WOMEN IN SCIENCE

International INNOVATION

Disseminating science, research and technology

ISSUE 171

A passion for progress

Showcasing the pioneering research of women scientists across the globe

POLICY

Promoting gender equality in science, with **Claudine Hermann** at the **European Platform of Women Scientists**

PRACTICE

The L'Oréal Group: advancing the careers of female scientists

RESEARCH

Addressing the gender gap in a **Research Roundtable** discussion with featured contributors

WWW.INTERNATIONALINNOVATION.COM

ARE YOU FULFILLING YOUR PROJECT DISSEMINATION OBLIGATIONS?

As a highly respected research dissemination publication with a huge global audience, *International Innovation* offers the ideal platform to present your project on the world stage in a way that is appealing and easy to understand.

95% of projects featured* said they would recommend *International Innovation* to:

- Communicate project impact and results to a wider scientific audience
- Reach global stakeholders and funding agencies
- Fulfil project dissemination requirements
- Increase project visibility
- Satisfy project partners and stakeholders

'International Innovation provided the perfect opportunity for NAMEPA to communicate its important work to a wider scientific audience. We are very pleased with the outcome of what was an easy process and overall an excellent experience.'

Clay Maitland, Founding Chairman / Carleen Lyden-Kluss, President of Morgan Marketing and Communications, NAMEPA

Contact us now quoting reference: 171

Call: +44 117 911 3470

Email: info@researchmedia.eu

Web: www.researchmedia.com

*Of those who replied to the follow-up client feedback questionnaire

RESEARCH MEDIA

Welcome to

International Innovation

PUBLISHED BY
Research Media Ltd
Trading address:
Whitefriars, Lewins Mead,
Bristol, BS1 2NT, UK

T +44 117 911 3477
F +44 117 981 1586

E info@researchmedia.eu
www.researchmedia.eu

Registered office: Howard House, Wagon Lane, Bingley, BD16 1WA, UK

CEO
Vicky Williams
vwilliams@researchmedia.eu

Commercial Director
Caroline Herbert
cherbert@researchmedia.eu

EDITORIAL
Editorial Director
Sarah Anderson

Editor
Rebecca Torr

Production Coordinator
Siân Yates

Senior Editors
Karen Lindsay
Benjamin Skuse

Associate Editors
Josh Gabbatiss
Lauren Haigh
Rosemary Peters
Katie Smith

Junior Editors
Frances Cartwright
Stephanie Spurr

Staff Writers
James Harle
Katie Harris
Eleanor Bird

Editorial Assistants
Jessica Greenhalgh
Rebecca Norman
Caitlin Sewell

Production Assistants
Kaz Armour
Katherine MacInnes
Ed Ramstedt
Gianina Turner

Contributors
Leah Eades
Sally Fowles
Anna Wilcox
Gwilym Lawrence

DESIGN
Head of Design
Paul Martin

Senior Designer
Mike Hill

Designers
Mark Evans
Claire Hatch
Orlagh Murphy
Iain Rex

Junior Designers
Laurie Atkins
Suzie Eland
Tom Sydenham

Project Managers

Josh Carpanini
+44 117 223 2273
josh@researchmedia.eu

Brett Langenberg
+44 117 911 3477
brett@researchmedia.eu

Carlton Romaine
+44 1172 232 581
cromaine@researchmedia.eu

Matthew Harrison
+44 117 223 2271
matthew@researchmedia.eu

Josh Hillier
+44 117 223 2580
jhillier@researchmedia.eu

MARKETING AND DISTRIBUTION

Head of Marketing
Laura Stanley
lstanley@researchmedia.eu

Digital Editor
Ben McCluskey
benm@researchmedia.eu

Marketing Executive
Alice Neill
aneill@researchmedia.eu

Marketing Assistant
Simone Bellofatto
sbellofatto@researchmedia.eu

WHILE WOMEN ACCOUNT for a significant proportion of the workforce in many countries around the world – 50 per cent in the US – they are generally underrepresented in the sciences, particularly within STEM fields and notably at senior levels. Stereotypes, cultural bias and lack of support for work-life balance are just some of the reasons preventing more women from pursing and progressing in scientific careers. There is evidence to suggest that if as many women as men were working in science, economies would be positively affected, and many argue the contribution of women and other minority groups is vital in order to solve the world's problems. In Europe, for example, a 2013 study on female representation in the ICT sector showed that if an equal number of women and men were employed in this field GDP would increase by about €9 billion.

Recognising the clear need to close the gender gap in science, governments and organisations worldwide have rolled out a number of initiatives to attract, retain and promote women in this sector. Countries such as Australia and the US, for instance, have created special programmes aimed at increasing the participation of women and underrepresented groups in science. In addition, funding agencies, such as the European Research Council, the Irish Research Council and the Canadian Institutes of Health Research now make it a prerequisite for applicants to include gender analysis in their funding proposals.

This third edition of Women in Science showcases the outstanding achievements of women working across the sciences, as well as the latest policies and projects furthering gender equality around the world. We also feature some of the pioneering research being conducted by female researchers in sectors including STEM, health and social sciences. WISE Campaign Director Helen Wollaston opens the issue by calling attention to the huge strides that have been made to boost the number of women holding STEM positions in the UK. In a similar vein, American Association of University Women Vice President for Campus Leadership Programs Kate Farrar highlights the programmes that are supporting the next generation of women leaders in the field. Later in the issue, in our editorial feature 'The female factor', we explore some of the challenges facing women in science and present case studies where initiatives are making a difference. We close the edition with an enlightening interview with Baroness Susan Greenfield who describes her experiences as a women working in neuroscience and what is takes to succeed in this field.

We are working hard to build a dynamic community, bringing together a diverse range of researchers, funders, policy makers and commercial partners to showcase the very best from across the research spectrum. As ever, do not hesitate to contact us with any feedback, registration enquiries or proposals for our next edition. Finally, if you are not already receiving *International Innovation*, don't forget to register free of charge at: **www.internationalinnovation.com/join-us/registration.** Enjoy the issue!

REBECCA TORR
rebeccat@researchmedia.eu

January 2015

International **INNOVATION** ISSUE 171
A PASSION FOR PROGRESS

RESEARCH MEDIA

Mixed Sources
Product group from well-managed forests and other controlled sources
www.fsc.org Cert no. TT-COC-2200
© 1996 Forest Stewardship Council

Working in partnership with

GOLD SPONSOR

Available on

ANDROID APP ON Google play

Download on the App Store

Contents

171

Regulars

Analysis

Research highlights

> We need all our talent to solve the complex and critical problems that we face. Diversity of all types brings new perspectives – these perspectives are vital for providing change and tackling complexity

Projects

Want more information?

To find out how you can feature in *International Innovation*, please contact Brett Langenberg: **brett@researchmedia.eu**

For more information about the contributors in this issue:

www.wisecampaign.org.uk

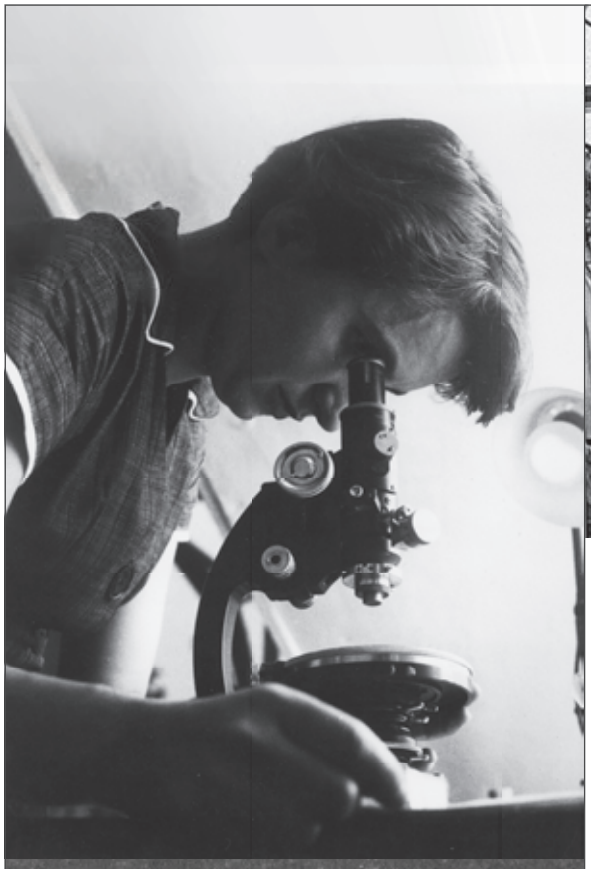
www.aauw.org

gender-summit.com

Register

Make sure you receive regular copies of *International Innovation* by completing and returning the enclosed registration form (page 24), or visit:
www.internationalinnovation.com/join-us/registration

WOMEN RESEARCHERS **MAKING THE HEADLINES**



Celebrating science

Now in its seventh year, the Women in Science Festival celebrates groundbreaking research in STEM

Taking place on 7-28 March in Dundee, UK, the 2015 Festival showcases cutting-edge research, inspiring girls and women to consider a career in science and, above all, celebrating the exceptional women contributing to STEM. The Women in Science Festival is a collaboration between the University of Dundee, Abertay University, the Dundee Science Centre, James Hutton Institute and Dundee Women's Festival, honouring scientific research, culture and heritage, as well as the stories of women behind some of the greatest discoveries.

For more information about the event, visit http://bit.ly/dundeeWiS

Better together

By bringing women scientists together, mentoring circles provide opportunities for sharing experiences, challenges and opportunities for development

Focused on career growth and problem solving, mentoring circles enable women working in academia or industry to develop skills and confidence. Mentoring circles also serve as safe environments for women scientists to talk openly about work issues and solve them together.

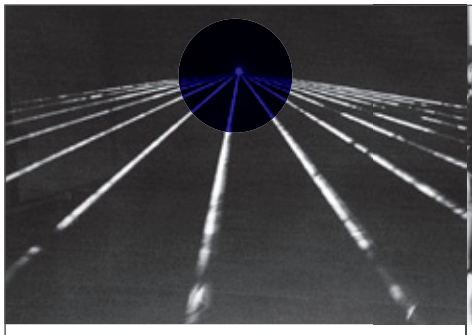
Sessions generally consist of three to five mentees, guided by at least one mentor who promotes productive discussions on a range of chosen topics. Once formed, the groups meet at monthly intervals for an agreed number of sessions that each last for approximately two to six hours.

Some of the benefits of joining a mentoring circle include:

- Learning from others' experiences
- Accessing solid career advice from more than one expert
- Gaining a broader perspective on issues
- Networking opportunities with fellow scientists in a comfortable environment

The Association for Women in Science chapter in Massachusetts, Philadelphia and DC Metropolitan holds regular mentoring circles.

To find out more, visit www.awis.org/news/193850/Mentoring-Circles.htm

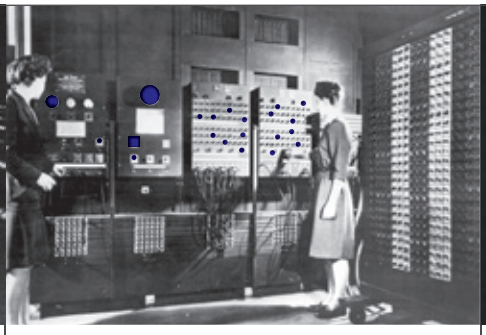


LIGHTING A NEW PATH

Shoe device offers cues to improve posture and balance for people with Parkinson's and multiple sclerosis

Clinical trials will soon begin for a walking aid designed for patients with Parkinson's. The aid, named Path and developed by engineer Lise Pape, can be simply fitted to the soles of the patient's shoes. Using a laser from the stationary foot, Path projects parallel lines up to 50 cm along the floor in front of the person, providing a visual prompt for where the opposite foot should step.

Pape was inspired to produce the device by her father, who was diagnosed with Parkinson's over 10 years ago. The device was tested at the Footwear Health Tech Conference in Eindhoven, Netherlands, by a patient with Parkinson's and two with multiple sclerosis. The patients gave positive feedback and Pape has plans to test Path on those with spinal cord injuries.



WISEING UP

Female STEM researchers honoured for their achievements

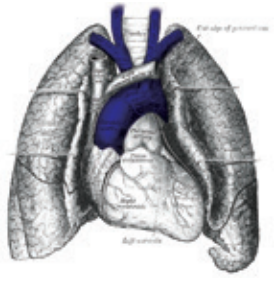
Last November, nine role models in STEM were awarded for their inspiring research by Women In Science and Engineering (WISE), an organisation aiming to promote gender balance in the UK's workforce.

Among those honoured was Dr Sarah Bohndiek of the Cancer Research UK Institute, University of Cambridge, who won the WISE Research Award for a tool she created for early cancer detection that uses imaging oxygen and oxidative stress. The WISE Lifetime Achievement Award went to Professor Dame Kay Davies, University of Oxford, for her work on Duchenne muscular dystrophy. Davies developed a screening test for women at high risk of having a child with muscular dystrophy and has supported many other researchers at all stages of their careers.

For the full list of winners, visit http://bit.ly/WiseCampaign

NEW LEGO SET FEATURING FEMALE SCIENTISTS

Dutch construction toy company The Lego Group has launched the 'Research Institute', a new research set depicting female scientists at work. The set was proposed by geoscientist Dr Ellen Kooijman and picked by popular vote on a Lego crowdsourcing website. The female scientists will serve as an alternative to the heavily stereotyped and controversial 'Lego friends' toy.

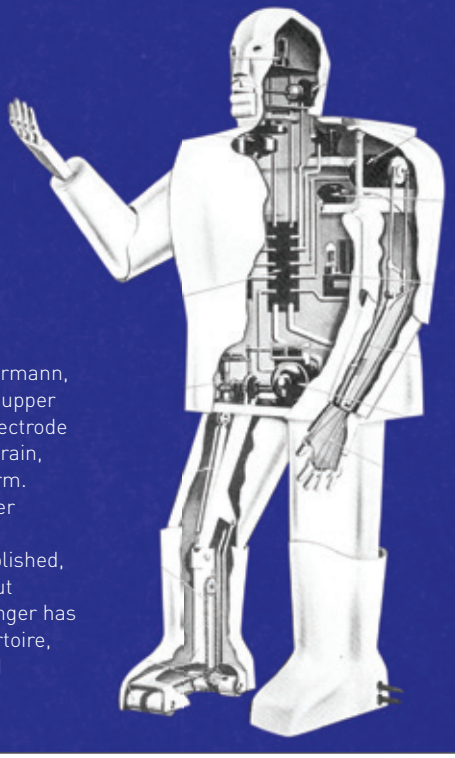


BRAIN POWER

A much improved prosthetic robot arm offers greater movement for paralysed patients

A system for moving a prosthetic robot arm using a patient's brain activity has received an upgrade by the original team of researchers at the University of Pittsburgh, Pennsylvania, USA, led by Assistant Professor Jennifer Collinger.

The unique prosthetic arm is used by Jan Scheuermann, a patient with tetraplegia who cannot control her upper limbs. Collinger and colleagues implanted two electrode grids in the left motor cortex of Scheuermann's brain, the area responsible for movement of the right arm. The electrodes analyse brain activity and computer algorithms and then match these patterns to the response of the arm. Once these have been established, the computer can direct the prosthetic to carry out Scheuermann's intended movements. Now, Collinger has added four new control signals to the arm's repertoire, allowing more complex movements such as hand shaping and thumb extension.



HOLD YOUR BREATH

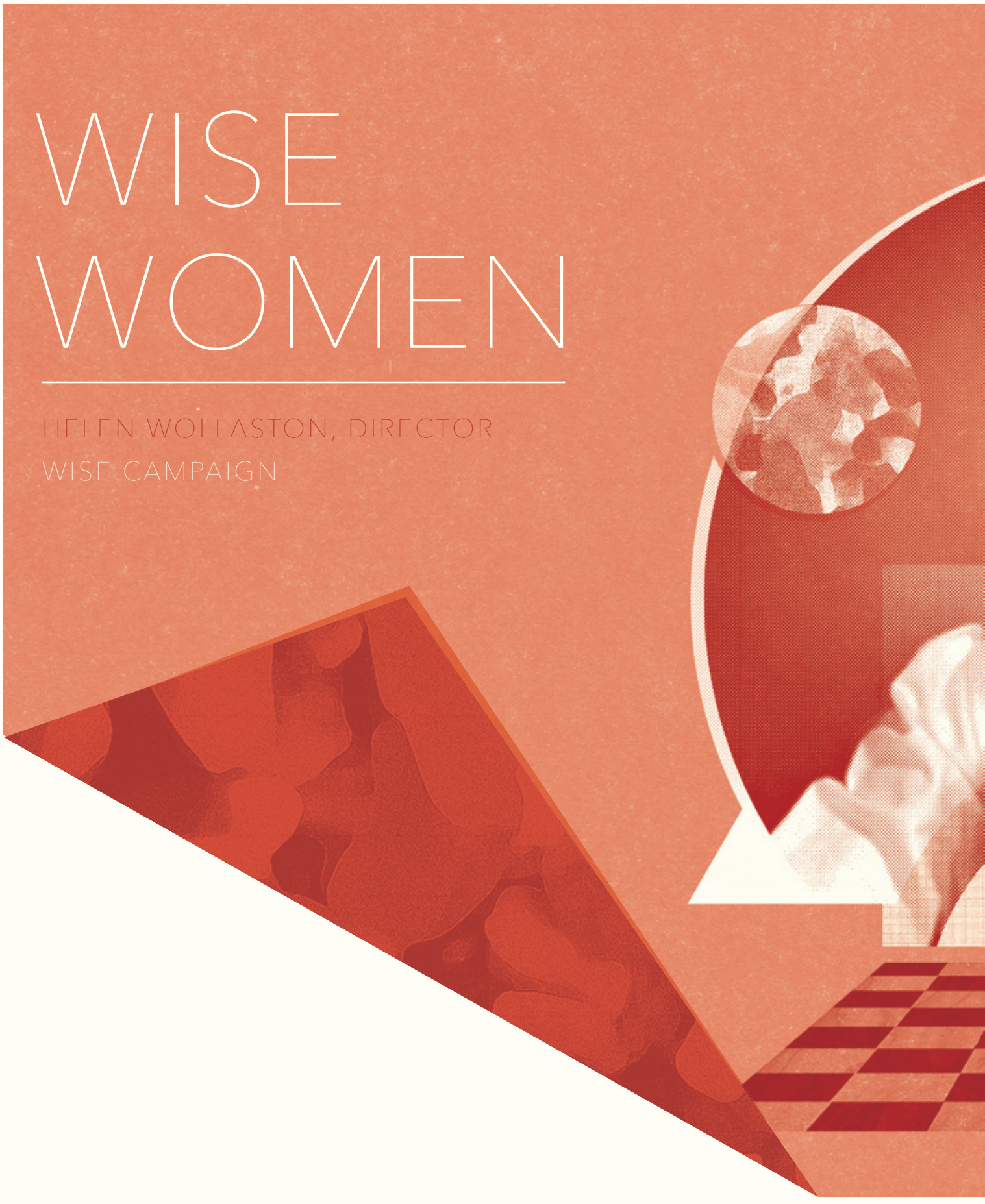
Women with breast cancer are less likely to develop heart disease if they hold their breath during radiotherapy treatment

Women who develop breast cancer in their left breast have shown an increased risk of heart disease, proportional to the dosage of radiation used to treat their cancer. But a team of researchers led by Rani Anne and Harriet Eldredge-Hindy of Thomas Jefferson University, have published work that showed a median reduction of radiation exposure of 62 per cent to the heart during breast cancer treatment using a straightforward technique.

In their study, Anne and Eldredge-Hindy found that having patients hold their breath during radiotherapy led to 90 per cent disease-free survival over the course of the treatment. The patients under study also showed a reduction of ischaemic heart disease risk after 10 years.

WISE WOMEN

HELEN WOLLASTON, DIRECTOR
WISE CAMPAIGN



ACTIVE WOMEN'S CAMPAIGNER AND DIRECTOR OF WISE, HELEN WOLLASTON MARKS THE ORGANISATION'S 30TH ANNIVERSARY IN THIS ENLIGHTENING INTERVIEW WITH *INTERNATIONAL INNOVATION*. HERE, SHE DISCUSSES THE PAST, PRESENT AND FUTURE OF THE CAMPAIGN, INCLUDING ITS CONTINUED DEDICATION TO SUPPORTING WOMEN AND GIRLS IN STEM

Firstly, *International Innovation* would like to congratulate the WISE Campaign on reaching its 30th birthday in 2014! How did you celebrate this momentous occasion?

The Campaign invited women who are now involved in STEM, and who have been influenced by WISE over the last 30 years, to tell us their stories. Each month we feature a blog on our website of the women who had contact with us when they were at school. We also held the WISE Awards in mid-November. These take place every year, but for the 30th anniversary there was an additional conference programme during the day as well – in particular, we featured a panel debate which asked people to think about what the STEM workforce will look like in another three decades from now and what actions need to be taken. People from leading companies and education shared their thoughts on this, and it was chaired by Anna Edwards, a journalist from Bloomberg TV. Bloomberg was a headline sponsor of the Awards this year. The debate was about exploring ways we can scale up the Campaign.

How has the Campaign grown over the past three decades?

Today, instead of trying to manage and operate all aspects individually at WISE, we are a membership organisation that facilitates other people to campaign by joining them together and providing them with the appropriate tools and resources. WISE launched a membership scheme at the beginning of 2013 for individuals – male and female – who support the cause as well as companies, professional institutions such as the Institute of Civil Engineering and the Chartered Institute for IT, trade unions, universities and colleges. It has changed greatly since the early days when people booked a WISE bus to come to their school. Now, we are supporting others to take action, which massively increases our reach and impact.

WOLLASTON OUTLINES THE CURRENT STATUS OF WOMEN IN STEM

Within the UK, females in the STEM workforce equate to 13 per cent. Within that, figures vary depending on the sector. If you look at engineering professionals, for example, the number of women is increasing rapidly, and growing faster than the number of men entering this field. In the last two years, the number of women who became professional engineers in the UK has doubled – that's about a 13,000 person increase. It's still a small percentage – 6 per cent of the total – but it's growing, which is very positive. On the other hand, in technology the gender gap is widening. It's important to drill down and look at the individual issues for each sector. WISE will monitor the overall percentage (with a goal of increasing 13 per cent to 30 per cent), but we will also examine what is happening in the different parts of STEM and the areas we need to target.

WISE services are designed to build and sustain the pipeline of female talent in STEM – from classroom to boardroom. Could you highlight these services and explain how they address the gender imbalance?

There are two activities. First, we encourage girls to want to study and work in STEM. The main way we achieve this is to give them access to inspirational role models, particularly young women and women from different backgrounds, who are passionate about what they do.

Second, we work with member organisations to create the right environments so girls have an equal chance of entering STEM employment, and have the same opportunities to thrive as their male counterparts. Here, we look at the recruitment and retention of women in STEM, as well as the policies and practices within the learning environment or workplace.

What educational opportunities does WISE provide?

We have training opportunities for women on career development and leadership. There are many leadership programmes for women, but the difference with WISE training is that the focus is on STEM, with effective peer support and relevant material for women who are likely to be working in a male-dominated environment. Women are able to talk in a safe space about different strategies for dealing with such issues.

WISE also provides training that is aimed at employers and focused on unconscious bias. We work with recruiters, managers and supervisors to make sure they are aware of this issue and have a strategy for dealing with it, so that it doesn't put women at a disadvantage.

Do you also supply media training?

We work with LeFevre media to provide training to WISE members. WISE has just appointed a young women's board – another step we took to commemorate our 30th anniversary – comprising 10 young women working in STEM who are WISE members. These young women have all been through the training to prepare them for the role. The aim of the board will be to ensure WISE is relevant to that generation, by giving their input to the campaign strategy. They will also serve as ambassadors, hence the media training. Some of them have already represented WISE at meetings with, for example, the Department for Education.

In late 2012 WISE incorporated the UK Resource Centre (UKRC). In what ways has this proved beneficial?

When the WISE Campaign was initiated, its focus was on the classroom. Today, we have the whole remit – from classroom to boardroom. That was the major advantage of UKRC; we are not only about inspiring girls to study and work in STEM, but we also aim to change the culture in the workplace and support organisations to make it more likely that women who are attracted to STEM will stay. That is where UKRC's expertise

STEM FOR PEOPLE LIKE ME

Network Rail and author Professor Averil Macdonald, Diversity Lead for the South East Physics Network, have produced a report entitled *Not for people like me?* which aims to encourage women into STEM by identifying best approaches and practices to get this important message across. Macdonald explores the reasons why STEM outreach and engagement activities have made limited impact on girls and young people who are underrepresented in STEM. It suggests that a fresh approach is required, that focuses on the person rather than the position itself. Macdonald is also on the WISE board.

To find out more about the report, visit **http://bit.ly/Notforpeoplelikeme**

Professor Averil Macdonald, in an exciting guest blog for *International Innovation*, discusses the *Not for people like me?* report in more detail **bit.ly//IIAverilMacdonaldBlog**

was – the retention and promotion of women in the workplace and universities. We've now got the expertise at all fronts, and can work with organisations to support women and girls at all levels of their journey in STEM.

Secondly, UKRC was funded publically by the government. WISE doesn't have any government grants, we are entirely funded through our membership and industry partners and sponsorship. This has given us more of a commercial focus and changed the character and nature of the organisation. WISE has to make sure it is delivering something of value to industry, because they would not continue to pay us and therefore it has to be very in tune with the needs of the employers. It makes us aware of where the opportunities are in the marketplace.

Ten Steps is an industry led programme that ensures women in STEM are provided with the same opportunities to progress in their career as their male counterparts. Could you discuss the latest successes to come out of the project?

Ten Steps is a good example of where WISE has become more commercially focused and industry led. Initially, we invited our corporate members to explain what has made the most difference in their organisations with regard to the retention and progression of women, and we facilitated a workshop that brought together those examples; that's how Ten Steps was born. One major success of that was our work with the Royal Academy of Engineering, who has a diversity leadership programme of about 40 companies. We now have 22 major employers signed up to implement Ten Steps, not just within their own organisation, but within their supply chain. This was only launched in September, and already some other companies have been contacting us to ask how they can become involved. I've been approached by the Confederation of British Industry (CBI) and have provided a blog for them.

During the WISE Awards, a woman working for an SME said she's pledged to take Ten Steps to her company and share it – that would be our first SME to adopt the programme. And we will be gathering examples of how it has made an impact, uploading them onto the WISE website and bringing those people together to share, learn and roll it out further. It's credibility lies in the seniority and influence of the industry leaders who have signed up.

You joined WISE as Director in June 2012. What was your vision for the Campaign? What skills and experience do you bring to this role?

My vision when I started was to mainstream the issues the Campaign addresses so that we weren't preaching to the converted. Increasing diversity in the workforce cannot be conducted single-handedly by someone with equality or diversity in their title, or an HR person in an organisation; it must be led from the top. And in order for that to happen, we need to put the issue onto a mainstream business platform and take the message to the public – to parents, teachers and girls.

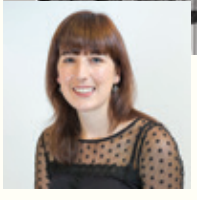
What I bring to WISE, and the reason I joined, is my campaigning and communications experience. I've worked on these issues in other sectors. I also bring management expertise and contacts with relevant organisations across the UK.

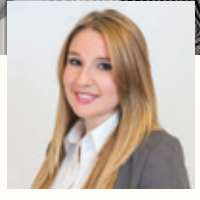
WOLLASTON HAS A TAKE HOME MESSAGE FOR THOSE LOOKING TO BECOME INVOLVED WITH WISE AND SUPPORT ITS SERVICES

My message is one of encouragement, and one that certainly extends to men and women, because we want champions of both genders to spread the word about the value of women and girls in STEM and the opportunities that are available for them to have a great career. We are harnessing that energy, enthusiasm and passion in two ways: our sectoral campaigns – one of these is led by energy sector leader Nina Skorupska on our board. And our regional campaigns, where we aim to bring together everybody in a particular town or region so that we can connect with girls in the area. The more members we have, the more sectoral and regional hubs we can develop.

WISE HERO AWARD

WINNER OF THIS YEAR'S WISE HERO AWARD, TARA MOORE, SPEAKS CANDIDLY ABOUT HER VIEWS ON WOMEN IN STEM, HER AMBITION TO BE A ROLE MODEL FOR GIRLS INTERESTED IN EMBARKING ON A CAREER IN SCIENCE, AND HER AIMS TO STRIVE FOR A WORK-LIFE BALANCE





WISE YOUNG WOMEN'S BOARD

FOLLOWING THE RECENT INAUGURATION OF THE UK WISE YOUNG WOMEN'S BOARD, *INTERNATIONAL INNOVATION* ASKS MEMBERS KEELEY BURKE (SYSTEM ENGINEER, HALLIBURTON), SIÂN CLEAVER (MISSIONS SYSTEMS ENGINEER, AIRBUS DEFENCE AND SPACE) AND SALLY WOOD (PLANT ENGINEERING MANAGER, ROYAL MAIL) TWO IMPORTANT QUESTIONS...

Congratulations on being appointed to the first WISE Young Women's Board. What attracted you to a career in STEM?

KB: I was always interested in STEM subjects at school, so I studied maths and science at A level and completed a degree in maths and statistics. After spending my industrial placement working as a statistician in pharmaceutical manufacture I decided to branch into engineering because I enjoy applying statistics to industrial issues, such as problem solving and process improvements. I like working in STEM because it gives me the chance to use my analytical skills and to work in a job that I find both interesting and challenging.

SC: I have always wanted a career in STEM; I decided I wanted to be an astronaut when I was six-years-old! This strong ambition has influenced most of my decisions to date, and has ultimately led me to where I am today – a Mission Systems Engineer for Airbus Defence and Space, Europe's leader in space. If I hadn't had this aspiration then I think that my choices throughout life (eg. A Level and degree choices) would have been quite different. I think it's so important for young people to have ambitions and to hold on to them and I want to try and get this message across to others through my work with WISE.

SW: I was interested in how things work and enjoyed using my hands to make things. I was good at maths and physics at school, and engineering seemed like a natural choice at university – especially after I attended some engineering taster sessions and work experience whilst at school. I really enjoyed my degree – I studied Manufacturing Engineering at Cambridge University – as there were so many different aspects to learn. One day we would be programming a robot and the next we were working in a jam factory. I now work for Royal Mail as the Plant Engineering Manager ensuring our machines deliver the mail in walk sequenced order to our postmen and women and to your door every day.

How are you working with WISE to encourage other women to enter these fields?

KB: I volunteer as a STEM ambassador, which gives me the opportunity to speak to secondary school girls about my career to date. STEM subjects offer a wealth of career opportunities but students often lack confidence or do not see benefits in pursuing STEM when they make subject choices. Seeing real examples of STEM careers can help to make these subjects seem more interesting and relevant to future career choices, and may inspire students to consider STEM careers.

SC: I'm working with WISE to try and inspire other young people – particularly girls – to consider STEM careers. I want to share my experiences with others, and show them it's possible to hold on to the dreams they had during childhood, even if they seem a little far-fetched and crazy to others! I want young people to see that they can take these ideas and dreams and turn them into a successful and fulfilling career. Sometimes it's the path towards your goal that is the most interesting part, rather than the end goal itself – I want young people to see that you shouldn't give up on something just because you perceive it to be 'challenging'.

SW: I am working with WISE and Royal Mail to drive female applications to engineering apprenticeships within the engineering side of our business. I see the importance of encouraging the next generation to learn and study STEM subjects at school to enable the future of women in STEM careers and will work with WISE on our strategy to address this.

By means of an introduction, could you outline your professional and academic background?

I undertook a degree in Microbiology and was fascinated by the study of viruses and the immune system. I then completed a PhD in Immunology and Virology, followed quickly by a number of postdoctoral research positions spanning across the world from Belfast to New York, including an amazing opportunity as a research fellow in Harvard Medical School and Brigham and Woman's Hospital in Boston. I returned home to Northern Ireland to take up an independent academic position at Ulster University and since then I have built a great team of researchers, been promoted to Professor and taken up roles as Vision Science Group Leader and Associate Director of the Biomedical Science Research Institute.

What have been some of your proudest achievements?

I love teaching and influencing young minds to ignite a life-long interest and enthusiasm for science and its potential to change our lives. Being awarded a National Teaching Fellowship Rising Star Award by the Higher Education Academy UK for my innovative teaching was fantastic, as it was based, in part, on student opinion of their learning experience under my tutelage. I was also privileged to receive Honorary Fellow from the Faculty of Forensic Medicine, Royal College of Physicians, an accolade for persons who rendered exceptional services to science and practice of forensic and legal medicine. In addition, I had the opportunity to be interviewed by an elite panel of scientists for a European Research Council Starter grant – a frightening but rewarding life experience. Recently receiving an award for advancing diversity in the workplace from Women in Business NI also ranks highly, and of course I have hardly recovered from the surprise of winning the WISE Hero Award in London, just a few weeks ago. All these moments make me feel so proud to be a woman in science.

If I absolutely have to pick one achievement, I would honestly say that out of all these academic-related prizes the most amazing and unbelievable prize is to have been able to do all this and raise my seven beautiful children simultaneously.

***International Innovation* was excited to learn about you becoming the winner of this year's WISE Hero Award. Can you explain the criteria for the award and what the win has meant to you?**

WISE nominated women are those who could be role models for young girls considering science as a career. Professor Hugh McKenna – Pro Vice Chancellor for Research and Innovation at Ulster University – nominated me. I was delighted to receive a phone call from WISE to say I was shortlisted and was to attend the awards ceremony in London, where the winner would be announced and presented with the award by HRH The Princess Royal – 'The Oscars of Science'.

During my career I have strived to improve health, wellbeing and safety of people through the use of technology to develop various eLearning training courses and an MSc in Forensic and Legal Medicine. In partnership with the Faculty of Forensic Legal Medicine, Royal College of Physicians and Department of Health, London, I have driven developments in eLearning courses at Ulster to enable doctors and allied health professionals to recognise, treat and prevent rape, child abuse and domestic violence.

Through my research I aim to discover the genes involved in causing genetic eye diseases, carried by parents and passed on to at least half of their children. These devastating diseases can strike at a very young age and it is heart breaking to hear a parent describe how the disease is stealing their child's vision. I now have a team of researchers working hard to discover the genetic reason for blindness and we are making great progress in developing new therapies.

In your current role as Professor at Ulster University, what do your responsibilities entail?

The reason I enjoy my job is because it is dynamic and every day is different. It is stimulating and challenging, but also rewarding when a day ends with success. As a research team, students and staff all contribute to writing papers and grants, and become familiar with the perils and pitfalls associated with this type of career. I think the biggest responsibility I have as an academic and a researcher is to ensure that all scientists that train in my laboratory leave with great potential to move on to anywhere in the world. The skills and training they obtain should open doors and allow them to explore the world as they explore science. As a group, we travel a lot either to carry out experiments in a collaborating laboratory or to present our findings at international conferences. I have travelled to the Middle East, China, many areas in the US and across all of Europe.

Where are you currently focusing your research efforts?

My main research focuses on the eye, and in particular, developing new therapies for blinding diseases caused by faulty genes. My team and I have gathered extensive evidence indicating that we can specifically target and silence or edit the bad gene causing the disease. We are achieving this through the use of siRNA gene silencing or CRISPR CAS9 gene editing. I find this approach and the success we are seeing in the laboratory truly remarkable. The power it gives us as scientists has no limits. I have colleagues who are using it to eliminate DNA viruses such as HIV, hepatitis and herpes. I can only imagine how this technology is going to spiral over the next year.

Have you personally witnessed any gender bias in your own line of work? Are you working to tackle such discrimination?

One gender bias we found, which is an action point as part of our University Athena SWAN Bronze award, is the decreased number of females at professorial level and the higher level of females staying in lower grade academic positions, such as Researcher or Lecturer. While this can certainly be attributed to personal choice or a work-life balance effort, we did find evidence of female members of staff being hesitant or not feeling as confident about applying for promotion. By way of addressing this, and in my attempt to be energetic in championing the promotion of women in STEM, I have developed and lead the University-wide female mentoring programme, which includes training sessions for mentor volunteers and establishing formal mentor-mentee relationships.

How do you see the STEM landscape developing, particularly for women in the next five to 10 years?

In terms of how females can be involved, evidence shows that while a growing number of women are enrolling in university, many opt out at the highest levels required for a research career. In Sweden, women form the majority (60 per cent) of students enrolled in a Bachelor's programme, but their numbers decline as they move up the education ladder, accounting for 49 per cent of doctoral students and only 36 per cent of researchers. The data trends across every region.

Some suggest this 'drop out' is due to the conflict that many women face as they try to reconcile career ambitions with family caring responsibilities. While I acknowledge this may be a concern and I know I have been incredibly lucky in my career, I hope I can serve as a role model for females pursuing a career in science and technology. I would definitely oppose the idea that to be a successful scientist females have to choose between having a family and enjoying other dimensions of your life.

I have progressed as a female in science and moved from lecturer to Professor within a 10-year period and during that time I had seven beautiful children. Yes there have been sacrifices and the odd school play missed but in that my six girls have learnt that 'mum works' and I hope that influences them in their life-choices in the future.

www.wisecampaign.org.uk

Kate Farrar
Vice President for Campus Leadership Programs
American Association of University Women

A primary goal for the **American Association of University Women** is to encourage college women to take up leadership roles and STEM careers by providing training and support workshops and programmes. Here, Kate Farrar explains how these activities are securing equality within the workforce

Throughout your career you have been an advocate for women and girls' leadership. Can you elaborate on the path that led you to become Vice President of Campus Leadership Programs at the American Association of University Women (AAUW)?

I joined AAUW almost seven years ago, and was attracted to working for the organisation through one of its core programmes called the National Conference for College Women Student Leaders – the only conference in the US that brings together female college leaders from all over the country. Remarkably, I attended this conference when I was in college, and it was extremely inspiring. The idea of returning to an organisation and working on the same conference that made such an impact on my life was one of the core reasons I decided to work at AAUW.

AAUW has more than 800 college and university partner members with thousands of student members

Since I started, we have tripled our programmes and quadrupled our college/university and student members. At AAUW, we've reinvested more resources into building up the confidence and skills of college women. Specific to STEM, we've started two national programmes for girls to ensure that middle school girls are considering STEM careers as a pathway. By focusing our STEM work on college-age and younger women and girls, AAUW has grown our impact for the next generation of leaders and STEM professionals.

What is the overarching mission and vision of AAUW?

AAUW is a remarkable organisation because our mission is tied to advancing equality for women and girls. The work we do covers advocacy, education, philanthropy and research, and we try to achieve our goal from all these angles. Since our founding in 1881, we have been working in this manner to empower tens of thousands of women decade after decade. We aim to face this inequality head-on, not only in STEM professions, but in a wide range of issues, from problems with campus sexual assault to inequality in social security.

We will continue to fight for our mission. Our founders, who were some of the first women to pursue higher education, would be astounded at the US today, which has more women on campuses and graduating than ever before; however, they would also be disturbed that we have so few women in leadership positions. I'm sure that they would be proud that we're continuing to fight the persisting inequalities.

AAUW has a strong history of worldwide collaboration. How has AAUW gone global?

There are many examples I can cite that show our global reach. Since the 1800s, we have been giving graduate fellowships to women to pursue higher education, and we are now the largest funder of postgraduate education for women in the world. Many of our fellowships are for women who come to the US to study, and we also offer grants when they return to their country to continue their education.

Another role that we play is through our consultative status at the UN; we seek to use our resources, research and experience to advocate for women internationally. We have proponents around the globe, and we also have several college and university partners worldwide who believe in our mission and want to expose their students to our organisation's offerings.

What have been the key takeaway messages from AAUW's upcoming research report, *Solving the Equation: Women in Engineering and Computing*?

This report is focused on how many women are working in engineering and computing, and how we can increase their representation in the workforce. These skills are paramount to solving a multitude of problems the world is facing. When women aren't represented in these areas, we are cutting our potential workforce in half. Uniquely, the report offers recommendations for specific audiences, such as policy makers, universities and industry. The reason we focused on STEM is that we are not making enough progress in this area and this is where we need to pinpoint concerns.

Can you discuss AAUW's Tech Trek programme?

Tech Trek is a week-long science and mathematics camp for girls; it was set up through a California AAUW branch member in 1998. In the past two years an AAUW branch member has taken this programme nationally. This year there will be 21 camps.

TRACKING TECH TREK TRIUMPHS

Recently, AAUW completed a survey of the Tech Trek programme:

- 73 per cent of the respondents stated that Tech Trek introduced them to STEM college majors of which they were previously unaware
- Tech Trek alumni are pursuing higher maths and science classes after the programme, many of which are precursors to earning academic credit for courses when they transfer into university
- 77 per cent of alumni completed pre-calculus mathematics, beating the national average of 37 per cent

According to Kate Farrar, Tech Trek can have a considerable lasting effect on participants: "Not only are participants being exposed and transformed in how they're perceiving STEM, but they're also pursuing the pathways that will set them up to take these subjects in college".

There are several reasons why these camps give a high impact experience for girls. They:

- Provide an opportunity to interact with women in STEM as role models
- Offer different workshops and core classes
- Spark awareness of career opportunities available
- Ensure that girls are empowered to see beyond the stereotypes and biases that they might be facing and not aware of in their own lives

Likewise, can you elaborate on the Tech Savvy Programme?

A day-long programme for girls and their parents, it includes workshops and college recruitment for the girls, but also ensures that parents are aware of the benefits of STEM careers for their daughters. The programme was founded by an AAUW branch member in 2006 in Buffalo, New York, and in the past two years, it has been rolled out nationally. We now host 15 Tech Savvy days. Tech Savvy has been widely commended – including by the White House – for its efforts to introduce girls to the variety and importance of STEM careers.

AAUW's 2015 National Convention will be held in San Diego, California, in June

Excitingly, a new Tech Savvy programme is being set up in Hungary, and it will incorporate a track for teachers to ensure that they are in the best position possible to encourage students to pursue STEM subjects. I suspect this is just one of many expansions to come.

In your opinion, what makes Tech Savvy and Tech Trek so effective?

What is unique about both programmes is that they are entirely volunteer run. These programmes really speak for how much our AAUW membership is passionate about not only giving back but making a difference for the next generation. We certainly provide a range of support, technical assistance and fundraising for programmes, but the actual implementation is carried out by volunteers. With this model, we can continue to grow the programme both nationally and globally. With Hungary as an example, there is exciting transferability to many other locations around the world.

Is AAUW looking to expand and build on the successes of these programmes in the future?

We are looking to ensure that both Tech Trek and Tech Savvy programmes have the same engineering and computing focus as our new report. One of the ways we have been doing that is through some of our corporate relationships. This year, we collaborated with the Verizon Foundation to offer a national app adventure course through our Tech Trek camps. We intend to expand these efforts over the next year. We have also been seeking other ways to build more activities related to coding and careers in developing areas, such as cyber security – areas to which girls have had little exposure.

Additionally, because we have such a strong model developing, we want to not only grow our footprint here in the US, but to build more international models so that our members and university partners abroad can implement these programmes too.

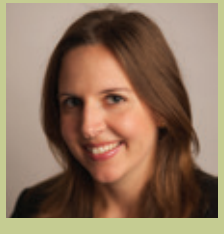
CAMPUS LEADERSHIP PROGRAMMES

AAUW has five national campus leadership programmes:

- National Conference for College Women Student Leaders (NCCWSL) – 1,000 women nationally and internationally attend the Conference every year in May/June
- National Student Advisory Council – a year-round leadership programme for 10 competitively selected students who then act as AAUW campus ambassadors and peer leaders at NCCWSL
- Campus Action Project (CAP) – every year AAUW grants US $5,000 to student-proposed projects based on AAUW research. This year, the CAP grants have aimed to tackle the biases and stereotypes that women face on college campuses
- Elect Her – a training workshop run on 50 college campuses for women aiming to run for student government or political office
- $tart $mart – takes place on more than 100 campuses a year to teach college women to negotiate their salaries to reduce the pay gap between men and women. An offshoot programme, Work Smart, performs a similar function but is aimed at professional women

"We reach tens of thousands of college women every year with these programmes and it is AAUW's capability to build the confidence and skills of these women that we hope will prepare them for taking on leadership roles after college," enthuses Kate Farrar, on the subject of AAUW's unique leadership schemes.

AAUW
empowering women since 1881



www.aauw.org

Inspirational innovators

Since its lauch in 1988, the L'Oréal-UNESCO For Women in Science programme has been striving to promote the position of women in scientific research. As a result of its annual UK and Ireland National Fellowships, four outstanding young female researchers based at universities across the UK have been awarded prestigious career-enhancing fellowships, each worth £15,000

Dr Clémence Blouet, University of Cambridge

Blouet's research focuses on the consequences of a high-fat diet on the hypothalamus and the mechanisms that underpin obesity. Particularly crucial in a world where obesity and its associated diseases represent a major and ever-increasing threat to global public health, Blouet's work will advance scientific understanding about the impact of a high-fat diet on the plasticity of brain cells in the hypothalamus and explain how this affects the body's energy balance. "This award will help me investigate risky science questions and collect some pilot data to help obtain additional and more substantial research funding," she enthuses. The hope is that the findings from her research will pave the way for the discovery of novel therapeutic targets to treat obesity.

Dr Eva-Maria Graefe, Imperial College London

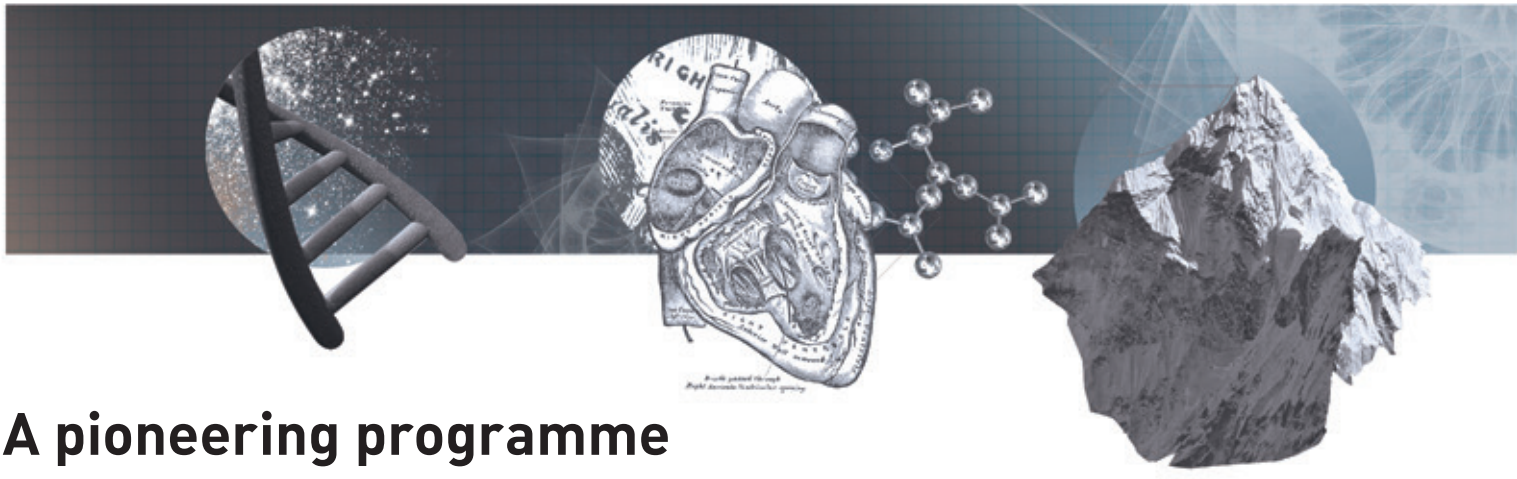
With a background in theoretical quantum dynamics in the context of atom physics, Graefe's current project is exploring how leaky quantum systems with engineered holes could in fact be advantageous. Using a formula known as non-Hermitian quantum mechanics – and drawing on her detailed knowledge of the mechanisms and effects of loss – she is forging exciting conceptual advances in this nascent field. Graefe is also aiming to develop new theoretical tools for the description and prediction of novel experimental applications. "This award [...] provides me with the financial means to invite and visit collaborators and to present my results on scientific meetings," she points out. "Second, it allows me to combine my family life and my research with much more ease, by providing resources for childcare as well as the opportunity to take my baby daughter with me when travelling. Finally, the prestige of the award has been very helpful in disseminating my research and I hope it will help me to achieve my long-term goal of building up a world leading research group in the area of quantum dynamics."

Dr Sneha Malde, Univerity of Oxford

Pushing past the boundaries of the Standard Model of the Universe, Malde is attempting to answer a pressing scientific question: namely, why is the Universe dominated by matter? By analysing the data collected from Large Hadron Collider experiments, she is seeking to build a deeper understanding of the fundamental difference between matter and anti-matter. Encouragingly, recent advances have allowed for a precise measurement of this difference – and Malde is accordingly aiming to develop her method of measurement to probe the vast realms of data that have not yet been analysed. Her research, which heralds significant progress in the search for New Physics, has been bolstered by receiving this award: "It is wonderful to gain recognition for my work," she states. "I am using the funds for travel so that I can spend more time at the European Organisation for Nuclear Research (CERN) and attend more conferences. Collaborating with others on a face-to-face basis is an invaluable asset to efficient and creative working."

Dr Tracy Briggs, University of Manchester

Lupus is a common and potentially life-threatening disease in which the immune system becomes overactive, causing the body to attack its own tissue. In order to further knowledge about the origins of this disease, Briggs is investigating how its onset may be linked to a change in a single gene. Her seminal work in this field is helping to establish the genetic basis for familial forms of lupus that start in childhood and primarily affect the skin. "Winning this award has allowed me to start my research and obtain key preliminary data," she elucidates. "This data will form part of a larger grant application in the future, which will be vital for my career development."



A pioneering programme

Despite the achievements made by women in science to date, gender distribution in STEM fields remains stubbornly imbalanced in favour of men. The L'Oréal-UNESCO For Women in Science programme is tackling this head-on by recognising exceptional female scientists and supporting early-career women researchers throughout the world

WHEN IT COMES to forging a successful scientific career, women in the 21st Century have much better prospects than their female counterparts from previous generations. Yet in spite of significant gender equality advances – set in motion during the 1960s and 1970s – women continue to be underrepresented at all levels of R&D in every region of the world. For instance, the UNESCO Institute for Statistics estimates that just 30 per cent of researchers worldwide are female, while in the UK and Ireland women comprise only 13 per cent of STEM employees. Multiple studies have identified a number of recurring barriers to women in STEM, including a male-dominated working culture, a 'chilly' classroom environment, the insecure nature of science research and a lack of access to mentors.

In response to the pervasive gender inequalities in STEM, a number of visionary organisations have launched initiatives aimed at attracting and retaining women in science. The L'Oréal Group, with its roots in science and beauty, has demonstrated its commitment to the field by promoting female participation in science and advancing the careers of female scientists. Its primary vehicle for achieving these aims is the innovative For Women in Science (FWIS) programme. Launched in 1998 in partnership with UNESCO, this programme offers fundamental support to women researchers across the world at different stages of their careers, as well as advocating scientific education through participation in exhibitions and joint ventures. "We are convinced that science and women bring hope and foster discovery, innovation and excellence," asserts Jean-Paul Agon, Chairman and CEO of L'Oréal and Chairman of the L'Oréal Foundation. "All the best talents must be called upon to accomplish this mission. L'Oréal believes in women, L'Oréal believes in science."

A LOCAL FOCUS

Importantly, the L'Oréal-UNESCO FWIS programme attempts to respond to pressing scientific challenges at a local, grassroots level – and the national fellowships it awards in almost 50 countries around the world are a strong testimony to this. For instance, the FWIS UK and Ireland fellowships provide four outstanding female postdoctoral scientists based in the UK and Ireland with flexible financial help to pursue their chosen research. Now entering their eighth year, these important fellowships – each worth £15,000 – help women to launch their scientific careers by giving them the freedom to choose how they want to spend the funds. Revealingly, of the 289 women who applied for the fellowships in 2014, one-in-four said they would use the money to fund childcare, emphasising the intrinsic value of flexible funding for female researchers.

Announced at a ceremony at London's Royal Society in June, the winners of the highly competitive 2014 awards were of remarkable calibre. "Choosing between the shortlist was an exceedingly difficult task, as all the shortlisted women were hugely impressive in their individual fields," admitted Katriona Methven, Director of Scientific and Technical-Regulatory Affairs at L'Oréal UK and Ireland. "However, it was inspiring to see the extraordinary work that is being carried out in diverse scientific disciplines all across the UK."

Each of the four prizewinning researchers came from different universities – the University of Cambridge, the University of Manchester, Imperial College London and the University of Oxford – and their diverse research topics ranged from investigating New Physics to mapping the genetic origins of disease. The researchers reported that they would be using their funds for equipment, field trips, attendance at conferences, collaborations and childcare – and, looking ahead, the hope is that much-needed financial support in these respective areas will help them to develop and flourish as early-career scientists. Going forward, from 2015 onwards the number of UK and Ireland fellowships will be increased to five.

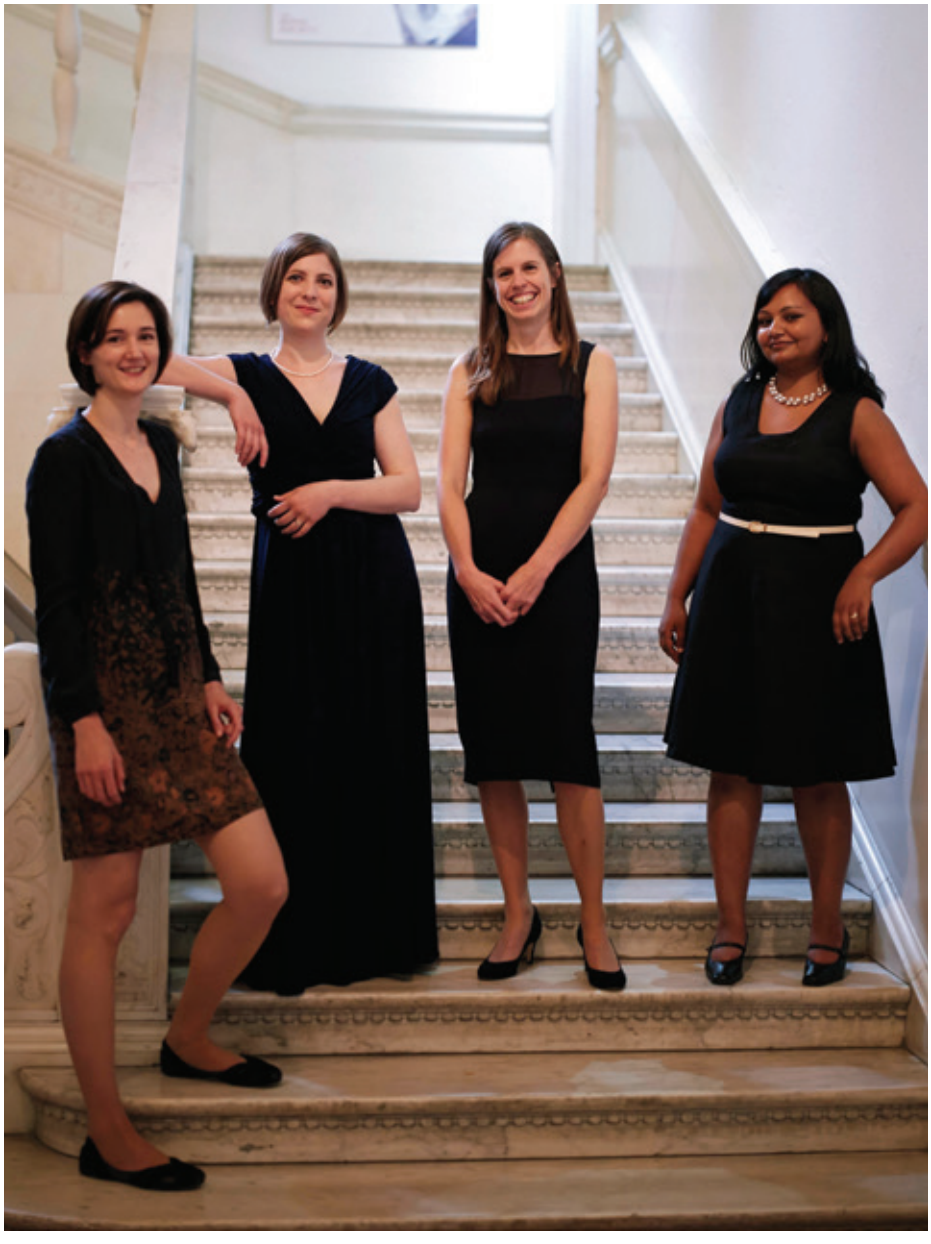
A GLOBAL PERSPECTIVE

The FWIS programme also offers national fellowships to women in science across the

By injecting vital funds into revolutionary science projects across the world, the L'Oréal Group has helped create a dynamic network of dedicated researchers – indeed, by the end of 2014, more than 2,000 women scientists from over 100 countries had received support from the FWIS programme

BROADENING STEM ACCESS

In early 2014, L'Oréal joined the UK Government's 'Your Life' campaign, which encourages young people to pursue science subjects at school and to consider entering a STEM career. It has pledged to dedicate an annual fund of £20,000 for the UK and Ireland Fellows community to support their roles as ambassadors for STEM in engaging the broader population – especially young people – in science. Additionally, in order to address the gender discrepancy in engineering – in the UK, just 6 per cent of the engineering workforce are female – from 2015 the FWIS programme will encourage young women to consider careers in the engineering, mathematics and computer science fields.



For Women in Science
FONDATION L'ORÉAL

L'ORÉAL
UK AND IRELAND

United Nations Educational, Scientific and Cultural Organization
UK National Commission for UNESCO
Irish National Commission for UNESCO

WITH THE SUPPORT OF
THE ROYAL SOCIETY

world and regional fellowships in the Arab States and sub-Saharan Africa. Since 2003, in India the FWIS programme has helped 10 young women annually to fund their studies at higher education institutes. By injecting vital funds into revolutionary science projects globally, the L'Oréal Group has helped create a dynamic network of dedicated researchers – indeed, by the end of 2014, more than 2,000 women scientists from over 100 countries had received support from the FWIS programme. Undoubtedly, two of the highest-profile and most important FWIS activities at a global scale are the L'Oréal-UNESCO International Awards and the International Fellowship programme.

The International Awards are devoted to women in science – their purpose is to celebrate the individual achievements of exceptional female researchers who, as a result of their passion and ingenuity, have made new discoveries and driven scientific progress. To contend for the International Awards, scientists worldwide are invited to nominate candidates, with a final selection of eminent female Laureates made by an international jury of top scientists chaired by Nobel Prize winners. The 2014 International Awards were presented to five women from five different regions – Latin America, Europe, North America, Asia-Pacific, and Africa and the Arab States – in recognition of the significant achievements they made in the respective fields of neurological disorders, mental health, immunology, cellular therapy and ecological food crop production.

The L'Oréal-UNESCO International Fellowships have been granted annually since 2000 to 15 promising young female scientists at the doctorate or postdoctorate level. Not only do they give these young high achievers the recognition they deserve, but they also provide them with the means to continue their scientific research journeys abroad and contribute to the development of collaborative, cross-cultural research networks.

FUELLING INNOVATION

In the present day, the world is facing more scientific challenges and opportunities than ever before. With a rapidly growing global population, threats to the environment and the explosion of new technologies, it is essential that both women and men participate in R&D, drawing on their unique experiences in order to contribute to the continued advancement of vital scientific knowledge. To this end, as a result of its tireless and forward-looking work, the L'Oréal-UNESCO FWIS programme is sowing the seeds for a fairer and more diverse future in STEM fields. As a benchmark for global scientific excellence, the programme will continue to help female researchers cultivate their commitment to scientific research, enabling them to make a tangible impact on society.

FORWARD thinking

Although there are many more women employed in academia than there were 30 years ago, significant challenges still remain. For nearly two decades, **Drs Rachelle Heller** and **Catherine Mavriplis** have been working towards addressing the gender gap

Could you provide a brief introduction to the Focus on Reaching Women for Academics, Research and Development (FORWARD) to Professorship project and explain why it was created?

CM: FORWARD started in 1996 as a programme to advance women and underrepresented minorities in STEM, including the deaf and hard of hearing, through the undergraduate to graduate level juncture. It soon became obvious to us that the structure of our FORWARD to Graduate School workshop could easily be adapted to address the graduate school to professorship juncture. FORWARD was developed to fill the gaps for women and underrepresented groups by providing information about the ways in which these populations can make successful transitions in STEM. The FORWARD to Professorship workshop covers the nuts and bolts of applying for and succeeding in a tenure-track professor position.

What are your respective roles in the project and what inspired your involvement?

RH: The project truly is a collaborative effort, and I do not think of it in terms of specific roles. That said, Catherine's memory for people we've met, articles we should relate to and tasks we have on our to-do list is much better than mine. So, I would say Cathy is the project memory. I am happy taking care of the administrative details. Together, we consider speakers, projects and new pathways to implement.

CM: We never set out with any respective roles, but we certainly brought different strengths and perspectives to the project. Our colleagues at Gallaudet University for the Deaf and Hard-of-Hearing, Charlene Sorensen, H David Snyder and, more recently, Paul Sabila, have provided much needed insight into the culture and challenges for the deaf in science. Each of us also brought our experiences from different disciplines and institution types. But together, we drew upon each others' strengths to spark creativity and come up with a unique programme that addresses a comprehensive set of challenges.

How does the FORWARD project compare to other educational or career support programmes?

RH: FORWARD was ahead of its time: in the 1990s, individuals were not organising workshops to discuss issues and skills necessary for women's advancement in academic STEM.

CM: At the time, as one of our participants said, the workshop provided information that was not available anywhere else. We really see it as 'insider information' that should be available to everyone: that is why we endeavoured to provide it for free to participants who were serious about becoming a professor in science or engineering. Furthermore, the uniqueness of FORWARD is gathering women from across a wide geographical, disciplinary, institution-type and ethnic background to converse in one time-intensive session about solutions to the challenges of becoming and succeeding as a professor: breadth and depth in a short powerful experience.

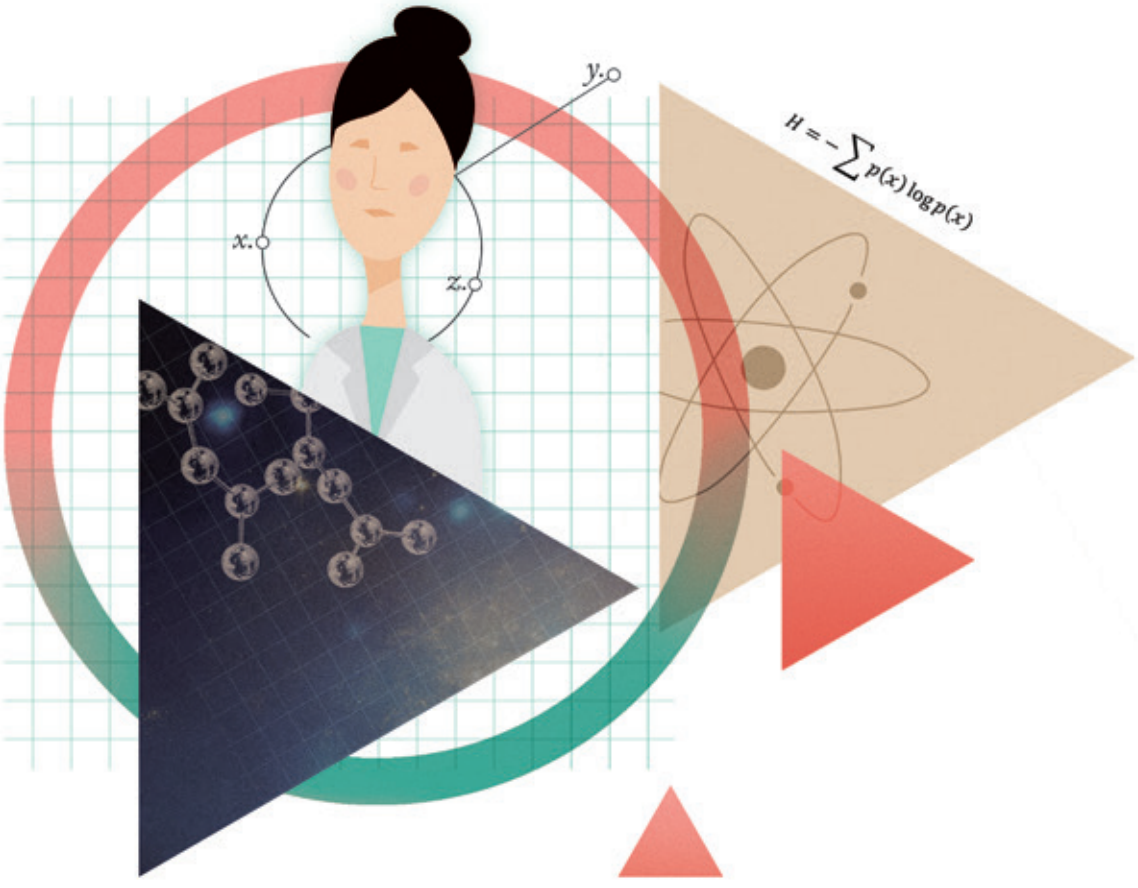
Are there any noteworthy achievements as a result of the programme that you wish to highlight?

RH: We have had a few notable successes. Firstly, we have interacted directly with over 400 women and indirectly impacted over 1,300. Secondly, through the Pay It FORWARD grant, 10 local adaptations of our model were created and offered to targeted geographic, social or discipline groups. Two models have become institutionalised, one at Massachusetts Institute of Technology and the other at Arizona State University.

CM: The greatest success of the project is definitely seeing the smiles on the faces of more than 1,300 doctoral women who thrive on science and engineering, when they recognise that they are not alone and can foresee a path for themselves to becoming successful researchers and professors. Beyond that gratifying moment, the creation of a legitimate structure for faculty development that has been institutionalised, adapted and adopted by several different groups and institutions across the US and Canada is a very tangible and enduring success.

Do you hope to use FORWARD as a global model for increasing the inclusion of women and minority groups in STEM leadership roles?

RH: The workshop model is adaptable, as we have already shown. FORWARD is an easily localised model – we have already seen it in use outside of the US where it was well received. Issues of advancement for women are bound into the social fabric of a community and our model supports adapting the programme to address social issues. For example, technical issues in funding vary from country to country. We urge organisers to conduct a session on funding with local leaders. Additionally, the 'Having It All' work-life balance panels are designed to bring in colleagues who have addressed their advancement within the social structure. We expect that our forthcoming book will incite new partners to advance the FORWARD model.



Equality in academia

On the path to the predominantly male upper echelons of STEM fields in academia, women and minority groups face many challenges. The long-standing **FORWARD** to Professorship project was one of the first to support such individuals to access these realms

IN THE US, the number of women employed in STEM academia has increased considerably over the last three decades, but progressing from doctoral and postdoctoral level to professorship has remained a predominantly male pursuit. At the end of their doctoral research, women are faced with the difficult choice of pursuing an academic career, working in private industry or government, or following another life path. Although most institutions now acknowledge that life events such as starting a family can impact a woman's ability to progress in academia, many women doctoral students are dissuaded from an academic career for a number of reasons – often influenced by what they have observed in their own institutions. These include the small or non-existent number of females already employed in professorships and the challenges of breaking into a rigid male-dominated culture, as well as a lack of clarity around the pathway to professorship.

WORKSHOP MODEL

Over the past 15 years, the Focus on Reaching Women for Academics, Research and Development (FORWARD) to Professorship project has been addressing these challenges for women, as well as other underrepresented groups such as individuals who are deaf or hard of hearing. The project was originally devised by Drs Rachelle Heller and Catherine Mavriplis at George Washington University, USA, and Drs Charlene Sorensen and H David Snyder at Gallaudet University, USA, in the late 1990s, when support for women's progression in academia was sorely lacking, mentoring was rare and no other similar initiatives existed. FORWARD was designed to demystify the process and bring women together to hear from women (and some men) who had successfully advanced their academic careers.

Funded by the National Science Foundation under the ADVANCE Leadership Award programme since 2001, FORWARD's primary method is a two and a half day workshop with a range of sessions on topics which include teaching styles, communication and negotiation skills, writing, seeking research funding, creating a career plan and discussion on work-life integration. Speakers, mentors and peers who can offer solutions to a variety of the challenges faced, or simply the encouragement to devise one's

FORWARD TO PROFESSORSHIP

OBJECTIVES

To address the significant challenges faced by women and underrepresented minorities in STEM and provide effective support and mentorship to help them advance from graduate education to professorship positions.

KEY COLLABORATORS

Dr Charlene Sorensen; **Dr H David Snyder**; **Dr Paul Sabila**; **Dr Yell Inverso,** Gallaudet University, USA

PARTNERS

Gallaudet University

FUNDING

National Science Foundation: ADVANCE Leadership Award programme

CONTACT

Dr Rachelle Heller
Professor and Associate Provost for Academic Affairs
Mount Vernon Campus
The George Washington University
USA

T +1 202 242 6698
E sheller@gwu.edu
http://bit.ly/1zidefr

Dr Catherine Mavriplis
Associate Professor
University of Ottawa
Canada

T +1 613 562 5800 x 8961
E catherine.mavriplis@uottawa.ca

http://bit.ly/17LlZmG
http://bit.ly/FORWARDToProf
http://bit.ly/Chair-WiS

@CWSE_ON

@sheller43

www.facebook.com/CWSE.ON

http://bit.ly/CatherineMavriplis

http://bit.ly/ShellyHeller

DR RACHELLE HELLER, Professor of Computer Science and Associate Provost for Academic Affairs, is a lifelong researcher into all areas of computing and education, starting with a text in 1984 called *Bits 'n Bytes About Computing*. She has also devoted herself to recruiting and retaining women in STEM from young girls to women in leadership.

DR CATHERINE MAVRIPLIS holds a PhD in Aeronautics from MIT. Her research is in computational fluid dynamics (CFD) and she is President of the CFD Society of Canada. As Associate Professor of Mechanical Engineering at the University of Ottawa in Canada, she holds the Natural Sciences and Engineering Research Council of Canada / Pratt & Whitney Canada Chair for Women in Science and Engineering to advance women 'from the classroom to the boardroom'.

uOttawa

THE GEORGE WASHINGTON UNIVERSITY
WASHINGTON, DC

own solutions, are selected to attend. At the end of each workshop, a career planning session is available in which participants are encouraged to build a near-term career plan that they can then discuss with experienced administrators such as department chairs and deans. "Our pre- and post-workshop surveys track career progression and have shown success of transition into tenure-track and tenured positions for many of the participants," Mavriplis reports.

Heller reflects that the problems and obstacles identified have not been easy to resolve and there are no quick fixes: "Changing a culture takes sustained effort in a variety of forms. FORWARD is one of those forms," she asserts. Addressing the challenges women face takes time, necessitates consideration of the problem from various angles, requires a team of people and takes perseverance. Furthermore, as the specific needs of the target population have changed, so have the potential resolutions.

TRANSFORMATIONAL MENTORING PROCESSES

The interactions of participants with the many peer, academic and other mentors are central to FORWARD's success, and provide the empowerment for attendees to forge ahead in a challenging environment. Both formal and informal mentoring takes place, in traditional senior-junior, near-peer, and peer mentoring dynamics. Because women and other underrepresented groups often find themselves isolated and with limited reference points from which to forge their own path, bringing role models and successful examples from these populations together in one intensive experience has proven to be transformational for many of the participants. "The mentoring relationships are extremely important to 'get the message' across. Some of the informal networking and mentoring that has taken place has had an enormous impact," Heller explains.

Although senior academic mentors can provide important career-advancing advice and important contacts for job searches and research funding, peer or near-peer mentoring has been found to be equally, if not more, important. "While the experienced research fund programme directors and other speakers were enormously helpful, it was the near-peers who captured the participants' attention more vividly, as people who had recently tackled the same challenges," Mavriplis explains.

She and Heller discovered that at the heart of most speakers' ability to connect with and mentor the programme participants was feeling compelled to share what they had learned, often the hard way, so that new candidates would not have to experience similar struggles. Where the mentor relationships were particularly strong, they attempted to offer support beyond the workshop through a telephone bridge at first, then through listservs and social media. Mavriplis adds: "The mentors themselves also felt inspired by the experience of sharing their paths with participants. Some even expressed surprise at this feeling. Overwhelmingly, participants, speakers and organisers reported the connection with other women in similar roles to be one of the most beneficial aspects of the workshop".

EFFECTING SYSTEMIC CHANGE

The FORWARD programme has been running annually at the Massachusetts Institute of Technology since 2005. In 2011 and 2012, the workshop model was disseminated and expanded, with training and financial support, to 10 teams across the US, who have adopted or adapted it to focus on specific disciplines, geographic regions or populations. Eventually, Heller and Mavriplis are keen for FORWARD to be used as a global model for increasing the inclusion of women and minority groups in STEM professorships. They continue to seek European partners to advance the FORWARD model or develop new ones, and workshop models are also now being adopted across Canada.

> The interactions of participants with the many peer, academic and other mentors are central to FORWARD's success

Ultimately, Heller and Mavriplis are aiming for the wider adoption of their model by the academic community, in order to effect systemic change for diversity in academic STEM departments going forward. "Women want to be STEM professors. Providing them with access to information, key contacts and a variety of role models is inexpensive and fairly easy to achieve with a workshop structure such as FORWARD to Professorship," Mavriplis enthuses. Furthermore, the experience of the workshop is empowering for participants, speakers and organisers alike, and benefits the careers of all involved.

The project is the subject of a forthcoming book to be published by Elsevier, *FORWARD to Professorship in STEM: Inclusive Faculty Development Strategies That Work*. Heller and Mavriplis have found the process of compiling the book a useful opportunity to reflect upon FORWARD's impact. They plan to disseminate the book widely. "Gathering the 11 teams who adapted the workshop to their regional, discipline or minority group focus and synthesising the experiences of these diverse groups contributed to a deeper understanding of what we had created and its importance," Mavriplis concludes.

THE Female Factor

The gender disparity in the STEM workforce is a well-charted phenomenon in countries all around the world. In view of this, there is an urgent need for targeted and imaginative policies that redress the male-dominated nature of this field

IN A WORLD that is facing numerous environmental, health and development challenges, the STEM sector is paramount. Not only is it critical for enhancing productivity and competitiveness, but it also helps to ensure the continued wellbeing of individuals and societies. In today's burgeoning knowledge-intensive economy, the STEM workforce is projected to undergo exponential growth in the coming years.

Unfortunately, however, women in countries throughout the world are vastly underrepresented in scientific and technological fields. When it comes to pursuing successful and long-lasting STEM careers, they often face multiple barriers including a male-dominated working culture, a 'chilly' classroom environment and a lack of access to female mentors.

Closing the shameful gender gap in the STEM sector is vital for improving fairness and opportunities for women. Yet above and beyond this, ensuring greater inclusivity and diversity in scientific fields is also conducive to innovation, firing growth through fostering a broader culture of scientific excellence. Indeed, the current lack of female representation in the STEM workforce means that the talents of half of the global population are not being exploited to their full potential.

In response, governments, universities, charities and organisations all over the world are ramping up efforts to close the STEM education gender gap and increase female participation in scientific and technological careers. For instance, the European Commission has set a target of 40 per cent by 2020 for the underrepresented sex in expert groups and evaluation panels, while the US-led TechWomen initiative is providing the next generation of women STEM leaders in Africa, Central Asia and the Middle East with access to mentors and educational exchange programmes. Importantly, national assessments conducted in 2012 by Women in Global Science and Technology in Brazil, India, Indonesia, the Republic of Korea, South Africa, the US and the EU highlighted that women researchers do better in countries that have effective policies for health, childcare and equal pay.

Yet while there is a growing acceptance of the importance of promoting greater female representation in STEM fields, the bulk of the literature on gender disparities – as well as the policies designed to combat them – relates to the European and North American context. At present, in many developing countries there is a lack of disaggregated data on the number of women in STEM careers, making it challenging for policy makers in these countries to draw up effective interventions.

Moving forwards, with the prosperity of future generations dependent on the inception of innovative solutions that resolve pressing challenges such as clean energy, cures for diseases and increased food production, it is crucial that all nations invest in encouraging more women to pursue STEM careers.

A GLOBAL PICTURE

By shining the spotlight on the position of women in science in different regions throughout the world, *International Innovation* takes stock of successful national and international strategies for promoting gender equality in STEM

NORTH AMERICA

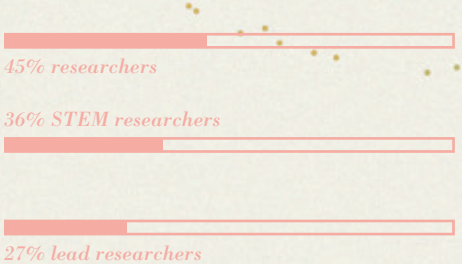
- In the US, women earn 41 per cent of the PhDs in STEM, but only comprise 28 per cent of tenure track faculty in these fields
- While women make up half of the US workforce, they only account for 25 per cent of the STEM workforce
- In 2011, 39 per cent of STEM university graduates aged 25 to 34 in Canada were female, compared to 23 per cent of STEM graduates aged 55 to 64

CASE STUDIES

- In May 2013, the Obama Administration released its five-year STEM Education Strategic Plan, which included increasing the participation of women and underrepresented groups
- The National Institutes of Health (NIH) Re-entry Program has been specially designed to support scientists returning to the workforce after raising children or engaging in other family duties. To date, over 90 per cent of the participants have been women

LATIN AMERICA

- Although 45 per cent of researchers in Latin America are women, only 36 per cent are STEM researchers
- In Brazil, 49 per cent of researchers are female – yet only 27 per cent of women lead research groups, compared to 32 per cent for men
- In Bolivia, 63 per cent of researchers are women, compared to just 37 per cent in Colombia



CASE STUDIES

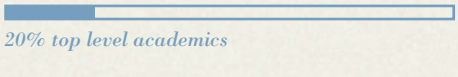
- The Venezuelan Academy of Physical, Mathematical and Natural Sciences launched Women for Science Venezuela in 2012 to connect women working in science and highlight their contributions. They are currently conducting a census of women working in the sciences in Venezuela
- UN Women has initiated projects to increase the digital literacy of rural women in Ecuador and Guatemala and of girls in the Dominican Republic. The Dominican Republic Government has set a national goal for achieving 50 per cent digital literacy among women in a four-year period

AFRICA AND THE ARAB STATES

- Of the 20 countries worldwide where women earn 50 per cent or more of the science degrees awarded, six of these are Arab states
- Only one in five countries in sub-Saharan Africa has achieved gender parity whereby 45 to 55 per cent of researchers are women
- In Namibia, 44 per cent of researchers are female while in Ethiopia women make up just 8 per cent of researchers

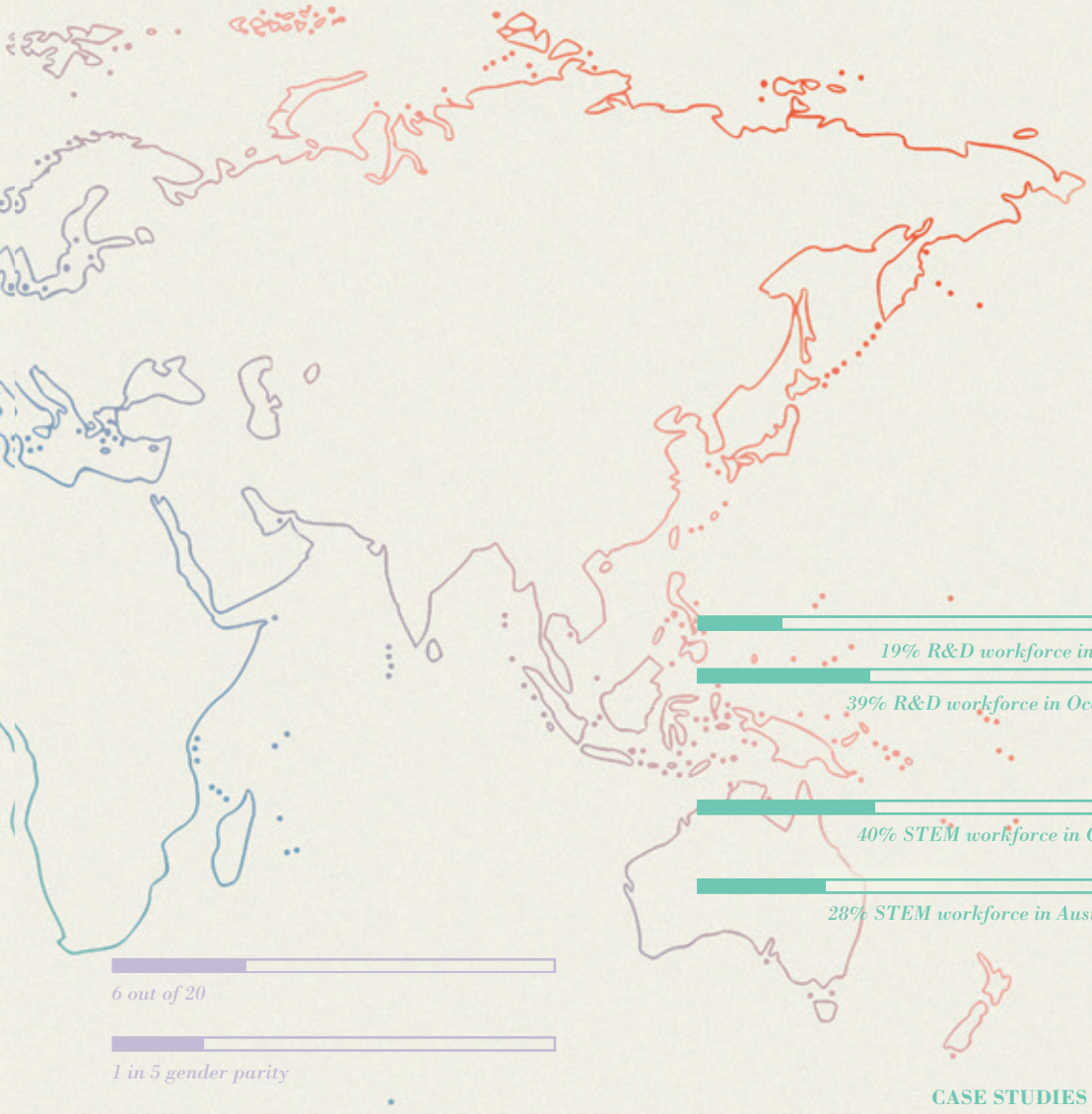
EUROPE

- Women make up 34 per cent of Europe's R&D workforce
- Only 20 per cent of top-level academics in Europe are women
- A 2013 study on female representation in Europe's ICT sector suggested that if as many women as men worked in this field, European GDP would increase by an estimated €9 billion. Yet at present only 30 per cent of the 9 million people in this sector are women



CASE STUDIES

- Most EU Member States have made concerted efforts to encourage gender equality in STEM, including the creation of national committees on women in science, commitment to gender mainstreaming, the publishing of sex-disaggregated statistics and the promotion of gender studies and research
- Gender equality is a key priority for the European Commission, enshrined in Horizon 2020. Applicants for research funding are strongly encouraged to ensure gender balance at all levels in their teams and management structures



ASIA-PACIFIC

- Women make up nearly 19 per cent of the R&D workforce in Asia and approximately 39 per cent in Oceania
- In China, it is estimated that women comprise approximately 40 per cent of the entire STEM workforce
- In 2011, only 28 per cent of employed STEM-qualified Australians aged 15 years or over were female

CASE STUDIES

- The Bunengi Group is a women-owned company that operates in South Africa's construction, mining and agricultural sectors to further the advancement of women and girls in STEM education by providing female students with scholarships and career information
- The US-launched TechWomen initiative supports the next generation of women leaders in STEM in Africa, Central Asia and the Middle East through providing them with access to inspirational mentors and offering educational and cultural exchange programmes

CASE STUDIES

- In response to India's burgeoning number of female engineering graduates and their current low representation in the workforce, the Anita Borg Institute and the Lean In Initiative have designed videos, training and resource materials and generated strategic networking opportunities for women engineers in India
- The South Australian Government provided professional development scholarships, each valued at AUD $15,000, to support a number of female STEM researchers in the early stages of their careers in 2011

Sources: http://bit.ly/whitehousestem, http://bit.ly/europagender, UNESCO Data Center, 2010

International INNOVATION
Disseminating science, research and technology

RESEARCH MEDIA

Your FREE OF CHARGE registration

International Innovation is a global resource providing insight and analysis on current scientific research trends, as well as funding and policy issues. Every issue of *International Innovation* reaches a global audience of over 20,000. Available both digitally and in print, *International Innovation* is free to access. Members can download, copy, distribute, print, search or link to all articles without asking prior permission from the publisher or author.

To access *International Innovation* free of charge, please complete the form below or go to www.internationalinnovation.com/join-us/registration and fill out our online registration form.

We look forward to welcoming you on board as an *International Innovation* member!

Becoming a member is easy. Simply:

1 Confirm your address

2 Tell us how you'd like to be contacted

3 Tell us which areas of research you are interested in

4 Sign and date the form

Then fax, scan or email it back to us!

STEP 1: Confirm your address

Title Mr ☐ Mrs ☐ Ms ☐ Miss ☐ Other ☐

First name **Middle name/Initial**

Surname

Job title

Organisation

Department

Organisation Address

City

State/County

Country

Post/zip/area code

Telephone (business)

Telephone (mobile)

Email

First two letters of your mother's first name ☐☐

STEP 2: Your preferences

Please tick:

☐ Yes - I would like to receive regular copies of ***International Innovation***

☐ Yes - I would like to receive the latest email news alerts from ***International Innovation*** and **Research Media**

☐ Yes - I would like to be informed of **Research Media's** products and services by post and or phone

STEP 3: Please indicate your thematic areas and locations of interest below, we can then ensure you only receive editions of *International Innovation* that are relevant to you:

Research locations of interest:

Africa	☐	Europe	☐
Antarctica	☐	North America	☐
Asia	☐	South America	☐
Australasia	☐		

Thematic areas of interest:

Environment and Climate	☐	Energy	☐
Food and Agriculture	☐	Healthcare	☐
ICT	☐	Nano and Materials Technology	☐
Transport	☐	Other	☐

STEP 4: How did you hear about *International Innovation*?

Contributor	☐	Received a free copy	☐
Colleague	☐	Contacted by Research Media	☐
Event	☐	Other	☐
Internet Search	☐		

if other please state

STEP 5: Please tell us a bit about you

If you will be sharing your copy of *International Innovation* with colleagues, please indicate with how many? ☐

STEP 6: Please sign below if you wish to receive copies of *International Innovation*

Signed .....

Date .....

Please fill out this application in full and either fax, or scan and email to:
Fax: **+44 117 911 3474** Email: **info@internationalinnovation.com**

A rationally designed vaccine

Professor Denise Doolan is passionate about driving scientific advances that improve the lives of individuals in developing countries. Here, she discusses her work on genome-based rational vaccine design and outlines her research successes and challenges to date

How has your research career developed up to this point? What inspired you to improve vaccine design?

I was born and raised in the highlands of Papua New Guinea, and so was exposed to the enormous impact that disease can have on individuals and communities from a very young age. After completing my BSc at the University of Queensland, Australia, I worked at the Commonwealth Scientific and Industrial Research Organisation in the field of animal health, with the goal of developing a vaccine against bovine ephemeral fever. However, I wanted to move back to human research in order to have an impact on public health in countries such as Papua New Guinea, so my PhD – conducted at the Queensland Institute of Medical Research – focused on the development of a malaria vaccine.

Following the completion of my PhD, I moved to the USA to work in the Malaria Program at the United States Naval Medical Research Center. In the 12 years I spent there, I gained invaluable experience in malaria vaccine development, spanning the areas of discovery research, preclinical research and development, and clinical trials. Unfortunately our candidate vaccines, based on only a small number of parasite proteins identified empirically, were not successful. Upon returning to Australia, I therefore decided to focus on the basic sciences and pursue a rational approach to vaccine development, using as a foundation the huge genomic-based datasets that had thus far not been exploited. I was fortunate to be awarded a Pfizer Australia Senior Research Fellowship, and subsequently a National Health and Medical Research Council Principal Research Fellowship, which have allowed me to pursue my research goals.

Can you describe the main objectives of your research into genome-based rational vaccine design?

Traditional empirical approaches to vaccine development, based on only one or a few pathogen proteins, have not been successful for a number of diseases. My research aims to develop and implement a rational approach to vaccine design for complex pathogens by bridging the fields of genomics and immunology – immunomics – using cutting-edge technologies. Specifically, we are mining genomic, proteomic and transcriptomic datasets using biological samples and clinically relevant selections to identify important antigens and epitopes targeted by protective immune responses. Genome-based rational vaccine design holds a lot of promise for the development of vaccines against many diseases that have so far proved elusive.

You have acted as a consultant for, and collaborated with, several biotechnology companies and in doing so helped to bridge the gap between academia and industry. What impact has this work had on your research?

I was fortunate to be in a position where I could collaborate with both academia and industry – and have benefited enormously from associations with small biotechnology companies as well as big pharma. These partnerships have taught me the industry perspective on the vaccine development pipeline and highlighted the core differences between industry-based, product-orientated research and academic research.

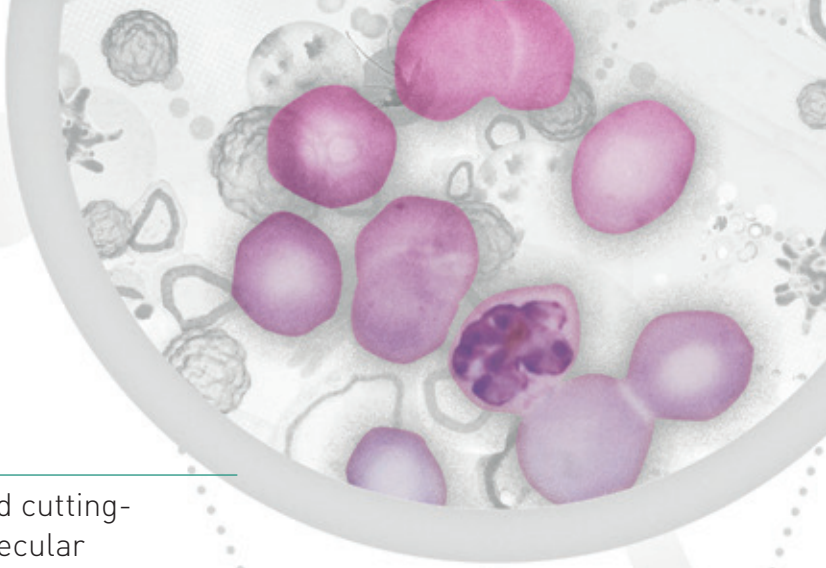
Additionally, my consultancies have enabled me to expand my knowledge of the business side of research. Overall, my involvement with industry has had a demonstrable impact on the direction and priorities of my work, in particular by emphasising the importance of translating research from basic science to practical application.

What have been the biggest challenges in your research and how have you successfully overcome these?

Like most scientists, the biggest challenge is funding. When I relocated from the US back to Australia, I had to build my laboratory and secure funding for personnel and resources. Importantly, my Pfizer Australia Senior Research Fellowship allowed me the freedom to pursue promising but less conventional avenues of research. My current challenge is to secure funding for research translation in order to move my basic science discoveries through the pipeline into clinical testing.

Looking back over your career, can you discuss your highlights to date?

My research has achieved key advances in our understanding of the mechanisms of infection-blocking immunity directed against the liver stage of the *Plasmodium* parasite and of the antigens and epitopes involved in this protection. I have also evaluated a range of molecular-based vaccine platforms in preclinical animal models, some of which were advanced to clinical testing in humans, including the first study of plasmid DNA vaccines in healthy humans. A more recent focus has been the mining of genomic sequences for vaccine development. I am also an inventor of a number of patents in the areas of antigen discovery, utilisation of genomic sequence information and vaccination strategies.



Advancing immunomics

Drawing on conceptual advances in genomics and cutting-edge technologies, researchers based at the Molecular Vaccinology Laboratory at the **QIMR Berghofer Medical Research Institute** in Brisbane, Australia, are striving to develop a rational and effective malaria vaccine

AS THE MOST efficient and cost-effective method of preventing infectious diseases, vaccination has saved countless lives and dramatically improved global public health. The earliest documented vaccines originated in China and India in the 17th Century, while the work of Edward Jenner and Louis Pasteur – in the 1700s and 1800s, respectively – established and refined the whole organism vaccine approach. The modern era has witnessed great strides in vaccine development, with the spread of vaccination campaigns across the globe successfully targeting many viral and bacterial pathogens.

However, there are still many chronic infectious diseases for which vaccines are ineffective or do not currently exist. For instance, it has been particularly difficult to develop effective vaccines for diseases such as tuberculosis, malaria and HIV – which together represent half of the global infectious disease burden – due to their complex pathogens with large genomes and multi-stage lifecycles. "At present, there are no licensed vaccines for humans against any parasitic or chronic infection caused by complex pathogens," details Professor Denise Doolan, a molecular immunologist who heads up the Molecular Vaccinology Laboratory at the QIMR Berghofer Medical Research Institute. "Historically, vaccines have been designed to mimic the immunity induced by natural exposure to the target pathogen – but complex pathogens have since evolved sophisticated immune evasion strategies and so it seems that we must try to do better than nature."

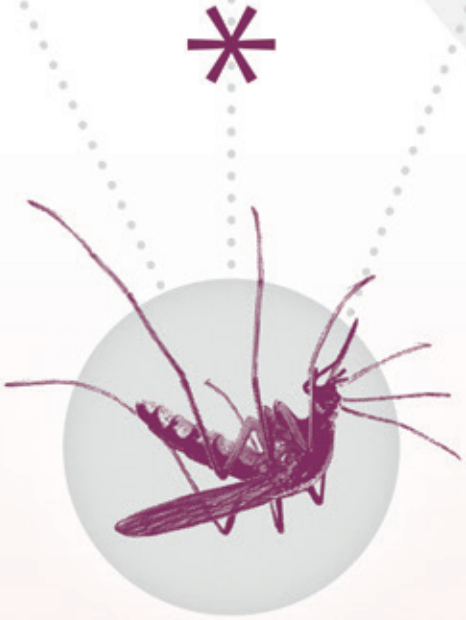
A NEW APPROACH

In response to this challenge, the researchers in Doolan's laboratory are attempting to produce an effective malaria vaccine that goes beyond the conventional strategy of reliance on a limited number of pathogen proteins. Indeed, since the mid-20th Century, in a quest to develop a pre-erythrocytic (sporozoite/liver) stage malaria vaccine, researchers have primarily focused on a single antigen: the circumsporozoite protein. Believing this conventional approach to be incomplete and insufficient, Doolan and her team are pursuing a new and innovative approach to vaccine design that taps into recent technological and conceptual biological advances.

Known as genome-based rational vaccine design, the strategy takes advantage of the enormous datasets available from the definition of the genomes, proteomes and transcriptomes of target pathogens. At present, using biological specimens from individuals with experimentally or naturally induced malaria immunity, Doolan and her colleagues are applying large-scale methods to screen proteins and peptide epitopes derived from the complete genome of the parasite that causes malaria. They are aiming to identify the key antigens and epitopes targeted by protective immune responses with a view to overcoming the problem of poorly immunogenic and protective vaccines.

LEADING-EDGE METHODS

The researchers are utilising human models as a starting point for their research into the development of an effective malaria vaccine for three central reasons. Firstly, sterile and infection-blocking immunity to the disease can be induced in both humans and animals via immunisation with *Plasmodium* sporozoites attenuated by radiation. Secondly, the passive transfer of immunoglobulin from those with lifelong malaria exposure to current malaria sufferers can reduce blood stage parasitemia and lessen the symptoms of the disease. Finally, individuals who survive past childhood in areas with a high burden of malaria develop substantial clinical immunity to the disease and rarely die from it in later life. "Importantly, these models provide a source of samples for *in vitro* screening," discloses Doolan. "We use cells and serum from individuals with immunity in order to assess the capacity of each protein or epitope



Professor Denise Doolan and her team are pursuing a new and innovative approach to vaccine design that taps into recent technological and conceptual biological advances

IMMUNODOMINANCE AND PROTECTIVE IMMUNITY IN THE CONTEXT OF A COMPLEX HOST-PATHOGEN SYSTEM

OBJECTIVE

To develop and implement a rational approach to vaccine design for complex pathogens by bridging the fields of genomics and immunology (immunomics), using cutting-edge technologies.

FUNDING

Australian National Health and Medical Research Council (NHMRC) • National Institutes of Health (NIH)

CONTACT

Professor Denise Doolan
Molecular Vaccinology Laboratory Group Leader and National Health and Medical Research Council Principal Research Fellow

QIMR Berghofer Medical Research Institute
300 Herston Road, Herston Queensland 4006
Locked Bag 2000 Royal Brisbane Hospital
Queensland 4029
Australia

T + 61 733 620 382
E denise.doolan@qimrberghofer.edu.au

http://bit.ly/denisedoolan

http://linkd.in/1t0aDs4

PROFESSOR DENISE DOOLAN is a molecular immunologist who heads the Molecular Vaccinology Laboratory at the QIMR Berghofer Medical Research Institute. She is an NHMRC Principal Research Fellow (2012-16) and was previously a Pfizer Australia Senior Research Fellow (2007-12). She is also a member of the QIMRB Director's Consultative Committee, Coordinator of the QIMR Biology Department, Honorary Professor at the University of Queensland (School of Medicine) and Adjunct Professional Research Fellow at the Australian Institute of Tropical Health and Medicine, James Cook University. She was on the Executive of the Australian Society for Parasitology 2010-14 (President 2011-13).

She graduated from the University of Queensland with BSc (Hons), completing a MPhil at Griffith University and a PhD at QIMR and the University of Queensland before undertaking a National Academy of Sciences postdoctoral fellowship in the US. She spent approximately 12 years in the US before returning to QIMR in mid-2007.

Doolan has published over 120 research articles, is an inventor on a number of patents, and has been a consultant for US-based biotechnology companies.

Currently, Doolan is investigating the molecular basis of immunity, with a focus on malaria and rational vaccine development. Her research programme encompasses core themes of: immune mechanisms, antigen and epitope discovery from genomic sequence data, and molecular vaccine technologies.

A FORWARD-LOOKING FIELD

As the study of a subset of pathogen-derived proteins or their epitopes that are recognised by the host immune system, immunomics is a burgeoning field of research that mines information from vast genomic, proteomic and transcriptomic datasets. By testing biological samples from humans or animals with immunity to the disease under scrutiny, immunomics researchers are able to define the set of antigens or epitopes at the interface between the host immune system and the pathogen proteome. Although no immunomics-derived vaccines have been clinically tested to date, using their malaria model Professor Denise Doolan and her team have successfully identified a number of promising candidate antigens. Looking ahead, the aim is that a rationally designed genome-based malaria vaccine will be brought to the clinic, ultimately making an impact on the lives of many people in the developing world at risk from this chronic disease.

expressed by the genome to be recognised by *Plasmodium*-specific immune responses."

Working in close collaboration with researchers at the University of California, Irvine, and Antigen Discovery Inc., USA, one approach is to develop and use protein microarrays that express most or all proteins in the *Plasmodium* genome to screen the serum of malaria-immune individuals to identify important antibody targets. A complementary approach, in collaboration with colleagues at Epimmune Inc. and the La Jolla Institute of Allergy and Immunology, USA, is to use computerised algorithms to predict the $CD8^+$ and $CD4^+$ T-cell epitopes that bind to common major histocompatibility complex alleles from all proteins expressed in the *Plasmodium* liver stage genome, and to screen synthetic peptides representing these epitopes with peripheral blood cells from the malaria-immune individuals. "We can then prioritise the antigens and epitopes on the basis of immune reactivity and to confirm that they are targets of protective immune responses in animal models," Doolan adds.

TECHNOLOGICAL SOLUTIONS

Although an *in silico* algorithm that pinpoints the key antigens and epitopes of protective immunity has not yet been developed, Doolan and her colleagues have made significant headway with their rational malaria vaccine design. Using advanced, -omics scale tools, they have generated unique, illuminating datasets of proteome-wide T-cell and antibody responses to *Plasmodium*. The researchers are analysing the most promising of these antigens, initially in mouse models of the disease and, further down the line, to the implementation of human clinical trials. In addition, they are currently working on the integration of their genome-based datasets in order to discover the main structural and genetic components linked to antibody or T-cell immune reactivity.

Pushing the boundaries of their extensive and ever-increasing knowledge, the researchers at the Molecular Vaccinology Laboratory are ultimately aiming to develop a vaccine platform that integrates multiple antigens and epitopes and is capable of inducing optimal antibody and T-cell responses. Excitingly, these technological solutions for malaria vaccine development have the potential to be translated to other chronic infectious agents with genomic sequence data in the future. "This should greatly enhance vaccine safety and simplify vaccine manufacturing, since the candidate vaccine would consist only of key well characterised components of the complex pathogen," Doolan concludes.

QIMR Berghofer
Medical Research Institute

Removing THE GENDER BIAS

PATRICIA REILLY

Member of the Cabinet of Máire Geoghegan-Quinn, European Commissioner for Research, Innovation and Science

The European Commission's new research funding programme – Horizon 2020 – has been designed to promote diversity and gender inclusion in order to minimise talent loss and support excellence. Patricia Reilly highlights the extent of gender discrimination in research and industry and the EC's strategies addressing these issues

Could you provide an overview of your role and key responsibilities at the European Commission?

I am a member of the Cabinet of Máire Geoghegan-Quinn, European Commissioner for Research, Innovation and Science. I'm one of a team of just seven people, and between us, we cover all areas of research, innovation and science policy. My particular areas of interest are agriculture, health, food, fisheries and the marine, biotechnology and gender.

The EC is committed to addressing gender discrimination within the scientific research arena. What are some of its activities in this regard?

There are three main issues that need to be addressed: gender balance within research teams, the relevance of sex or gender to the research itself, and gender balance at management level in research.

In Horizon 2020, the EC's new €80 billion research framework programme, and within our actions to support the completion of the European Research Area (ERA), each of these issues is addressed:

Gender balance in research teams – for the first time ever, the gender balance of research teams is a ranking factor in the project evaluation process. Proposals are evaluated and ranked according to their score. The top ones in the ranking list get funded. Without compromising excellence, where two proposals score identically, the proposal with the most gender balanced team will be ranked first. I think this is a very fair and effective way to ensure that the issue of gender balance is taken seriously by teams when they are putting together their proposals.

The sex/gender dimension of the research itself – those making project proposals are asked to consider sex or gender factors relevant to their work, and to explain how, if at all, they intend to address them in their

project. The quality of their response will be evaluated and influence their overall evaluation score. We have made it as easy as we can for applicants, identifying or 'flagging' particular topics in the Horizon 2020 work programmes, which definitely do have a sex/gender aspect.

These measures are new to EU research funding, and place Horizon 2020 at the cutting edge worldwide. It's the first time the gender balance of teams will be taken into account as part of the evaluation process, and though the gender dimension of the research itself has featured in some calls in the past (for example, in the area of clinical trials), this is the first time it has been integrated and highlighted systematically across the programme.

Gender at management level – this is an issue that concerns us greatly. While Europe now produces high numbers of female PhDs, only 20 per cent of top level academics are women and just one in 10 universities in the EU has a female rector. It is essential to remove the longstanding cultural and institutional barriers that are behind the persisting gender discrimination in research. We are working with all Member States, associated countries and bodies representing universities and research institutes to enable the institutional change necessary to remove barriers to female scientists' careers and ensure more gender balance at management level.

How is the EC helping to support female researchers advance in their careers?

In Horizon 2020, we set a target of 50 per cent of the underrepresented sex in the advisory groups, which assist the EC in preparing the biannual work programmes. A target of 40 per cent of the underrepresented sex is set for the evaluation panels, which assess and rank the submitted proposals. Furthermore, while signing the grant agreement, beneficiaries commit to taking all possible measures to promote equal opportunities and aim at gender balance at all levels of personnel engaged in the research project.

One of the cornerstones of ERA policy is to ensure open, transparent recruitment and promotion policies in Member States. This improves the prospects of the best candidates, whether women or men, and we see that where recruitment practices are most open, women do better. Furthermore, research organisations are invited to set up gender equality plans to remove remaining gender bias in their practices.

The EC is taking a range of other actions to help women in their research careers. For example, we support a network, or ERA-Net in Commission jargon, which brings together national ministries, research programme funders and managers in order to identify and scale up best practice. The participants learn from each other and implement joint activities on institutional change. The EC also provides funding support for universities and research organisations to set up and implement their own gender equality plans. Up to now, 11 projects have been funded involving over 70 universities and institutions, and this initiative will continue under Horizon 2020.

Do you have any statistics that represent how far female researchers lag behind their male counterparts, for example, in terms of the percentage of European Research Council (ERC) grants awarded, patents filed, positions held, etc.?

Recent statistics show that while the gender gap is improving, the pace of change is disappointingly slow. In the case of the ERC, only 30 per cent of applications for Starting Grants and only 25 per cent of successful proposals come from women. The picture is even less encouraging when it comes to Advanced Grants. On a positive note,

Professor Jean-Pierre Bourguignon, President of the ERC is very committed to addressing gender inequality. The ERC recently commissioned two studies on the topic of gender. One is looking into career paths and patterns, in particular into differences and similarities in the career paths of female and male ERC grant holders. The second study began in April and is looking into the ERC's practices and processes in the context of gender mainstreaming, in particular during proposal submission and peer review. The ERC is also working to combat gender bias in the selection process.

In the Seventh Framework Programme (FP7), the framework programme previous to Horizon 2020, the participation of female researchers remained rather low. Women represented only 21 per cent of the project leaders (the EC contact person for scientific aspects) and 19 per cent of the ERC principal investigators. The Marie Skłodowska Curie fellowships did better with 35 per cent of women, according to the *Sixth FP7 Monitoring Report* of 7 August 2013.

Commenting on the above findings, could you highlight the personal, research and economic impact of gender inequality?

The effects of gender inequality are both obvious and discrete. The obvious effects, other than the clear inequity of the current situation, include the loss of talent from the pool of highly skilled women in Europe – a critical issue when Europe faces a large deficit of researchers. This has clear economic implications – we risk falling behind our competitors if the pool of researchers is inadequate.

By failing to take account of the gender dimension in research, we risk missing out on important societal and economic opportunities. For example, we know that men and women both suffer from heart disease – in fact, heart disease is the number one killer of European and American women. However, for years, research relied on reference models that treat men as the norm. Happily, that has changed, and all EU-funded health research must take account of gender factors. We have examples of computer game designers who missed out on 50 per cent of their potential markets by simply designing consoles for boys alone, and for years, car seatbelt design was using male-only models, resulting in poor-quality products.

Could you elaborate on the EUGenMed initiative?

EuGenMed is an FP7-funded project that's working to produce an innovative roadmap for the implementation of the sex and gender dimensions in biomedicine and health research. This is a very valuable piece of work with practical implications. We hope that the roadmap will improve the treatment of chronic diseases that affect women and men worldwide, such as diabetes, cardiac infarction and autoimmune diseases. Women and men often present with very different clinical pictures with these illnesses, and understanding this, and the underlying biological pathways, will help produce much better outcomes for patients.

What initiatives and policies should stakeholders apply in support of gender equality?

As mentioned above, research-performing organisations (including universities) and research-funding organisations are invited to set up gender equality plans. It is not enough to support individual female scientists' careers. Research shows that there are still many gender biases concealed within current practices that look harmless at first sight. In the ERA policy we encourage research organisations to audit their own practices and remove remaining gender bias. The 'Science with and for Society' work programme provides financial support to research organisations that set up gender equality plans.

Does the EC have any initiatives that are helping to further gender inclusion in industry?

Gender equality and inclusion have been a cornerstone of the EU since it was formed. A great deal of the progress that has been made over the last decades has been born of EU legislation on equal treatment, the mainstreaming of gender into all policies, including industrial policy, and specific measures for the advancement of women. Challenges undoubtedly remain, however, otherwise we would not be having this conversation! Gender gaps persist and in the labour market, women are still overrepresented in lower paid sectors and underrepresented in decision-making positions. The Strategy for Equality between Women and Men outlines the EC's work programme on gender equality in all EU policies and highlights the contribution of gender equality to economic growth and sustainable development in the context of the Europe 2020 Strategy.

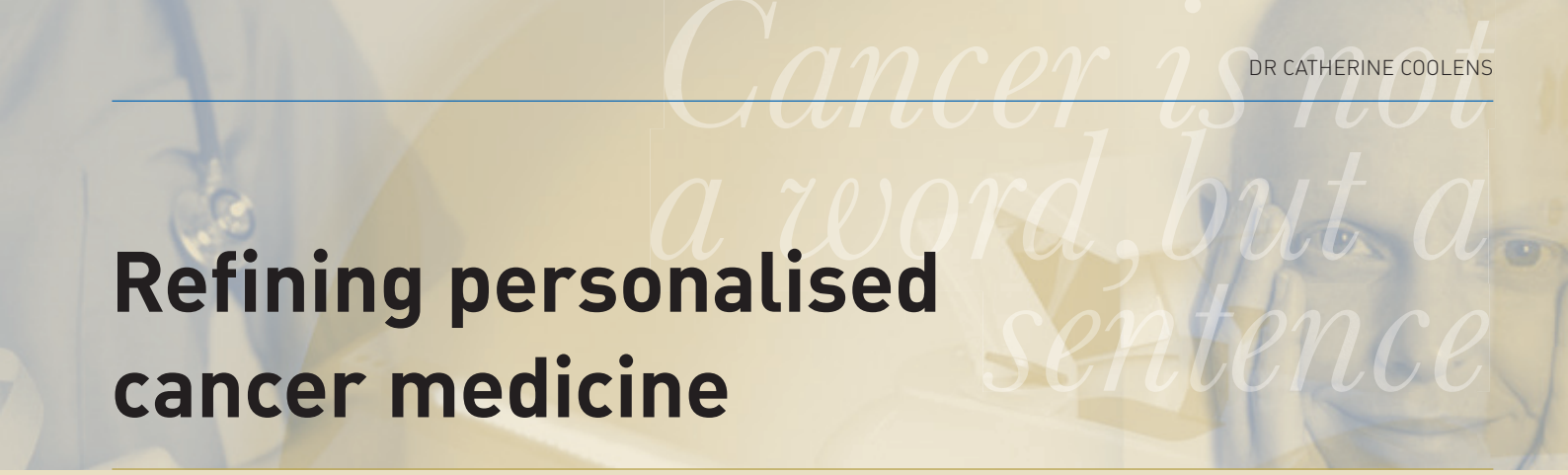
You recently gave a talk at Gender Summit 4; what were the main points you highlighted in that speech?

I outlined some recent statistics that have struck me as important, namely that in 2012 in the EU, women represented 46 per cent of PhD graduates but only 33 per cent of researchers, and that there are still far too few women in senior positions in research institutes and universities. I gave an overview of the measures we in the EC are taking to tackle this, how Member States and individual research institutes and universities need to play their part, and I spoke about some of the excellent work that is already happening.

I described the new gender-related features of Horizon 2020 and gave an update on the EC's initiative aimed at attracting more young women into science – our 'Science; it's a girl thing' campaign, which has over 70,000 Facebook fans and a very significant internet presence. I thanked the organisers of the Gender Summit 4, who are doing terrific work, our ERA-Net leaders, our 'Science; it's a girl thing' role models and the many national and institutional organisations that are trying to improve gender balance and content in research. I also thanked our own team, whose hard work has resulted in a major advance for gender equality in Horizon 2020.

Above all, I emphasised that gender equality is not a matter of being nice to women. It's about ensuring that the very best people go into and remain in research, achieving the greatest results and ensuring the best products and services end up on the market for the benefit of everyone.

http://ec.europa.eu/justice/gender-equality



Refining personalised cancer medicine

In pursuit of improved cancer treatments, **Assistant Professor Catherine Coolens** is employing a broad and distinguished array of approaches, encompassing disciplines from basic engineering and physics to clinical translation and radiation oncology

What stimulated your interest in cancer diagnosis and treatment technology, and how has this led you to your current research?

I grew up in a family of business executives so when I started talking about astrophysics and medicine, it was met with healthy scepticism and confusion, but nevertheless strong support. During university I gradually became more and more interested in the medical applications of physics and interactions of radiation with DNA and cells. Radiation oncology is probably one of the most technically challenging and interesting fields in medicine, and when I was offered a doctoral position at The University of London, days after my grandfather was diagnosed with lung cancer, it seemed the choice had come full circle. Over the last few years I have been very focused on the development and validation of functional imaging techniques to non-invasively assess how a tumour is behaving and growing, and using that information to evaluate the efficacy of radiation treatment.

How do you balance your clinical and academic responsibilities? Are the lines between the two ever blurred?

Working in an applied field can also make it quite challenging to balance these responsibilities, mainly because purely clinical and academic research have traditionally been rooted in two different modus operandi. Clinical responsibilities typically require faster decision making and, although significant planning is involved in commissioning new technology and treatment approaches, the patient's needs come first so your daily schedule is much more unpredictable. On the other hand, academic responsibilities and traditional research goals are inherently more long-term, as ideas often need to percolate. Finding the time in a busy schedule to write grant proposals and get back into your train of thought can be difficult, and time management is essential. One of the reasons I joined the Princess Margaret Cancer Centre at University Health Network (UHN) is the organisational recognition that good quality research and development will ultimately advance clinical care, making the research translation here very successful and interesting indeed.

Why is there such a need for personalised cancer treatment? Can you outline the advantages of careful measurements or markers of the patient's genetic, proteomic and physiological state?

Dr Robert Buckman, who was a tremendous medical oncologist and a very funny humanist, always said: "Cancer is not a word, but a sentence". We have come a long way in treating cancer thanks to improved technology and population-based knowledge gathering, but this can only take you so far. It has long been known from laboratory experiments that people have different sensitivities to radiation, as well as from population studies following Hiroshima, Nagasaki and Chernobyl. In addition, it is becoming increasingly clear that every tumour environment is different. Therefore, having improved prognostic and/or predictive information on individual tumour behaviour and genetic makeup that can better discriminate which type of treatment will be most beneficial for a particular patient is essential in improving outcomes, as well as taking cancer from a potentially life threatening disease to a cure, or chronically manageable disease. These personalised measurements are likely to consist of complementary genetic and molecular profiling as well as functional imaging, since tumour biology can be sampled invasively over time but only imaging can provide simultaneous geometric information.

Have there been many challenges or setbacks during your research career, and what role do you foresee your studies playing in future diagnosis and treatment technologies for cancer patients?

There are always challenges or it wouldn't be research, but I have found that staying rooted in the clinically relevant questions has helped me to focus on how to best overcome them. In terms of the future of my research, I would hope that validating our pioneering functional imaging methodologies will make for faster, easier and non-invasive methods that can help guide patients' treatments in a more informed, personalised and human way.

Clearly, your role is both exciting and altruistic. However it is also challenging. Other than your education and experience, what do you attribute your accomplishments to?

I have lived in other big cities such as London, Boston and San Francisco, and one of the reasons I accepted a position at the Princess Margaret Cancer Centre – in addition to the fantastic team and reputation – is the diversity and work-life balance that both the programme and Toronto offer. I've always believed in the 'healthy mind, healthy body' philosophy. I take time to practise mixed martial arts, yoga, music and spend time with my family. Toronto has spectacular restaurants, excellent nightlife and numerous offerings in arts, culture and events that celebrate personal diversity, which I happily participate in. This provides me with enjoyable 'downtime' away from the office which makes me more focused professionally.

How does collaboration contribute to the realisation of your research aims?

I very much enjoy collaborating with scientists from different disciplines, and the University of Toronto and UHN provide ample opportunity for these types of multidisciplinary interactions. The best ideas often come from being challenged to substantiate your work, and doing so amongst different disciplines brings out that extra level of effort in the attempt to speak a common language. For example, over the past five years, I have collaborated with institutions in the US, Netherlands, UK, Norway, Spain, France, Germany and Australia. Some of my closest collaborators are radiation oncologists running the clinical trials needed to answer the important questions. The availability of clinical data to work on new techniques is really an iterative process that benefits all of us in translating innovation from the bench to the bedside.

Advanced imaging of tumour biomarkers

Ongoing research projects at the **University of Toronto** and the University Health Network's **Princess Margaret Cancer Centre**, Canada, are breaking new and exciting ground in the quantitative uses of dynamic contrast-enhanced computed tomography

THE WAYS IN which cancer is detected, diagnosed and treated are currently on the brink of major change. Increasingly, clinicians and researchers are seeking to take a more precise, personalised approach, involving the gathering of highly specific biomarkers from each patient. These biological markers not only shed light on the complex mechanisms by which cancers develop and spread, but are also expected to unlock the door to the identification, design and administration of optimal treatment combinations for individual patients, boosting cancer control and reducing unnecessary toxicity.

Before this pioneering approach can become widespread, however, a lot of work remains to be done to improve the precision and accuracy with which biomarkers can be measured. Without the necessary detailed biomarker information, both the quality of cancer care and the medical community's wider understanding of these biological measurements will continue to suffer. In response, a series of groundbreaking studies are currently underway at the University of Toronto (UofT), Canada, and affiliated University Health Network (UHN). The multidisciplinary projects, encompassing basic engineering, physics, clinical translation research and development and clinical radiation oncology, are already making significant headway in their attempts to develop and deploy image-based biomarkers for personalised cancer medicine.

ESTABLISHING VALIDITY

The researchers at UofT and UHN have been focusing their efforts on establishing the clinical applicability of new uses for dynamic contrast-enhanced computed tomography (DCE CT), an advanced imaging technology underpinned by the intravenous injection of a contrast agent that makes blood-flow visible to regular CT scanning devices. By harvesting images that elucidate the speed and direction of the flow of blood through tissue, it becomes possible to both model and calculate the permeability of tumour microvasculature. Given this information, researchers are able to ascertain how effectively specific drug molecules can deliver therapy to the desired location.

Dr Catherine Coolens, Assistant Professor at the Institute of Biomaterials and Biomedical Engineering and Radiation Oncology at UofT and radiation physicist at Princess Margaret Cancer Centre – part of the UHN – explains that the technology itself is not new: "DCE CT has long been used to highlight areas of concern and to better visualise tumours, but mainly as a qualitative test; we are trying to use this information quantitatively as the basis for evaluating a response to treatment". The researchers are aware that tumour volume is not necessarily a good indicator of treatment efficacy, especially early on in the process, so if DCE CT demonstrates that a tumour is showing a reduced capacity to grow, and this can be measured early on during treatment, then clinicians could adapt their treatment plan accordingly if this change was not seen. In order for this approach to become clinically commonplace, however, the process would need to be properly validated and standardised. Currently, this cannot happen in patients due to the impossibility of knowing the so-called 'ground truth', leading Coolens and her colleagues to trial an innovative solution.

PHANTOM SIMULATION FRAMEWORK

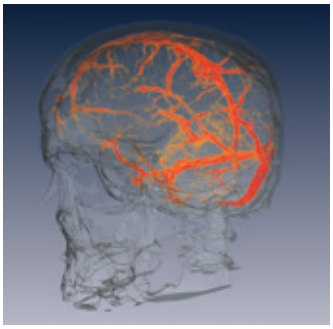
In addition to the validation of measurements, appropriate tracer kinetic modelling and analysis methods are required for the quantitative use of DCE CT to be successfully incorporated into radiation treatment response and assessment. To bridge this gap, Coolens and her fellow researchers have established a cutting-edge phantom simulation framework capable of using biopolymers and tissue printing to accurately represent perfusion of the lungs, liver and cardiovascular system. At a basic level, the dynamic flow phantom effectively simulates the injection of a contrast agent into the bloodstream, controlling the exchange of the agent into the simulated extravascular interstitial space. "Depending on the operating settings, one can create different contrast enhancement curves that are reproducible and predictable, allowing quality assurance and the investigation of other variables such as the choice of kinetic model, type of contrast

agent and imaging technique," elaborates Coolens, underlining that the flexibility of this technique is perhaps its strongest attribute.

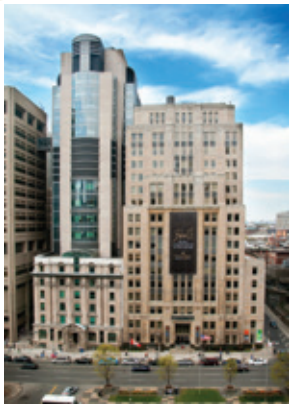
Having strived to develop a quality assurance framework capable of delivering testing and analytic tools that can be of use to clinicians and researchers throughout Ontario, the work of Coolens and her collaborators is paying off as the research community is coming on board. Indeed, the pressing need for standardisation of the team's advanced imaging techniques is being acknowledged, and requests have already come in for clinical trials from all over North America into the newly set up QIPCM office supported by both the TECHNA Institute – led by Dr David Jaffray – and the Ontario Institute of Cancer Research. Ultimately, it is only through the type of validated and standardised technology which Coolens and her colleagues are developing that oncologists, radiologists and other clinicians will be able to introduce these innovative therapeutic methods into their programmes of care and treatment management.

OUTPERFORMING CONVENTIONAL METHODS

A vital part of the research at UofT has lain in assessing whether the innovative 4D DCE CT is more accurate in measuring tumour perfusion than traditional region-of-interest approaches. Through the study of preliminary evaluations of metastatic brain cancers, Coolens and her colleagues have successfully gleaned that the availability of true volumetric DCE CT data opens up a fresh approach to analysing the relevant kinetic problem. The novel technology being developed has allowed the researchers a method of temporal dynamic analysis that was particularly salient in the examination of extremely small metastases. This investigation is very much ongoing: "I am currently writing up the results of a study which demonstrates that the dynamic and automated method throws up some interesting and promising results with regards to liver tumours, even in the presence of breathing-induced deformable motion," Coolens elucidates. Subsequently, the team has extended its approach in order to design software capable of considering



Three-dimensional rendering of a volumetric perfusion map within the brain.



Princess Margaret Cancer Centre on University Avenue, Toronto, Canada.

DCE-MRI as well as PET data, opening up new avenues for exploring the various imaging techniques currently available. For example, once the contrast enhancement measurements are complete, the kinetic analysis methods between imaging techniques are very similar, therefore a common platform for automated voxel-based analysis is highly relevant.

INTERSTITIAL FLUID PRESSURE

Alongside this research, the team at UofT and UHN is also planning investigations into the potential of interstitial fluid pressure (IFP) as an important biomarker, particularly in cervical cancer. Led by Coolens' colleague Dr Michael Milosevic, the investigators are analysing the elevation of IFP in solid malignant tumours as a direct result of vascular abnormalities. High IFP has already been shown to have links with a range of critical processes including changes in gene expression, accelerations in tumour proliferation, development of metastases and resistance to radiation treatment. In addition, Milosevic's group has succeeded in showing that it can also serve as a strong adverse predictor of survival following radiation treatment, and can be used to identify those individuals most likely to benefit from concurrent cisplatin chemotherapy.

Whilst IFP has great potential value as a biomarker for the improvement of personalised cancer treatment, at present it is only measurable using invasive needle-based techniques. As a result, Coolens, Milosevic and their colleagues are striving to develop a project that capitalises on current knowledge regarding tumour hypoxia and microenvironmental research; biophysical modelling of transport within tumours; and cutting-edge imaging techniques in order to design and develop a consistent, minimally invasive magnetic resonance approach to measuring IFP. If successful, this would enable the widespread adoption of IFP measurement in clinical practice and across a range of forms of cancer, leading the way for new personalised treatments that could ultimately improve the quality of care, reduce the invasiveness of therapy and significantly boost survival rates.

VALIDATION FRAMEWORK FOR 4D PERFUSION COMPUTED TOMOGRAPHY

OBJECTIVES

- To model tracer kinetics used in dynamic contrast-enhanced computed tomography (DCE-CT)
- To establish a validated functional imaging framework for use in radiation treatment and assessment with DCE-CT

KEY COLLABORATORS

Dr Michael Milosevic; **Dr David A Jaffray**; **Dr Caroline Chung**; **Dr Laura Dawson**; **Dr Cynthia Menard**, Princess Margaret Cancer Centre and University Health Network, Canada • **Professor Hani Naguib**, University of Toronto, Canada

PARTNERS

National Institutes of Health / National Cancer Institute • Cancer Care Ontario • Ontario Institute for Cancer Research • Radiological Society of North America • American Society for Radiation Oncology • American Association of Physicists in Medicine • Institute of Physics and Engineering in Medicine • European Society for Radiotherapy and Oncology • Modus Medical Devices • Shelley Medical Imaging Technologies • Toshiba • Philips • Siemens • Elekta • Varian • RaySearch Laboratories

FUNDING

National Institutes of Health • Canadian Institutes of Health Research • Ontario Institute of Cancer Research • Ontario Research Fund • Natural Sciences and Engineering Research Council of Canada

CONTACT

Dr Catherine Coolens
Assistant Professor

Princess Margaret Cancer Centre
610 University Avenue, Room 5-632
Toronto, Ontario, M5G 2M9, Canada

T +1 416 946 4501 x 5011
E catherine.coolens@rmp.uhn.on.ca

http://bit.ly/radonc-coolens

http://bit.ly/ibbme-coolens

http://qipcm.technainstitute.com

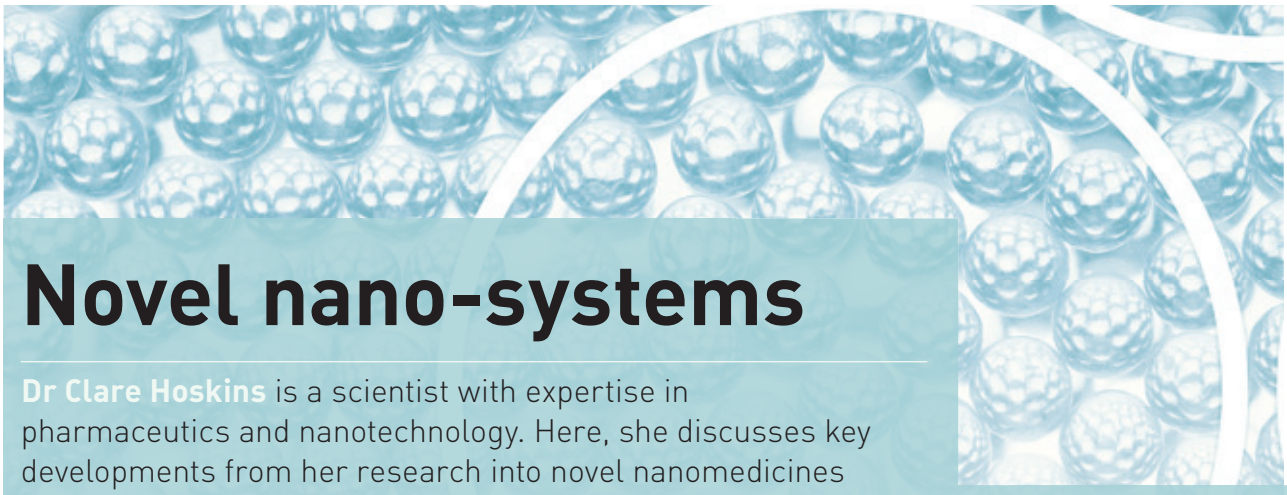
http://modusmed.com/qa-phantoms/dce-ct

http://bit.ly/simutec

http://bit.ly/sciencedirectpii

http://bit.ly/scitationmedphys

DR CATHERINE COOLENS received her PhD in Medical Physics from the Institute of Cancer Research, University of London, UK, in 2005. Subsequently, she has held positions at the Royal Marsden Hospital and is currently Assistant Professor at the University of Toronto, Canada in the department of Radiation Oncology, IBBME as well as Medical Imaging. She is also Adjunct Faculty at the TECHNA Institute and Staff Medical Physicist at the Princess Margaret Cancer Centre.



Novel nano-systems

Dr Clare Hoskins is a scientist with expertise in pharmaceutics and nanotechnology. Here, she discusses key developments from her research into novel nanomedicines

What led you to develop an interest in nanopharmaceutics?

My PhD project focused on the use of polymeric nanoparticles for the solubilisation of poorly soluble drugs. This work captivated my interest and exposed me to a whole new area of science. Ever since then, I have been involved in the development of novel nanosystems for various healthcare-related issues. My research group – Keele Nanopharmaceutics – is concerned with the application of metallic and polymeric nanoparticles in targeted drug delivery, with the bulk of our work focusing on the use of hybrid iron oxide-gold nanoparticles. I believe that nanopharmaceutics will drive healthcare into a new era and provide treatments for diseases that are currently very difficult to treat.

How did you establish your research group Keele Nanopharmaceutics?

When I arrived at Keele University in 2011 as a lecturer in pharmaceutics, I was keen to set up a laboratory that was fit for purpose and to commence independent research. I received strong support from both the Keele School of Pharmacy and the Institute of Science and Technology in Medicine. Initially, nanopharmaceutics research was carried out in my free time between teaching sessions. I identified gaps in the literature and developed a research strategy. I supervised final year project students carrying out their Masters projects, and began to apply for funding, publish my work and advertise PhD studentships. Currently, the group consists of two academics, including myself, four PhD students and an Erasmus student from the University of Gothenburg. In 2015, we will expand further, with three more PhD projects scheduled to commence.

One of your projects focused on the use of hybrid nanoparticles (HNPs) in pancreatic cancer therapy. What have your findings revealed to date?

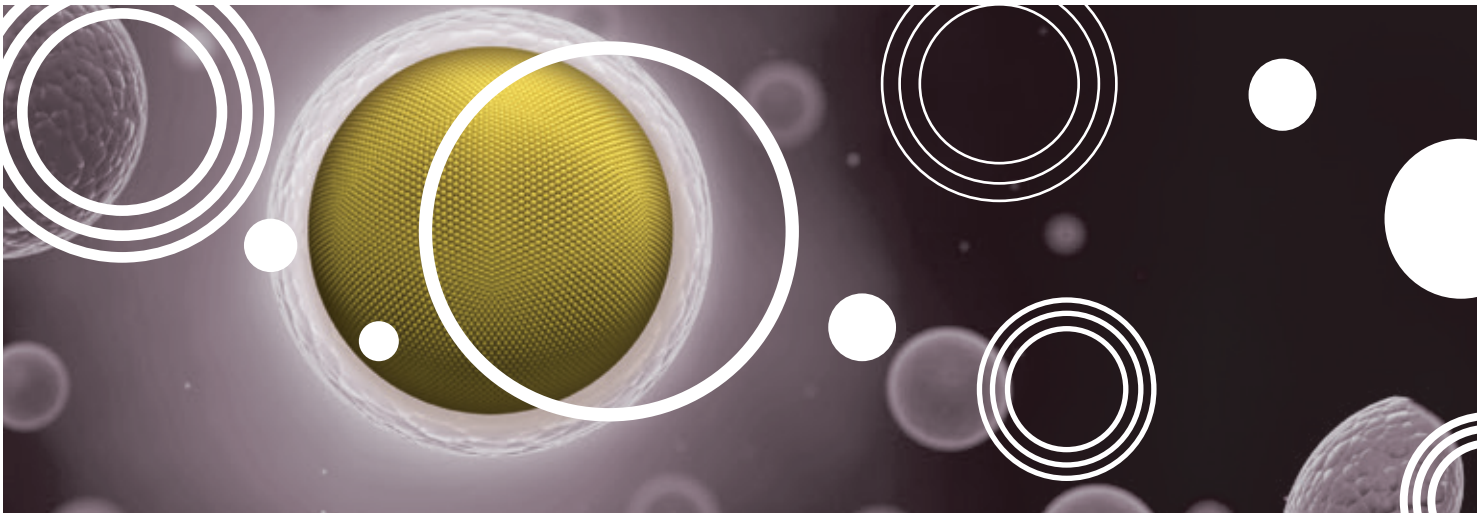
Preliminary work in this field was concerned with HNP fabrication and characterisation. We have published various articles demonstrating the use of these particles as image-guided drug delivery vehicles. Moving forwards, we are working to synthesise a thermo-responsive linker that breaks down after heating in order to free the drug contained inside it. As a group, we have examined the literature to find out whether similar linkers have been reported in other fields or applications. We discovered that the retro Diels-Alder reaction is capable of providing a linker that breaks down at elevated temperatures. This reaction is ideal for use with HNPs as they undergo localised heating after laser irradiation. Thus, drug molecules may be bound onto the HNP surface until they arrive at the desired site of action where heat activated drug release can occur. This will lead to enhanced drug targeting and, hopefully, to decreased patient side effects. So far we have observed linkage breakdown and drug release at temperatures around 70 degrees – and are currently working on optimising this system to achieve drug release at more favourable temperatures of around 45 degrees.

To what extent is collaboration essential to your team's investigations?

The work my group carries out is highly multidisciplinary. Our projects focus on organic synthesis, as well as inorganic, physical and analytical chemistry, surface engineering, optical and magnetic physics and biological investigations. The wide scope of our work means we rely heavily on a network of multidisciplinary collaborators to achieve success. These collaborators include former mentors, friends, colleagues and other key academics in the subject disciplines. Dissemination of our work at both conferences and via platforms such as *International Innovation* is crucial to fuel our work. Through collaboration, new ideas and concepts are formed and new technologies are driven forward. Our team is eager to work with other groups and individuals worldwide, and always welcomes suggested synergies and project ideas.

In which direction might nanomedicine develop over the coming decade?

The era of nanomedicine is upon us, with multidisciplinary teams breaking boundaries and finding more sophisticated answers to current medical problems. Although only a small range of nanotechnologies have made it through the rigorous testing of clinical trials and into the market, this can be attributed to their relatively young age. In the coming decade I anticipate that the market will become awash with a vast array of multifunctional, efficient, low-cost solutions in this ever-evolving climate where healthcare expenses are spiralling out of control. Ultimately, patients are at the heart of healthcare research – and any breakthroughs that improve quality of life are more than worthwhile.



Theranostic advances

Keele Nanopharmaceutics is a based in the Institute for Science and Technology in Medicine at Keele University. It hosts a small but dynamic group of visionary researchers who are pushing the boundaries of clinical applications in nanomedicine

TODAY, THOUSANDS OF patients are diagnosed with cancer every year – chances of survival increase when the disease is caught in its early stages. With delays in cancer diagnoses linked to lower survival rates, an early diagnosis can mean the difference between life and death. However, a speedy diagnosis itself is not enough to make a tangible impact; it needs to be followed up with an effective and robust therapeutic strategy. Indeed, according to Cancer Research UK, scientists estimate that up to 10,000 cancer deaths each year could be avoided through earlier diagnosis and access to optimal treatment.

Recent years have seen one particularly exciting and innovative development in the field of cancer diagnostics and therapeutics: namely, theranostics. As a completely new class of agent that offers simultaneous diagnosis and therapeutic delivery, theranostics closes the sometimes detrimental gap of time between diagnosis and drug administration, resulting in increased functionality and efficacy: "By coupling the controlled treatment of cancer with diagnosis, a rapid and localised clinical effect can be achieved," discloses Dr Clare Hoskins, a lecturer in pharmaceutics at Keele University and head of the Keele Nanopharmaceutics research group. "This reduces patient discomfort and results in decreased treatment times."

The scientists in Hoskins' research group are attempting to fuel new advances in the rapidly evolving field of theranostics. Primarily concerned with exploring the application of metallic and polymeric nanoparticles in nanomedicine, their studies have so far focused on the use of hybrid iron oxide-gold nanoparticles across three respective platforms: pancreatic cancer therapy, image-guided polymers for the drug delivery of insoluble compounds and heat-triggered scaffolds for the controlled release of pharmaceuticals. Importantly, their cutting-edge work in these areas is challenging traditional approaches and pushing past current boundaries in cancer diagnosis and treatment.

COMBATING PANCREATIC CANCER

In their first project, Hoskins and her team are designing and characterising complex nanoparticles that enable the imaging and treatment of pancreatic tumours. As the fourth leading cancer killer in the Western world, only about one-third of pancreatic cancer patients survive five years after diagnosis – so the intention is that this new approach will lead to the earlier treatment of pancreatic tumours and, consequently, to better outcomes. "The particles used in this study consisted of an iron oxide core, allowing for the diagnostic imaging of the tumours by magnetic resonance imaging," Hoskins outlines. "They are coated with a gold shell that, when activated by laser light, will heat the nanoparticles, in turn allowing the controlled release of anti-cancer medicines

Primarily concerned with exploring the application of metallic and polymeric nanoparticles in nanomedicine, the research at Keele Nanopharmaceutics focuses the use of hybrid iron oxide-gold nanoparticles across three respective platforms

THE USE OF METALLIC NANOPARTICLES IN NANOMEDICINE

OBJECTIVE

To design and fabricate novel nano-sized constructs for delivery, solubilisation, image guidance and targeting of pharmaceutical compounds. This work is carried out in collaboration with researchers at Keele University, Robert Gordon University, University of Dundee and Warwick University.

KEY COLLABORATORS

Dr Paul Roach; **Dr Anthony Curtis**; **Dr David McGarvey**, **Dr Richard Darton**, Keele University

Professor Paul Kong Thoo Lin, Robert Gordon University, UK

Dr Martin Lees, University of Warwick, UK

Dr Mariana Gueorguieva, formerly University of Dundee, UK

FUNDING

Iraqi Ministry of Higher Education and Scientific Research (MOHESR)

Engineering and Physical Sciences Research Council (EPSRC) – grant no. EP/J501591/1 'Bridging the Gaps Additional Sponsorship-Keele University'

CONTACT

Dr Clare Hoskins
Lecturer in Pharmaceutics

School of Pharmacy
Keele University
Hornbeam Building
Keele University
Keele, Staffordshire
ST5 5BG
UK

T +44 1782 734799
E c.hoskins@keele.ac.uk

http://bit.ly/1wvPm56

@KeeleNanoceutic
http://linkd.in/1Aj9N4k

CLARE HOSKINS completed her PhD in Pharmaceutics at the Robert Gordon University, UK, followed by a postdoctoral position at the University of Dundee, UK, and was appointed as Lecturer in Pharmaceutics at Keele University, UK, in 2011, where she leads the Nanopharmaceutics group. She is a member of the Royal Society of Chemistry, United Kingdom & Ireland Controlled Release Society, British Nanomedicine Association and the Institution of Engineering and Technology.

From left to right: Maryam Malekigorji, Dr Clare Hoskins, Adeolu Oluwasanmi, Dr Tony Curtis and Mohanad Alfahad.

only within the tumour. These particles are referred to as hybrid nanoparticles (HNPs)."

In contrast to the non-porous and well-formed blood vessels in normal tissue, the capillaries that supply the cancerous tissue with blood are leaky, disorganised and highly permeable, therefore allowing the HNPs to enter them. Upon entry, these tiny nanostructures naturally accumulate within the poorly-formed tumour tissue and, due to the poor lymphatic drainage, they remain inside the tumour. Crucially, the attachment of ligands to these nano-carriers facilitates targeted drug delivery within the tumour, opening up the possibility of administering lower drug doses that reduce negative side effects and promote therapeutic benefits. Initial publications from this project have highlighted the strong potential of HNPs as image-guided drug vehicles.

A DUAL OUTCOME

Hoskins' research team is also working on the design of image-guided polymers for the drug delivery of insoluble compounds. Here, the scientists are concentrating on incorporating HNPs into polymers for drug solubilisation. This is an important area as poorly soluble drugs represent a major challenge to drug development – indeed, an estimated 40 per cent of all new drugs in the developmental stage are water insoluble. To address this, delivery systems such as amphiphilic polymers are currently used to increase the solubility of drug compounds. "Most of these polymers share a common architecture consisting of both water-loving and water-hating segments within the same system," explains Hoskins. "When the polymers are in an aqueous environment, they form core-shell aggregates in which the water-hating portion of the polymer clusters together to form a waterless core where the insoluble compounds reside."

In their project, Hoskins and her colleagues decided to add HNPs to the structure of the amphiphilic polymers, thus endowing them with extra imaging and guidance properties. They found that the addition of these nano-carriers resulted in a doubly beneficial outcome: it both increased the solubilisation of the hydrophobic drugs and, as a result of enhanced imaging performance, improved the site-specific drug delivery capacity. Specifically, the core-shell structures constructed by the researchers turned out to be promising carriers for a novel anticancer agent: bisnapthalamidopropyldiaminooctane, or BNIPDaoct. "*In vitro* assays carried out using human pancreatic adenocarcinoma (BxPC-3) cells showed that treatment with the polymer-HNP formulation resulted in a significant increase in drug uptake and decrease in cell viability," Hoskins enthuses.

HEAT-TRIGGERED SCAFFOLDS

In a further area of work, Hoskins' team is investigating the addition of HNPs to polymers that undergo conformational changes at high temperatures. Together, they are fabricating smart, biodegradable scaffolds based on thermoresponsive(polyN-isopropylacrylamide), or pNiPAM, with HNPs incorporated into the polymer matrix. Biodegradable scaffolds are beneficial for long-term use as they do not need to be surgically removed, while the addition of nanoparticles generates key functional properties such as the ability to remotely control drug release or structural collapse.

In this project, the researchers found that the heating of HNPs – through exposing them to laser irradiation – causes these nano-particles to act as localised trigger heating switches. The elevated internal temperatures result in the collapse of the scaffold, in turn enabling the release of the drug encased within. In their studies using methylene blue as a model drug, Hoskins and her team found that the addition of HNPs caused scaffold deformation after just seconds of irradiation. Promisingly, these initial findings demonstrate the strong potential of smart hybrid-scaffold constructs for enhancing targeted drug delivery.

DRIVING INNOVATION

Moving forwards, Hoskins and her research group are planning to continue forming new ideas, exploring innovative concepts and creating new technologies in the area of nanopharmaceutics. With an eye on the potential future clinical benefits of their basic research, the team at Keele University is currently working on the development of clinically relevant smart scaffold systems and the synthesis of thermo-responsive linkers at lower, more favourable temperatures. Hoskins is confident that her research will have a demonstrable impact on the quality of cancer care: "I believe theranostics holds the key to modern healthcare and that in future we will see these agents advance into the clinic," she concludes.

Keele University

INSTITUTE FOR SCIENCE AND TECHNOLOGY IN MEDICINE

ORGANIZATION FOR WOMEN IN SCIENCE FOR THE DEVELOPING WORLD

OWSD aims to bring women scientists together to strengthen their position in scientific and technological leadership. **Professor Xin Fang**, President of OWSD and **Dr Tonya Blowers**, Programme Coordinator, elucidate the Organization's current objectives, with input from **Sophia Huyer**, Director of the GenderInSITE – Gender in science, innovation, technology and engineering campaign, and **Dorothy Ngila**, OWSD South Africa National Chapter

From what context did the concept for establishing a developing world organisation for women in science emerge?

The idea was first discussed at a conference on 'The Role of Women in the Development of Science and Technology in the Third World', which was convened by The World Academy of Science (TWAS) and the Canadian International Development Agency in Trieste, Italy, held on 3-7 October 1988.

The participants of the conference – including 218 leading women scientists from 63 developing countries – recommended that a study group be set up to explore the possibility of creating an organisation that would address the lack of representation and participation of women in science from developing countries.

Subsequently, the group was formed and, at its meeting in Trieste on 20-22 March 1989, it was decided to establish the then named Third World Organization for Women in Science (TWOWS) and to adopt a constitution for the organisation.

TWOWS was officially launched in Cairo, Egypt, on the occasion of its first General Assembly, a major conference that took place on 10-13 January 1993 and was generously supported by the Kuwait Foundation for the Advancement of Science.

OWSD OBJECTIVES

- Increase the participation of women in scientific and technological research, teaching and leadership in developing countries
- Promote the recognition of the scientific and technological achievements of women scientists and technologists in developing countries
- Encourage collaboration and communication among women scientists and technologists in developing countries and with the international scientific community as a whole
- Increase access of women in developing countries to the socioeconomic benefits of science and technology
- Promote participation of women scientists and technologists in the development of their country
- Increase understanding of the role of science and technology in supporting women's development activities

Could you outline your respective roles in the organisation, including your backgrounds and areas of expertise?

XF: I live in China, and have been President of OWSD since 2010. I am a long-term researcher in the fields of S&T developmental strategy and policy. My major contributions are to technological innovation and institutional reform of the Chinese S&T system. I am also a member of the Presidium of the Chinese Academy of Sciences.

As President of OWSD, I have the final approval for its strategic decisions and actions. The President presides over the meetings of the General Assembly (made up of OWSD members) and the Executive Board (made up of four vice presidents and four regional members).

TB: I have been Programme Coordinator of OWSD since August 2013. This was a new role created by extra funding from the Swedish International Development Cooperation Agency (Sida) in order to have a fulltime member of staff based at the Organization's headquarters in Trieste who could develop and implement communications, strategy and fundraising as well as coordinate the current programmes. This includes up to 50 PhD fellowships awarded per year (again through the Sida grant) to women scientists from developing countries and five prizes per year to outstanding women scientists from the least developed countries, sponsored by the Elsevier Foundation.

What unique issues are women scientists in the developing world facing?

SH: In general, there are few differences in the challenges faced by women in the developing and developed worlds. The main challenge is domestic and family responsibilities. A recent global survey conducted by scientists at the American Institute of Physics found that globally women in both the developed and developing worlds feel their domestic obligations are affecting their careers and rate of advancement.

If you look at the data collected on women's representation in national science academies in several countries, the numbers of female members in US academies is as low as or lower than some developing countries. These data can be viewed on the Women in Global Science and Technology (WISAT) website – the STI section of the Global Analytical Report of the OWSD-WISAT *National Assessments on Gender and STI*, www.wisat.org/national-assessments. It also has data on women's representation as heads of research institutions, where they are available. The OWSD National Chapter in South Africa is currently collecting data on women's representation in African science academies.

A second issue affecting women's advancement and success is access to resources: research grants, travel grants, travel to conferences, assistants, etc. Research in South Africa, Brazil and Argentina has

THE OWSD EXECUTIVE BOARD IS RESPONSIBLE FOR:

- Setting the time and venue for the meetings of the General Assembly
- Preparing the agenda and the decisions of the General Assembly
- Implementing the decisions taken by the General Assembly
- Deciding on membership applications
- Developing a strategic action plan
- Securing funding for programmes and activities
- Approving programmes and activities, as well as their budgets
- Ensuring that actual spending is in accordance with these budgets

GenderInSITE

Sophia Huyer discusses GenderInSITE, an international campaign aimed at both men and women

GenderInSITE is a multistakeholder global initiative to create greater awareness about the gender dimensions of science, innovation, technology and engineering (SITE).

The initiative has seen a number of achievements to date. We have established Regional Focal Points in: 1) Latin America with the UNESCO Chair on Women in S&T in Latin America (Argentina); 2) the Academy of Science of South Africa (ASSAf); and 3) Eastern Africa at UNESCO (Nairobi) with the Africa Network of Science and Technology Institutions (ANSTI). The Latin America RFP has recently signed an agreement with the Argentina Council for Research on Science and Technology (CONICET) to co-coordinate a research grant programme in gender, science and technology. The current focus areas are:

- Women´s educational and professional careers in engineering
- Gender differences in use and appropriation of ICT by youth
- Gender representation in decision making of S&T policies

They have also convened a regional Advisory Committee on Gender, Science and Technology which includes representatives of CONICET in Argentina, the Organization of American States (OAS), UNESCO, and the InterAmerican Network of Science Academies (IANAS) Women for Science Working Group (WfS-WG), among others.


Fang Xin


Tonya Blowers


Sophia Huyer


Dorothy Ngila

shown that women's access to research funding is lower than male researchers' in sciences, and they tend to be less represented as leaders or principal investigators of research teams. See the National Country Reports of the OWSD-WISAT project for these data.

Sociocultural attitudes do affect women in the developing world differently in that in some regions or countries, it is more difficult for women to travel away from home, either when they are single or married. In some Arab countries, for example, female science students study at national universities, while the males tend to be sent overseas for their education more often. A study of women scientists in East Africa found that less ability to travel for research and international conferences – for reasons of family responsibilities and finances – affected women's scientific careers (Campion and Shrum, 2004).

How is OWSD encouraging both men and women to participate in the gender equality debate, particularly within the STEM disciplines?

SH: GenderInSITE does this in two ways: 1) by making it a priority to bring men into its programmes and activities, and 2) by looking at impacts and trends in science, innovation, technology and engineering from both male and female perspectives.

For example, we have made it a priority to include men on our governing committee — the male members are Professor Mohamed Hassan, Chair of the InterAcademy Panel, Professor Romain Murenzi, Executive Director of TWAS, and Professor Geoffrey Oldham, Science Policy Research Unit (SPRU), University of Sussex. They work with our co-Chairs, Professor Xin Fang and Dr Shirley Malcom (AAAS and Gender Advisory Board) and other members from the Africa Centre for Technology Studies, Chinese Academy of Sciences and the Elsevier Foundation. At recent workshops on gender mainstreaming in science journalism with SciDev.Net, we discussed the relations between women and men, as well as how to understand the differential impacts on women and men of S&T — with an almost equal distribution of both genders. Similarly, an upcoming workshop at SPRU will engage both female and male experts and researchers, with an almost equal gender balance.

What inspiring activities are currently taking place at OWSD's South Africa National Chapter?

DN: The OWSD South Africa National Chapter is producing two important books on the profiling of women scientists. The first will chronicle the career pathways of young scientists (both women and men) in South Africa and select African countries with the aim of inspiring young girls and boys to take up a science career. The second will chronicle the journeys of South African young women scientists who are moving up the career ladder, and select current women PhD students, providing stories on the challenges these young women have faced so far – and so inspire future science leaders of South Africa.

The Chapter is also spearheading a project on the collection of gender disaggregated data within science academies who are members of IAP – the global network of science academies. This will be the first ever comprehensive survey on science academies. The results will be presented at the IAP General Assembly in February 2016 in South Africa.

Furthermore, the Chapter is committed to supporting capacity building efforts geared at OWSD postgraduate fellowship holders, the majority of whom are based in South Africa. As such, it will host an annual training workshop on scientific writing and science communication

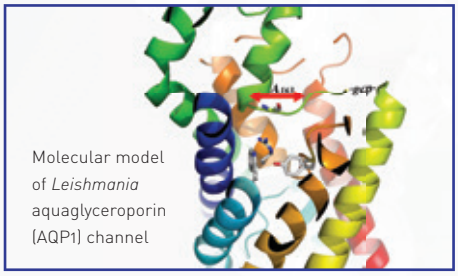
Does OWSD have any ambitious or exciting plans for 2015?

TW: OWSD is hoping to double the number of fellowships we can award, from 50 to 100 per year – so we must get new funders on board! The launch of the new website will ensure OWSD is much more visible, and will link our members and showcase all the amazing work they are doing. It will also ensure that members are able to network in such a way that stimulates national, regional and inter-regional groups and brings together crossdisciplinary research teams. In addition, we are hoping to set up a mentoring scheme whereby successful OWSD fellows and prize winners mentor onsite PhD fellows, and an online writing buddy scheme.

HTTP://OWSD.ICTP.IT

The resistance roadblock

For over two decades, **Dr Rita Mukhopadhyay** has been fascinated by the deadly parasite responsible for causing leishmaniasis. Here, she discusses how her extensive research is paving the way for the identification of promising new drug targets



Molecular model of *Leishmania* aquaglyceroporin (AQP1) channel

How did your interest in the drug resistance of *Leishmania* develop? In what ways has your research focus evolved over the course of your career?

As a Master's student, I regularly volunteered at the Calcutta School of Tropical Medicine, India, and it was there that I saw several patients suffering from visceral leishmaniasis. A few were not responding to the treatment, which intrigued me and motivated me to start reading about it. I had already participated in classes on parasitology so I knew about the causative agent, *Leishmania donovani*. Further down the line, when I was in the graduate school at Jawaharlal Nehru University, New Delhi, I changed labs – and the opportunity to work with this parasite practically landed in my lap. I fell in love with parasitic research and today our 25-year love affair is still going strong. The way that this parasite always manages to stay one step ahead of our efforts to control it never ceases to amaze me.

Can you explain the mode of action of the existing antimonial treatments – Pentostam and Glucantime?

Several mechanisms have been proposed regarding the mode of action of antimonials. However, in my opinion, the key factor is the reduction of pentavalent antimonials through a reductase in macrophages and the subsequent transport of the trivalent form through *Leishmania* aquaglyceroporin (AQP1) – the only trivalent antimony facilitator in *Leishmania*. Since trivalent antimony reacts very strongly with thiols, it kills the parasite by depleting free thiols and deactivating key enzymes with cysteines in their active sites. The parasite depends on thiols such as trypanothione in order to combat oxidative stress while living inside the phagolysosome of the host's macrophage.

Can you summarise the evidence that has led you to investigate the potential of aquaglyceroporin channels as a novel drug target to address this resistance?

Back in 2003, my group was investigating human AQPs as trivalent arsenic channels

A growing threat

Researchers at **Florida International University**, USA, are investigating the molecular mechanisms behind the alarming increasing virulence and resistance of *Leishmania* parasites

Leishmania parasites

EVERY YEAR ABOUT 12 million people are infected with a protozoa parasite spread by biting sand flies. Known as leishmaniasis, the resulting disease is endemic in areas of 88 countries across five continents, with the greatest burden found in the tropics and subtropics. Associated with malnutrition, poor housing and a weak immune system, it primarily afflicts the poorest people in the world and is responsible for an annual death toll of between 20,000 and 30,000. The disease exists in three main forms: visceral, cutaneous and mucocutaneous leishmaniasis.

Worryingly, over the course of the past decade a sizeable increase in the global incidence of leishmaniasis has been reported, as well as a wider geographical spread. These patterns have been linked to a combination of environmental and socioeconomic factors – such as deforestation, urbanisation, conflict and the collapse of public health infrastructure – and the emergence of HIV/leishmaniasis comorbidity. Unfortunately, the growing incidence of this disease coincides with its proliferating drug resistance. At present, pentavalent antimonials – namely, Pentostam and Glucantime – are the first line of defence against leishmaniasis-causing parasites – yet, in northern India alone over 50 per cent of visceral leishmaniasis cases are resistant to Pentostam. Antimonial resistance is thought to be a consequence of patient noncompliance, which facilitates the slow, underlying exposure of the parasite to the drugs.

One researcher who is taking the threat posed by leishmaniasis very seriously is Dr Rita Mukhopadhyay, Associate Professor in the Department of Cellular Biology and Pharmacology at Florida International University. Having devoted the past 25 years of her research career to studying *Leishmania* parasites, one of her main research objectives is to forge a deeper understanding of the molecular mechanisms that underpin their growing drug resistance. "The *Leishmania* genome is highly plastic and constantly employs novel mechanisms to survive in hostile environments," she elucidates. "Pinpointing these mechanisms is extremely challenging, especially as *Leishmania* also displays strain-specific variability when responding to antimonial drugs – yet it is essential if we are to combat clinical resistance."

Mukhopadhyay and her colleagues have focused on mapping the mechanisms of drug action and resistance in the treatment of leishmaniasis

STUDIES IN RESISTANCE

In their research, Mukhopadhyay and her colleagues have focused on mapping the mechanisms of drug action and resistance in the treatment of leishmaniasis. Supported by the findings of other researchers, they

in collaboration with Professors Peter Agre and Barry Rosen. At this time, we also discovered modulation of arsenic sensitivity in leukaemia cells by human AQP9. Since nothing was known about antimony uptake systems in *Leishmania*, I was intrigued by the fact that arsenic and antimony are related metalloids and therefore there must be an AQP responsible for their uptake. Thus, my group identified the first AQP in *Leishmania* and showed its involvement in antimonial resistance. Several groups have since corroborated our findings with the filed isolates. Since AQP1 is essential for the parasite's survival inside the macrophage, as well as during transmission, our rational conclusion was that it could be used as a drug target.

Are there any other mechanisms of resistance that you are investigating as potential drug targets?

Dr Goutam Mandal, a member of my research faculty, and Srotoswati Mandal – my research assistant – are currently working to identify the RNA interactome of AQP1. At the same time, my graduate student Mansi Sharma is investigating the post-translational regulation of AQP1 through the use of global interactome methodologies. From this research, we expect to identify novel targets that could also be used as drug targets.

What progress has your research made towards finding a treatment to overcome this resistance? Have you identified any other promising drug candidates?

We are on the tip of the iceberg in our research and still have a long way to go. At present, we are exploring the possibility that unique regulators of AQP1 could be reasonable targets. For example, since protozoan MAP kinases are distantly related to human MAP kinases, it might be possible to design compounds that specifically target the protozoan enzymes. We previously showed that *Leishmania* MAPK2 stabilised AQP1 by phosphorylation. Thus, one approach could be the development of specific small molecule inhibitors of *Leishmania* MPK2 activity. Such compounds would prevent the phosphorylation of the protozoan AQP1 channel, resulting in its increased turnover. We predict that these parasites would be killed by osmotic stress. A second approach could involve identifying small molecule inducers of MPK2, which may stabilise AQP1 and either reverse drug resistance or lower drug toxicity by reducing the effective dose.

The Mukhopadhyay Group

Dr Rita Mukhopadhyay's most recent publications can be viewed here: **http://bit.ly/RM_publications**

have clearly highlighted the multifactorial nature of the antimonial resistance of *Leishmania*, noting that parasites use one or several biochemical mechanisms to generate resistance. For instance, these mechanisms may include the overproduction of thiols, the lack of reduction of the pentavalent form within the parasite, intracellular sequestration and/or efflux of antimony-trypanothione conjugates and the downregulation of the aquaglyceroporin channel (AQP1).

A recent study conducted by Mukhopadhyay's team has demonstrated that species-specific antimonial resistance is largely driven by *Leishmania* AQP1. As a channel protein that enables the passage of small, uncharged molecules across biological membranes, AQP1 also plays a key role in facilitating the passage of antimonite, the active form of pentavalent antimonial drugs. In their study, the researchers showed that variations in the levels of AQP1 in different *Leishmania* species could dictate their intrinsic antimony sensitivity and behaviour in vertebrate hosts. As a greater consequence this may enable them to respond to species-specific osmotic challenges during their life cycles. Importantly, because AQP1 is vital for the parasite's survival inside the host's macrophages and transmission from the vector, it could represent a promising drug target.

A BRIGHTER FUTURE

The research conducted by Mukhopadhyay and her colleagues is generating a fuller knowledge of the complex mechanisms that underlie *Leishmania* drug resistance. Moving forwards, the hope is that this knowledge will not only help clinicians to implement alternate or combination therapies at earlier stages of the disease, but also contribute to the development of a new class of drug that offers improved treatment for leishmaniasis. This would have a significant impact on the lives of millions of the world's most poverty-stricken people who are suffering from or at risk of this devastating disease.

INTELLIGENCE

A NOVEL AQUAPORIN FROM *LEISHMANIA*: ROLES IN PHYSIOLOGY AND ANTIMONIAL RESISTANCE

OBJECTIVES

To investigate the underlying mechanisms causing increased antimonial resistance in *Leishmania* parasites and identify novel therapeutic targets and drugs that could improve the effectiveness of treatment for leishmaniasis.

COLLABORATORS

Professor Barry P Rosen; **Professor Hiranmoy Bhattacharjee**, Florida International University, USA

Professor Peter Agre, Johns Hopkins Malaria Research Institute, USA

Professor Scott Landfear; **Professor Larry David**, Oregon Health and Science University, USA

Professor Marc Ouellette, Canadian Institutes of Health Research, Canada

Professor Barbara Papadopoulou, Université Laval, Canada

Professor Dr Eric Beitz, University of Kiel, Germany

Professor Markus Tamas, University of Gothenburg, Sweden

FUNDING

National Institutes of Health (NIH)

Florida International University – Herbert Wertheim College of Medicine

CONTACT

Dr Rita Mukhopadhyay
Associate Professor
Cellular Biology and Pharmacology

Herbert Wertheim College of Medicine
Florida International University
Miami 33199
Florida
USA

T +1 305 348 1472
E rmukhop@fiu.edu; rmukhopa@gmail.com

RITA MUKHOPADHYAY gained her PhD from Jawaharlal Nehru University, India, in Parasitology and Biochemistry before moving to the US for a postdoctoral position at Wayne State University. In 2008, she moved to Florida International University. Mukhopadhyay has authored 43 peer-reviewed articles and 10 book chapters and, in addition to her research, teaches passionately at the undergraduate and postgraduate levels and supervises postgraduate research.

FIU Herbert Wertheim College of Medicine
Florida International University

Empowering older adults

As a geriatrician and palliative medicine physician based in California, **Dr Rebecca Sudore** explains how she developed an interest in caring for older vulnerable adults and why she is committed to putting people at the centre of healthcare

What sparked your primary passion – direct patient care for vulnerable older adults?

My passion has always been to ensure that people have a voice in the healthcare system. I first became interested in vulnerable populations when I helped to create a student-run homeless clinic for women during medical school. It was then that I began my life's work creating easy-to-read patient health information. I was astounded by the effects that social factors such as homelessness and poverty had on health and healthcare access and by the way these individuals were often disrespected by the healthcare system.

During internal medicine residency at the University of California, San Francisco (UCSF) and at a county hospital in San Francisco, I again witnessed the disastrous effects of longstanding poverty and poor medical care on older adults, as well as the ramifications of not providing easy-to-understand medical information that would allow people to make informed medical decisions. I felt I could have the most impact by caring for these older adults and their families and by creating health education materials that would allow them to make informed medical decisions.

Why are you interested in this demographic in particular?

The rich interactions I have with my patients, their families and caregivers, as well as my colleagues, makes my job as a geriatrician and palliative medicine physician incredibly rewarding. Geriatric medicine focuses on care for older adults, while palliative medicine focuses on relieving the symptoms of illness and maximising quality of life for patients of any age and any stage of illness. Both geriatrics and palliative medicine are highly collaborative team efforts; and, as multidisciplinary specialties they allow me to work closely with other clinicians, families, and caregivers in the care of patients. People are much more than their illnesses, and working with older adults in my respective geriatrics and palliative medicine fields allows me to focus on my top priority of understanding the patient as a person.

Could you describe what you perceive as the most salient challenges facing the US healthcare system?

A major challenge is maintaining the person's voice in a healthcare system that has almost limitless options for tests and treatments. Studies show that people want to talk to their clinicians about what is important to them and that clinicians really do want to do what is in the best interest of their patients. However, discussions about patients' overall values and goals – which would help guide individualised and tailored treatment plans – rarely occur due to lack of time, inadequate clinician training and medical culture.

Without understanding the patient as a person, treatments, tests and medical decisions are at risk for not honouring patients' values and goals. If the first procedure in a clinic or hospital consultation were a discussion about the patient as a person and their values rather than a laboratory or radiology test, this would go a long way in improving the quality of care in the US.

Mentoring is a key part of your role. Why is it so important to you?

I take mentoring very seriously. I have had the benefit of excellent mentorship myself and have learned that mentoring can occur in many different contexts. For example, through a formal one-to-one relationship with regular meetings over time, through one-off or chance meetings, through higher-level intermittent life coaching or through collaboration with colleagues. I therefore try to make myself available for all types of mentoring encounters and through this have helped others become published, obtain grants, negotiate new jobs and be accepted onto graduate and medical programmes.

You are the site Director for the Medical Student Training in Aging Research (MSTAR) Program at the UCSF. What aspects of this role do you most enjoy?

For the past three years I have directed the UCSF MSTAR Program, sponsored by the American Federation of Aging Research and the National Institutes on Aging. The Program allows medical students to conduct research projects on ageing and matches them with a research mentor during the first summer of medical school. I enormously enjoy meeting students from all over the country, hearing about the amazing projects they complete over the summer and watching many of these students mature into trainees who eventually pursue careers in geriatric medicine.

Helping people understand medical information

In response to a lack of comprehensive and patient-centred advance care planning tools, researchers based in the Division of Geriatrics in the School of Medicine at the **University of California, San Francisco**, USA, have developed a website that enables patients to make more informed decisions about medical care

IN A WORLD with a rapidly ageing population, increasing numbers of older people are suffering with severe and chronic illnesses. As a result, individuals from this vulnerable group often face complex choices regarding their current and future medical care and support. Despite the fact that physicians urge older people and their families to engage in planning for future medical care, conversations about values for current and end-of-life care can be difficult and deeply emotive – and are thus avoided by many. Unfortunately, when it comes to making some of the most important decisions in their lives, many elderly people are disempowered and unsupported.

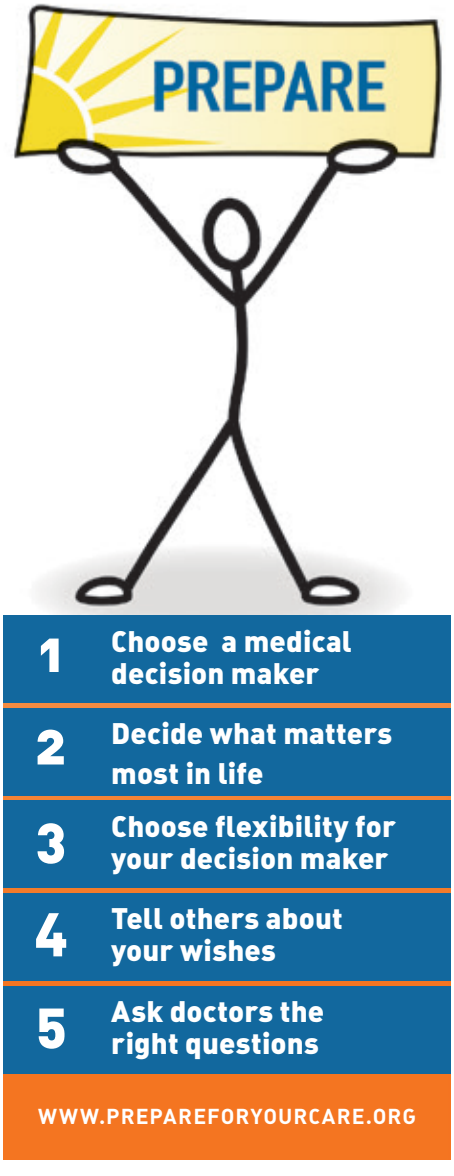
This problem often stems from inadequate healthcare systems that fail to provide older people and their caregivers with a cohesive framework to plan ahead for complex medical scenarios. Additionally, many physicians are not given sufficient training to hold appropriate advance care planning conversations, while many health organisations do not place enough emphasis on advance care planning. All too often the concept of advance care planning is reduced to filling out complicated forms that centre on hypothetical health scenarios and preferences for life-sustaining treatments such as cardiopulmonary resuscitation (CPR). Although such forms are important, and Dr Rebecca Sudore has worked to make these forms easier to understand (see http://bit.ly/iha4health-directive) they fall short of teaching people how to identify their deep-seated values and priorities, how to cope with sudden and frightening medical decisions or how to have meaningful conversations about these issues with their doctors and families.

It is these shortcomings in healthcare that have motivated Sudore – Associate Professor of Medicine at the University of California, San Francisco (UCSF) and the San Francisco VA Medical Center– to focus on empowering patients and their families to engage in meaningful advance care planning. With almost two decades of experience in designing health education materials for adults with limited health literacy, Sudore is passionate about putting patients at the centre of health systems by developing tools that facilitate optimal health communication. "When caring for older adults or individuals with serious illness, I am deeply honoured to connect with people on a personal level and get to know their histories, stories and life experiences," she affirms.

A CUTTING-EDGE RESOURCE

Most recently, Sudore and her colleagues have focused on developing an advance care planning website called PREPARE – www.prepareforyourcare.org. As a free-of-charge, interactive and user-friendly website, its main aim is to help as many people as possible to proactively engage in advance care planning and to have open, honest discussions about their desires with clinicians and loved ones. Since its inception in 2013, PREPARE has had almost 50,000 unique visitors from 115 countries – and the launch of a Spanish-speaking version in November 2014 means that it now appeals to a broader and more diverse audience. "PREPARE is novel because it is meant to help older adults identify what is most important to them and make informed medical decisions regardless of their stage of life or illness," Sudore points out. "It walks people through an easy five-step process, including how to identify a potential surrogate or proxy medical decision maker, how to determine what is most important in life and how to communicate decisions to family and clinicians. It shows individuals how to do this through videos and by giving people the exact words they can use to start a conversation." Importantly, the content on the website was formulated from a series of focus groups with seriously ill patients and their families who shared what would have helped them to make informed medical decisions.

A key feature of PREPARE is its accessibility to an older audience that may not be familiar with the internet or with complex medical concepts. Indeed, the use of large fonts, voiceovers of written text and a simple, easy-to-navigate layout ensures that the content is non-threatening and readily understandable – and in recognition of the diverse needs of different patients, the



With almost two decades of experience in designing health education materials for adults with limited health literacy, Sudore is passionate about putting patients at the centre of health systems by developing tools that facilitate optimal health communication

PREPARE

OBJECTIVES

- To help patients make informed decisions about their medical care
- To develop tools to help older adults engage in advance care planning

KEY COLLABORATORS

Dr Dean Schillinger MD, Professor of Medicine, University of California, San Francisco (UCSF) and the Center for Vulnerable Populations, San Francisco California, USA

Dr Deborah Barnes MD, Associate Professor of Psychiatry, UCSF

PARTNERS

People Designs, Inc. **David Farrell, MPH**, President

Institute for Healthcare Advancement, **Michael Villaire, MSLM**, CEO

FUNDING

National Institute on Aging • Veterans Affairs Health Services Research and Development • Patient Centered Outcomes Research Institute • Robert Wood Johnson, Donaghue and the Harmon Family Foundation • UCSF Catalyst Award in Digital Health Innovation

CONTACT

Rebecca Sudore, MD
Associate Professor of Medicine

San Francisco VA Medical Center
SFVAMC 4150 Clement Street, 151R
San Francisco, California 94121, USA

T +1 415 221 4810 x 3475
E rebecca.sudore@ucsf.edu

http://geriatrics.medicine.ucsf.edu
www.prepareforyourcare.org
http://bit.ly/1IJHeR5

@prepareforcare
@es_Prepare
http://linkd.in/1xos0KK

REBECCA SUDORE received her BSc in Microbiology at the University of Washington before completing her MD at UCSF in 1999. Now Associate Professor of Medicine at UCSF, she is an expert in geriatrics, palliative care, advance care planning and health communication. In 2012 she was awarded Best Junior Investigator from the Society for General Medicine. For nearly 20 years, she has also designed easy-to-understand health education materials for older adults.

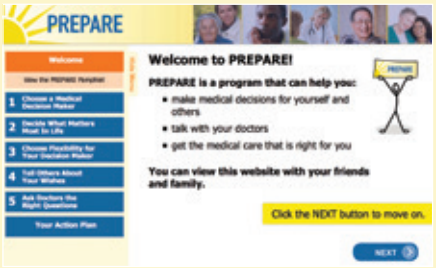
information is presented through written text, video, audio and pictures. Furthermore, the use of lay language for medical concepts enables individuals to understand and interpret complex information, while tailored algorithms generate a unique values summary for each user that can be saved, printed and shared with caregivers and clinicians. By answering questions that identify what is important in life and by fully understanding the medical pathways available to them, individuals are empowered to make informed medical choices that reflect their personal values and beliefs. "From my perspective, PREPARE empowers patients and their families to have their voice heard regardless of age or stage of illness," Sudore states.

Encouragingly, a pilot study of the PREPARE website conducted by Sudore and her colleagues found that it substantially increased patients' willingness to engage in advance care planning. For instance, before viewing PREPARE only 40 per cent of the participants had taken steps in advance care planning; however, after they viewed the website, this statistic increased to 100 per cent one week later.

FUTURE STEPS

At present, Sudore and her team are in the middle of three randomised control trials to determine the efficacy of PREPARE in helping older adults engage in advance care planning. These studies are being conducted in several different locations in the US with both English-speaking and Spanish-speaking cohorts. As the data become available over the course of the next few years, this will enable the researchers to assess the impact of the website on the lives of older people.

Moving forwards, Sudore and her colleagues are currently attempting to obtain additional funding that will allow them to expand the scope of PREPARE. As well as translating the website into additional languages, they are also planning to include specific sections dedicated to providing information about different diseases and for caregivers who may need to make medical decisions on behalf of elderly patients. Additionally, the establishment of research partnerships with several international colleagues could lead to the widespread implementation of similar websites in different countries, thus benefiting the older population on a global scale. "Looking to the future, we are eager to forge additional collaborative research relationships," Sudore affirms. "In addition, one of our main long-term goals includes finding funds to keep PREPARE up-and-running and free-of-charge for everyone to use."



WWW.PREPAREFORYOURCARE.ORG

PREPARE is a valuable, free resource that focuses on teaching patients the skills they need in order to identify their values and communicate their wishes to loved ones. It is innovative in the following ways:

- It is easy to read and is presented in an easy to follow five-step process
- Rather than asking people to make premature medical decisions, it encourages users to prepare for these decisions in the future and to build their communication skills
- Its patient-centred approach focuses on empowering individuals
- It is based on video demonstrations
- The content is tailored to each person's individual needs and preferences
- Users are guided to make action plans based on the information they are given
- It is culturally sensitive and features images and videos of people from a variety of ethnic backgrounds
- It allows users to create a tailored values summary that can be shared with clinicians and loved ones

PREPARE

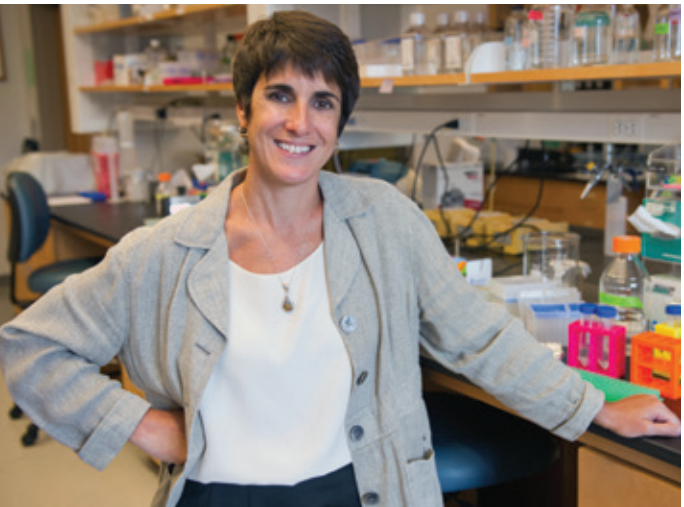
UCSF Division of Geriatrics
Department of Medicine

Of mice and molecules

With expertise in neuroscience and biology, **Professor Sandra Hewett** discusses how her ambitious research is helping to unveil the mechanisms that underlie cell death in the central nervous system and explain the complex interplay between excitotoxicity and inflammation

Can you provide an insight into your background and outline what sparked your current research interests?

It was during my postdoctoral studies at the Washington University School of Medicine that I began studying the mechanisms that underlie acute neuronal injury – particularly regarding stroke, which is caused by cerebral ischaemia, or the loss of blood flow to the brain. Although the laboratory in which I was based was predominantly focused on understanding the mechanisms by which neurons die in an autonomous fashion, I was fascinated by the potential that stroke could result in non-autonomous neuronal cell death – namely, that other cells mediate the injury. I therefore started to explore how astrocytes respond to the injured environment and whether these cells contribute to injury. As for my current research interests, they are an extension of this work. As a postdoctoral researcher, I was very lucky to have a wonderful mentor who allowed me to study the potential for inflammatory astrocyte signalling to contribute neuronal injury and who encouraged me to continue this initial work in my own laboratory.



What are the core aims and objectives of your laboratory's work?

The work in my laboratory focuses on elucidating the molecular and biochemical mechanisms by which inflammatory factors upregulated during and following acute injury – for example, in stroke, trauma and epilepsy – can either promote or protect neurons (that is, nerve cells). In particular, we are concentrating on the interactions between neurons and astrocytes.

How is the combined usage of *in vitro* and *in vivo* experimentation helping to facilitate your work?

As both *in vitro* and *in vivo* models of injury are employed in my research, I am fond of saying that we take a 'molecules to mouse' and 'mouse to molecules' approach to the essential questions posed. Combining these two approaches is a very powerful method. Our cell culture models allow us to look at the cellular interactions that follow injury with specificity and detail, leading us to make insights into potential therapeutic targets. In turn, we are then able to test these potential therapies in animals as part of an applied research strategy. This is appropriate since mice and humans share many of the same neurobiological properties.

In what ways does cyst(e)ine/glutamate antiporter (system xc) influence hypoglycaemic neuronal cell death?

We found that the excitotoxic neuronal injury that follows glucose deprivation – aglycaemia – is initiated by glutamate extruded from astrocytes via system xc-, an amino acid transporter that imports L-cystine and exports L-glutamate. Thus, the release of astrocyte glutamate appears to be a primary contributing factor to hypoglycaemic neuronal injury, at least in our cell culture model. Our next steps are to confirm this in an animal model.

Could you discuss your lab's most exciting findings to date?

Something that is truly unique and exciting is our work on the bimodal actions of IL-1ß – intriguingly, it can either contribute to or protect from neural injury via what is essentially the same mechanism: the upregulation of astrocyte system xc-. The concept that IL-1ß and system xc- are at the crossroads of injury and protection is the factor that is especially original and intriguing about the work in our lab. Indeed, while our published data predict the ability of IL-1ß enhanced cyst(e)ine/glutamate antiporter activity to contribute to injury in cerebral ischaemia and hypoglycaemic injury, we have recently generated new, as-yet unpublished results that indicate this activity could also be potentially protective in direct models of oxidative stress. Hence we posit that IL-1ß-mediated upregulation of astrocyte system xc- represents a protective mechanism, which under certain conditions, will ultimately go awry. For these reasons, understanding the regulation of system xc- by IL-1ß at the molecular level is of utmost importance, so that we may use this information to devise strategies that harness the beneficial effects and, when appropriate, employ strategies that reduce its activity in order to decrease the probability of neuronal injury.

Astrocyte-neuron interactions

Based in the Department of Biology at Syracuse University, USA, researchers at the **Sandra Hewett Lab** are making inroads into understanding the molecular and biochemical mechanisms by which upregulated inflammatory factors fuel the progression of acute neuronal injury

PRIMARILY THE RESULT of trauma, stroke or epilepsy, acute brain injury represents a prominent cause of death and disability worldwide. Yet, despite its prevalence, the complexity of the pathophysiological processes involved in such injuries means that they are not fully understood. For instance, in addition to the damage inflicted on the brain at the moment of injury, further damage is incurred as a result of a series of cellular events that occur minutes or even days afterward. The outcomes of these dangerous secondary processes are capable of inflicting as much (or more) harm as the initial moment of trauma. Importantly, if viable therapeutic targets for acute brain injury are to be identified, it is imperative to forge a detailed and robust understanding of the cellular interactions that occur following the initial injury, in order to determine their contribution to subsequent brain damage or their potential to participate in cellular protection and/or repair.

In response, researchers at the Sandra Hewett Lab in the Department of Biology at Syracuse University are conducting rigorous investigations into the molecular and biomechanical mechanisms that drive the progression of neuronal injury. Using a combination of *in vitro* and *in vivo* models, Professor Sandra Hewett and her team are making innovative insights into the upregulation of inflammatory factors in the brain following injury. Notably, their studies have pinpointed an intriguing dichotomy: namely, the pro-inflammatory cytokine interleukin-1ß (IL-1ß) appears to have a dual role in which it both advances the pathophysiological process under certain contexts, yet in other paradigms could also facilitate repair. Moving beyond the traditional view – which holds that brain damage associated with acute injury is mediated by the overstimulation of inflammatory factors and excitatory amino acid receptors – Hewett's team has found compelling evidence that demonstrates inflammatory genes expressed in parenchymal cells in the central nervous system may also play a key role in protection and repair.

EXPLORING CEREBRAL ISCHAEMIA

In their studies, the researchers at the Sandra Hewett Lab are focusing on the processes that underpin cerebral ischaemia and hypoglycaemia. Firstly, as a subtype of stroke, cerebral ischaemia occurs when the blood flow to the brain is interrupted and consequently fails to meet metabolic demand. This limits oxygen and nutrient supply to the brain, in turn triggering a series of biochemical reactions that result in the death of brain cells, or cerebral infarction. Causes of cerebral ischaemia can range from sickle cell anaemia to congenital heart defects, while symptoms can include impairments in vision, speech and movement, paralysis and unconsciousness. When tissue cell death occurs – the symptoms become permanent.

Importantly, Hewett's research on cerebral ischaemia has demonstrated that the brain damage arising from loss of blood flow involving IL-1ß occurs via signalling through interleukin 1 receptor, type I (IL-1RI). The team's results additionally emphasise the significance of astrocytes – namely, the star-shaped glial cells found in abundance in the brain and spinal cord – in the mechanisms that underpin the pathology of cerebral ischaemia. Indeed, their work on the regulation of the cysteine-glutamate antiporter (system xc-) via IL-1ß has flagged up that IL-1ß-potentiated hypoxic neuronal injury is associated with the upregulation of system xc- in astrocytes. "As a result of this discovery, we have now begun to work on understanding the molecular mechanisms that occur in this cell type,"

Hewett's team has found compelling evidence linking the inflammatory genes expressed in parenchymal cells in the central nervous system to both injury and protection

Hewett outlines. "We have elucidated that IL-1ß works to increase transcription of the gene for system xc- (increased xCT mRNA) and stabilises xCT mRNA. Overall, the effect is to increase the number of transporters on the cell's surface."

COMBATING HYPOGLYCAEMIA

In addition, the team is also exploring the cellular and molecular mechanisms involved in severe hypoglycaemia, the process whereby brain glucose levels can reach zero. Hypoglycaemia occurs during strokes but is also an event most commonly connected to diabetes – for instance, it occurs in diabetic patients who may take too much insulin, who might not eat enough or who exercise too intensively. It is a serious medical emergency that causes cognitive impairment, seizures, unconsciousness, coma and neuronal cell death. Additionally, it is known that individuals who experience one or more episodes of severe hypoglycaemia are at increased risk of dementia. Hence, it is imperative to understand the cell and molecular processes initiated in the brain by hypoglycaemia.

In spite of solid evidence from previous *in vitro* and *in vivo* models that hypoglycaemic neuronal cell death is induced as a result of glutamate excitotoxicity, the cellular source from which glutamate is released – as well as the molecular mechanisms that underpin this process – were incompletely defined prior to the work of the Hewett Lab. "Previous work from my laboratory determined that the astrocyte system xc- contributed to hypoxic neuronal injury via a glutamate-mediated mechanism, thus leading us to attempt to determine whether a similar mechanism might be in play during hypoglycaemia," Hewett reveals. Excitingly, their results demonstrated that glutamate efflux from astrocytes – via system xc- – contributes to glucose deprivation-induced neuronal cell death *in vitro*.

SPOTLIGHT ON EPILEPSY

In a further line of research, Hewett is also investigating the cellular and molecular mechanisms that cause seizures in epilepsy. Here, she is collaborating with Dr James Hewett, an associate professor who is also based in the Department of Biology at Syracuse University. Their work in this area stemmed from a finding reported in several studies that the supplementation of polyunsaturated fatty acids (PUFA) – which accumulate in the brain following seizure – can increase seizure threshold in some animal models of epilepsy. "Because nearly 30 per cent of individuals diagnosed with epilepsy do not respond to current anti-epileptic drugs, there is a pressing need to understand the cellular and molecular mechanisms that underlie seizure genesis so that new therapies can be developed," Hewett emphasises. "Using our mice models, we found that seizure threshold is regulated by the PUFA-metabolising enzyme L-12/15 Lipoxygenase. It could be that PUFAs accumulate in the animals that lack L-12/15 Lipoxygenase and that this is what underlies this effect – but that remains to be experimentally determined."

FASCINATING FINDINGS

- Hewett and her team discovered that IL-1ß fuels the activity and expression of the cyst(e)ine-glutamate antiporter (system xc-) in astrocytes
- Under conditions of energy deprivation, system xc- induces excitotoxic neuronal cell death; however, the same transporter also drives the synthesis of the antioxidant molecule glutathione
- Their findings suggest that in addition to its pathogenic role, IL-1ß also upregulates processes that protect the brain against oxidative stress

MOVING FORWARDS

To date, Hewett and her team have made important strides in carving a clearer knowledge about the molecular and biochemical processes that underlie pathophysiological processes in the brain. Looking ahead, it is possible that as a result of their findings the astrocyte will become a more viable therapeutic target to address ischaemic and hypoglycaemic injury than the inhibition of downstream neuronal effectors. However, in order to design the most effective therapies, the researchers are currently planning to focus on forging a deeper understanding of the timing and duration of the dual inflammatory-repair response mediated by IL-1ß.

INTELLIGENCE

THE ROLE OF INFLAMMATORY FACTORS IN ACUTE NEURONAL INJURY

OBJECTIVES

- To understand the cellular and molecular mechanisms that drive the progression of acute neuronal injury
- To clarify the role of interleukin-1ß in pathology and repair

KEY COLLABORATOR

Dr James Hewett, Syracuse University, USA

FUNDING

US National Institutes of Health

CONTACT

Dr Sandra Hewett
Executive Director of Neuroscience Studies and The Beverly Petterson Bishop Professor of Neuroscience

Syracuse University
362 Life Sciences Complex
Syracuse
New York
13244
USA

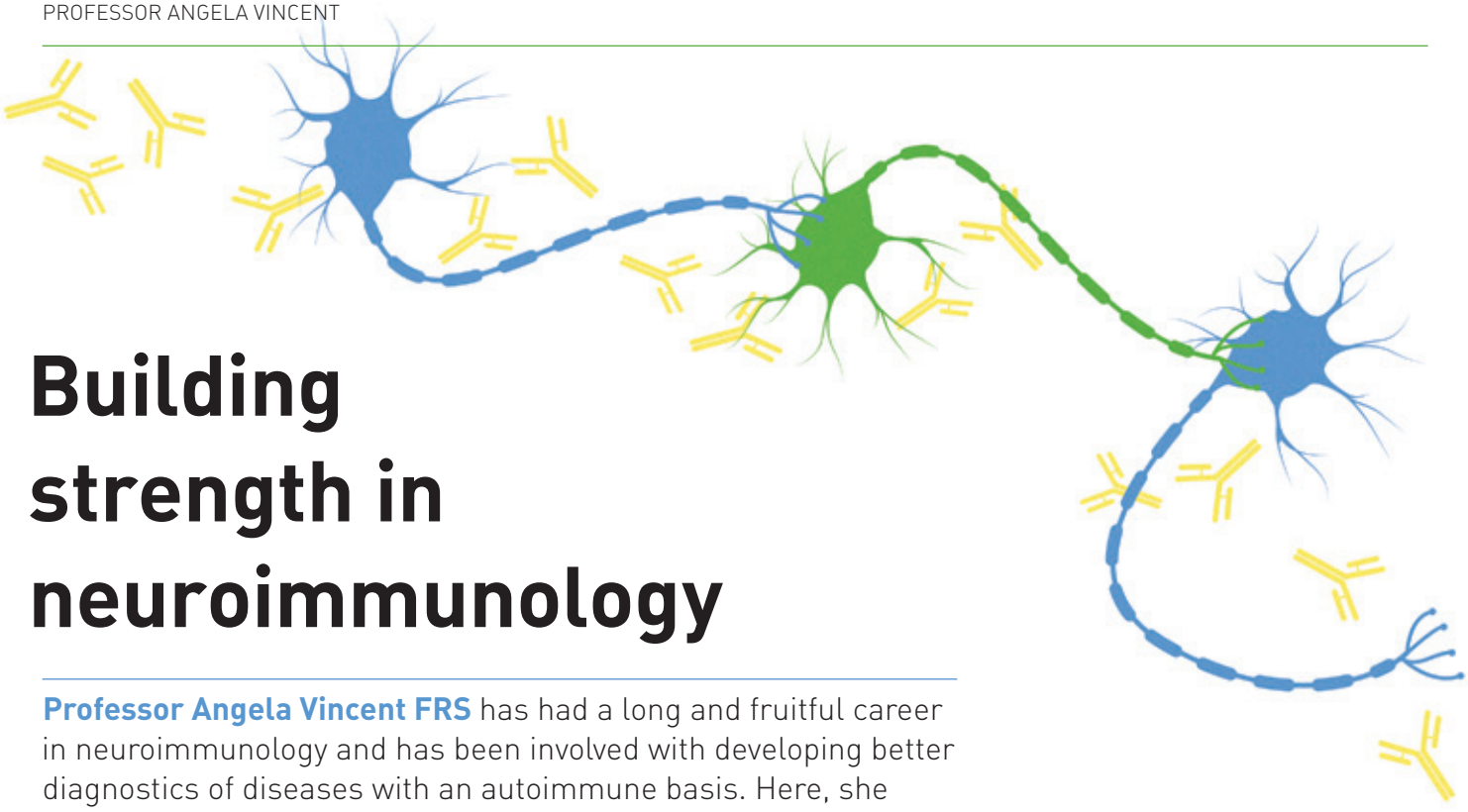
T +1 860 212 1378
E shewett@syr.edu

http://bit.ly/SandraHewett

@NeuroscienceSU

SANDRA HEWETT completed a BSc in Biology before receiving her PhD in Pharmacology/Toxicology in 1992 from Michigan State University, USA. After completing postdoctoral research at Washington University School of Medicine, she worked at the University of Connecticut Health Center. In 2011, Hewett became the inaugural Beverly Petterson Bishop Professor of Neuroscience and Executive Director of Neuroscience Studies at Syracuse University, New York, USA.

SYRACUSE UNIVERSITY
The College of Arts and Sciences
Interdisciplinary Neuroscience Programs



Building strength in neuroimmunology

Professor Angela Vincent FRS has had a long and fruitful career in neuroimmunology and has been involved with developing better diagnostics of diseases with an autoimmune basis. Here, she discusses the current priorities of her lab

Which experiences from your academic and professional background do you think have played the biggest role in shaping your research today?

I am a qualified doctor and spent a year working as a doctor, but then turned to science. I was lucky to experience first-hand the pioneering research into the function of the neuromuscular junction by Nobel laureates Bernhard Katz and Bert Sakmann, and Ricardo Miledi at University College London in the late 1960s, which was crucial for the understanding of transmission across synapses in the peripheral and, later, the central nervous system. In 1969, Miledi had already used snake toxins to purify the post-synaptic 'acetylcholine receptors' that received the acetylcholine signal from the nerve, and after three very unproductive years in a different department, I began to work with Miledi on these receptors and the neurological disease myasthenia gravis, beginning a collaboration with neurologist John Newsom-Davis. All of my work today stems from these very fortuitous experiences.

Can you discuss some of the work taking place at the Vincent lab? Why are you focusing on antibodies in particular?

If a patient has an antibody to a neuromuscular junction or central nervous system receptor, or another membrane protein, it is highly likely that their symptoms will improve if you can reduce the levels of the offending antibodies. Therefore, if a patient presents to a neurologist with symptoms of muscle weakness, or epilepsy, for instance, it is now common to ask whether they have one of the known antibodies. It is akin to performing a genetic test to identify a particular form of disease. My laboratory has two main aims. First, to help diagnose these patients, which we do by running a clinical service that is used by most hospitals in the UK, and many around the world. And second, to identify new antibodies, look for them in patients with diseases for which there is no current diagnostic test, and study how the antibodies affect neurological functions. We are also interested in asking whether there were antibodies to neuronal proteins in some pregnant mothers whose children subsequently developed diseases such as autism or schizophrenia.

Are you collaborating with any individuals, groups or institutions that you would like to highlight?

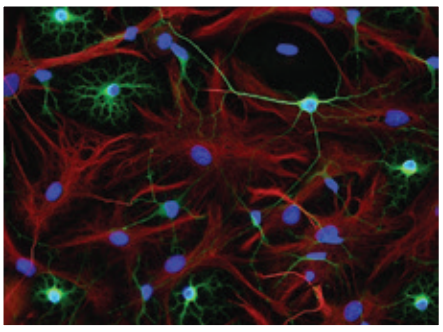
We collaborate worldwide with neurologists on many clinical studies of individual patients and examine the antibodies and clinical features of patients with specific neurological diseases. At the moment, we have a particular interest in improving the diagnosis and treatment possibilities of patients with myasthenia gravis, which involves many of the myasthenia centres in the UK, Europe and Japan. We are also looking for specific antibodies in children and adults with unexplained epilepsy or psychosis, partly in collaborations with the Institute of Psychiatry in London, and the Universities of Sydney and Groningen. The maternal antibody studies are being performed in collaboration with the Department of Economics and Business – National Centre for Register-based Research in Aarhus Denmark.

Having been elected to prestigious positions such as Fellow of the Academy of Medical Sciences and Fellow of the Royal Society, and as a past President of the International Society for Neuroimmunology, you are well positioned to inspire young women looking to enter a career in the field. Is this a significant aspect of your work?

I am very committed to helping young people, of either sex, fulfil their hopes of combining a clinical career with laboratory-based science, and act as a mentor through the Academy of Medical Sciences, which is highly active in this field. I also informally mentor a number of younger scientists and clinician scientists in Oxford.

What are your main objectives over the next five years?

I am already past the normal retirement age but would like to complete some of the projects that have been intriguing me over the last decade or two: looking at the relative roles of serum antibodies and cerebrospinal antibodies in causing central nervous system diseases; showing whether or not maternal antibodies can be an important factor in causing neurodevelopmental disorders in the offspring, using a combination of serum studies and animal models; and exploring whether there is a role for antibodies in patients with some unexplained conditions such as pain or sleep disorders. The main objective must be to leave the Neuroimmunology Group in good hands and with a sensible strategy for the future.



Cultured cells from brain tissue grown in the lab. One large and several small neurons (green) lying on a bed of astrocytes (red). These cultures can be used to show that antibodies in patients bind to the surface of live cells. The nucleus of each cell is in blue.

Courtesy of Dr D Menassa, University of Oxford

Antibody, brain proteins

Starting at the Royal Free Hospital School of Medicine in 1977, and moving to the **University of Oxford**, UK, in 1988, the Vincent Neuroimmunology Group was created to understand the mechanisms underlying nerve and muscle diseases. The contributions to understanding the links between autoantibodies and neurological diseases has been considerable

UP UNTIL THE 1960s the brain and other components of the nervous system were a largely mysterious and uncharted territory of the human body, and neurological diseases were diagnosed based on descriptions of symptoms and simple investigations. However, during the last few decades the understanding of neurological diseases has developed beyond recognition and now almost all disorders are investigated in terms of their molecular mechanisms. This paradigm shift was in part due to the increasingly interdisciplinary nature of research, encompassing clinical genetics, physiology, pharmacology and molecular biology. "This now allows any individual disease to be defined at the level of the gene, the protein, the cellular function, the influence on function of the nerve cells, and ultimately, on the behaviour of mouse and man," explains Professor Angela Vincent, who embraced the change in neurology early on in her long career, and is now based at the Nuffield Department of Clinical Neurosciences at the University of Oxford.

Vincent runs the Clinical Neuroimmunology service, analysing patient samples for diagnosis, and has been well placed to carry out work at the interface between the clinical and experimental sides of science. She originally trained as a doctor but joined the eminent neurologist John Newsom-Davis, developing together an interest in myasthenia gravis, a disease that leads to muscle weakness. Newsom-Davis and Vincent then began to make strides in the recognition of other neurological disorders caused by autoimmunity, and set up the Neuroimmunology Group at the Royal Free Hospital School of Medicine.

AN AUTOIMMUNE BASIS FOR A NEUROLOGICAL DISEASE

Autoimmunity plays a well-known role in diseases such as diabetes, but less is known about its role in neurological disorders. In autoantibody diseases, the body produces antibodies that target its own proteins resulting in loss of these proteins or damage to the cells in which they function. The first neurological disease with autoantibodies was myasthenia gravis, a rare disorder of the neuromuscular junction where communication between the nervous system and muscular system is impaired, resulting in muscle weakness. At the neuromuscular junction, the acetylcholine receptor (AChR) is clustered on the muscle surface during development, so that the muscle fibre can efficiently receive the chemical signal (acetylcholine) that is released from the motor nerve; this signal triggers muscle contraction. The AChR clustering is dependent on another nerve signal that activates a protein, muscle specific kinase (MuSK).

For myasthenia gravis, Vincent and Newsom-Davis confirmed that the majority of patients with the disease have antibodies to AChR, resulting in loss of AChR from the muscle fibre surface and consequently the symptoms observed in the disease. Importantly, they showed that removing the antibodies with a treatment called plasma exchange resulted in dramatic clinical improvement. Subsequent work by Vincent showed that some myasthenia patients without AChR antibodies had antibodies to MuSK, resulting in reduced levels and dispersion of AChR due to inhibition of MuSK clustering activity. Understanding which autoantibodies a patient with myasthenia gravis is producing, and how they result in disease, can be key in ensuring they receive the most effective and relevant treatment.

AUTOANTIBODIES AGAINST NEURONAL CELL SURFACE TARGETS

Since 2001, a number of antibodies to brain proteins have been discovered by Vincent and others. These include autoantibodies against parts of the voltage-gated potassium channel complex (VGKC) and the N-methyl-D-aspartate receptor (NMDAR), both linked to brain inflammation (encephalitis) and epileptic seizures.

To measure the antibodies, Vincent uses human embryonic kidney (HEK) cells expressing the expected target of the antibodies. Adding the serum or cerebrospinal fluid (CSF) of a patient with appropriate symptoms, and identifying whether antibodies bind the target expressed by the HEK cells, will determine if the patient has the specific autoantibodies in their serum or CSF. In some cases, it is also helpful to confirm that the antibodies bind to the surface of live brain neurons that can be cultured in the laboratory (see figure above).

The reason for these elaborate and time-consuming tests is that autoantibodies directed towards the cell-surface are more likely to be causative then those that bind intracellular antigens. This is borne out by the treatment responses of many patients,

ANTIBODIES CAN DAMAGE THE BRAIN

OBJECTIVES

To identify antibodies to specific proteins that are essential for brain, nerve or muscle function. Patients with these antibodies have neurological diseases that may include epilepsy, loss of memory, psychosis or abnormal movements, and can be treated by reducing the levels of the antibodies with drugs or other treatments. Babies of mothers who have these antibodies, even if the mothers are not showing signs of disease, may be at risk of neurodevelopmental disorders.

KEY COLLABORATORS

Dr Ming Lim, Evelina Children's Hospital, St Thomas' Hospital, London, UK • **Professor Oebele F Brouwer**, University of Groningen, University Medical Center Groningen, Netherlands • **Professor Preben Bo Martensen**, Department of Economics and Business - National Centre for Register-based Research, Aarhus, Netherlands • **Professor Christian Bien**, Mara Hospital, Bethel Epilepsy Centre, Bielefeld, Germany

PARTNERS

The Guthy-Jackson Charitable Foundation for neuromyelitis optica

FUNDING

The Wellcome Trust •The National Institute of Health Research • Oxford Biomedical Research Centre • The Watney Trust and Myasthenia Gravis Association (Myamar) • GlaxoSmithKline • The NHS National Commissioning Group for neuromyelitis optica

CONTACT

Professor Angela Vincent FRS
Head of Neuroimmunology

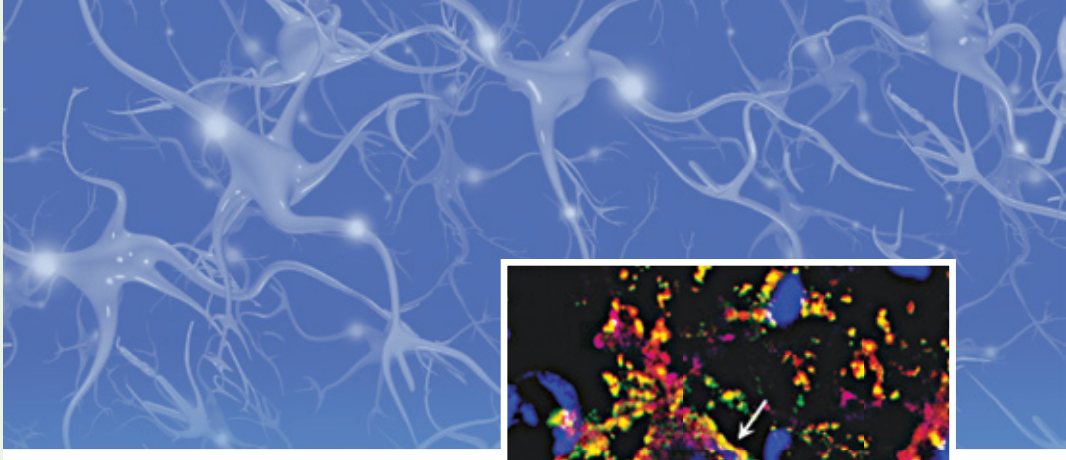
Nuffield Department of Clinical Neurosciences
Level 6, West Wing
John Radcliffe Hospital
Oxford
OX3 9DU
UK

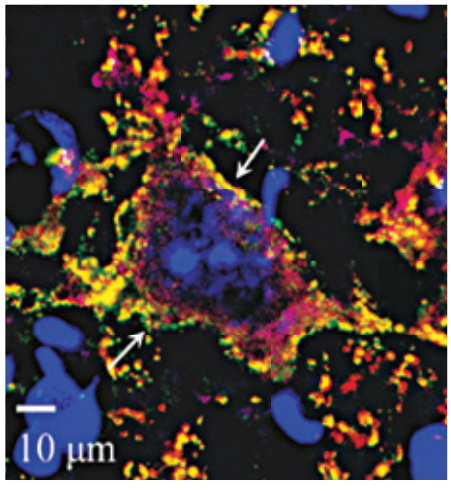
T +44 781 7224 849
E angela.vincent@ndcn.ox.ac.uk

www.imm.ox.ac.uk/professor-angela-vincent

ANGELA VINCENT qualified as a doctor, but after practicing for one year she obtained an MSc in Biochemistry at University College London. She worked with Ricardo Miledi on acetylcholine receptors in myasthenia gravis, and began a long partnership with neurologist John Newsom-Davis, moving with him and their team to the (Weatherall) Institute of Molecular Medicine in Oxford in 1988. In 1992, she established a national and international referral centre for the diagnosis of immune-mediated neurological diseases, and since Newsom-Davis' retirement in 1998, she has led the Neuroimmunology Group, researching antibody-mediated neurological diseases. She was elected FMedSci in 2003 and Fellow of the Royal Society in 2011.

NUFFIELD DEPARTMENT OF CLINICAL NEUROSCIENCES
Medical Sciences Division





A motor neuron in a thin slice of spinal cord from a healthy mouse and incubated in serum from a patient with muscle spasms and rigidity. The bead-like structures (yellow) on the surface of the motor large neuron show where patient's antibodies have bound to glycine receptors on the surface of the cell.

Reproduced with permission from Carvajal-Gonzalez et al *Brain: a journal of neurology*, 2014

both children and adults, who have been identified by the Vincent lab in the last 10 years. The antibodies in these patients now include not only NMDARs and VGKC-complex proteins, LGI1 and CASPR2, but also glycine and γ-amino butyric acid (GABA) receptors, and surface proteins on glial cells associated with demyelinating diseases. However, how any of these antibodies, which are produced initially in the periphery, gain entry into the brain tissue to cause disease is still hotly debated.

AUTOANTIBODIES AGAINST INTRACELLULAR BRAIN TARGETS

Antibodies to glutamic acid decarboxylase, an intracellular enzyme, are more of a mystery. They are found in a chronic progressive disease called stiff person syndrome (SPS), which leads to extreme muscular rigidity. Work by the Vincent Group showed that these patients often had additional antibodies to neuronal surface proteins that are more likely the cause. In fact, some patients with similar, but more extensive and life-threatening symptoms, have antibodies to surface glycine receptors. These are responsible for controlling many neuronal cell functions, and current experiments in mice are showing that these antibodies can access the brain and bind to the glycine receptors in the brain and spinal cord.

DIAGNOSIS OF TREATABLE AUTOIMMUNE DISORDERS

Partially due to Vincent's background as a clinician, her work is well translated into informing the diagnoses used for these rare and often severe neurological disorders. If an adult or child presents with symptoms of brain disease and a test of their serum reveals autoantibodies against any of these proteins, the patient's doctor can make a diagnosis and consider treating with immunotherapies aimed at reducing the levels of these autoantibodies. As Vincent notes, her work on developing and refining patient diagnostics may also develop further: "Together with the tools provided by molecular biology and biochemistry one can also begin to explore why some patients get these diseases, the molecular mechanisms, drug targets and how these differ between individuals, leading to patient-specific approaches to treatments".

Current work by Vincent's Group at Oxford includes research on maternal antibodies and their role in causing neurodevelopmental disorders in the future child. This is conducted via experimental techniques, most likely first used by Vincent and colleagues, including a maternal-to-foetal transfer model with postnatal behavioural testing in mice, which can be used to demonstrate the pathological effects of maternal antibodies on foetal development. Through this model Vincent has shown that maternal antibodies that inhibit foetal AChR can be transferred to the foetus, causing musculoskeletal problems in the child. The maternal-to-foetal transfer model is now being used to explore maternal antibodies in autism and schizophrenia. "We have established approaches that we use in our work which are now recognised and used much more widely," summarises Vincent on the impact of their methodologies.

SOLID GROUND FOR NEUROIMMUNOLOGY

Despite retiring officially in 2008, Vincent continues to run the clinical service, searches for new antibodies and investigates their mechanisms, and lectures widely. The information that Vincent and her team produce can help doctors confirm the diagnosis and likely response to immunotherapies. Vincent's lifetime achievements were recognised in 2009 with the prestigious Association of British Neurologists Medal, but as she continues to work indirectly and directly for patients with these rare and severe neurological disorders her scientific legacy will be felt for years to come.

RESEARCHER PROFILE

VERA NENADOVIC

CONTACT

Vera Nenadovic
Project Investigator

Centre for Brain and Mental Health
The Hospital for Sick Children
555 University Avenue
Toronto, Ontario M5G 1X8
Canada

T +1 416 709 8372
E vera.nenadovic@sickkids.ca

www.sickkids.ca

VERA NENADOVIC is a nurse practitioner in paediatric neurology at SickKids, Toronto, Canada. As a PhD-prepared neuroscientist her research applies complexity theory and principles of nonlinear dynamics to real-time understanding of brain function in both health and disease. Watch out for her BrainRattle blog coming March 2015.

SickKids®

RESEARCH GOALS

Brain injuries represent the biggest cause of death and acquired disability in paediatric patients. These can be caused by, for example, infections, trauma or cardiac arrest. Due to the economic and social cost, improvements in accurately determining the prognosis of patients are urgently needed. This information could inform clinicians on the best course of treatment for individual paediatric patients.

Researchers led by Vera Nenadovic, a nurse practitioner in paediatric neurology at The Hospital for Sick Children, Toronto, Canada, have been working to develop accurate numerical indices that indicate the clinical outcome of brain injury in paediatric coma patients at an early stage. The group wants to measure the brain activity of comatose children in real time. Continuous measurements using electroencephalography (EEG) are currently used to detect subclinical seizures but these methods create large amounts of data that are typically unmanageable by clinicians and prevent real-time feedback.

Ultimately, this lack of real-time information on a child's injury status stands in the way of clinicians making well-informed decisions on the most successful course of treatment.

Neurons in the brain show complexity in the way they interact and transmit data. Information exchange takes place through phase synchrony between neurons and, in a healthy brain, this is variable across neuronal networks in space and time. However, in a patient with brain injury, this trend changes, resulting in an increase in phase synchronisation and a reduction in variability. This also leads to reduced complexity in the brain as demonstrated by many previous studies. Increasing variability of phase synchrony also correlates with patients' emergence from comas. In light of these changes, Nenadovic focused her research on the development of algorithms that could communicate numerical indices of patient prognosis from brain activity data using phase synchrony and variability, ultimately hoping to revolutionise clinicians' abilities to predict complications and outcomes.

METHOD

For their research, Nenadovic and her team are using an EEG – a device that is typically portable and can record brain activity changes on the scale of milliseconds, making it a powerful technique for rapidly reporting changes in a patient's status. The phase synchrony of neurons can be reported using EEG readings and is termed the R index. Modulations in R index occur prior to subclinical seizures and are therefore useful as an early warning of a change in the patient's status. This spatio-temporal variability of the R index can also be analysed by EEG, proving the perfect tool for Nenadovic's work.

Nenadovic has developed a series of algorithms called EEG for Knowledge Integration and Decision Support (KIDS) that can be integrated into current data monitoring systems. These algorithms track both phase synchrony and variability and act as indicators of the disease state. They take the complex waveforms produced by the EEG machine and translate them into comprehensible indices for clinicians.

IMPACT

The algorithms developed by Nenadovic and her colleagues have resulted in a tool that can continuously reflect alterations in cortical activity in terms of brain injury outcome. Their studies found that increased complexity of neuronal patterns was associated with a good disease prognosis. As well as providing clinicians with invaluable information regarding a patient's brain activity status, the group's algorithms also created a method by which the impact of current treatment options can be analysed by studying the association with changes in phase synchrony variability. The EEG-KIDS system can therefore initiate several strands of novel research aiming to improve knowledge of routine brain injury treatments.

Nenadovic is now looking for integration of the EEG-KIDS system with other monitoring systems, for use in critical care units with existing continuous EEG monitoring capabilities nationally and internationally. These methods will hopefully make a real difference in the way clinicians and families plan for the care of paediatric patients and fully understand the impacts of treatment on altering brain injury prognoses.

PULLING DOWN THE WALLS OF GENDER INEQUALITY

Dr Elizabeth Pollitzer
Founder and Director, Portia

Leading expert on gender, STEM and innovation, Dr Elizabeth Pollitzer discusses her work which spans two decades, within these three key realms, as well as Portia's contribution to tackling gender inequality in STEM

What skills and experiences have shaped your career trajectory?

My involvement in STEM began in the Biophysics Department at King's College London, a department created by Maurice Wilkins who was one of the solvers of the structure of DNA, and, as a consequence of being involved in the Manhattan project that produced the first atomic bombs, wanted to make a positive impact on society. He was my mentor, although the concept (as it is interpreted today) did not exist then. Wilkins introduced me to social responsibility of science through a course he set up under the same name. Another person who influenced my thinking during that time was Geoffrey Brown, who worked with Maurice. Brown was interested in the philosophy of science and we went to endless lectures together where philosophers talked about Karl Popper, Thomas Khun and Levi Strauss.

My degree was in biology/physics but it covered a whole range of STEM subjects: chemistry, biochemistry, all kinds of physics, biology and maths, microscopy, and of course genetics, which I loved. It was an intellectual tour-de-force. It was also a time when the first personal computers started appearing and having had to write computer program using punch cards, I thought this was amazing. My friend, Severyn Chomet started 'publishing on demand' with a Commodore PET computer, which had only 1 KB of RAM! The future had to be either biophysics or computing. The choice was forced by the opportunity to do a PhD, the aim of which was to look at how physics developed and was influenced by the availability of resources.

Three years after completing my PhD, I took a short career break to have children, and was then lucky enough to return to STEM with the help of the newly set up Daphne Jackson Fellowship scheme, which led me to work for over 20 years at Imperial College London, first in the School of Management and then in the Department of Computing. It was there, together with a group of other women scientists that we set up Portia. At the time, the UK Government was very concerned about the underrepresentation of women in ICT, so this is where our work started. But then, the European Technology Assessment Network on Women in Science (ETAN) report was published, which introduced the statistics behind the 'leaky pipeline' phenomenon, and we saw that we had a serious task ahead.

Can you discuss some of your most recent activities in the STEM workplace and educational setting to further gender equality?

From the late 1990s until 2008, I continued to be involved in the Daphne Jackson Trust as Fellowship Coordinator whilst also working at Imperial. The Trust was unique in that it specialised in women returning to research careers through a two-year part-time fellowship. Since then, other organisations (Wellcome Trust, Science Foundation Ireland) have adopted a similar approach, but still, taking a career break in STEM for women remains a risky step, bound to have negative effects on their future career prospects. In general, I would not advise doing this unless it's the only option. Portia's involvement in educational activities started with retraining women who were educated in STEM, had taken a career break and then wanted to return to the field. We worked with universities and industry and, as part of EU funded project, Equalitec, over a three-year period have

Gender Summit conference
© Ben Pollitzer

supported more than 300 women to re-establish their careers.

Then, when London was preparing for the 2012 Olympics, we used sport as a hook for promoting engineering in schools, especially those located in the more deprived areas, where there are many migrant groups and very few engineering role models. We collaborated with the Learning Trust in Hackney and the Institution of Mechanical Engineers to create a day-long event for schools in which young female and male engineers participated. We would come to a school with a variety of creative and sporty materials and engaged the children in many different interactive tasks each designed to help them discover what engineering was about, and give them confidence to use engineering concepts. The day would start with imagining the future and end with a debate on 'Should there be a limit to how much engineering is good for sport?' It was remarkable, how after just four-five hours the children were able to produce well-argued for and against arguments.

GenSET

Pollitzer outlines the core objectives of the genSET project, and explains how it aims to improve the European R&D landscape

GenSET was very timely, though we did not appreciate this when we planned it. Having by then spent more than a decade on gender issues in science, I felt the biggest obstacle was the unquestioned assumption that science is gender neutral. In 2008, I came across a book edited by Londa Schiebinger, *Gendered Innovation in Science and Technology*, which included chapters about gender bias in science knowledge making. The opportunity to pursue this came about through the Framework Programme's Science in Society (SiS) theme and we decided to apply with a proposal to engage scientists in the gender discourse, since they were mostly excluded from discussions in this area.

Our idea was to adapt the consensus conference format and create a series of seminars where a panel of science leaders would examine available research evidence demonstrating gender issues in science and decide what it meant. The plan was to assemble 14 science leaders from across Europe as the 'lay panel' and a large gender 'experts panel' to answer their questions. We collected extensive empirical research evidence and asked the science leaders: 'how can European science benefit from integrated action on gender?'

The result of these deliberations was a report with 13 recommendations, written by the science leaders for science institutions to adopt. It provided the blueprint for creating institutional gender action plans. The University of Tromsø, Norway, was the first to adopt these recommendations, led by Curt Rice the Vice-Rector for Research at the time, however, the science leaders panel did not stop there: they wrote to the European Commission advising that others should be also exposed to the persuasive research evidence and gender scholarship they had just witnessed, and this was why the Gender Summit was created.

We recently interviewed Janet Bandows Koster, Executive Director of the Association for Women in Science (AWIS), with whom you occasionally work alongside. In what capacity are you collaborating with the Association?

We are concerned about the same issues and share the same end goal, namely to make gender equality a norm in science, but our histories and structure, through which to make progress, are different. This is very helpful since a variety of approaches is needed to persuade and embed new thinking about the role of gender in science. For this, we share experiences of successful measures, such as the career development support method we have established for women at the early stages of their science careers when uncertainty about the future and the risk of them giving up on their aspirations to work in STEM are the greatest. The method uses a scenario building approach that is translated into building future CVs. This work was made possible through a grant from the Elsevier Foundation's New Scholar Programme. We have tested it in three different institutions in three different countries with excellent results, and have now been exploring with the New York chapter of AWIS how this could be adapted to support women at PhD level across universities in the area.

Where would you next like to focus your efforts in the gender, STEM and innovation fields?

For the first time in the history of the EU Framework Programmes, the importance of gender in research and innovation has been fully recognised in Horizon 2020 (H2020), but also in the European Research Area (ERA). In particular, in the current H2020 programme for 2014-15, gender has been defined as a criterion of success that has to be demonstrated through actions improving gender equality in scientific roles, the incorporation of gender dimension in investigation design and process, and as a cross-cutting issue that applies to all research themes. Our concern is that in the next phase of H2020 gender may slip from the policy attention radar and the progress made will stagnate or dissipate. This risk is real: almost all EC working papers relating to the thematic aspects of the H2020 programme for 2016-17 fail to mention gender.

The second concern is that although the 1997 Amsterdam Treaty recommends that gender is mainstreamed into all EU policies, other EU R&D&I policy initiatives such as Innovation Union have failed to do this. 'Gender as the norm' in research and innovation should replace the obsolete 'science is gender neutral' paradigm, otherwise science will be failing in its obligations to work through and with research evidence. There are so many opportunities, not only better knowledge but also new markets for science knowledge and more holistic and sustainable applications of knowledge.

One example is climate change: this debate has been pursued without including women as a source of knowledge, as decision makers, or seeing them as 'victims' of climate change. People influence their environment and are influenced by it. Important gender differences act in these processes. At the biological level, women's physiology differs in many respects from men's and they will find it harder to adapt to hotter temperatures. With a warmer world, diseases such as malaria will expand to new regions and the effect on pregnant women will be particularly negative. In the developing world, women spend up to five hours a day looking for fuel, primarily biofuel, they use rudimentary stoves to prepare meals and inhale indoor pollutants that damage their health (and that of their children), but nearly all that we know about the effects of pollutants is based on studies that used male animals and men.

Gender Summit conference
© Ben Pollitzer

GENDER SUMMITS

Pollitzer outlines how the Gender Summits provide a forum for stakeholders from research, industry and policy to jointly explore gender equality and explains how they can stimulate innovation and scientific excellence

WE SET UP the Gender Summit platform with the idea that it would be a European event, but the vision and approach, namely to use scientific research evidence and consensus established jointly through discussions involving scientists, policy makers and gender scholars, attracted attention from other parts of the world. The first Gender Summit in 2011 attracted 400 participants and 65 speakers, this was large for a gender event.

Since then, other stakeholder groups with interests in STEM became involved: industry, civil society, educators, national policy makers, etc. People like the link between research quality and gender equality because it can be demonstrated along the continuum of research process, from idea creation to application of results and development of new products. A good example is biomarkers. Gender (strictly speaking sex) differences at chromosome expression level influence metabolic processes and contribute to the differences in the metabolic profiles of women and men. Such differences have consequences for the progress and severity of diseases linked to metabolism, such as diabetes and Alzheimer's. Research shows that we may need separate biomarkers for women and for men to ensure diagnostic efficacy, which will lead to better health economics.

SPECIFIC OBJECTIVES OF THE SUMMIT

- To develop national, regional and global communities as agents of change
- To develop evidence-based consensus on the actions needed and the ways of implementing them in specific national or regional contexts
- To demonstrate positive effects of gender balance and gender diversity in research and innovation process
- To demonstrate how integrating gender dimension in research and innovation content improves quality of results and outcomes
- To promote gender aware solutions to societal problems, eg. urban quality, human adaptation and climate change, food security, transport and mobility

ACHIEVEMENTS FROM THE SUMMITS

One of the greatest achievements of the Gender Summits has been the transition from an event to a movement driven by the growing community of researchers, experts, practitioners, science leaders, policy, industry and civil society. We hope this emerging community will evolve into a multi-stakeholder alliance of individuals and organisations as 'agents of change'.

The greatest moment has been at the Gender Summit – Europe, in June 2014, where it was pointed out by the participants that the theme 'Research and Innovation Quality through Equality' can also create impact in the other direction; that is, equality can be brought about by science that is truly excellent. In other words, by admitting that science is not gender neutral, science can lead cultural change in society towards accepting gender equality as the norm, because this is what research evidence demands.

GOOD FORTUNE

We are fortunate in having wonderful partners as co-conveners for each of the summit events, and also organisations, such as Elsevier, the Bosch Foundation, Research Council Norway, and the European Commission that have supported this work. It is critical for each regional platform to be guided by leading science institutions in that region who know and understand local research and innovation communities and can engage important local stakeholder groups. The conditions that we have in Europe, eg. Horizon 2020 and equality legislation, do not exist in other parts of the world. We were lucky that the way the National Science Foundation (NSF), and in particular Wanda Ward and her team, led the introduction of the Gender Summit to North America, provided a blueprint for transferring Gender Summit to other regions.

PREVIOUS EVENTS

Gender Summit 1 **(Europe) 2011** – Quality Research and Innovation through Equality

Gender Summit 2 **(Europe) 2012** – Aligning Agendas for Excellence

Gender Summit 3 **(North America) 2013** – Diversity Fuelling Excellence in Research & Innovation

Gender Summit 4 **(Europe) 2014** – From Ideas to Markets: Excellence in mainstreaming gender into research, innovation and policy.

TOWARDS THE FUTURE

It does not need explaining, that Africa and Asia represent new challenges because of the huge diversity of nations, languages and countries, as well as institutions, agendas, histories, cultures and people. The subtheme for the 2015 5th Gender Summit – Africa (April 2015 Cape Town) is Knowledge from Africa for Africa. 2015 has been designated by the European Commission as Development Year, and we very much hope that the Gender Summit will contribute to this. Similarly, for the 6th Gender Summit – Asia-Pacific (September 2015 Seoul), we are talking about South Korea, China, Taiwan, Japan, Australia, New Zealand and the many countries in Southeast Asia. So again, multiplicity of national, institutional, language and cultural conditions. The idea that science is gender neutral is rooted deeply in the scientific thinking and gender bias disadvantaging women is pernicious in all cultures.

One exciting aspect of the forthcoming 7th Gender Summit – Europe (November 2015) is that we plan to dovetail the event to the Falling Walls activities in Berlin that celebrate the destruction of the Berlin Wall. Gender bias and gender inequality in science is perhaps the most important wall that has to fall.

UPCOMING EVENTS

Gender Summit 5 Africa 2015 – Poverty alleviation and economic empowerment through scientific research & innovation: Better Knowledge From and For Africa

28-30 April 2015, Cape Town, South Africa

The meeting will be led by the Human Sciences Research Council (HSRC) in South Africa. The main aim will be to address issues within gender and society that impact on research and innovation processes. With Africa's research agenda at the forefront on discussions, the Summit will reflect on how science, technology, infrastructure, capital and skills could help to realise the full potential of the country's citizens and societies.

Gender Summit 6 Asia Pacific 2015

27-28 August 2015, Seoul, South Korea (26 August – Pre-Summit on Curriculum & Education on Gendered Dimensions)

The Asia-Pacific Summit is both significant and timely as there is a large gender gap in the Asian region. This event will be hosted by the National Research Foundation of Korea, Korea Institute of Science and Technology Evaluation and Planning (KISTEP) and the Center for Women in Science, Engineering and Technology (WISET). The theme of the Summit will be to encourage better science for a better world, by promoting gender equality and diversity as a means of achieving this goal.

Gender Summit conference
© Ben Pollitzer

GENDER SUMMIT STEERING COMMITTEE

The vision and mission of the Summits are guided by the Steering Committee, many of whom served on the genSET science leaders panel or represent leading partners of previous regional committees. This includes:

Hans M Borchgrevink MD, Special Adviser, International Staff, Research Council Norway (RCN), Norway, Europe

Simone Buitendijk PhD, MPH, MD, Vice-rector Magnificus and member of the Board, Leiden University, Netherlands, Professor and Chair, Women's and Family Health at the Leiden University Medical Center (LUMC), Netherlands

Daniela Corda PhD, Director, Institute of Protein Biochemistry (IBP), National Research Council of Italy (CNR), Italy

Elizabeth Pollitzer PhD, Director, Portia Ltd, UK (Chair)

Curt Rice PhD, Professor, University of Tromsø, Norway, Head, Norway's Committee on Gender Balance and Diversity in Research (KIF)

Ylann Schemm, Program Director, Elsevier Foundation, USA

Martina Schraudner PhD, Head of the Department of Gender and Diversity in Organizations, Technical University Berlin, and Director of Responsible Research and Innovation Unit, Fraunhofer Gesellschaft, Germany

Rolf Tarrach PhD, Rector, University of Luxembourg, Luxembourg

Wanda Ward PhD, Director, Office of International and Integrative Activities, National Science Foundation (NSF), USA

Ingrid Wünning Tschol, Senior-Vice President and Head of Science, Robert Bosch Stiftung (Germany)

SAVE THE DATE

Gender Summit 7 Europe 2015
6-7 November, Berlin

GS7EU will be a two-day event, the first day devoted to advancing gender equality and gender dimension in research and innovation, and the second day will tackle policy issues and actions needed to achieve sustainable change.

Gender Summit 8 North America 2016
Mexico, March 2016

gender-summit.com

Gender Summits®

PORTIA gender and science

Multifaceted probes

Dr Akane Kawamura and her team are developing a comprehensive toolkit to lay bare complex epigenetic mechanisms that alter gene expression and contribute to diseases such as cancer

Could you introduce your research into the molecular mechanisms of epigenetic processes?

While each cell in the body contains identical copies of DNA, different genes are turned on or off depending on cell types or cellular states. These changes are regulated and maintained by a combination of epigenetic instructions, annotated by covalent modifications on DNA and histone proteins that package DNA.

My research aims to understand the methylation of histones in epigenetic regulation, focusing on a family of enzymes called histone demethylases (KDMs). We are interested in how these enzymes function and regulate gene expression at the molecular level, and are developing chemical probes against them to study their function in cells.

Why have you decided to focus specifically on KDMs?

Methylation is one of the major modifications found on histone tails. Histones are highly basic, consisting of multiple lysine and arginine residues. Lysines on histone tails can be mono-, di- or trimethylated. Different degrees of lysine methylation, as well as the location of the modification on the histone tail, can confer different outcomes for the associated gene, making methylation a complex yet fascinating post-translational modification to study.

Can you offer an insight into your research methodologies?

We have recombinantly produced the majority of the KDM enzymes found in humans and developed activity assays to screen for chemical inhibitors of their activities. This screening platform has been fundamental to the development of inhibitors for KDMs.

We have utilised strategies such as high throughput screening and focused libraries to identify and generate KDM inhibitors with different profiles (such as broad-spectrum inhibitors and subfamily selective inhibitors). We have demonstrated inhibition of KDMs in cells where histone methylation levels are increased according to the dose of inhibitor treatment, in some instances having anti-proliferative effect in certain cancer cell lines.

How does a multidisciplinary approach benefit your work?

A multidisciplinary approach is essential for an ambitious and challenging project such as this. We work alongside the Epigenetics Chemical Probes Consortium, led by the Structural Genomics Consortium, to generate and share chemical probes with the epigenetic research community. The project requires expertise from chemistry, biochemistry, assay development and screening, structural biology and cell biology. We also collaborate with researchers from medicine interested in testing our compounds in different disease areas, and working together to investigate epigenenetic observations.

What obstacles have you faced over the course of the project and how have they been overcome?

Chemical probe development for KDMs has been very challenging due to difficulties in obtaining selectivities and potencies between the different KDM subfamilies. We are currently working on improved compound screening methods and novel approaches, such as substrate competitors and cyclic peptide development to target new chemical space and increase the selectivity, potency and cellular activities of our inhibitors. We believe that combining different strategies will generate promising new leads for KDM probes.

Enhanced knowledge of epigenetics processes will contribute to more effective treatment of disease and augment understanding of how cells and tissues adapt to disease in general

Decoding disease

Multidisciplinary research at the **University of Oxford**, UK, aims to decipher the molecular mechanisms of certain enzyme-induced epigenetic processes that underlie the onset and progression of both inherited and somatic diseases, as a precursor to developing new, targeted treatments

THE IDENTITY, AND thus, the function and fate of each cell in the body are determined by the regulation of gene expression through a complex set of molecular processes that are yet to be fully understood. However, it is clear that when the mechanisms of regulation are disturbed, disease states such as cancer, or inherited conditions including mental illness, can result.

Among the actors and factors involved in gene expression, the histone proteins play a particularly crucial role, ensuring that DNA is correctly compacted and packaged into nucleosomes within the cell nucleus; as the main protein components and regulators of chromatin, any changes to the ways in which histones perform can have far-reaching effects on the balance of the cellular epigenetic landscape.

Histones undergo post-translation modifications that can activate, enhance or repress their interactions with other proteins and DNA. Some have particularly long tails that may be modified in various locations, usually as a result of interactions between enzymes and their lysine or arginine residues, through processes such as methylation, acetylation, ubiquitination and phosphorylation. However, whereas some modifications such as lysine acetylation have consistently positive effects, histone methylation can either activate or repress transcription, depending on context, timing, residue and the level of methylation.

For a greater understanding of the family of enzymes involved in modulating the methylation levels of histone tails, the histone demethylases (KDMs), Dr Akane Kawamura from the University of Oxford is focusing on the development of chemical probes. Thus, in her post as British Heart Foundation Centre of Research Excellence Senior Fellow in the Radcliffe Department of Medicine, and with support from a Royal Society Dorothy Hodgkin Research Fellowship, Kawamura has assembled a team to decipher the roles of KDMs through chemical inhibition.

FURTHERING DISCOVERY

The project has a dual aim: to increase knowledge of the roles of KDMs, including their activities in the epigenetic regulation of gene expression, and provide a robust set of chemical tools and probes that can modify their structures – with the ultimate goal of leveraging development opportunities for novel personalised approaches to treating disease. "Many KDMs are potential therapeutic targets. We hope that our chemical tools and probes will be useful for further target validation and serve as potential starting points for new drug development," Kawamura elucidates.

The KDM family of enzymes includes the KDM1s and six subfamily of 2-oxoglutarate (2OG)-dependent JmjC KDMs (KDM2-7). 2OG oxygenases are ubiquitous iron dependent enzymes that, in humans, orchestrate a wide range of important biological processes including the biosynthesis of collagen, metabolism of fatty acids, DNA repair, RNA and chromatin modifications and hypoxic sensing. 2OG oxygenase inhibitors thus have particular promise for therapeutics, with several currently being investigated for treating diseases including anaemia, inflammation and cancer.

SCREENING AND TOOLSETS

In conjunction with the Structural Genomics Consortium and the Oxford University Target Discovery Institute, Kawamura's project has established a robust and comprehensive screening platform for KDM probe discovery: "The platform covers all of the KDM subfamilies, including production of active proteins, assay setup, crystallography and cell assays," Kawamura explains, adding that the platform has already been used widely in both industry and academia. The team has also developed and disseminated chemical tools which are now in general use for studying KDMs and 2OG oxygenases.

Kawamura anticipates that enhanced knowledge of epigenetics processes will contribute to more effective treatment of disease and augment understanding of how cells and tissues adapt to disease in general, such as the response of heart tissue to ischaemia following a heart attack or the growth and mutation of cancerous tumours: "Epigenetics research holds huge potential in delivering new drug targets and therapeutic strategies in medicine," she enthuses. "I am very fortunate and thrilled to be working in this expanding field."

THE ROLE OF MODIFIERS OF HISTONES IN EPIGENETIC REGULATION AND GENE EXPRESSION

OBJECTIVE

To gain further insight into histone methylation in epigenetic regulation, focusing on a family of enzymes called histone demethylases (KDMs) within the context of disease.

KEY COLLABORATORS

Professor Christopher J Schofield; **Dr Paul Brennan**; **Dr Susanne Müller-Knapp**; **Professor Udo Oppermann**; **Professor Peter Ratcliffe**; **Dr Emily Flashman**, University of Oxford, UK

Professor Hiroaki Suga, The University of Tokyo, Japan

PARTNER

Structural Genomics Consortium

FUNDING

Royal Society, UK

British Heart Foundation Centre of Research Excellence Oxford

Engineering and Physical Sciences Research Council, UK

Cancer Research UK

CONTACT

Dr Akane Kawamura
Chemistry Research Laboratory
University of Oxford
12 Mansfield Road
Oxford
OX1 3TA,
UK

T +44 1865 285 000
E akane.kawamura@chem.ox.ac.uk

http://bit.ly/AkaneKawamura
http://bit.ly/chemakane

AKANE KAWAMURA completed her undergraduate degree in Chemistry at Oxford University and obtained her doctorate in Pharmacology in Professor Edith Sim's group, focusing on the biochemistry of xenobiotic metabolism and small molecule interactions of phase II drug metabolising enzymes. She then spent three years in industry as a senior biologist, where she led multiple drug discovery projects across a wide number of therapeutic areas. In 2009, Kawamura returned to academia and joined Professor Chris Schofield's group. During this time she worked on developing chemical probes for epigenetic targets in collaboration with the Structural Genomics Consortium. In July 2012, Kawamura was appointed as a British Heart Foundation Centre of Research Excellence Senior Fellow in the Department of Chemistry and Division of Cardiovascular Medicine, Radcliffe Department of Medicine. She was also awarded a Royal Society Dorothy Hodgkin Fellowship, which commenced in January 2013.

A blended intervention

In a large-scale collaboration with researchers and physical therapists based in the Netherlands, **Professor Cindy Veenhof** and **Corelien Kloek** have played leading roles in devising an eHealth learning approach that aims to increase physical activity among patients with osteoarthritis

Dr Veenhof, you were recently appointed Professor in Physical Therapy Sciences at the University Medical Center (UMC) Utrecht. Can you provide an introduction to the career path that led you to this position?

CV: After graduating in Human Movement Sciences and Physical Therapy, I worked as a physical therapist and researcher at the Netherlands Institute for Health Services Research (NIVEL). In 2000 I started my PhD at NIVEL, during which I studied the effectiveness of behavioural graded activity in patients with osteoarthritis of the hip or knee. This led me to take up a position as the research coordinator of the research programmes Allied Health Care and Sport, and Physical Activity and Health at the NIVEL Institute. It was only in October 2014 that I was appointed my current position as Professor in Physical Therapy Sciences at UMC Utrecht in the Department of Rehabilitation, Nursing Sciences and Sports.

The e-Exercise programme aims to help reduce physical therapy costs. How does the programme achieve this goal?

CV&CK: In the Netherlands, the mean number of treatment sessions (physical therapy) of patients with osteoarthritis is 17. By developing a blended intervention which integrates face-to-face sessions with an online program, we reduced this to four or five sessions. A large part of the exercise can be performed at home with support of the online tool.

The e-Exercise programme helps to tackle non-adherence to home exercises in physical therapy. How does this work?

CV&CK: In our blended e-Exercise intervention, we use technology to influence patients' behaviour. This strategy is called 'persuasive technology' and we have incorporated several specific technical components in order to

Fuelling physical activity

Researchers from the **Netherlands Institute for Health Services Research**, the **University of Tilburg** and the **University Medical Center Utrecht**, have developed e-Exercise – a new health intervention for patients with osteoarthritis that combines face-to-face physical therapy sessions with a web-based exercise programme

AS THE MOST common form of joint disease, osteoarthritis is one of the leading causes of chronic pain and disability worldwide. Although it can occur in younger people, it primarily afflicts adults over the age of 45 and, as a result of the ageing population and the growing obesity epidemic, its incidence is likely to increase. As a group of mechanical abnormalities that involves the gradual degradation of joints, osteoarthritis has a range of symptoms that include stiffness, muscle weakness, a reduced range of motion and deformed joints.

Due to the intense pain and stiffness experienced by individuals with osteoarthritis, it is common for many patients to reduce their level of daily physical activity. However, a significant body of evidence suggests that exercise is in fact beneficial for these patients, with inactivity linked to reduced muscle power and a subsequent deterioration of physical functioning. Multiple studies have emphasised the positive effects of face-to-face exercise therapy for reducing pain and increasing physical function. Despite this, such programmes also place a weighty financial burden on health systems, particularly as the number of patients with osteoarthritis increases.

Indeed, in view of the prohibitive costs of face-to-face physical therapy programmes, a number of recent studies have focused on exploring the effectiveness of web-based interventions. These are cheaper because of the absence of face-to-face interaction with a qualified therapist. Additionally, these fully web-based interventions have the advantage of constant accessibility to patients. However,

stimulate adherence to home exercises. Firstly, each week automatic reminder emails are sent to inform the patient about new assignments and instruction videos on the e-Exercise website. Secondly, exercises and information are supported with videos, which help to make the programme more attractive. Thirdly, after each activity or exercise, the patient is asked to evaluate the assignment – and tailored feedback is automatically generated based on this evaluation. Finally, the patient's number of website visits is visible to the physical therapist and low adherence can be discussed during the face-to-face sessions. Compared to usual physical therapy – mainly comprising of face-to-face sessions combined with home exercises – the patients using our blended e-Exercise intervention receive more reminders at home about their exercises.

What criteria did you use to decide to include five sessions with a physical therapist?

CV&CK: Based on the literature, we were able to establish that the average number of physical therapy sessions for patients with osteoarthritis is 17 in the Netherlands. Yet, in order to develop a cost-effective intervention, the number of sessions had to be much lower than 17. We therefore organised a focus group with seven physical therapists to discuss the number of physical therapy sessions needed in addition to the web-based element of the intervention. Additionally, we ran a discussion group with different stakeholders – researchers, physical therapists, eHealth experts and insurance companies – to debate the perceived number of sessions. Finally, we reached the consensus that four sessions would be the ideal situation, with five sessions for patients in need of additional guidance. Having said this, we do not believe that this intervention will fit all patients with osteoarthritis – a subgroup has more complex problems and probably needs more face-to-face sessions.

The e-Exercise programme is a collaboration between the researchers of NIVEL, Tilburg University and around 250 physiotherapists. What are the challenges of collaboration on this scale?

CV&CK: The challenge is to keep all the physical therapists motivated throughout the duration of the study, both in terms of including patients in the study and treating patients according to the protocol. Importantly, all physical therapists received thorough training prior to their participation in the study and, in order to generate motivation and inclusivity, a digital newsletter is sent out twice per month. e-Exercise researchers also send out frequent messages on Twitter. The physical therapists that successfully recruit an above-average number of patients are rewarded with flowers and a notification in the digital newsletter. Twitter messages are also frequently made by the researcher of e-Exercise.

How do you see the future of e-Exercise developing?

CV&CK: In the future, we anticipate that one online platform will be used for physical therapists. This platform will consist of different e-Exercise programmes, which are applicable to different types of chronic conditions such as diabetes mellitus, lower back pain, chronic obstructive pulmonary diseases or cancer. It will also incorporate a range of general exercises and instruction videos that will be suitable for patients with other acute injuries. Encouragingly, to date, physical therapists and patients have expressed enthusiasm about e-Exercise – however, its future depends on its financial feasibility. By reducing the number of sessions from 17 to four or five, physical therapists will need financial compensation, which may occur if more patients are keen to take advantage of this intervention.

PROGRAMME IMPLEMENTATION

From the inception of e-Exercise, Veenhof and her team have devoted significant time and attention to exploring its implementation. To this end, they created a project group – comprised of patient representatives, physical therapists, a health insurance company, a rehabilitation centre and an online physical therapy company – with a specific mandate to focus on the practicalities surrounding its implementation. Moving forwards, the hope is that the wider implementation of e-Exercise will have a positive effect on the lives of patients afflicted with osteoarthritis. There could also be broader applications of e-Exercise if adapted to other chronic diseases.

low adherence rates are a commonly reported pattern, with the lack of a professional presence thought to have a negative effect on patient motivation for exercise. As a result, there is therefore an urgent need for the development of cost-effective interventions that successfully encourage patients with osteoarthritis to engage in physical exercise.

AN INNOVATIVE INTERVENTION

It is in response to this need that a group of physical therapy researchers from the Netherlands Institute for Health Services Research (NIVEL), the University of Tilburg and the University Medical Center (UMC) Utrecht in the Netherlands have been working on the development of a cost-effective and implementable intervention for patients with osteoarthritis. Back in 2013, they created a fully automated and self-paced physical activity web-based programs for in-home use by patients with osteoarthritis. Entitled Join2move, it worked by slowly increasing the patient's favourite recreational activity over the space of nine weeks. "We noticed that a lot of patients with osteoarthritis adhered to the mistaken belief that there was nothing they could do about the disease," explains Professor Cindy Veenhof, currently based in the Rehabilitation, Nursing Sciences and Sports Department at UMC Utrecht and the former Research Coordinator at NIVEL. "A large group of these patients did not have the skills to self-manage their osteoarthritis, were not physically active and did not access support from caregivers – so we decided to develop an intervention that reached patients at home." Encouragingly, Veenhof and her colleagues found that Join2move resulted in positive changes, leading them to conclude that it could be a useful means of promoting physical activity in sedentary osteoarthritic patients. However, Join2move only worked for a subgroup of patients. Others missed the face-to-face contact with the physical therapist. This inspired the researchers to develop a blended intervention.

Building on the success of Join2move, the researchers have since developed e-Exercise – a 12-week blended intervention for osteoarthritis, which combines a web-based exercise program with four or five face-to-face sessions with a physical therapist. Together, they are aiming to determine both the short- (three months) and long-term (12 months) effectiveness and usability of the intervention in comparison to conventional physical therapy care programmes. "Our hypothesis is that

E - EXERCISE

OBJECTIVES

- To develop a blended intervention for patients with osteoarthritis of the hip and/or knee
- To study the cost-effectiveness of e-Exercise in patients with hip and/or knee osteoarthritis
- To discover the applicability of e-Exercise for other patient groups

KEY COLLABORATORS

Daniël Bossen PhD, Netherlands Institute for Health Services Research (NIVEL), Utrecht

Professor Dr Dinny de Bakker, NIVEL, Netherlands and Tranzo, Tilburg University

Professor Dr Joost Dekker, PhD, Department of Rehabilitation Medicine & Department of Psychiatry, EMGO Institute, VU University Medical Center Amsterdam, Netherlands

Dr J M van Dongen, Department of Health Sciences, EMGO Institute, VU University Medical Center Amsterdam, Netherlands

PARTNERS

Sint Maartenskliniek Nijmegen • Reade Amsterdam • Achmea • Fysiovoorjou • KNGF • Dutch Rheumatoid Arthritis Foundation • Patients with Osteoarthritis

FUNDING

The Netherlands Organisation for Health Research and Development (ZonMw) • The Dutch Rheumatoid Arthritis Foundation • KNGF

CONTACT

Dr Cindy Veenhof
Chair in Physiotherapy Sciences, Department of Rehabilitation, Nursing Science & Sports

Brain Center Rudolf Magnus
University Medical Center Utrecht W01 121
PO Box 85500, 3508 GA, Utrecht, Netherlands

T +31 6 28 909 596
E c.veenhof-2@umcutrecht.nl

www.e-exercise.nl

CINDY VEENHOF, PHD, is Professor in Physical Therapy Sciences at the Department of Rehabilitation, Nursing Sciences and Sports at the University Medical Center Utrecht in the Netherlands. Until November 2014, she worked as research coordinator at the NIVEL-institute in Utrecht. Her research focuses on physical therapy, physical (in) activity and technology.

CORELIEN KLOEK has studied physical therapy (BSc) and Health Sciences (MSc). After four years of working as a physical therapist, she is now working as a PhD student on the e-Exercise project at Tilburg University, Netherlands. Kloek also works as a physical therapist in a research project about the effectiveness of home-based exercise in patients with brain tumour.

There is an urgent need for the development of cost-effective interventions that successfully encourage patients with osteoarthritis to engage in physical exercise

e-Exercise is both at least equally effective and more cost-effective in terms of increasing physical functioning and physical activity compared to traditional therapy," elaborates Corelien Kloek, a researcher who is working on the development of e-Exercise for her PhD project at the University of Tilburg.

OUTLINING THE METHODS

Importantly, the e-Exercise intervention combines around-the-clock accessibility to exercise with motivational patient support. For instance, in the first week of the programme the patients work with their physical therapist to select one physical activity – such as walking, cycling or swimming – for the web-based intervention. "Once the patients have logged in to the programme, they will be asked to determine their physical load ability based on a three-day self test, the results of which will be logged on the website," elucidates Kloek. "During the second face-to-face session in week two, the patient's physical load ability will be discussed with the physical therapist, – and short- and long-term goals will be formulated based on the idea that goals encourage action."

As a result of the assigned goals, the e-Exercise website automatically generates a number of targeted exercise assignments, with the duration of the selected activity gradually increasing until the patient reaches his/her personal short-term goal. Additionally, another section on the website focuses on increasing strength and stability, with specific exercises illustrated through interactive instruction videos that incrementally increase in number every four weeks. The website also includes a comprehensive 'resources' section, with information about the aetiology of osteoarthritis, physical activity, pain management, weight management and medication, among other topics. Automatic emails are sent to notify the participants about new assignments or fresh content uploaded to the site, helping to keep the users up-to-date.

Finally, in order to keep track of their progress, the patients are required to complete weekly evaluations that their physical therapist is also able to access. The information from these evaluations represents a useful resource for the third and fourth face-to-face sessions, which take place in week six and week 12, respectively. "In the final face-to-face session, physical therapists will support and encourage patients to maintain a physically active lifestyle," states Veenhof. "If necessary, they can plan an additional fifth session – something that is especially useful for patients who are less capable of performing unsupervised physical exercises."

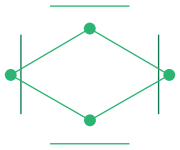
FUTURE STEPS

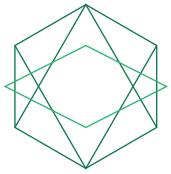
By blending human support and personal guidance with an accessible, self-directed online program for physical activity, the e-Exercise intervention successfully promotes patient motivation and adherence to exercise at home. Importantly, increased physical activity as a result of the programme has the potential to improve the health of osteoarthritis patients by providing pain relief and increasing physical functioning. Another key advantage of the intervention is that it generates a wealth of information about the patients' experiences of home exercises, in turn enabling the physical therapists to tailor their face-to-face sessions to specific individual needs.

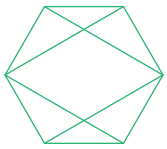
Looking ahead, Veenhof and her colleagues are confident that the blended eHealth approach they have adopted in e-Exercise has great potential for use in other healthcare fields, including speech therapy and occupational therapy. "Provided that it is used as an objective to achieve behavioural change and that patients visit a healthcare provider several times, this highly cost-effective approach could result in enormous health benefits at both individual and societal levels," Veenhof concludes.

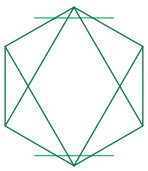
United for health

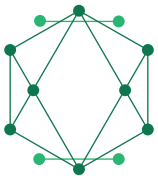
Fulfilling three separate but complementary roles, **Dr Helen Lunt** is well placed to help increase collaboration and interaction between sectors within New Zealand's healthcare systems

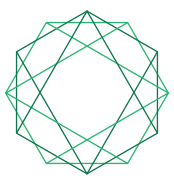


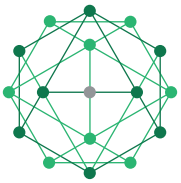












You have three distinct positions as a physician, Clinical Director of Health Innovation at the Canterbury District Health Board (CDHB) and Associate Professor at the University of Otago. How do these three roles enhance one another and improve your breadth of expertise?

Working across all three sectors has given me insights into the different drivers, incentives and resources that innovators, researchers and clinicians bring to projects. This helps me identify and work through the effect of possible misalignments on specific projects, and try to come up with 'win-win' solutions that are acceptable to all parties. Sometimes you have to acknowledge that the goals and resources available to potential collaborators are not sufficiently aligned to enable an idea to progress. In this situation, it is nevertheless important to remain open to future dialogue, as situations change and ideas can always be revisited.

How has your background and previous training contributed to your success in your current roles?

Sometimes you have to move out of your primary role before you realise that you have multiple 'soft' skills that are transferable to other roles. In terms of a personal example, I've never really enjoyed managing the contractual side of clinical trial work. This background has, however, been invaluable in my Clinical Director role, as I'm working with people who are drafting contractual documents about innovations for projects that require clinician input. I'm able to offer insights into the clinician's perspective and how this might be incorporated into the details of contractual arrangements.

In what capacity were you involved with the establishment of New Zealand's Health Innovation Hub? What is the purpose of the Hub and why is it a particularly unique part of a healthcare system?

I was involved with the Health Innovation Hub during its very early start-up phase, acting as its clinical representative at a time when we were all trying to work out what it would look like. As the Hub has broad connections throughout New Zealand's research, innovation, enterprise and clinical systems, it links businesses with clinicians and vice-versa at the national level. It can also connect innovative clinicians with other regional health systems, so their ideas can be tested outside of their own regional health system.

Might your work with CDHB serve as an example for healthcare systems internationally of how to ensure sustainable collaboration between academics, clinicians and industry?

We are only just moving out of the start-up phase of our development, so it is a little too early to comment on sustainable collaborations with any degree of authority. However, I believe a key element to sustainability is having a high level of trust between parties. This only works if you have visible support for innovation from your CEO and executive management, as their support instils confidence in the system. Another important lesson for me is acknowledging the huge impact of innovative incremental changes to clinical service delivery that are made by clinicians and patients. I try and remind others about this work, which is sometimes not that visible to outsiders, as it reinforces the fact that innovations can come from anywhere and that it is not just about research and enterprise.

How have those involved in these new partnerships responded to changes in the local healthcare system?

Innovative clinicians have always worked with industry but this is/was often ad hoc, with a focus on separate departments and clinical disciplines. I'm hopeful that the power of an increasingly united regional health innovation ecosystem, with a greater potential for sustained partnerships across multiple sectors, will be enough to offset the work needed to achieve this shared vision. Getting to this point will require a better understanding of the compliance and regulatory requirements of all partners within this ecosystem.

What expectations do you have for your work in the future? Would you like to spend more time on research or do you have further plans for the initiatives you developed at CDHB?

My passion is around translational research, so I like to work nearer the 'D' end of the R&D spectrum. My ideal job would therefore be to combine research with enterprise, both in terms of being an active member of an R&D team in my area of clinical expertise, and facilitating the work of others who are translating their R&D findings into routine clinical care.

Overhauling care provision

Effective cooperation between clinical, industrial and academic sectors are vital for the delivery of improvements to healthcare. **The Canterbury District Health Board** of New Zealand is leading the way towards overcoming the barriers that impede this goal

INTERNATIONALLY, MANY HOSPITAL and healthcare systems are under pressure to improve the quality of care, reduce the usage of unnecessary resources and lower costs. Such outcomes require continuous improvements in the ways in which care is delivered operationally and clinically. It is becoming increasingly recognised that in order to innovate rapidly and continuously, high levels of collaboration and interaction between clinicians, the local and international biotechnology and medical technology industries and the academic sector are required. However, in many healthcare systems, a silo approach to disciplines and services can act as a barrier to effective partnerships, with goals and resources often misaligned within sectors.

COLLABORATION IS KEY

In New Zealand, Dr Helen Lunt is working to increase collaboration within healthcare systems, helping to address many of the associated obstacles. In fact, the focus of her first year as Clinical Director of Via Innovations, the Health Innovation arm of the Canterbury District Health Board (CDHB) in 2011, was to act as a clinical representative during the establishment phase of the national Health Innovation Hub. This initiative was designed to provide industry with access to clinicians and their new ideas, and clinicians with advice on product design and health innovation funding options. "My role was to explain to non-clinical colleagues the personal and professional drivers that make clinicians get up and go to work each morning and how this might interact with the agendas and incentives of the biotechnology and medical technology industries," Lunt elaborates.

At the regional level, Lunt has been working to improve understanding and reduce the barriers faced by members of the local biotechnology sector seeking closer engagement with the public health system. Finally, she has been engaging and empowering clinicians and scientists working within the regional health system, so that they are better able to interact more closely with the health technology sector.

CHRISTCHURCH EARTHQUAKE

Although the Canterbury Health System had long recognised the importance of collaboration, the devastating Christchurch earthquake of 2011 was a catalyst for change. The earthquake damaged much of the city's infrastructure, reducing the functioning of many of its hospitals and clinics. Recognising an opportunity to restructure, Lunt explains how an optimistic outlook can be a strong motivator: "Whilst it is easy to focus on your difficult working environment, this approach is not very good for business! Instead, you have to remind yourself to put local problems into a broader perspective and see the positives".

A reduction in office space has meant employing an innovative approach to working virtually, a concept which is being increasingly embraced. Furthermore, the loss of clinical space has required clinicians to seek out ways of delivering care that are less reliant on hospital bricks and mortar. "Trying to reduce hospital bed day stay and deliver more care in the patient's home environment is a great driver for innovative clinical thinking," Lunt explains. "Clinicians are more willing to try out new ideas that might help achieve these goals, when they know there are increasing constraints on space." In effect, the earthquake helped accelerate that work that was already underway to transform the Canterbury Health System, which provides services for a population of around half a million people. The population, including clinicians, were more open to embrace changes to clinical service delivery that were already beginning to take place. "You could say the earthquake has accelerated the search for innovations that are beneficial to patients and which also represent efficient use of the health dollar," Lunt adds.

VIA INNOVATIONS

Over the past two years, Lunt has been working at the local level to set up Via Innovations – a unit within the Canterbury Health System that connects clinicians with industry. In a virtual environment, she has been collaborating with a diverse group of

INCREASING COLLABORATION WITHIN HEALTHCARE SYSTEMS

OBJECTIVES

To promote multidisciplinary partnerships between academia, industry and clinicians to improve quality of care and reduce expenditure through the development of innovative strategies and increased communication.

KEY COLLABORATORS

Clinical research: **Associate Professor Chris Florkowski**, Canterbury Health Laboratories, New Zealand

PARTNERS

New Zealand Health Innovation Hub

Canterbury Development Corporation, New Zealand

PowerHouse Ventures, New Zealand

EverEdgeIP, New Zealand

FUNDING

The high intensity interval training exercise study was funded by the District Health Board Research Fund, New Zealand

CONTACT

Dr Helen Lunt

Diabetes Centre
550 Hagley Avenue
Christchurch Central
Christchurch 8011
New Zealand

T +64 33 640 860
E helen.lunt@cdhb.health.nz

@CanterburyDHB

Canterbury District Health Board

Canterbury District Health Board

Canterburydhb@gmail.com

DR HELEN LUNT is a medical graduate from Bristol University, UK. She undertook most of her postgraduate clinical training in New Zealand, specialising in acute general medicine and diabetes, and completed her doctoral studies in Southampton, UK. Lunt is the Inaugural Clinical Director of Via Innovations, the Health Innovation arm of the Canterbury District Health Board (CDHB) in New Zealand, where she is also a practicing specialist diabetes physician. In this role, she has been the local principal investigator for numerous pharmaceutical trials. She also has a teaching and research role with the University of Otago, where she is Clinical Associate Professor. Lunt's current research focuses on understanding how best to interpret glucose measurements in routine clinical practice.

experts in fields which include intellectual property, law, business development, technology transfer, regulation and compliance, and marketing and communications.

As part of this initiative, Lunt has met with local businesses that have a health innovation focus and has hosted or co-hosted events to facilitate better interactions between industry and clinicians. As a result, it has become apparent that industry professionals often experience difficulties in accessing clinicians and their patients, and sometimes perceive clinicians as being slow adopters of innovation. Conversely, clinicians are likely to become frustrated by industry offering technology-driven solutions, rather than solutions that are focused on providing realistic answers to unmet clinical needs. "Ongoing conversations as a result of Via Innovations have led to a better, more mature understanding of each other's perspectives, and we are now working on several new projects between the CDHB and local industry partners," Lunt reveals. The initiative has already helped to propel a number of new ideas into everyday patient care.

DRIVING CHANGE

Despite the demands of her Clinical Director role, Lunt also undertakes patient care and clinical research in diabetes. "Doing so gives me credibility when I let fellow clinicians know I understand their frustrations, when they encounter the inevitable barriers on the journey to implementing clinical innovations," she explains. Lunt's recent research has included the applicability of high intensity interval training, a popular form of a time-saving exercise, to a group of mid-life participants at risk of developing diabetes and cardiovascular disease. Moreover, she explored ways to reduce some of the pitfalls involved in the measurement and interpretation of patients' glucose values in clinical practice.

Having worked with both clinical and non-clinical colleagues, Lunt has developed a new perspective on the range of collaborative skills that physicians possess – they are team players, able to work across multidisciplinary and inter-sectorial groups, and listen and translate the language of one discipline or speciality into another. Furthermore, physicians working within the clinical trial environment have skills in contracting and compliance that aid understanding in related sectors. "Working with a diverse group of non-clinical colleagues over the last few years has taught me just how flexible and transferable the physician's toolkit of skills is; I think this fact is under-appreciated," Lunt enthuses.

Lunt anticipates that her own clinical and research efforts will benefit from the new, integrated ways of working that she is driving forward, which will make clinical change easier to implement. "If you can deliver a story to your colleagues about the need for change and back this up with scientific evidence, plus budgetary information and detail about mitigating the inevitable downsides to implementation, then you are 90 per cent there in terms of driving through clinical changes," she asserts. With this approach, Lunt believes that she and her team will be able to transform the way glucose blood samples are prepared for analysis in local laboratories, effecting very rapid changes within the local healthcare community.

Having worked with both clinical and non-clinical colleagues, Lunt has developed a new perspective on the range of collaborative skills that physicians possess – they are team players, able to work across multidisciplinary and inter-sectorial groups, and listen and translate the language of one discipline or speciality into another

International Innovation showcases the most exciting highlights and interviews on research centred on healthcare published in recent editions, available free-to-access online

Q. What can other sectors learn from medicine when it comes to encouraging equality in the workforce? Looking forward, what progress needs to be made to promote the involvement of women in the medical science disciplines in which they are still underrepresented?

Professor Monica Lakhanpaul (University College London, UK):

Medicine has been tackling gender issues for many years. Universities have reviewed entry requirements and university application assessments to try and make sure men and women are equally able to engage with them, and have also proactively reached out to schools to encourage women to apply, using role models to allay some of the fears young women typically raised when applying to medicine. The profession itself has also increased the number of flexible working posts available so that women can juggle the difficult task of being a mother and a doctor. There are, however, still many disciplines where women are underrepresented. It appears that where women have managed to enter the discipline and have been successful, more women have followed – which in itself means more women are attracted to the discipline. While we have done well in achieving our current position, we must recognise that there is not an even distribution of women across all disciplines and more needs to be done.


Issue 162


Issue 137


Issue 170

THE PROBLEM WITH POLYPS

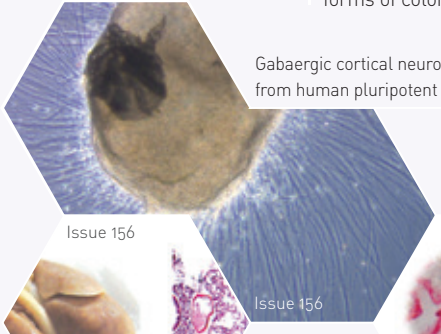
Molecular biologist and cancer researcher **Dr Vicki Whitehall** from the QIMR Berghofer Medical Research Institute in Australia provides an insight into her research on the different varieties of polyps found in the human bowel and their significance in oncogenesis. Her team is conducting novel studies into the genetic and molecular characteristics of different forms of colorectal cancer.

FIXING THE MEMORY MODEL

Although the hippocampus has been intensely investigated for over 70 years, one region has remained largely understudied. In an interview with International Innovation, **Dr Rebecca Piskorowski** from Université Paris Descartes, France, explains her focus on the cornu ammonis 2 and its role in memory formation, and the aim to produce a new and more encompassing model of hippocampal function using the latest optogenetics and biophysical tools.

BEAUTIFUL SCIENCE

IMAGE ANALYSIS


Issue 156

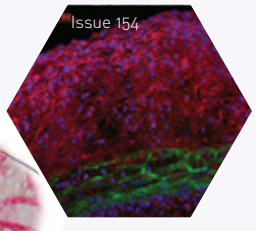
Gabaergic cortical neurons derived from human pluripotent stem cells.


Issue 156

Assay of melanoma metastasis: +B16f10 MAb4C5 treated.


Issue 168

Polymer-based biodegradable nanoparticles are injected into the maternal circulation of a mouse model to initiate the expression of insulin-like growth factor 1 in the placenta.


Issue 154

Confocal microscopy micrograph of an experimental atherosclerotic plaque from an apolipoprotein E knockout mouse.

AN AGE OF OPPORTUNITY

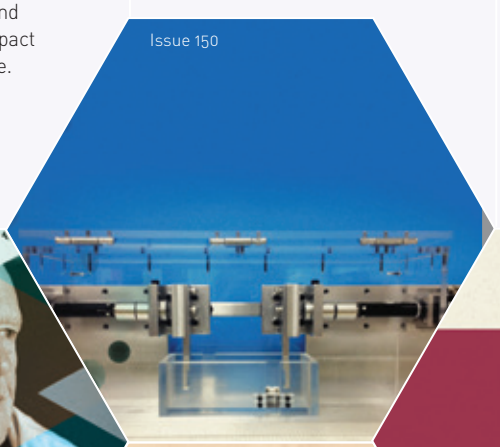
Professor Diana Kuh and **Dr Rachel Cooper**, participants in the UK's longest-running birth cohort study, the Medical Research Council National Survey of Health and Development, discuss the need for rich life course data on health and ageing. From a sample of 5,000 British men and women since their birth in 1946, the emerging data reveals the social, psychological and biomedical factors that impact wellbeing and quality of life.

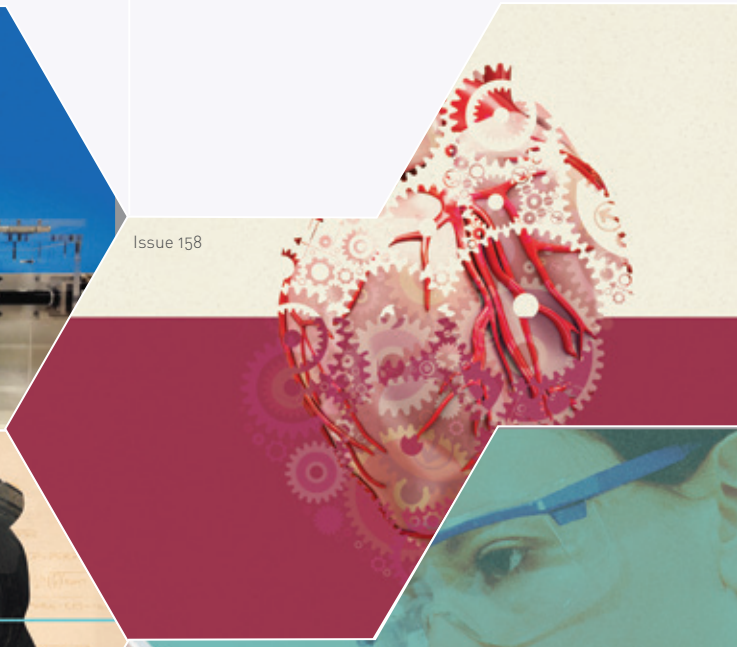
MECHANICAL METHODS

In the Department of Biomedical Engineering at the University of Akron, USA, **Dr Marnie Saunders** investigates cellular interactions and mechanotransduction, taking her cue from the natural world to advance modern technologies. The lab is developing models that accurately mimic the *in vivo* bone environment for the effective study of bone multicellular interactions.

A SPECIFIC SOLUTION

As cardiovascular disease is on the rise, the need for new treatment options is greater than ever before. **Dr Julie Goodwin** from Yale University, USA, is exploring the correlation between glucocorticoid receptors, which are expressed by most cells in the human body, and hypertension, in search of new targets for potential avenues of treatment.





FEED YOUR HEAD

Neurologist **Dr Sophie Layé** and nutritionist **Professor Véronique Pallet** from the Laboratory of Nutrition and Integrative Neurobiology in France share the inspiration that led them to collaborate on research dedicated to better understanding neurological disorders and their relationship with nutrition, with a focus on cognitive and emotional disorders such as depression.

ASSOCIATION FOR WOMEN IN SCIENCE

Janet Bandows Koster, Executive Director and CEO of AWIS champions the interests of women in science, technology and engineering across all disciplines and employment sectors, and explains the importance of working towards a positive system transformation to ensure that women in these fields can achieve their full potential.

EUROPEAN PLATFORM OF WOMEN SCIENTISTS

In pursuit of gender equality in science and innovation, **Drs Brigitte Muehlenbruch** and **Dora Groo** have been influential ambassadors for women working within academia and industry. EPWS endeavours to promote networking among female scientists, enhance the understanding and inclusion of gender issues in science and research policy and ensure that women's interests are taken into consideration when setting the political agenda.

Observing omega-3 in obesity

Associate Professor Lindsay Robinson explains how her interest in nutrition and immunometabolism led her to begin conducting research on fish oil-derived omega 3-fatty acids, with the aim of promoting a healthy lifestyle

You are currently based at the University of Guelph where you are an associate professor. What is your field of study?

My research programme at the University of Guelph, Ontario, is focused on nutrition and immunometabolism in obesity. I am particularly interested in how dietary fatty acids, like fish oil-derived omega-3 fatty acids, modulate inflammatory mediators and immune processes within adipose tissue, and the ensuing implications for obesity-related chronic diseases, such as type 2 diabetes. My interests are both at the basic science level of these relationships (understanding mechanisms by which fatty acids modulate immune function), and also in determining nutritional strategies, such as increased consumption of omega-3 fatty acids that may be incorporated into a healthy lifestyle to promote optimal health.

How has your background shaped the research you conduct today?

My interest in this area developed from two key events that occurred during my fourth year of undergraduate studies in biology at Acadia University in Nova Scotia. The first was taking an elective nutrition course and the second was my laboratory-based research project. These actions revealed my love for both nutritional sciences and research. Combining these interests led me to the University of Alberta, where I obtained my PhD in Nutrition and Metabolism with a focus on dietary fat, immunology and cancer. Following this, I held a Natural Sciences and Engineering Research Council of Canada (NSERC) Postdoctoral Fellowship at the University of Guelph to study carbohydrate metabolism in insulin resistant states, such as obesity and diabetes. Altogether, this

Fighting fat with fish

A team based at the **University of Guelph** is testing unique methods in a bid to uncover the true potential of omega-3 polyunsaturated fatty acids in preventing and treating obesity-associated diseases such as type 2 diabetes

IN MODERATION, AND in the right composition, fat is an essential part of any human diet. High-fat diets, for instance, particularly those that are rich in saturated fatty acids, have been strongly linked to the onset and prevalence of obesity – a growing epidemic of the 21st Century – as well as a number of other chronic diseases, such as type 2 diabetes. Research into the types of fatty acids being consumed in the diet, and the extent to which individual fatty acids exert unique biological effects, is therefore fundamental to adequately manage such conditions.

Obesity occurs as a result of excessive adipose tissue mass – adipocytes (more commonly known as fat cells) are a predominant component of metabolic control, the secretion of which can lead to an accumulation of fat. As a result, it is important to examine the physiological characteristics of adipose tissue to better understand the mechanisms by which obesity-associated inflammation arises. Led by Associate Professor Lindsay Robinson, a team of researchers based at the University of Guelph's Department of Human Health and Nutritional Sciences is examining this link in the hopes of identifying preventive and treatment options to reduce obesity-related inflammation.

OPPORTUNITIES FOR OMEGA-3

At Robinson's laboratory, which is currently funded by the Natural Sciences and Engineering Research Council of Canada (NSERC) and receives an infrastructure grant from the Canadian Foundation for Innovation, the main focus is on fish oil-derived omega-3 polyunsaturated fatty acids, namely eicosapentaenoic (EPA) acid and docosahexaenoic (DHA) acid. The unique characteristics of these acids could potentially lead to a multitude of physiological benefits, including the capability of mitigating dysregulated inflammatory processes.

The team has shown that EPA and DHA increased secretion of adiponectin – an anti-inflammatory, insulin-sensitising adipokine – from 3T3-L1 murine adipocytes and primary human adipocytes. "In addition, we have also shown that DHA may lessen the degree of inflammatory mediators (eg. MCP-1 and IL-6) secreted from adipocytes, and may reduce the degree of pro-inflammatory M1 macrophages recruited to adipose tissue, thereby decreasing the intensity of pro-inflammatory communication between adipocytes and macrophages in obese adipose tissue," Robinson enthuses. She hopes their research will contribute towards the improvement of the inflammatory microenvironment in adipose tissue, and ultimately, the related metabolic processes and functional outcomes that impact the pathogenesis of obesity-associated diseases.

METHOD LAB

Robinson and her group are spearheading efforts to monitor responses to nutritional manipulation in various systems, including adipocytes and immune cells grown in cell

work has led to my research programme and the work we are currently doing in the area of nutrition and immunometabolism in healthy and obese states.

In your scientific investigations, you have zeroed in on omega-3 and omega-6 polyunsaturated fatty acids (PUFAs). Why have you focused on these two acids?

My reasons for focusing on omega-3 and omega-6 fatty acids are threefold. Firstly, given that omega-3 fatty acids are increasingly found in a plethora of functional foods and supplements in the marketplace and are widely consumed by many individuals as a strategy to promote health, it is important to continue studying their effects on various aspects of health, including inflammation and metabolic processes in the body. Secondly, although many health benefits of omega-3 fatty acids have been reported, it is important to understand the basic biological processes by which these bioactive nutrients impact health and disease. Finally, it is typically believed that omega-6 fatty acids promote inflammation in the body, whereas omega-3 fatty acids, especially fish oil-derived eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), exert anti-inflammatory effects and thus may be beneficial under situations of too much inflammation in the body.

Have you made any novel discoveries to date, either in this study or in other investigations you have undertaken?

Most recently, we have shown that the early obese adipose tissue cellular microenvironment of CD8+ T cells and adipocytes can be recapitulated in a co-culture model *ex vivo*. We investigated fish oil-enriched CD8+ T cells in co-culture with 3T3-L1 adipocytes in a CD8+ T cell: adipocyte ratio to mimic CD8+ T cells in obese adipose tissue in the absence or presence of the inflammatory stimuli, lipopolysaccharide. Using this model, we have provided the first evidence that fish oil-enrichment of CD8+ T cells can drive subsequent CD8+ T cell -adipocyte communication in a beneficial anti-inflammatory and anti-chemotactic direction that reduces subsequent macrophage chemotaxis, providing a basis for further studies assessing the mechanisms that underlie interactions among CD8+ T cells, adipocytes and macrophages. This is an exciting direction for us as we aim to further understand the inflammatory microenvironment in obese adipose tissue.

Is there a particular aspect of your work or discovery you have made of which you are most proud?

We are very excited to be moving beyond the macrophage in adipose tissue to study other immune cells, such as T cells and how they can be affected by omega-3 fatty acids within adipose tissue. This will help us to develop a more comprehensive picture of the inflammatory microenvironment in obese adipose tissue.

culture and rodent adipose tissue organ culture. "In our rodent work, we manipulate the diet composition to study the impact of bioactive nutrients on aspects of adipose tissue biology and inflammation," she explains. "We use mice *in vivo* and the isolation of primary adipose tissue immune cells from mice for use in co-culture with established cell lines *ex vivo* in order to provide a comprehensive picture of the anti-inflammatory influence of omega-3 fatty acids on obese adipose tissue composition, structure and function."

The team also boasts extensive experience and knowledge in using a range of methods, including flow cytometry and immune cell purification, enzyme-linked immunosorbent assay (ELISA), Western blotting, quantitative polymerase chain reaction (qPCR), multiplex for analysis of plasma and cell/tissue levels of cytokines and inflammatory signalling proteins in response to nutritional manipulation.

LOOKING FORWARD

With research lined up to develop more rodent and cell culture models, the team is excited about the future potential of their work: "We aim to establish the underlying mechanisms by which omega-3 fatty acids exert their effects, the time-course of immune cell infiltration into obese adipose tissue, and functional consequences related to diet-induced changes in the adipose tissue inflammatory microenvironment," Robinson outlines. The researchers hope their work will ultimately lead to human clinical trials, allowing them to investigate the impact of omega-3 fatty acids on obese adipose tissue, and processes such as insulin sensitivity.

COME TOGETHER

For the Robinson lab, collaboration is key to propelling their work forward

Alongside Dr David Ma at the University of Guelph, the team is using a wide range of mouse models, including the novel delta-6 desaturase knockout model, as well as a mammary cancer model to further explore the role of omega-3 fatty acids in modulating immune function and inflammation. Dr Krista Power at Agriculture and Agri-Food Canada in Guelph is a leading collaborator with the group, working on an exciting project to explore the role of the gut and gut microbiota in obesity-associated inflammation and the role of other bioactive dietary nutrients, including those found in pulses such as beans. Finally, Power and Robinson are co-advising Dr Jennifer Monk, a postdoctoral fellow with expertise in nutrition and immunology who, along with other graduate students, continue to be the force driving their research forward.

INTELLIGENCE

FATTY ACIDS AND INFLAMMATORY MEDIATORS IN HEALTH AND DISEASE

OBJECTIVE

To investigate the impact of omega-3 fatty acids on adipose tissue biology, inflammation and metabolic processes, such as insulin resistance, that are implicated in obesity-related diseases, such as type 2 diabetes.

KEY COLLABORATORS

Dr David Ma, University of Guelph, Canada

Dr Krista Power, Agriculture and Agri-Food Canada, Canada

FUNDING

Natural Sciences and Engineering Research Council of Canada (NSERC)

Canadian Foundation for Innovation (CFI)

CONTACT

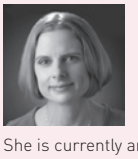
Dr Lindsay Robinson
Associate Professor

Department of Human Health and Nutritional Sciences
336-B Animal Science/Nutrition Building
University of Guelph
Guelph, Ontario N1G 2W1
Canada

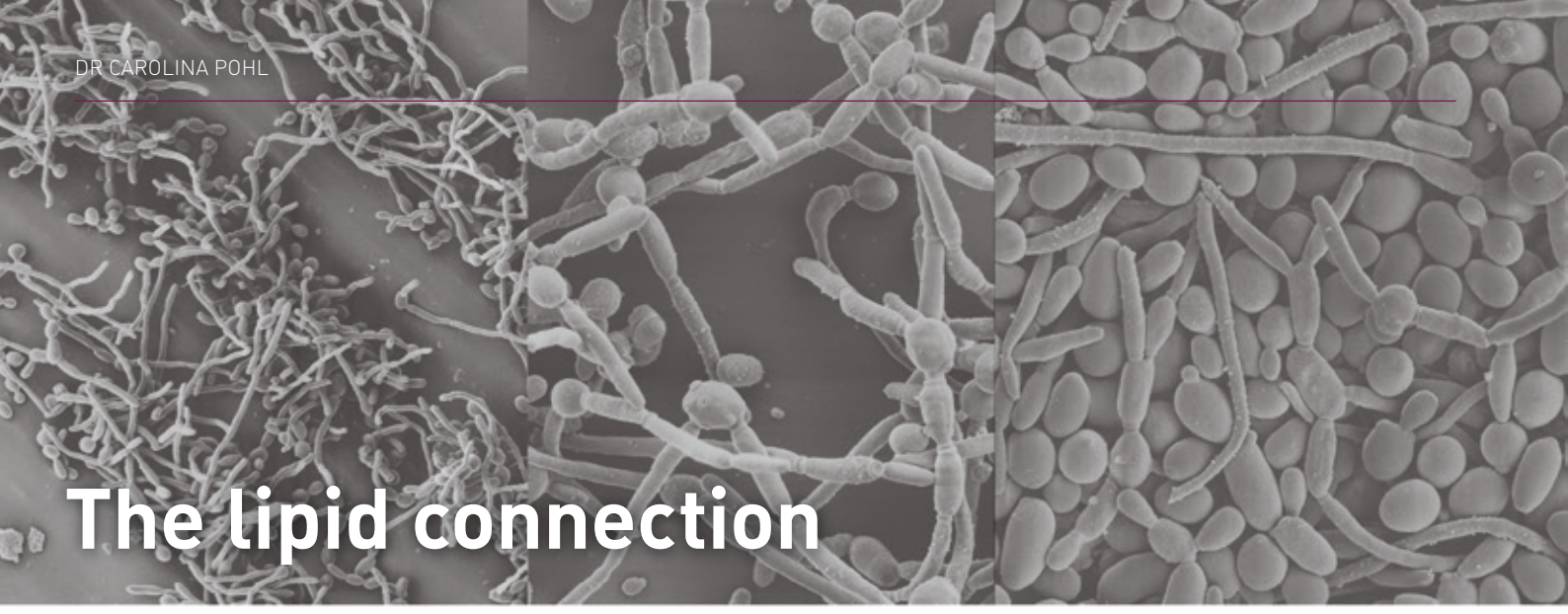
T +1 519 824 4120 x 52297
E lrobinso@uoguelph.ca

bit.ly/ResearchGateLindsayRobinson

@LRob_NutrExProf



LINDSAY ROBINSON received her BSc in Biology from Acadia University and her PhD in Nutrition and Metabolism from the University of Alberta. She is currently an Associate Professor at the University of Guelph and is interested in the role of bioactive nutrients in health and disease.



The lipid connection

Dr Carolina Pohl describes the work of her research team, one of few groups in the world that are exploring the roles of bioactive fatty acids in the development of yeast infections

Could you begin by introducing the work of the Pathogenic Yeast Research Group?

The Pathogenic Yeast Research Group focuses on diseases caused by yeasts, especially those belonging to the *Candida* and *Cryptococcus* genera. My focus is the role of bioactive lipids produced by *Candida* species. I am interested in understanding how fatty acids, including those obtained from the host, are used by these yeasts to produce lipid metabolites (oxylipins) that contribute to their survival in the host, as well as to tissue damage caused by the yeast during infection.

What is the immunological role of bioactive lipids in hosts of these diseases?

Certain oxylipins can modulate the mammalian immune system and often have several different functions in distinct cell types. One of the best-studied oxylipins produced by both the host and pathogenic yeasts is prostaglandin E_2 (PGE_2), which can shift host immune responses in favour of the pathogen. It can inhibit the type of immune response needed to protect against *Candida* infection and induce an immune response that may lead to associated chronic or disseminated diseases. It can also stimulate another type of immune response that may cause uncontrolled inflammation and damage to the host. Thus the production of PGE_2 during infections can benefit the pathogen.

Another important effect caused by PGE_2 is tissue eosinophilia leading to tissue damage, which is characteristic of some chronic fungal infections. Interestingly, it is not only the host that is affected: PGE_2 has biological activity on yeast by stimulating germ tube formation in *Candida* species. This change in morphology, from unicellular to filamentous, is considered the start of biofilm formation and is associated with an increased ability to invade tissue. Interestingly, biofilms also produce more PGE_2 than unicellular yeast forms.

Can you highlight some of the roles that lipids have as 'inter-kingdom' signalling molecules in yeast-associated multispecies infections?

This is an exciting new research focus for us. It is increasingly being recognised that many infections are not caused by one organism. Interaction between pathogen and host may be influenced by other non-pathogenic organisms. Although it is known that lipid metabolites can act as signals between organisms – even those belonging to different kingdoms – very little work has been done on the bioactive lipids produced by mixed communities. An example of a multispecies interaction is the biofilms consisting of *Candida albicans* and the *Pseudomonas aeruginosa* bacterium in the lungs of patients with cystic fibrosis.

Are there particularly advanced imaging techniques that you incorporate in your studies?

Most studies of different antimicrobial effects start with the production of standardised biofilms, which are notoriously resistant to antifungal treatment. To assess the effectiveness of potential antifungal drugs, biofilms are stained for viability and visualised using a confocal laser scanning microscope.

The potential of drugs to decrease biofilm viability or metabolic activity is assessed in an XTT-assay based on the ability of mitochondrial dehydrogenases to convert a substrate to a coloured formazan. The effect of compounds on the ultrastructure – including surface characteristics and organelle structure – is examined by electron microscopy.

Our group pioneered the use of nano-scanning Auger microscopy (Nano-SAM) on yeast cells. With Nano-SAM, nanometre-thin slices of a yeast cell enable observation of its 3D structure. The cell elements can also be mapped. Similarly, time-of-flight secondary ion mass spectrometry (TOF-SIMS) is used to map the distribution of certain compounds, including oxylipins, in cells. We also use various assays to measure oxidative stress.

Has collaboration with other research groups aided your research?

My own speciality is enhanced by that of Dr Olihile Sebolai who focuses on *Cryptococcus* species and immunology. Dr Chantel Swart is an expert in ultrastructural analyses and was a leading member of the group that pioneered the application of Nano-SAM to yeast research. In this, we also collaborate with our university's physics department. The fourth member of the group is Professor J Albertyn, who is an expert in yeast molecular biology and yeast signal transduction.

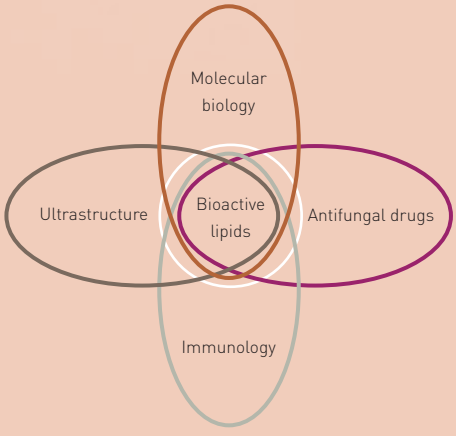
To date, has your work drawn any interesting conclusions?

An obvious conclusion is that the lipids of pathogenic yeasts are much more than structural compounds or reserve material; like mammalian and plant lipids, they have other functions. It has also become obvious that much of the knowledge regarding metabolic pathways and enzymes responsible for production of mammalian oxylipins does not translate directly to yeasts. With the completion of each project, we end up with more questions – the study of these bioactive compounds is always exciting.

Pathways of infection

Research into the molecular mechanisms of common yeasts and bacteria at the **University of the Free State** in South Africa seeks to exploit the roles of lipid molecules as instigators of disease symptoms towards development of new therapeutics and antifungal agents

Oxylipins are central elements in adaptation and survival; in some instances they aid organisms to defend themselves, propagate or prompt symbiotic relationships, whereas in other situations they can induce pathogenesis



A RICH AND diverse population of bacteria and fungi live in a mutualistic fashion within the human body. Unfortunately, when their normal balance is disturbed, their populations can respond with rapid growth, giving rise to infection. Because such disturbances typically follow an event of ill health, the impact of such infections may have severe consequences, especially for already immune-compromised individuals. For example, fungal infections caused by the *Candida* yeast are common among individuals who are HIV-positive and can inhibit their nutrition. *Candida* species infections can also exacerbate infection by the tuberculosis bacterium or lead to deterioration in patients with cystic fibrosis or head and neck cancers. Similarly, infection by pathogenic *Cryptococcus* causes serious fungal infections that can result in pneumonia-like symptoms, infertility, central nervous system damage, encephalitis or death.

In the Republic of South Africa – where the incidence of tuberculosis is high, low birth weight and infant mortality are prevalent, sexually-transmitted infections are widespread and HIV infection is at epidemic proportions – pathogenic yeasts lie at the intersection of a number of priority health issues: women and children's health, and infectious and noncommunicable diseases.

ADDRESSING THE PROBLEM

The Pathogenic Yeast Research Group at the University of the Free State in South Africa is focused on the role of bioactive lipids, the fatty molecules fundamental to cellular growth in both hosts and pathogenic yeasts, with the aim of furthering development of new drugs and treatments to counteract yeast infections. The Group is particularly interested in the role of these lipids in multispecies infections, as found in cystic fibrosis, peritonitis and tuberculosis, and in cancer-related and female reproductive tract infections. In addition, they aim to discover more about the vulnerability of yeasts to antimicrobial compounds, in order to counteract the growing problem of multidrug-resistant yeast strains.

This Group was the first to discover yeast oxylipins, or oxidised fatty acids, including prostaglandins. One member, Dr Carolina Pohl, is an expert in lipid metabolism in yeasts and has been involved in the discovery of the antifungal effect of acetylsalicylic acid – an oxylipin that is a mitochondrial inhibitor and anti-inflammatory compound. Since making these findings, her work has mainly concentrated on biofilm formation and subsequent infection by the *Candida* species *C. albicans* and *C. dubliniensis* – highly related strains that behave in similar ways, which makes them ideal as model systems of pathogenic yeasts. "These two species both have the ability to produce the lipid signalling molecule prostaglandin E_2 (PGE_2), and react in the same way to this chemical by producing germ tubes," Pohl explains. "With both, the formation of biofilms, and subsequent increase in ability to form PGE_2, is an important disease-causing mechanism through the stimulation of inflammation."

THE ROLE OF OXYLIPINS

Oxylipins have ancient origins as signalling molecules, elements of which are conserved across different kingdoms of life. Pohl recently undertook a review of oxylipin mediation of diverse inter-organism communication that leads to beneficial or deleterious interaction: between plants, animals, fungi and bacteria. Although the mechanism by which yeasts 'sense' the presence of bioactive lipids in their environment or host remains unclear, the review has led Pohl to conclude that oxylipins

The Pathogenic Yeast Research Group

EFFECT OF POLYUNSATURATED FATTY ACIDS ON PATHOGENICITY OF *CANDIDA ALBICANS* AND *CANDIDA DUBLINIENSIS*

OBJECTIVES

- To understand the metabolism of arachidonic acid to proinflammatory oxylipins by *Candida* species
- To understand the signalling pathways of oxylipins leading to morphological changes in *Candida* species
- To investigate the lipid metabolisms of mixed species biofilms and the influence of the produced oxylipins on the host

KEY COLLABORATORS

Professor J Albertyn; **Dr O Sebolai**; **Dr C Swart**, University of the Free State, South Africa

FUNDING

South African National Research Foundation

CONTACT

Dr Carolina Pohl
Associate Professor

University of the Free State
PO Box 339
Bloemfontein 9300
Republic of South Africa

T +27 824 540 072
E pohlch@ufs.ac.za

twitter.com/PathYeastRes

www.facebook.com/PathYeastRes

www.linkedin.com/pub/carlien-pohl/53/7a7/905

http://bit.ly/RGPohl

DR CAROLINA POHL is an associate professor in the Department of Microbial, Biochemical and Food Biotechnology at the University of the Free State, South Africa. Her research focus is Bioactive Lipids in pathogenic *Candida* species. She had been part of a research group studying the distribution and functions of these compounds in environmental yeasts since completing her PhD in 1999. She started her own research group in 2006, focusing on yeasts that are important human pathogens.

are central elements in adaptation and survival; in some instances they aid organisms to defend themselves, propagate or prompt symbiotic relationships, whereas in other situations they can induce pathogenesis.

Pohl's research has shown that some yeast oxylipins work by mimicking host signalling molecules to induce an immune response. They can also bring about structural changes in the yeast that then assist its colonisation activities or help it to evade host defences. Additonally, lipids are involved in cross-talk between different cellular compartments, such as cell walls and mitochondria, which can aid the acquisition of multidrug resistance, but also underlies their potential as antifungal agents. Hence Pohl recently conducted an assessment of the effects of an omega-3 fatty acid on *C. albicans* and *C. dubliniensis* growth. In this study, the long-chain stearidonic fatty acid stopped biofilm formation by increasing reactive oxygen species production and the rate of apoptosis. The study also suggested that stearidonic acid can act in synergy with some antifungal compounds. This was the first finding that it is not just medium-chain fatty acids that can stop the growth of pathogenic yeasts.

OXYLIPINS IN MULTISPECIES INFECTION

Pohl's investigation into the effects of supplementing levels of an omega-6 fatty acid, sciadonic acid, in epithelial cells on infection with *C. albicans* and *C. dubliniensis*, showed changes in PGE_2 concentrations, but no reduction in those of benign anti-inflammatory omega-3 fatty acids. Furthermore a trial of the effects of aromatic amine phenothiazine – a constituent of several types of drugs in medical and veterinary use – on *C. albicans* biofilms, demonstrated significant reductions in biofilm metabolic activity and biomass and large reductions in PGE_2 production.

Given their abilities to mediate communication between species, bioactive lipids in single-species yeast or host contexts are not, however, Pohl's only line of research. Multispecies infections, particularly concerning the production of oxylipins and subsequent reactions of the host and pathogens in mixed populations of yeasts and bacteria, are a current key area of study: "Finding out more about the types and levels of oxylipins produced by different organisms when growing together may tell us more about the influence of interaction on each microbe, and the potential effects on the host," she elaborates. Such information would be particularly relevant for understanding the oxylipin role in generating the symptoms of mixed pathogen diseases, such as cystic fibrosis.

TRANSLATING *IN VITRO* RESULTS

In a recent project, Pohl explored the principle of inhibiting the release of arachidonic acid – a necessary component of the PGE_2 production pathway. This was achieved by substituting sciadonic acid for arachidonic acid in *C. albicans* and *C. dubliniensis* biofilms grown *in vitro*. Her team found that the levels of PGE_2 were indeed reduced and now aim to further validate this result in experiments using *in vivo* infection models.

Potential approaches to mitigating yeast infections currently being tested by Pohl's team include preventing the production of PGE_2 in yeast biofilms, so reducing their proinflammatory effects: "An ideal drug target may be a metabolic pathway that is unique to yeasts and not found in the host," Pohl muses. She is also working to identify the pathway that allows *Candida* species to react to the presence of oxylipins produced by either the host or other yeast cells.

Pohl is confident that greater knowledge of the role of lipids and the mechanisms of lipid metabolism of pathogenic yeasts will lead to significant advances in the near future. With a focus on their structures and their ability to metabolise fatty acids, she now plans to follow up several candidate enzymes that her team have already identified as being implicated in prostaglandin production and virulence in *Candida*. With the support of the rest of the Pathogenic Yeast Research Group, Pohl also intends to further explore the influence of arachidonic acid on gene expression of pathogenic yeasts, using genomic and proteomic analysis techniques. She intends for this to deliver as yet unanticipated antifungal drug targets and lead to new applications in diverse fields, from medicine to agriculture.

A vital vitamin

Professor Carol Wagner is a paediatrician with expertise in neonatal-perinatal medicine. Here, she discusses how her research into the vitamin D status of pregnant and lactating women is filling a significant knowledge gap and fuelling innovative public health initiatives.

What inspired you to begin studying vitamin D status in pregnant and lactating women and how have your background and previous experiences helped your current research?

I was inspired to study vitamin D requirements during pregnancy and lactation because of my collaboration with biochemist Dr Bruce Hollis, one of the world's leading scientists in vitamin D research. Back in 2000, we were discussing the vitamin D requirements of lactating women and the issue of supplementation in breastfeeding infants. I became intrigued by the fact that human milk, always viewed as the 'perfect' first food for babies, was deficient in vitamin D and began to question why this was the case. Together, Dr Hollis and I began to conduct vitamin D supplementation studies in lactating women in an attempt to answer this question. Later, we studied pregnant women in order to understand why vitamin D metabolism is so dramatically different during pregnancy. From that point on, I have not looked back.

Do you think that the impact of vitamin D deficiency on pregnant and breastfeeding women has been underresearched prior to your studies? Why do you think this is?

My answer to this is a resounding yes! Vitamin D deficiency during pregnancy and lactation has been understudied because until very recently it was thought that vitamin D was only involved with calcium homeostasis and bone integrity – and that beyond childhood there was little need for vitamin D. Now, with an exponential growth in vitamin D research, we are able to explore the mechanisms of action of vitamin D at the cellular level and, importantly, we see that it affects every cell in the body, just as other steroid hormones such as thyroxine and cortisol do. As a result of previous misunderstanding and a lack of robust research on the effects of vitamin D, there is much 'catch-up' that needs to be done in this area.

You and your team collaborate with non-profit organisation GrassrootsHealth. How is this partnership facilitating the translation of your research into public health initiatives?

It has been a tremendous experience to work with GrassrootsHealth. As a clinician scientist, I did not have any prior experience in translating research into practice. When speaking about our research findings, I would often communicate in terms that were not easily understood by nonmedical folks – and as a result this minimised the impact of our findings. Partnering with GrassrootsHealth – which is directed by Carole Baggerly – has allowed us to make the transition from using technical jargon to explaining health impact factors in terms that are accessible to everyone.

What factors stand in the way of patient adoption and adherence to vitamin D supplementation during pregnancy? How will these challenges be tackled by your project?

The main impediment to adoption and adherence to vitamin D supplementation is lack of understanding on the part of the medical community, which in turn limits end-user understanding. In response, we are developing educational materials for healthcare professionals about vitamin D metabolism, evidence about vitamin D deficiency and its impact on health and, finally, practical steps that can be taken to achieve the sort of vitamin D sufficiency that would be attained if one lived in a sun-rich environment. We also have partnered with an insurance company, Select Health of South Carolina, to inform their pregnant clientele about vitamin D deficiency and other risk factors that affect pregnancy outcomes. Providing pregnant women access to this information will empower them.

What do you see as the next steps in promoting vitamin D supplementation and adherence to supplementation programmes during pregnancy nationwide?

We are currently planning to launch community-based programmes in Charleston, South Carolina; San Diego, California; Chicago, Illinois; and Omaha, Nebraska, through our collaboration with GrassrootsHealth. Such programmes are important because they provide an educational forum for both healthcare providers and the women themselves. Additionally, the involvement and support of insurance companies – which shoulder the burden of escalating costs incurred with adverse pregnancy outcomes – will ensure the sustainability of these programmes. Indeed, with the US ranking much higher than many other countries for adverse pregnancy outcomes, there is an urgent need to turn the tide.

Spotlight on deficiency

Researchers based in the Division of Neonatology in the Department of Pediatrics at the **Medical University of South Carolina** in Charleston, USA, are investigating the optimal vitamin D status for the improved health of pregnant and lactating women and their babies

LARGELY DERIVED FROM sunlight on bare skin, vitamin D is essential for human health – and recent years have witnessed enhanced interest in the many and varied functions of this vitamin. For instance, in addition to maintaining calcium homeostasis in the body – consequently preventing rickets and osteomalacia in children and osteoporosis in adults – the deficiency of vitamin D has been linked to multiple chronic conditions such as cancer, diabetes and the development of neurological diseases. Although it is possible for individuals with vitamin D deficiency to survive for many years, their quality of life and overall health status are often severely compromised.

Unfortunately, vitamin D deficiency is becoming much more common in the US and in many other nations throughout the world. This is largely due to modern lifestyle factors; for example, the prevalent indoor culture means that people are less likely to spend extended periods of time outside in the sun and, if they do, they will usually be covered with sunscreen, which prevents their skin from absorbing sunlight and making vitamin D. Additionally, because vitamin D is fat-soluble and can be stored in fat, overweight and obese individuals are prone to deficiencies due to reduced amounts of vitamin D circulating in their blood. Thus, the growing obesity epidemic – a trend that is particularly marked in the Western world – is also a contributing factor to the increasingly widespread phenomenon of vitamin D deficiency.

PREGNANCY AND LACTATION

Two particularly worrying subpopulations subject to large-scale vitamin D deficiency are pregnant women and breastfed infants – a number of observational studies have revealed correlations between low vitamin D levels and comorbidities in pregnancy including preeclampsia, lower birth weight and a higher rate of preterm delivery. Unfortunately, these patterns have been vastly underresearched to date, largely due to the mistaken association between vitamin D and toxicity during pregnancy. Based on observations that hypercalcaemia led to facial and other deformities in the foetus following the supplementation of milk and other food sources with vitamin D, in the past the root cause of these deformities was wrongly attributed to vitamin D. In fact, the problem of metabolising vitamin D is a symptom of Williams syndrome, a genetic disease. Vitamin D has nothing to do with causing this condition, yet even today many clinicians remain reluctant to prescribe vitamin D supplements to pregnant women.

Motivated by the lack of research and the misconceptions surrounding vitamin D deficiency and supplementation in pregnant and lactating women and their infants, Professor Carol Wagner is attempting to

VITAMIN D: FACING THE FACTS

- The active form of vitamin D is produced from previtamin D_3, derived from sunlight, dietary supplements or certain foods. Before it becomes biologically available, D_3 must be metabolised in a series of steps, first in the liver, then the kidneys, and finally released into the circulation in its active hormone form (1,25(OH)2D)
- Vitamin D enables the body to use calcium ingested in the diet. More recently, research has emphasised that, due to its effect on both innate and adaptive immunity, vitamin D has multiple roles in protection against a plethora of chronic conditions
- The populations at highest risk of vitamin D deficiency are those of African, Hispanic and South Asian origin because the melanin in their skin reduces their ability to make vitamin D in response to exposure from sunlight

VITAMIN D REQUIREMENTS DURING PREGNANCY AND LACTATION

OBJECTIVES

To define optimal vitamin D status for improved health of pregnant and lactating women and their babies, with a focus on immune function.

KEY COLLABORATOR

Bruce W Hollis, PhD, Medical University of South Carolina, USA

FUNDING

Eunice Kennedy Shriver National Institute of Child Health and Human Development

Thrasher Research Fund

Kellogg Foundation

CONTACT

Professor Carol Wagner
Professor of Paediatrics

Medical University of South Carolina
Division of Neonatology
Department of Pediatrics
Medical University of South Carolina
165 Ashley Avenue, MSC 917
Charleston, South Carolina 29425-0917
USA

T +1 843 792 8829
T +1 843 743 5384
E wagnercl@musc.edu

PROFESSOR CAROL WAGNER is a board-certified paediatrician and neonatologist at the Medical University of South Carolina (MUSC). She is currently Associate Director of the Clinical and Translational Research Center and Associate Fellowship Director of Neonatology. Wagner received her undergraduate degree from Brown University and her MD degree from Boston University School of Medicine with subsequent training in paediatrics and neonatology at the University of Rochester, New York. She came to MUSC in 1992 and has advanced along the tenure track, being promoted to Professor of Paediatrics in 2006. Her clinical questions have been the driving force for her research. For the past 15 years, Wagner has partnered with Dr Bruce Hollis to conduct vitamin D research. They have completed two large randomised control trials of vitamin D supplementation during pregnancy and an additional vitamin D supplementation trial involving lactating women and their infants. This work has led to an ongoing public health initiative on vitamin D during pregnancy funded by the Kellogg Foundation.

A number of observational studies have revealed correlations between low vitamin D levels and preeclampsia, lower birth weight and a higher rate of preterm delivery

forge a deeper understanding of the optimum vitamin D dosage for these populations. As a prominent clinician-researcher in the Division of Neonatology at the Medical University of South Carolina (MUSC), Wagner has devoted the past 15 years to studying the benefits of vitamin D supplementation in both lactating and pregnant women and, more recently, has begun to explore the role of vitamin D in early infancy. Her innovative research has benefited from her longstanding collaboration with Dr Bruce Hollis, an expert in vitamin D and Professor in the Department of Pediatrics at the MUSC Children's Hospital. "The importance of vitamin D in health has expanded in the last decade as we have deciphered the role of this steroid hormone in cellular metabolism that includes, but goes well beyond, bone and calcium metabolism," Wagner points out. Indeed, recent studies have highlighted that vitamin D plays a key role in immune function and general health throughout life.

FAR-REACHING FINDINGS

In order to determine the effectiveness of vitamin D supplementation in pregnant and lactating women, Wagner and Hollis have conducted important clinical trials. Funded by the National Institute of Child Health and Human Development and the Thrasher Research Fund, the data from their studies on pregnant women suggest that maternal supplementation with high doses of vitamin D leads to a reduction in risk of infection, preterm labour and preterm birth. As for the lactation trial, the results showed that high-dose maternal supplementation of vitamin D during lactation could substantially improve both maternal and neonatal nutritional vitamin D status: "Significantly, we found that if the mother is vitamin D replete, which can occur with 6400 IU vitamin D3/day, then her milk is replete and her infant's vitamin D status will be similar to those infants who receive 400 IU vitamin D3/day as a supplement," Wagner elucidates. "Thus, when mothers have adequate vitamin D status, their milk is enriched with vitamin D and their infants achieve healthy vitamin D levels without any need for supplements." Importantly, this finding helps to dispel the myth that human milk is an inherently poor source of vitamin D.

FORGING A FULLER UNDERSTANDING

So far, Wagner's cutting-edge research has helped to address a significant knowledge gap regarding the role of vitamin D in pregnancy, lactation and early childhood. Yet much more work remains to be done in this field and, together with her colleagues, she is currently seeking to establish the mechanisms that underpin the link between vitamin D deficiency and the risk of complications in pregnancy. Moreover, Wagner is also eager to translate her research findings into practice; to this end, she has partnered with a not-for-profit health organisation to run community-based programmes that educate women and healthcare professionals about vitamin D supplementation during pregnancy and breastfeeding.

Excitingly, Wagner and her research team have recently been awarded a grant by the Kellogg Foundation to embark on a study that aims to prevent health disparities in pregnancy outcomes through the supplementation of vitamin D. "This project involves a comparison between women who are receiving the current standard of care for vitamin D of 400 IU received in a prenatal vitamin with women receiving the much higher dose of 4400 IU/day," she explains. "We are focusing on immune function – T cell morphology, inflammatory and anti-inflammatory cytokine profiles and placental changes – as a function of maternal vitamin D status." Looking ahead, the hope is that the completion of this project will result in a more in-depth understanding of the mechanisms exerted by vitamin D during pregnancy and, ultimately, that this knowledge will generate wider acceptance of the importance of maintaining vitamin D sufficiency in pregnant women.

MUSC MEDICAL UNIVERSITY OF SOUTH CAROLINA

MUSC Children's Hospital
Discovering. Understanding. Healing.

GrassrootsHealth
Moving Research into Practice

For a sector at the cutting edge of scientific progress, it is surprising that equally forward-looking policies to ensure female scientists' development, retention and progression have not been successfully implemented. *International Innovation* explores this issue in a roundtable discussion with key contributors from this edition

RESEARCH ROUNDTABLE

Q: What are the main barriers facing women in science? How can universities, research institutions and industry attract and retain more women in these disciplines?

DR MEREDITH S BERRY
University of Montana, USA

A significant barrier is the lack of visible role models and institutional support. Organisations could design a built-in infrastructure that increases visibility of successful women role models and provides information or workshops on how to overcome challenges faced by women in science (eg. discrimination, sexual harassment, potentially elevated financial or childcare burden).

Stereotyping of women's career options and fulfilling teachers' expectations of gender differences between men and women is also a problem. It would be ideal to develop a training programme for teachers of all levels to increase awareness of the effect of stereotyping on children and adult learning.

Another difficulty lies in a lack of financial independence to pursue higher education. Wherever possible, merit- and need-based scholarships should be offered to women in STEM fields, as well as internship opportunities. We need to eliminate income inequality within organisations and speak out against the gender gap in income publicly.

PROFESSOR ANGELA VINCENT
University of Oxford, UK

A major barrier in my view is the lack of women in positions where they can support and promote younger women – one token woman is not enough. It is important that the institutions and committees that run them realise that women should not only be represented on all committees, but there should be at least two or preferably three women, and they should not just act like men, but bring a different perspective to the table. These women should be listened to because their attitudes and views can add to the decision-making process, and may even, over time, gently modify male attitudes!

DR SYLVIA E MCLAIN
University of Oxford, UK

This is a question we have been asking ourselves since the 1970s, but clearly it isn't improving very quickly. Fundamentally, these issues are not very straightfoward to address as I believe they are largely about culture and unconscious bias.

I think there should be much more emphasis on departments, institutions, etc., focusing on what their particular problems are with respect to diversity and trying to actively solve them. It is often easy to say 'women don't apply' and leave it at that. If women don't apply, then actively seek women out to apply – this would be a much better solution than just passively waiting for a change.

ASSOCIATE PROFESSOR LINDSAY ROBINSON
University of Guelph, Canada

My most significant barrier in my career relates to my ongoing efforts to successfully balance academic research with raising, along with my husband, our two children, currently aged seven and five. The time in which I was establishing a productive and successful research programme coincided with starting our family, making work-family balance my biggest challenge to date.

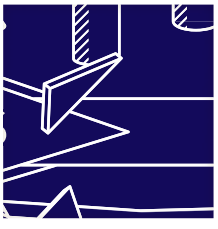
To attract and retain more women in science, there needs to be increased understanding and recognition of the time and commitment to home life and raising a family. The ability to have somewhat flexible work hours and to work from home are critical factors that allow me to balance family and work commitments on a daily basis.

DR CATHERINE MAVRIPLIS
University of Ottawa, Canada

I hate to speak of barriers because the word makes it sound like it's impossible to move forward. Certainly there are difficulties along the path to a successful career in science. No doubt men also recognise difficulties, but the difference for women is one of a minority, just as other minorities or underrepresented groups feel within a structure shaped and run by the majority group.

Learning to fit in and succeed in a profession depends on one's ability to understand and adapt to the culture of that profession. Unfortunately for women, that culture has been shaped exclusively by generations of males, and adapting to it is not straightforward: it's foreign to us and we are not particularly welcome. Adapting to a male model does not work: women are perceived differently than men in society and adopting male methods tends to isolate women even more. Staying true to their female ways, however, is not always seen as serious or scientific. Furthermore, male scientists in particular seem to be, on average, less open to changing the culture or changing their standards, which they see as rooted in 'the scientific truth', when in fact, as has been shown in the literature, they are rife with bias, conscious or unconscious. What makes a good scientific talk? What makes a good teacher? How do you manage graduate students? Should you publish as a single author or in a collaborative team? How important was your part on that team? All these 'truths' are up for discussion, but in some departments there is no discussion.

What universities, research institutions and industry can do is to work towards a more open discussion of accepting diverse approaches to scientific work and to broaden diversity within their work groups. In attaining a critical mass, the conversations and recognition of diverse approaches will start to change and allow more women and minorities to fully contribute to the scientific enterprise. The richness of those results will be amazing.



PROFESSOR DENISE DOOLAN
QIMR Berghofer Medical Research Institute, Australia

I think the main barrier facing women trying to establish a career in science is the need to return to full-time research as soon as possible after having children. Science is not a part-time career, and it is not a career that can be put on hold for too long given the rate of technological and conceptual advances. Furthermore, parental responsibilities extend beyond infants to include children who are of school age – so even when a woman has returned to work following maternity leave, there will still be additional demands on her time that need to be managed.

In addition to implementing flexible hours for working mothers and family-friendly meeting times (eg. between 9.15 am and 4.30 pm), fellowships to support the return of females to the workplace following maternity leave would be helpful. The provision of technical support to female early-career researchers while on maternity leave to facilitate research productivity in that critical career stage would probably be invaluable.

DR CLARE HOSKINS
Keele University, UK

I have seen so many women leave science to start families and not return; and I can understand this and sympathise since I am a mother. The long hours and dedication required do not always lead to an easy work-life balance, and the cost of childcare and emotional strain put on mothers is difficult to reconcile at times.

I was keen to return to work as soon as possible after taking maternity leave as I was scared I would lose my passion for science. However, I returned after three months even more driven than before. Although this was difficult, tiring and a steep learning curve, the support I received from Keele University made this a smooth transition. I believe the key to being a successful working mum is to have a supportive institution with line management who understand and are flexible to the demanding role of parenthood.

PROFESSOR SANDRA HEWETT
Syracuse University, USA

In my field of neuroscience, women actually comprise the majority of PhDs. However, women's representation in the field declines at every career transition. This is particularly evident in US academic institutions, where only approximately a quarter of full professors are women. So what appears to be happening is that we have a leaking pipeline.

Places of employment can surely do more to help recruit and retain excellent female scientists. First, they can educate both men and women about implicit or unconscious gender bias, which has been empirically demonstrated to adversely affect women when it comes to initial appointments and promotions. Next, they can actively recruit women into tenure-track positions and provide effective mentoring. Mentoring of junior faculty of both sexes leads to greater professional success. Finally, it is a reality that there never seems to be a good time for a female scientist to have a child. More family-friendly policies and affordable onsite childcare services for trainees and faculty alike can help. Academic institutions could implement automatic tenure extension (stop the clock) policies for new parents of either sex who are on the tenure track, thereby removing the stigma that some females feel about taking it. Society as a whole could help all working families by adjusting school schedules to match work schedules.

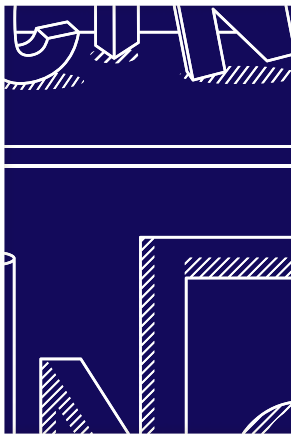
On a more personal note, women must choose their partners wisely. Having a life partner that is willing and able to support one's professional choices, to shoulder home and childcare duties proportionally, if not disproportionally, and understands and doesn't fully lament the long hours it takes to have a career in science – or in any discipline for that matter – is key to success.

PROFESSOR CAROL WAGNER
Medical University of South Carolina, USA

As a woman clinician-scientist, I have experienced considerable change during my career that has allowed women to be productive members of the scientific community. Working with a group of paediatricians who value research has allowed me to follow my vision.

Some of the barriers I see that impact the success of women in science include the lack of adequate training and rigid schedules that are inflexible to the lifestyle issues that women in particular have if they choose both a career and family. Universities that lack onsite day-care facilities do a disservice to women and men alike who are pursuing careers in science. Ancillary support services to assist young investigators to receive grant support may be sporadic or less suited to certain avenues of STEM.

One approach to ensuring women continue to participate in scientific disciplines is to facilitate the building of a multidisciplinary team, which allows greater depth and vision that translates into better science. I have benefited enormously from the team that surrounds me. It truly takes a village to be a successful scientist and having the opportunity to collaborate across scientific disciplines provides the necessary platform to achieve this.



DR CAROLINA POHL
University of the Free State, South Africa

This is a difficult question to answer as I do not believe that the barriers are easily defined. My feeling is that a part of the answer as to why less women than men enter STEM careers starts with how girls are generally socialised to be less curious than boys. They are not encouraged to spend hours observing and wondering about the behaviour of ants or to figure out how a vacuum cleaner works – they should rather learn how to use it.

This points to fundamental issues in society that ultimately lead to certain careers, including STEM, still being viewed as 'man's work', while other areas are dominated by women. As such, there are easy interventions that could be applied to immediately change this situation. One possible way is to increase the visibility of female scientists as positive role models in society.

DR REBECCA SUDORE
University of California, San Francisco, USA

I believe increasing the number of women in science will require a multipronged approach. Messaging starts early and can have a large impact on women. The media has been shown to change people's perceptions for other causes. Positively depicting women and girls with STEM interests and careers in movies, television and stories may be helpful. The burgeoning market for toys that encourage building and mathematics for girls could also prove fruitful. Furthermore, primary and secondary education could create curricula that highlight successful women and role models in STEM careers.

In terms of institutions attracting and retaining more women in these disciplines, transparency may be important. For instance, publishing the admission rates to universities and the hiring rates of women at all levels in an organisation may provide some accountability and competition to improve the percentages. To counteract potential unconscious biases, universities and organisations could accept blinded application policies. Furthermore, salaries and expectations for advancement could also be made transparent. Finally, allowing flexible schedules for women with children would allow them to stay in the workforce and work around their family needs. Women should not be penalised for attempting to have a work-life balance.

DR CAROLINA D WELLER
Monash University, Australia

The main barrier facing women in science is sometimes women. The 'imposter syndrome' is a trait that many women carry – the fear of not being good enough, not going for that promotion, not asking for a pay rise.

Universities, research institutions and industry could retain more women if they supported women with mentorship programmes. I believe our challenge is to have the courage to be more like ourselves than anyone else and play to our strengths. We need to be clear about what we stand for, and allow our research and evidence to inform our practice.

In my case, my vision for the future was realised by following my passion. I know the future I want to create and I can see a number of possible ways to achieve this. My research can speak volumes in a congress or seminar on the world stage. In the future, my hope is that there will be no need to label 'female' leaders, there will just be leaders.

DR YOLANDA COMEDY
American Association for the Advancement of Science, USA

I think one of our advisory committee members, Sharon Vosmek of Astia said it best: "Stop fixing, mentoring and supporting women – just invest in them". I think this is the key. Once women and underrepresented minorities have opportunities, we rise to the occasion. For me, the creation of 21st Century talent is one of the most important things in the world. We need all our talent to solve the complex and critical problems that we face. Diversity of all types brings new perspectives – these perspectives are vital for providing change and tackling complexity.

Community

Keep in touch with the latest in research dissemination

Funding calls

The Wellcome Trust International Engagement Awards

The Wellcome Trust International Engagement Awards provide funding for innovative public or community engagement projects that explore biomedical research or health in Africa and Asia. The awards provide grants up to £30,000 for up to three years. Projects should:

- Stimulate dialogue about biomedical research and health and its impact on the public
- Promote innovative partnerships between community organisations, the cultural sector, and scientists/researchers
- Strengthen capacity to conduct future public or community engagement with biomedical research and health

Deadline: 15 February 2015
See more at: http://bit.ly/wellcome-engagement

10th IBRO/Kemali Prize

A prize of €25,000 will be awarded by the International Brain Research Organization-Dargut & Milena Kemali Foundation to a scientist less than 45 years of age on 31 December 2014, who has made outstanding contributions to basic or clinical neuroscience.
Deadline: 15 April 2015
See more at: www.ibro.info

New bioinformatics approaches in service of biotechnology

One of the greatest challenges facing the biotechnology community today is making use of the vast and dynamic influx of 'omics' data. The synchronised development of bioinformatic concepts and related computational tools for prediction and modelling is a prerequisite to exploiting this wealth of biological data as a source of new biotechnological applications. These can range from industry and health to the environment and agriculture. Proposals should develop innovative bioinformatics approaches to close the gap between data availability and the discovery of new biotechnological applications.
Deadline: 11 June 2015
See more at: http://bit.ly/bioinformatics-biotech

Keeping in touch

@IntlInnovation
International Innovation
International Innovation
+44 117 3700 828
International Innovation
info@researchmedia.eu

Calendar

17-19 February 2015 ..... **Silicon Valley, USA**
Global Innovation Summit
www.innosummit.com/home#global-innovation

25-27 February ..... **Madrid, Spain**
Energy & Materials Research Conference
www.emr2015.org

10-11 March 2015 ..... **London, UK**
Alzheimer's Research UK Conference 2015
www.arukconf.org

28-29 March 2015 ..... **New Haven, USA**
Global Health and Innovation Conference
www.uniteforsight.org/conference

12-15 April 2015 ..... **Edinburgh, Scotland**
British Neuroscience Association's Festival of Neuroscience
www.bna2015.org

8-12 May 2015 ..... **New Orleans, USA**
Immunology 2015
www.immunology2015.org

28-30 May 2015 ..... **Istanbul, Turkey**
World Conference on Technology, Innovation and Entrepreneurship
www.istanbuluniversityinnovation.org

8-10 June 2015 ..... **Manchester, UK**
British Cardiovascular Society Annual Conference
www.bcs.com/ace/default2015.asp

6-9 September 2015 ..... **Vienna, Austria**
4th European Congress of Immunology
http://bit.ly/efis-immunologycong

Online

Missed a recent issue?

International Innovation is available to view digitally via
www.internationalinnovation.com

Free registration

Register for free today. For more details, visit:
www.internationalinnovation.com/join-us/register.php

For distribution or membership queries, contact
info@internationalinnovation.com

NATIONAL CENTRE FOR UNIVERSITIES AND BUSINESS

Olivia Jones, Project Manager for Talent, Enterprise and Development, reveals some of the exciting projects she is facilitating at NCUB to encourage girls to pursue a career in engineering

What work is the National Centre for Universities and Businesses (NCUB) conducting in order to promote gender equality?

I run two programmes associated with gender equality. The first is our Women in Engineering programme and the second is a newer programme on Women in Leadership. One of the key drivers behind both of these programmes is the economic benefit of a more diverse workforce, whether in leadership positions, the engineering sector or in general. There is a lot of information about the lack of women in engineering and we need so many more engineers – one source highlights nearly 850,000 by 2020, but only 7 per cent of professional engineers are women. So, the reason for our Women in Engineering programme is to increase the number of engineers – the best source is women because that's half the population.

The Women in Leadership programme is still fairly new. There are very few women in leadership positions, particularly at the most senior levels. But diverse boards and teams have proven to be more successful. Steered by our Women in Leadership group, which is led by the new Chairman of the BBC Trust, Rona Fairhead, we're going to design bold, practical actions to increase the number of women in leadership positions using university-business collaboration.

Could you describe some of the obstacles that girls and women currently face in science fields and the ways in which you are working to overcome them?

We are targeting girls early in the pipeline into engineering, going right back to choosing the right GCSE, A level and degree subjects. There are many influences dictating whether girls choose science. In terms of careers advice, there are many misunderstandings about engineering. Teachers are a big source of advice for girls – Engineering UK conducted a survey citing that nine out of 10 teachers provide careers advice to pupils but only 56 per cent of them deemed engineering as a suitable career. This shows how much more work is needed. Among teachers, parents and girls there are still huge stereotypes that we are trying to eliminate.

The substantial shortage of physics teachers is another factor. In addition, only 50 per cent of women that obtain a STEM degree go into STEM industry, whereas 65 per cent of men do. There is a higher dropout rate and the attrition rates are generally higher for women throughout their careers in engineering.

Have you read the *Not for people like me?* (see pg 9) report by Professor Averil Macdonald?

It's fantastic! Some of it I had come across before, but the area I found most enlightening, as the title suggests, is the part around self-identity. Our Women in Engineering programme includes a campaign called Talent 2030 to encourage girls into engineering, and that comprises the website, social media, outreach trips and a competition. On our website, and promoted through social media, we try to focus on role models – we call them heroes – and that ties in with what Macdonald's report says about being able to identify with people. We should no longer be saying 'be an engineer and build things', where the focus is on the product and not the person, as this is not always attractive to girls. It's a great report and I plan to use some of the ideas to shape our campaign.

You are the Project Manager for Talent, Enterprise and Development. What skills and expertise do you bring to the role?

At NCUB, I manage all of our talent projects. Some of this work is sector-specific, like the Women in Engineering programme, and some is more general. I focus on how we can encourage universities and businesses to collaborate to improve graduate skills.

Over the past 18 months, I have developed an expertise in STEM skills research and policy. However, our Women in Engineering programme is the reason I started at NCUB, as I am a chartered civil engineer by background. I've worked as a consulting engineer for a large international company and a small specialist company, and before this chose to study maths and physics at A level and

In a recent examination, NCUB asked students who could have studied engineering, but chose not to, the three most influencing factors that would have made them change their minds:

- Knowing there are '*green*' opportunities in engineering
- Knowing the earning potential
- Seeing more role models

engineering at university, all of which means I have faced the same experiences as the girls I'm trying to reach are going through.

Would you say that you have personally experienced gender stereotyping in your field?

I've had two advantages that many girls aren't so fortunate to have. First, I attended an all-girls school, and secondly, I had a physics teacher who had actually completed a physics degree. I chose engineering because I loved physics, which is quite a common reason among girls. A substantial amount of physics is now taught by teachers with biology and chemistry backgrounds, because there is a shortage of physics graduates going into teaching, and they don't have the passion and depth of understanding to encourage girls into physics.

In addition, research cites that girls perceive physics as too difficult, or a 'boys' subject, and that's where the advantage of all-girls schools come into play, because you can't make that comparison. However, no one in my family had studied engineering, and I was very much in the minority during my degree – just under 20 per cent of my course were female. When I worked in a small company of 20 people I was the only female engineer. I personally haven't come across any discrimination, being female, however, occasionally my age is an issue – but I think most graduates experience ageism when they are thrown into the workplace. I have read reports of women saying that it is tough and definitely would have appreciated more senior role models – that is something we are trying to address at NCUB.

The Talent 2030 Campaign is targeted at every girl in secondary education in the UK. Could you provide an overview of the Campaign, including its objectives and the reason for its initiation?

Talent 2030 was launched as a result of one of the recommendations from NCUB's Engineering and Manufacturing taskforce. They identified that future talent – or lack of it – was going to be one of the most influential issues on the sector and that failing to harness the whole of the talent base put it at risk of losing its competitive edge.

The National Engineering Competition for Girls is the most exciting aspect of the Talent 2030 campaign at the moment. It's national and has good publicity. We are working with many organisations to promote it – the Women's Engineering Society and British Science Association, for example. Some find it a little controversial, that it's a competition just for girls, but by promoting the event it sends out the message that engineering is for girls too.

Aside from the Talent 2030 website, social media, outreach and competition, as part of our Women in Engineering programme we also aim to influence policy makers. For example, we were asked to write a paper for Number 10 last year, which argued for changing the STEM acronym to MTEC – manufacturing, technology, engineering and computing. There isn't a problem with female participation in all sciences – women make up over half of individuals in biological sciences and there are many in chemical sciences. Our paper said that when encouraging more women into science, the focus must be on the industries where the proportions remain very low.

What criteria must the girls meet in order to be eligible for entry into the competition, and what prizes are awarded to the winners?

Talent 2030 is open to girls aged 11-18. The 2014 competition started in September and was open until 19 December. The competition is sponsored by Rolls-Royce and EDF Energy, and prizes include £1,000 for the winner of each age category, split: £500 for the winning girl(s) and £500 for their school.

All the shortlisted entrants are invited to attend an event called the Big Bang Fair in March – last year we took 70 girls. They set up their entries on stands and are given the chance to showcase their hard work to the public.

We posed a very open question for the competition: how can engineers solve the challenges of the 21st Century? We deliberately made it open, stating 'engineers' not 'engineering', so that it focused on the person. As part of the criteria, entrants were required to brainstorm some of the challenges, which meant they started to realise there's more to engineering than what is seen in the press – trains, people in hard hats looking at buildings, etc. – but areas such as the global energy crisis, food shortages, overpopulation. They seemed very enthusiastic about it.

JONES DISCUSSES SOME OF THE MOST EXCITING PROJECTS FROM TALENT 2030

Some of the entries from last year were fantastic, and the girls had clearly spent hours on them. The winning entry for the eldest category was by a girl who wrote a report and created a website on a super power plant. She developed an idea for a plant that featured many different renewable energy technologies. She built a computer-generated imagery model on her website, and it was amazing. Personally, I thought it was a higher standard than some of the first- and second-year projects I saw when I was at university.

In the younger age category, we had some really fun entries. They tend to be less serious because they aren't gearing up for university, and much more creative. There were designs for living on Mars and one girl built a working robot to do with recycling. My favourite entry was by a group of girls who developed a proposal for an app that would translate sign language, and they shot an excellent video to go with it. All the entries had some real variety.

How do you work to foster a community between the girls once the competitions have ended?

This is the third year we have run the competition. There was a pilot conducted soon before I started and then I took it on board and created the full version. We have two years' worth of winners and runners up and created an alumni group of previous winners. Rolls-Royce organises an annual trip to their site in Derby and we also send newsletters encouraging them to speak with each other.

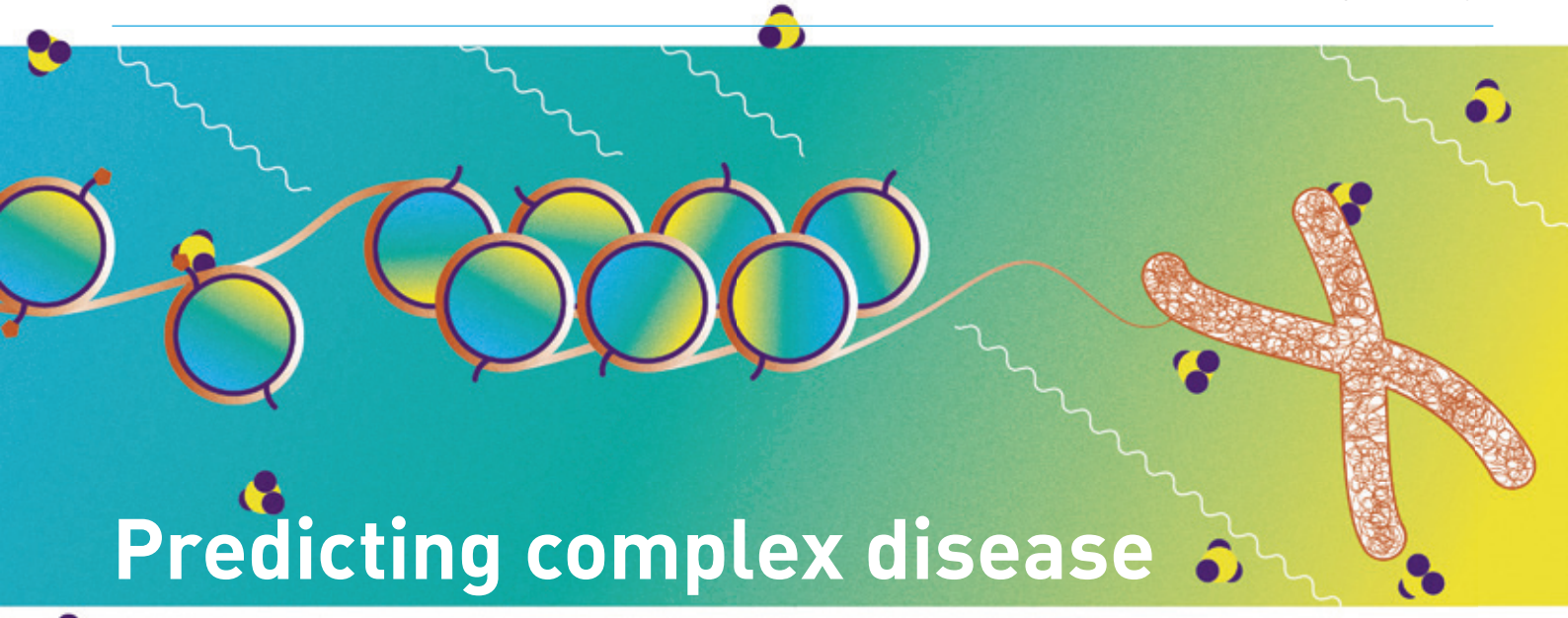
What are your expectations for 2015?

Next year, to make it bigger and better, we are planning to carry out some more work with universities and businesses, as part of our wider Women in Engineering programme; to look at the leak in the pipeline between A level and degree to see if we can increase recruitment onto engineering and technology courses. Some universities we are working with have simply changed the name of their degree and as a result have got a much larger percentage of women applying – implementing the word 'design', for instance. Interviewing candidates so that they can come to the campus and speak to someone about the course appears to be successful (girls generally take longer to make decisions, conduct more research and need more reassurance, so interviewing might help with that). These are quite anecdotal at the moment, so we would like to create a programme to look at the recruitment practices, monitoring them over time to be able to understand what really makes a difference.

NCUB
National Centre for Universities and Business

www.talent2030.org

www.ncub.co.uk



Predicting complex disease

Dr Sabine Langie, an expert in genotoxicology and epigenetics, describes her personal connections within the field, and how her early interest evolved into her current efforts to link early life exposures to biomarkers of complex diseases

Your research career has been very varied. Can you identify the common themes that have underpinned your work?

My research career has indeed undertaken some interesting turns. Overall, biomarkers of genome instability has been the common theme of my research. I obtained my PhD from Maastricht University in the Netherlands, studying the nutritional modulation of DNA repair, adapting a modified comet assay for DNA repair phenotyping purposes, and setting up a SNaPShot-PCR technique to determine genetic polymorphisms in DNA repair genes. Following this, I decided to obtain some experience abroad. Working as a postdoctoral researcher at Newcastle University, UK, allowed me to continue to research the effects of gene-environment/diet interactions on phenotypic markers like DNA repair and genome stability and, moreover, to learn new techniques, especially in epigenetics and early-life exposures. Since November 2012, I have been working at the Flemish Institute for Technological Research (VITO) in Belgium where I examine early-life exposures and their association with epigenetic marks (DNA methylation patterns) that underlie the developmental origin of complex diseases such as respiratory allergies.

What initially led you to work in this area? Were there any particularly inspiring events or people that drove your interest?

My parents for sure! They allowed me to choose science early in my studies. At 13, I had already chosen to study technical sciences. Biology and chemistry were my favourite topics. Moreover, my father is a doctor, which might have directed me towards biomedical sciences. In addition, when I was in my fifth year of secondary school my mother developed breast cancer. This background triggered me to pursue a scientific career, in order to be able to study the underlying mechanisms of complex diseases like cancer.

How have the fields of epigenetics and nutrigenomics developed since you began working in them?

I started working in the field of nutrigenomics during my PhD, and observed that the carriers of two variant alleles of XPC showed enhanced nucleotide excision repair capacity after a blueberry-apple juice intervention. Gene-diet interactions became a hot topic at the beginning of the 21st Century, moving from gene-targeted to genome-wide approaches once DNA micro arrays grew more popular and affordable. The first report on nutrigenomics was in 2001 and, since starting my PhD in 2004, reports on nutrigenomics/nutrigenetics increased about fivefold by 2008.

The term epigenetics on the other hand has been around since 1942. Before 1975, there had only been 13 scientific reports on epigenetics, but towards the late 1970s publications started increasing exponentially, reaching over 6,525 by the end of 2014. Mainly, associations between changes in DNA methylation and human health, ageing and age-related diseases were studied until 2008; at which point, consensus was reached on a definition of an epigenetic trait. When I started working on epigenetics in 2009, the focus shifted towards the developmental origin of complex diseases.

You were recently awarded a European Chemical Industry Council Long-Range Research Initiative Innovative Science Award. How important are awards such as this for young researchers, both in terms of recognition within your field and funding?

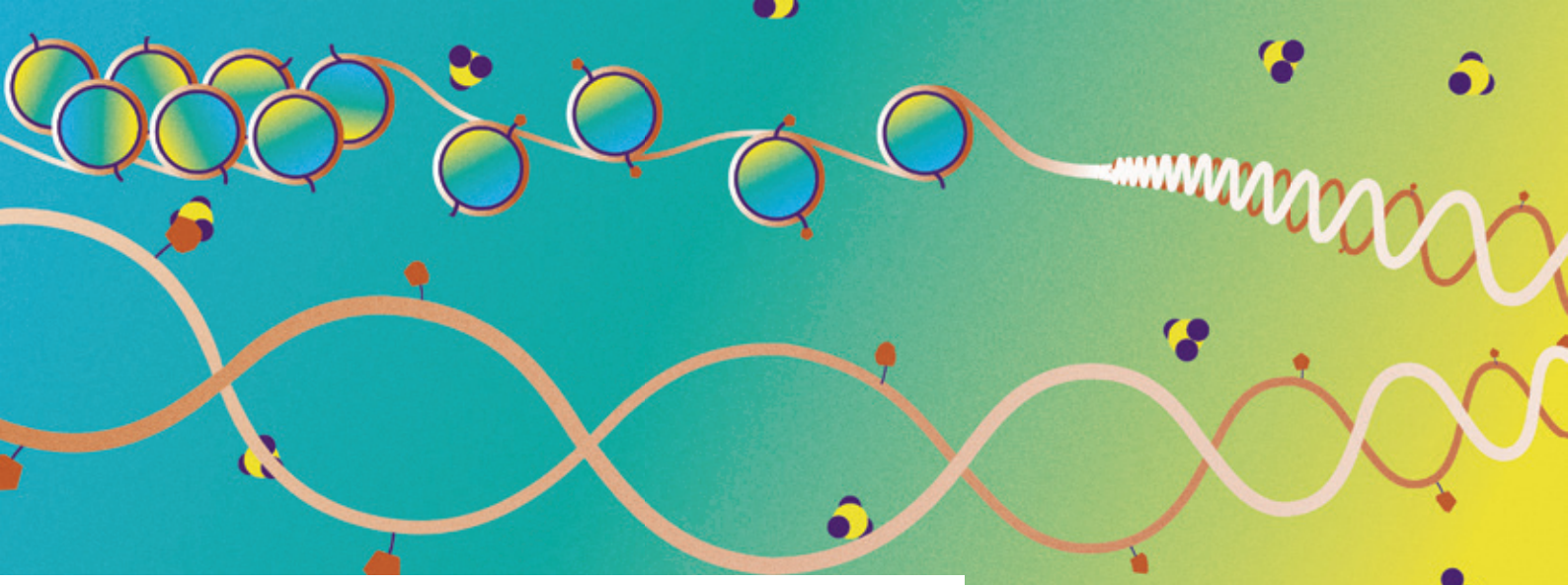
It is a real honour to win such a prestigious grant as a young scientist. It gave me the confidence that I am on the right research path. Such awards are a great opportunity to confirm the relevance of your work and to give your research project an extra boost. In my case, it enabled me to extend my research funded by AXA. These 'small' grants help you catch the bigger fish in the end, since they show your international mobility and that your research has been found relevant by the research community.

Looking back over your research career, is there a particular moment that makes you proud?

Although being granted awards, including the UK Environmental Mutagen Society Young Scientist Award of 2014, made me feel proud, finishing my PhD at the age of 25 is definitely the major milestone in my career so far. Hopefully, securing a European Research Council starting grant will be my next.

To close, what do you consider most important to successful research?

The key to success is not just papers in high impact journals, but also building an international network, mobility and acquiring new experiences and expertise in another institute or abroad. Science is a competitive world, but the die-hards always win.



The effect of early life exposures

Early life exposures can alter our phenotype as adults. Investigators based at the **Flemish Institute for Technological Research (VITO)**, Belgium, are studying this aspect of gene-environment interactions in order to understand the earliest beginnings of disease

THROUGHOUT OUR LIFESPAN, we are exposed to countless chemicals in the environment. Moreover, exposure to certain foreign agents or dietary compounds early in life can lead to susceptibility to diseases in adulthood. It is well known that chemicals in the environment can cause damage to our DNA. If this damage is not corrected by DNA repair mechanisms, damaged sites (lesions) can become mutations and ultimately lead to cancer. This predisposition to disease can also be mediated via epigenetic changes – the modifications that take place 'on top of' genes, without altering the DNA sequence. There are many chemical tags covering our DNA (which together make up the epigenome) that are able to activate and inactivate particular genes.

A growing body of evidence suggests that environmental exposures can change the methylation status of regulatory elements in DNA, which change the way genes are expressed, and therefore phenotype

Unlike the DNA sequence, the epigenome is flexible, and can respond to environmental factors, like diet and stress. These changes could explain the origin of complex diseases, from neurological disorders to allergies. Indeed, epigenetic factors can have an important influence on health, and epigenetic changes caused by environmental factors could be the missing link between early development and complex disease later in life.

Exploring this possibility is Dr Sabine Langie, research fellow at the Flemish Institute for Technological Research (VITO). Working in the Environmental Risk and Health Unit, she is studying the genetic impact of early life exposures. Langie hopes to identify the markers of epigenetic change, assess their relationship with environmental factors and, ultimately, use them to predict the onset of disease.

A DELICATE BALANCE

In 2010, Langie investigated one of the major DNA repair processes: nucleotide excision repair (NER). NER removes bulky DNA adducts resulting from exposure to chemical carcinogens, such as ultraviolet irradiation, and is important for maintaining genomic integrity.

The vital process of DNA repair is modulated by oxidative stress, the imbalance between the formation of reactive oxygen species and antioxidants. In 2010, building on previous *in vitro* studies showing inhibition of NER by oxidative stress, Langie obtained further insight on the links between oxidative stress and NER activity. She achieved this by inducing oxidative stress in newborn piglets, chosen for their poorly developed antioxidant systems.

The team also investigated the effect of maternal supplementation with an antioxidant-enriched diet. Amazingly, they found that supplementation reduced the number of adducts found in DNA. In addition, NER capacity in offspring that did not receive antioxidants was significantly reduced after birth. Taken together, their findings suggest that NER is reduced by oxidative stress *in vivo*, however, this effect can be counterbalanced with an antioxidant-enriched diet.

Langie has more recently studied the early-life exposures process in mice. In a paper published in *The FASEB Journal*, Langie examined the combined effects of maternal folate depletion and high-fat feeding from weaning, hoping to shed light on the mechanisms through which nutritional factors modulate DNA repair in the offspring. This time, they focused on base excision repair (BER), the primary repair pathway for damaged bases. Interestingly, they found that low folate increases BER in early life (at weaning), but the effect is the opposite in adulthood, when the offspring showed decreased BER. When combined with a high-fat diet, the reduction was even more pronounced. Thus, it seems a lack of folate during early life may inhibit DNA repair in adulthood, having a damaging health impact and perhaps predisposing an individual to other adverse life styles.

METHYL MARKS

After dedicating much of her early career to the nutritional modulation of DNA repair, Langie is now mainly focusing on epigenetics. Epigenetics responds dynamically to the environment, reacting to stress, diet, behaviour and toxins to regulate gene expression. "While our DNA, our genetic blueprint, determines the way we appear, epigenetics is responsible for the details," explains Langie.

There are many different types of epigenetic mark, each of which leads to different processing of DNA. The particular mark Langie is researching is DNA methylation, the most studied epigenetic modification, in which a

methyl group is added to DNA on a cytosine residue. DNA methylation is used to 'switch genes off', and is important in many cellular processes, including embryonic development.

A growing body of evidence suggests that environmental exposures can change the methylation status of regulatory elements in DNA, which change the way genes are expressed, and therefore phenotype. "Exposure of mothers-to-be to chemical compounds can alter epigenetic marks on their babies' DNA, turning some genes on and others off, and consequently changing the baby's risk for allergy," Langie elaborates.

AN ENVIRONMENT-DRIVEN EPIDEMIC?

Understanding risk for allergy is important, as allergic diseases are a significant global health problem, increasing both in frequency and severity. Although genetic predisposition is a known risk factor, the recent increase in prevalence has taken place too quickly to be put down to genetic changes in the population alone. Instead, it is thought that lifestyle factors have contributed to risk. In particular, prenatal and early life exposures are of great interest. While the underlying molecular mechanisms are largely unknown, it appears that epigenetic changes could be responsible.

To investigate this further, in an ongoing AXA-funded project Langie is exploring the idea that environmental exposures during pregnancy can affect the immune system in the child, studying the correlation between epigenetic marks found at birth and the later development of allergic disease. Using the combined power of molecular biomarkers and birth cohort data, the study has made impressive progress towards identifying risk factors: "We have found differentially methylated regions on DNA from allergic compared to non-allergic children. Interactions of dietary and environmental exposures during pregnancy with these allergy-related changes are now under investigation," adds Langie.

Thanks to funding from the European Chemical Industry Council Long-Range Research Initiative, Langie has been able to extend the project. She has now collected questionnaires and saliva samples from over 133 mother-child pairs, which she will use to determine if epigenetic changes in allergic children are due to chemical exposure during pregnancy, and if such epigenetic marks can be detected in saliva.

Together, these two studies have enabled Langie to establish a novel epigenetics platform to analyse DNA methylation patterns, using both a gene-targeted and a whole-genome approach. The results of these projects may lead to a preventive method to protect the children of exposed mothers-to-be, reducing the global burden of allergic disease. An impressive and motivated early career researcher, Langie has similarly ambitious plans for the future: "I aspire to have my own small group one day. At the moment, I am applying for a European Research Council starting grant. So fingers crossed!" she concludes.

THE COMET-BASED DNA REPAIR ASSAY

In her studies of early-life exposures, Langie has applied the comet-based *in vitro* DNA repair assay, which can be used to assess the capacity of cells for DNA repair.

Previously, experiments to measure DNA repair relied on following the decrease in DNA damage over time after exposing the cells to chemicals or ionising radiation – a time-consuming and laborious approach.

The comet-based *in vitro* DNA repair assay is much more effective for biomonitoring studies. It is based on incubating a cell extract with a DNA substrate containing specific lesions, such that DNA incisions accumulate. First developed to measure base excision repair in lymphocytes in the early 2000s, it has since been adapted for other lesions and their repair pathways, and for tissue as well as cells.


©CBAV, Newcastle University

ENVIRONMENTAL PROGRAMMING OF RESPIRATORY DISEASE

KEY COLLABORATORS

Professor Wim Vanden Berghe; **Dr Katarzyna Szarc vel Szic**, Department of Protein Chemistry, Proteome Analyses and Epigenetic Signaling, University of Antwerp, Belgium • **Professor Guy Van Camp**, Department of Human Molecular Genetics, University of Antwerp, Belgium • **Dr Diether Lambrechts**; **Matthieu Moisse**, Vlaams Instituut voor Biotechnologie, Vesalius Research Center, KU Leuven, Belgium

Ongoing collaborations on the comet-based DNA repair assay:

Professor Andrew R Collins, Institute of Basic Medical Sciences, Department of Nutrition, University of Oslo, Norway • **Dr Amaya Azqueta**, Department of Pharmacology and Toxicology, University of Navarra, Spain

PARTNERS

University of Antwerp, Belgium • Vlaams Instituut voor Biotechnologie, Belgium • Provincial Institute of Hygiene, Belgium • The Flemish Policy Centre of Environment and Health, Belgium

FUNDING

The Flemish Environmental Health surveillance programme is commissioned, financed and steered by the Ministry of the Flemish Community.

Postdoctoral fellowship from the AXA Research Fund and Cefic-LRI Innovative Science Award 2013.

Previous postdoc at Newcastle University, UK, supported by the Centre for Brain Ageing and Vitality (CBAV) and funded through the Lifelong Health and Wellbeing cross council initiative by the Medical Research Council, Biotechnology and Biological Sciences Research Council, Engineering and Physical Sciences Research Council and Economic and Social Research Council in the UK.

CONTACT

Dr Sabine Langie
Research Fellow

Flemish Institute for Technological Research
Environmental Risk and Health unit
Industriezone Vlasmeer 7, 2400 Mol
Belgium

T +32 14 33 51 36
E sabine.langie@vito.be

https://vito.be/en

http://bit.ly/ResearchGate-SabineLangie

http://bit.ly/Linkedin-SabineLangie

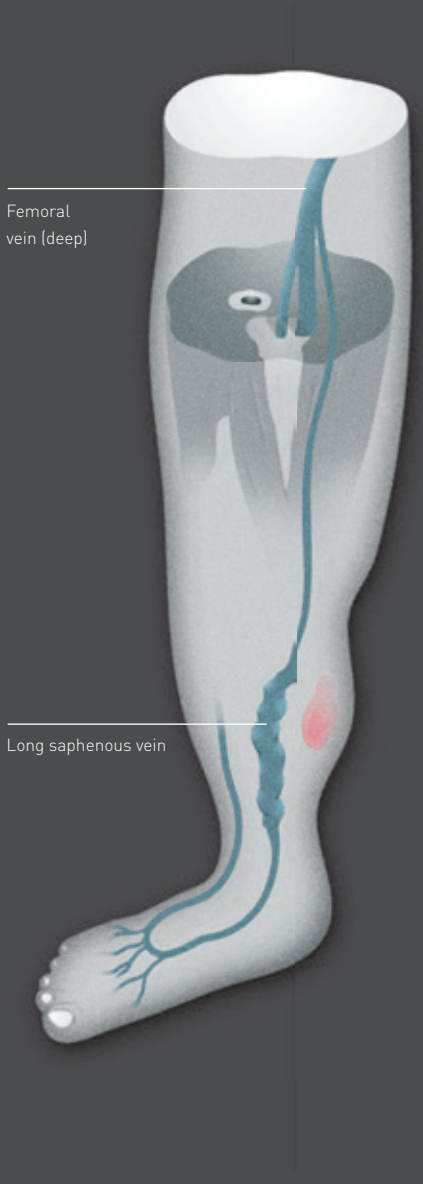
Frontiers: http://bit.ly/Frontiers-SabineLangie

SABINE LANGINE has been working at the Flemish Institute for Technological Research (VITO) in Belgium since 2012 on an AXA and Cefic-LRI funded project studying 'Allergy: environmental and nutritional programming in childhood'. As a postdoc she worked at Newcastle University, studying the modulation of epigenetic modifications and DNA repair in brain. Langine's PhD at Maastricht University focused on nutritional modulation of DNA repair.

Assessing aspirin in venous leg ulcers

Dr Carolina D Weller is conducting a world-leading study to assess the effects of aspirin on venous leg ulcers. Here, she explains the important potential of this common medication for a condition that is likely to increase in prevalence as the population ages

VENOUS LEG ULCER



Could you briefly discuss the Aspirin in Venous Leg Ulcer (ASPiVLU) study?

The aim of ASPiVLU is to ascertain whether low-dose aspirin should routinely be given to people diagnosed with a VLU to improve wound healing and decrease ulcer recurrence. This research is important because VLU is a common and costly condition that results in significant patient suffering. If an already approved drug could be used to reduce healing time, this would significantly reduce resource use and improve patient quality of life. Since aspirin is generally safe, cheap, well tolerated and widely available, the potential impact on this population is important.

The primary objective of this study is to determine whether aspirin, as an adjunct to compression, improves venous ulcer healing. The secondary aim is to determine the effects of aspirin on venous ulcer recurrence after healing. We will measure serum inflammatory markers and hospitalisations to shed light on the mechanism of aspirin's effect and to explore its impact on other important health outcomes.

Can you elaborate on the possible causes of VLU and how the condition affects everyday life?

Chronic VLUs are wounds of the lower limb caused by a diseased venous system resulting in chronically swollen legs and damage to the tissues around the ankles. VLUs take several months and sometimes years to heal, during which time they result in significant patient suffering and substantial cost to the health system.

Many patients do not adhere to compression therapy – a tight bandage applied to the lower limb – mainly because it can be painful, inconvenient for everyday life and may prevent the use of normal shoes. If aspirin could reduce the time of healing, this would be a significant breakthrough.

Could you describe the methodology you propose to use in your double-blind, multicentre, placebo-controlled trial on the effect of aspirin treatment?

We will recruit participants to investigate the effect of aspirin when combined with compression, compared to placebo combined with three-layer compression in adults confirmed to have a VLU.

We will assess the effect of aspirin on healing and ulcer recurrence. The primary outcome will be assessed at 12 weeks and, once healed, all participants will be followed monthly up to 52 weeks to measure the number of VLU recurrent episodes. We will recruit 286 patients over the next three years from hospital outpatient wound clinics in Australia.

By what means will you assess proof of healing?

The primary endpoint will be the time to complete healing of a participant's target ulcer at or before 12 weeks after randomisation. Proof of complete healing will be measured by an independent expert review of digital photos of the ulcer taken at baseline and fortnightly to 12 weeks or until healed, whichever occurs first.

The ulcer will be photographed using a digital camera to allow independent verification of ulcer size and proof of healing – 100 per cent epithelialisation with no scab and no exudate. A paper ruler with mm/cm markings will be used in each photo next to the ulcer to verify size.

Do you foresee any major challenges associated with this study? If so, what actions will you take to mitigate them?

The main challenge that we might have is recruiting sufficient participants into the trial. To ameliorate this, we have identified additional wound clinics across Australia that we can incorporate into the trial if necessary to ensure that the required number of patients can be recruited within three years.

Are you collaborating with any other researchers or laboratories in the course of your investigations?

Researchers based at Monash University are collaborating internationally on the largest trial conducted in Australia. An individual patient data meta-analysis with research groups from the UK and New Zealand is being discussed by principal researchers from Monash University, the University of Auckland and St George's, University of London. The study will assess the potential advantages of daily low-dose aspirin for healing VLUs.

Ulcer healing

Researchers at **Monash University** in Melbourne, Australia, may have found an affordable and accessible new treatment for the most common type of leg ulcer, which causes pain and incapacitation in the elderly

VENOUS LEG ULCERS (VLUs) are painful sores, most often on the inside of the leg just above the ankle, which can take many weeks to heal. In over 90 per cent of cases they are due to the improper functioning of the venous valves in the legs. This condition becomes more prevalent with age, and thus represents an increasing burden on healthcare systems as a consequence of population ageing, and as the risk factor-associated epidemics of obesity and diabetes continue to expand.

In Australia, this condition affects an estimated 400,000 people, with an annual economic burden of billions of dollars. Dr Carolina Weller is a senior research fellow in the Department of Epidemiology and Preventive Medicine at Monash University, where she is working to address this problem; developing and testing interventions to improve the quality of care received by those with such chronic wounds.

Weller wants to improve the treatment of VLUs which, in its existing state is not only costly, but also ineffective. The current standard is the use of compression bandaging to counteract the elevated pressure in the leg veins and allow the ulcer to heal. Two to four layers of bandage are usually placed over a dressing, with high pressure particularly applied at the ankle. Patient adherence to compression therapy, however, is poor, and bandage applications are inevitably inconsistent. As a result, one in three patients with a VLU will experience over 10 episodes of ulceration in their lifetime, with recurrence rates placed between 30 and 80 per cent. A 2004 study found that almost half of venous ulcers had recurred by the fifth year of healing, and it is not uncommon for them to reappear as soon as three months after healing. The need for an alternative is clear.

ASPiVLU IS INVESTIGATING THE EFFECTIVENESS OF ASPIRIN IN VLUs IN ORDER TO:

1. Improve healing in people with leg ulcers in Australia
2. Help policy makers to reach more informed decisions on VLU programme funding
3. Improve the treatment advice offered by clinicians
4. Help patients with VLUs make decisions about preventive treatment

AN UNLIKELY SOLUTION

There is evidence to suggest that aspirin – a common and readily available drug – could address this need. The therapy suppresses platelet aggregation and reduces inflammation to minimise pathogenicity and vessel permeability. Corroborating the theory, data from two clinical studies in the UK and Spain show that aspirin, when paired with compression therapy, can improve VLU healing rates, prevent recurrence and reduce treatment costs.

Unfortunately, the previous two trials were small, in total assessing only 71 participants, and insufficient to meet the high standard of randomised controlled trial required to demonstrate aspirin's potential. Hence, Weller set up the Aspirin in Venous Leg Ulcer (ASPiVLU) study to test the clinical effectiveness of aspirin as an adjunct to compression therapy for healing chronic VLUs. This randomised, double blind, placebo-controlled trial will provide robust evidence of aspirin's action. "We have sought to address the methodological and clinical limitations of previous studies and produce conclusive results," enthuses Weller.

One in three patients with a venous leg ulcer will experience over 10 episodes of ulceration in their lifetime

CLINICAL EFFECTIVENESS OF ASPIRIN IN HEALING CHRONIC VENOUS LEG ULCERS

OBJECTIVES

To investigate the potential benefit of using aspirin in addition to compression treatment for venous leg ulcers in order to improve rates of healing, reduce recurrence and decrease the financial burden that this condition places on healthcare systems.

KEY COLLABORATORS

Professor John McNeil; **Professor Martin Underwood**; **Associate Professor Ian Darby**; **Associate Professor Anna Barker**; **Associate Professor Terry Haines**; **Dr Stephanie Ward**

PARTNERS

Austin Health; Alfred Health; Western Health, Victoria • Royal Hobart Hospital, Tasmania • Westmead Hospital Vascular Clinic, New South Wales • Prince Charles Hospital Wound Clinic, Queensland

FUNDING

National Health and Medical Research Council (NHMRC)

CONTACT

Dr Carolina D Weller
NHMRC Postdoctoral Research Fellow and Senior Research Fellow

Faculty of Medicine, Nursing and Health Sciences
School of Public Health & Preventive Medicine
Department of Epidemiology & Preventive Medicine
The Alfred Centre 99 Commercial Road,
Melbourne 3004, Australia

T +61 399 030 623
E carolina.weller@monash.edu

www.med.monash.edu.au/epidemiology
www.med.monash.edu.au/sphpm/aspivlu-study.html

@CarolinaDWeller

DR CAROLINA WELLER is a NHMRC/Primary Health Care Research, Evaluation and Development fellow in the School of Public Health & Preventive Medicine based at the Alfred Hospital. She is an emergency nurse who completed her PhD in Epidemiology in 2011, investigating interventions to improve quality of care for people with venous leg ulcers.

Weller's research interests are in clinical epidemiology, evidence based practice, health services research including randomised controlled trials and translational research. Her past career appointments have included clinical consultant, researcher, health policy advisor and academic. She leads a research team to test interventions to improve patient safety and quality of care for people with chronic wounds.

In addition, Weller is the Early Career Research representative of Australian Wound and Tissue Repair Society, a founding member of the NHMRC venous ulcer guideline development advisory group, a member of the Council of Australian Governments Long Stay Older Patients' Advisory Group (skin integrity), an expert panel member on the Therapeutic Guidelines Wound Group and advisor to the Department of Health Victorian Wound Management Project Group.

STUDY DESIGN

In the trial, participants recruited from seven speciality wound clinics in Australia will be randomly assigned to use aspirin combined with three layer compression, or placebo pills and compression, every day for a year. The primary outcomes will be assessed at 12 weeks and once the participant's ulcer has healed. After this time participants will be monitored for recurrence at monthly intervals until the year is up, but all participants will remain in the trial for wound management, regardless of whether their wound has healed.

The dosage of aspirin to be used is critical, and was carefully decided based on evidence. The previous trials showed that 300 mg of aspirin administered daily can effectively accelerate ulcer healing and reduce recurrence rate, with minimal adverse effects. Alongside this, *in vivo* studies have shown that this dosage can suppress inflammatory markers and promote ulcer healing, while taking more aspirin can be associated with a larger risk of bleeding and gastrointestinal side effects. Thus, those randomised to the aspirin arm will receive 300 mg of aspirin daily.

Many outcomes will be measured throughout the trial (see boxout right), to assess the effectiveness of the treatment but also to understand its mechanism. Using serum collected from patients, the team will measure their inflammatory cytokine profiles. This will help to explain aspirin's effects on harmful pro-inflammatory macrophages, and perhaps shed new light on how inflammatory mediators impair healing in chronic VLUs.

A POWERFUL CONCEPT

If aspirin coupled with three-layer compression is found to be effective in this trial, it could have a significant impact on medical care and health policy worldwide. "The ageing of the population will progressively increase the numbers for whom these results are applicable," hypothesises Weller. "A method of effectively improving the healing rates with an ageing population is a high priority."

If the trial is successful, it could revolutionise the treatment paradigm for this common and painful ailment; improve healing rates, reduce the time to healing, and decrease ulcer recurrence. In addition, as aspirin is an affordable medication, its access will not be limited by the income or insurance status of a patient.

Following the ASPiVLU trial, Weller may be able to demonstrate a partial solution to the increasing burden of VLUs. Her study stands to increase confidence in the clinical use of aspirin, demonstrating not only that the drug works, but also that its benefits outweigh its risks. When the final results are published, attention will turn to clinical use. As aspirin is already an approved drug, the translation of this novel finding to the clinic should proceed rapidly, just as aspirin quickens the pace of recovery for VLU patients.

TRIAL ENDPOINTS

The primary endpoints of a clinical trial measure outcomes that will help answer the most important question being asked, in this case, does aspirin improve the healing of VLUs?

Ulcer size
The size of the ulcer will be measured at baseline and fortnightly until the ulcer is healed

Proof of healing
Healing will be measured via an independent expert review of digital photographs

Secondary
The secondary endpoints ask other relevant but less important questions, for example, does the therapy reduce the cost of treating patients?

Serum samples
At baseline and at week six, blood will be taken from participants for later assays of inflammatory markers

Wound pain score
The participants' assessment of pain will be measured on a standardised 0-100 scale

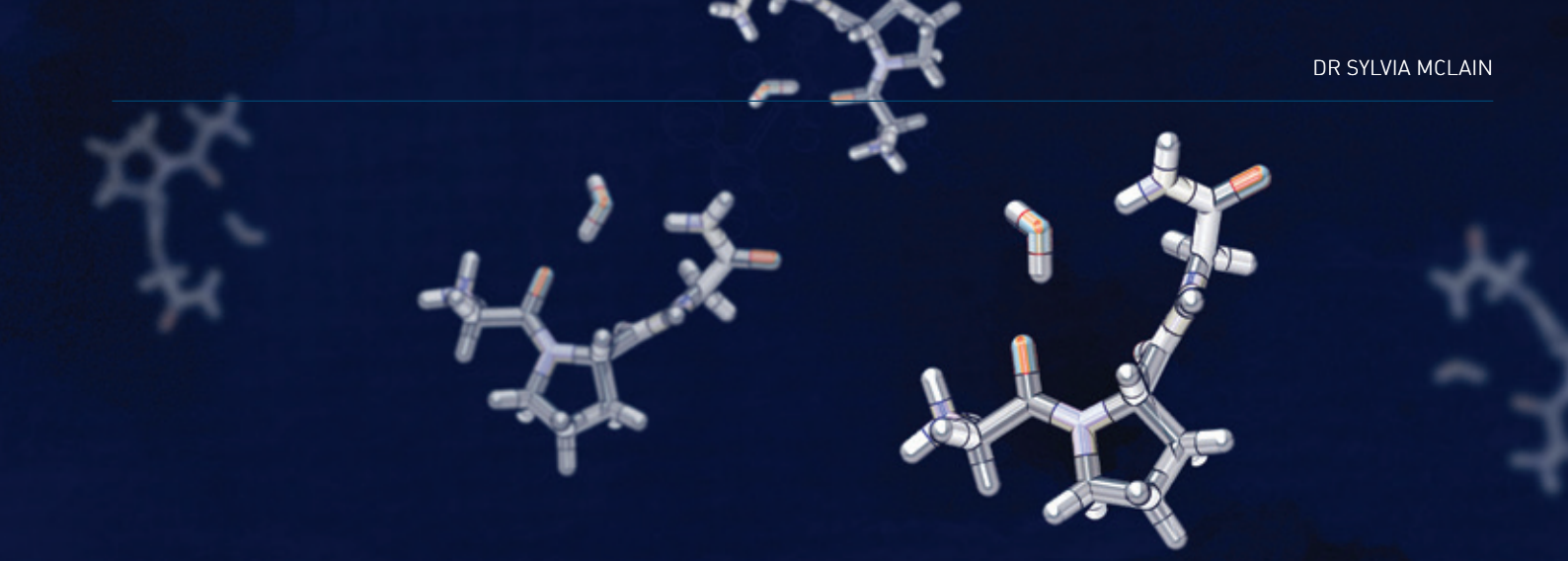
Quality of life
Health-related quality of life and wellbeing instruments will be used

Recurrence
The trial will assess ulcer recurrence in participants with healed VLU at monthly intervals

Adherence to compression
Participants will report how often they adhered to wearing their bandage

Adherence to medication
At treatment visits, participants will be asked to present medication containers for a pill count

Adverse events
Each follow up visit will assess adverse events using open-ended questions and a checklist



Biomolecular interactions

Dr Sylvia McLain is fascinated by how biological systems function and form at the atomic and molecular scale – and her dynamic research group, which operates at the intersection between biology and physics, is attempting to forge a deeper understanding of this

What are the primary aims and objectives of the McLain Group within the Department of Biochemistry at St Peter's College, University of Oxford, UK?

My research group focuses on understanding how biological molecules interact with each other at the atomic scale in solution. To this end, we investigate the association and structure of biomolecules – such as lipids, peptides and sugars – in physiological solutions. This research aids understanding of the fundamental principles that underpin molecular association and hydration and how this leads to the development of life at the microscopic level. Additionally, at St Peter's I tutor undergraduates in biophysics and biological chemistry.

Having gained wide and eclectic personal and professional experience, do you feel well-prepared to tackle your current research into understanding the physics of life?

I certainly feel prepared to tackle this research, but it is difficult to know which part of my training this can be attributed to. From my perspective, one of the key characteristics of scientific research is its dynamism. It is not simply a case of doing experiments and obtaining obvious answers – instead, the pursuit of science necessitates flexibility, readiness to admit mistakes and willingness to carry on conducting experiments.

Who currently makes up the McLain Group and what expertise do they provide your studies?

My research group contains myself, a postdoctoral researcher, two PhD students and a Master's student. My current postdoc, Dr Richard Gillams, has a PhD in Computational Chemistry while my two PhD students have backgrounds in physics and biochemistry. As our group relies on an eclectic mixture of experimental techniques and computation, I find that it is more stimulating and scientifically productive to have a range of group members with a variety of different experiences and backgrounds. In addition, we collaborate with the biochemist Professor Christina Redfield, also based at Oxford University, who is an expert in solution nuclear magnetic resonance (NMR) of biomolecules.

How important is collaboration with researchers outside the University who possess complementary skills?

Collaboration with other scientists is very important to the work of my team. At present, we are engaged in collaborations with several scientists from different universities but our main partners are Dr Chris Lorenz from the Department of Physics at King's College London, who is a molecular dynamics simulation expert for biological systems, and Dr Luis Carlos Pardo from the Department of Physics in the Universitat Politècnica de Catalunya in Spain, who is an expert in disordered materials and the simulation of liquids.

You provide open access to your RDF (g(r)) database. Do you feel it is important to be open about the scientific process as a whole?

I think that providing data, once published, is fundamentally important and that openness about results and methodology is essential for furthering the scientific process. In an ideal world, all results would be open to everyone and this is what we should be aiming for. In principle I support open-access journals, but the difficulty is how this is funded since publishing is expensive. With research budgets becoming even more limited, I worry that enforcing publication in open-access journals would take more money away from research budgets so that science – rather than the publishing journals – would take the hit.

Do you see your studies continuing along the same path or changing course in the coming years? If the former, on what elements of protein folding will you focus your attention?

In truth I would envision a bit of both. In terms of the Group's current work, we are still in the process of collecting evidence to support our working hypotheses; in science this can take a very long time and, as always, access to research funding. However, there are always new interests within the Group and we are already thinking about how we can branch out our research into a number of other areas, such as understanding drug interactions in solution.

In regard to our protein folding studies, we have already begun looking at larger peptides with β-turn motifs, and we are now starting to look at small peptides which form helices in solution and can be denatured with urea. In addition to allowing us to assess the role that water plays in the formation of secondary protein structures, this will also allow us to address protein-urea interactions.

The water impact

The McLain Group is a multidisciplinary biophysics research team based in the Department of Biochemistry at the **University of Oxford** in the UK. Together, the researchers are providing new insights into the complex interactions of biological molecules in solutions

AS THE FOUNDATION of life on Earth, water plays an essential role in facilitating multiple biological processes. The adult human body, for instance, is comprised of about 60 per cent water and the solutions within the body enable the delivery of vital nutrients and oxygen to organs. However, little is known about the impact of water on the interactions of molecular biological processes. This is a significant knowledge gap, particularly because almost all natural biological processes occur in solution.

For instance, despite considerable progress in understanding the structure of folded proteins, it is unclear as to the exact role that water has in the folding process itself, in which amino acid chains form stable and biologically functional 3D structures. Starting with the Nobel Prize-winning scientist Christian Boehmer Anfinsen in the 1970s, many experiments over the past few decades have probed the driving force behind protein folding – and today technological advances have opened new possibilities for scrutinising this process through computational investigations. However, investigations in this field have been hampered by the high speed at which amino acid chains fold and by the fact that it is very difficult to determine how water interacts with proteins in solution at an atomic scale. There is therefore a need for further experiments that use cutting-edge techniques to examine the complex interactions between biological molecules in solution.

INGENUITY AND INNOVATION

The McLain Group – based in the University of Oxford's Department of Biochemistry – is a team of forward-looking scientists who are attempting to carve a deeper knowledge of biological interactions in physiologically relevant environments at the molecular level. Led by Dr Sylvia McLain, a UK Engineering and Physical Sciences Research Council Fellow and lecturer in Biophysics and Biochemistry in St Peter's College, this small but innovative group is drawing on a combination of experimental and computational methods to examine the interplay between biological molecules in nature. Excitingly, their research is paving the way for a more complete understanding of the biophysical mechanisms that underpin how biological systems function.

The small but innovative McLain Group is drawing on a combination of experimental and computational methods to examine the interplay between biological molecules in nature

The insights made by McLain and her team are only possible through the powerful technologies and novel experimental techniques that are at their disposal. For example, their neutron experiments take place at the ISIS neutron and muon source, a large-scale facility based at the Rutherford Appleton Laboratory in Oxfordshire, while detailed data is collected from solution-state nuclear magnetic resonance (NMR) and neutron scattering techniques performed in the Department of Biochemistry at Oxford. Neutron diffraction on solutions is particularly important as it represents a physiological environment and allows the measurement of the role of water in the hydration and molecular associations of biological molecules. Importantly, the

experimental data that the researchers collect feed into the creation of computational models that display 3D representations of biological molecules in solution.

PROBING PROTEIN FOLDING

The McLain Group's research findings are challenging historical assumptions about the hydrophobic and hydrophilic interactions involved in the protein folding process. While the traditional view holds that protein folding is induced as a result of water being expelled from the hydrophobic parts of the protein – a process termed the 'hydrophobic effect' – there is a lack of robust experimental data supporting this assumption. Indeed, recent studies conducted by McLain and her team – in collaboration with researchers at the University of Oxford, Kings College London and the John Carroll University, USA – have questioned this conventional understanding by providing initial evidence that points to the active role of water in the protein folding process. "Our investigations on small peptides and other biological molecules indicate that water might have a more direct role in biological association, structure and function than previously thought," elucidates McLain. "Specifically, the hydrogen bonding and water association with different parts of the biological molecules we have investigated imply that water is more than just the medium in which molecules interact with each other in nature."

In their studies, the researchers focused in particular on exploring the role of water in forming ß-turns. As a commonly occurring structural motif that enables the protein chain to fold back on itself, this characteristic – which is often found on the water-exposed surfaces of proteins – was traditionally thought to have been initiated by the amino acid sequences within it. However, experiments and computer simulations of the small peptides that form these folds in solution imply that water plays a fundamental role in guiding the protein to fold into a ß-turn conformation in the early stages. It is thought that water is able to do this as a result of hydrogen bonding interactions between Gly1 reside peptide oxygen with the amide(NH_2) cap of the peptide.

FUNDAMENTAL IMPLICATIONS

McLain and her team have begun to make important advances in determining the interplay between hydrogen bonding and hydrophobic forces that establish structure and subsequent function in cell membranes. However, much work remains to be done in this area – and the researchers are planning to continue their studies into how water affects biological phenomena such as protein folding, the formation of biological membranes and the penetration of small molecules into these membranes. To this end, they have launched several investigations into the complex role that water has in the formation and hydration of lipids in biological membranes. Moving forwards, they are particularly keen to interrogate different biological systems for evidence that confirms their working hypothesis that hydrophilic interactions are more important than hydrophobic interactions in molecular biological processes.

Excitingly, this small research group in Oxford could hold the key to understanding protein folding and other biological phenomena such as drug-protein interactions. Looking ahead, the implications of potentially overturning the dominant and widely held belief that hydrophobic interactions are at the root of the protein folding process are enormous: "It would have a major impact on our understanding of a large range of biological phenomena, including interactions in our bodies," McLain concludes. "It would change the fundamental way that we understand biology on the molecular scale."

PROMOTING PUBLIC ENGAGEMENT

As well as conducting research that grapples with questions on the physics of life, McLain is also passionate about engaging the public with science issues. She is therefore active in many outreach activities – including blogging, podcasts and media interviews – and takes her undergraduate teaching responsibilities very seriously, as this motivates her to think about scientific topics in new and innovative ways. Additionally, she is eager to see more diversity in STEM and to challenge the notion that it is an elitist field: "Science and other STEM subjects should be recognised to be as important as art, literature or indeed any other aspect of society," she asserts. "Science is for everyone and, as such, education and careers in the scientific field should be open to everyone."

MCLAIN GROUP

OBJECTIVES

To understand how biological molecules interact with each other on the atomic scale in solution, investigating the association and structure of biomolecules – such as lipids, peptides and sugars – in physiological solutions with an aim to understand the fundamental principles which underpin molecular association and hydration and how this leads to the development of life at the microscopic level.

GROUP MEMBERS

For a full list of Group members, please visit **http://bit.ly/mclaingroup**

KEY COLLABORATORS

Dr Chris Lorenz, King's College London, UK

Professor Christina Redfield, University of Oxford, UK

Dr Luis Carlos Pardo, Universitat Politècnica de Catalunya, Barcelona, Spain

FUNDING

Engineering and Physical Sciences Research Council (EPSRC)

CONTACT

Dr Sylvia E McLain
Group Leader, UK Engineering and Physical Sciences Research Council Fellow and Lecturer for St Peter's College Oxford in Biochemistry

New Biochemistry
Biochemistry Department
University of Oxford
Oxford
OX1 3QU, UK

T +44 1865 613 279
E sylvia.mclain@bioch.ox.ac.uk

www2.bioch.ox.ac.uk/mclaingroup

@girlinterruptin

DR SYLVIA E MCLAIN received her Bachelor's degree in Zoology from the University of Tennessee in 1994. After four years as a genetics technician in the Ecology and Evolutionary Biology department (University of Tennessee) she returned to the University and received her Master's degree in Science Education in 1999 and her PhD in Chemistry in 2004. High profile positions in the US and UK followed, until moving to the Department of Biochemistry, University of Oxford in 2011, where she now teaches biochemistry and biophysics whilst undertaking cutting-edge biophysics research.

DEPARTMENT OF BIOCHEMISTRY
UNIVERSITY OF OXFORD

CLOSING THE

ADVANCING GENDER EQUALITY IN SCIENCE HAS BECOME AN IMPORTANT GOAL FOR MANY ACADEMIC AND RESEARCH INSTITUTIONS IN THE UK AND WORLDWIDE. *INTERNATIONAL INNOVATION* SPEAKS EXCLUSIVELY TO SEVERAL LEADERS IN THE FIELD, ALL STRIVING TO COMBAT UNDERREPRESENTATION AND FURTHER THE CAREERS OF WOMEN SCIENTISTS

GENDER GAP

ATHENA SWAN CHARTER

In an exclusive interview, **David Ruebain**, CEO of Equality Challenge Unit, and **Sarah Dickinson**, Manager of its Athena SWAN Charter, talk to *International Innovation* about their work to promote gender equality in the STEMM subjects

ECU's Athena SWAN Charter has been developed to encourage and recognise commitment to combating underrepresentation of women in STEMM and advancing their careers in research and academia

How have your careers and past experiences led to your involvement in the Athena SWAN Charter?

DR: I'm a solicitor by background and used to be a partner in a law firm with a specialist practice in education and equality law. We took cases mainly involving children and students, particularly in the areas of equality issues, gender, race etc. When I left private practice I joined the Equality and Human Rights Commission as their Director of Legal Policy. I left there to become Chief Executive at the Equality Challenge Unit (ECU). My career path has always related to equality and diversity in some way or another.

SD: I'm a social scientist by background. After university I worked for the Royal Society of Chemistry. There I focused on the differences in the PhD experiences of men and women. After that I went to the University of Cambridge and oversaw the Women in Science, Engineering and Technology Initiative, and then I came to ECU to manage the Athena SWAN Charter. Although it was great to be involved at a local level in Cambridge, I was really keen to come back and work at a national level again.

Can you provide some examples of the broad problems that ECU was established to address and the context in which you work?

DR: ECU was established in 2001 in the context of the race equality duty. Most people think of equality law as the basic prohibitions – things you must not do: directly discriminate, indirectly discriminate, victimise, harass and, in the case of disabled people, not make reasonable adjustments. Some of these duties have been around since 1965. However, the law changed in 2000 to address systemic exclusion and disadvantage. So instead of just waiting for somebody to discriminate, harass or victimise, for example, the public sector duty requires public bodies, including universities, to take positive steps to try to eliminate any inherent bias or disadvantage against a community. ECU was set up then, to provide a central resource for universities to try to address the increasingly complicated areas of equality and diversity.

Our remit now is to advance equality and diversity for staff and students in the UK higher education sector. We are essentially a policy and research agency. All of our work is evidence-based. We have colleagues that conduct quantitative and qualitative analysis, from which we develop programmes such as Athena SWAN.

Why are the science, technology, engineering, maths and medicine (STEMM) subjects particularly affected by inequalities in gender and how do UK institutions compare to other countries in Europe and further afield?

DR: One activity that ECU does on an annual basis is to map the demographics of the UK higher education sector by protected characteristics: how many men and women there are, what jobs they do, who progresses and so on. In the case of students, we analyse and produce statistical reports looking at who studies what, who goes to university and what degrees they obtain. If you look at the professoriate in STEMM subjects – the most senior level in academia – there is a clear underrepresentation of women; around 15 per cent of all professors in those subjects are women. In engineering it's only about

CLOSING THE

THE ATHENA SWAN CHARTER COVERS:

Women in academic roles

Progression of students into academia

Working environment for all staff

9 per cent, and it is as low as 5 per cent in mechanical engineering. So in one sense SWAN focuses on those subjects where the underrepresentation of women is most acute. That doesn't mean to say there aren't problems in other disciplines. In fact, we are developing another charter – the gender equality charter mark – building on the knowledge and experience of SWAN to work with other disciplines.

SD: The lack of female professors means there are few role models. A lot of women feel they can't conduct research as well as have a family, and many leave at the transition between PhD and postdoc, or during their postdoc where the necessity to move between institutes can be off-putting to women thinking of starting a family. In lab-based research especially, a culture of presenteeism can lead to the perception that you can't leave your work or go home. There's a perception that you can't balance having a life with being a scientist.

There is evidence to suggest that some subjects, eg. chemistry, have a particularly masculine culture that can also deter women from wanting to continue an academic career.

There are other aspects of STEMM academia aside from culture and a lack of flexibility that seem to pose barriers to women's career progression. These include appointment and promotion processes, policies that may not be clear or transparent and a lack of career development support.

Similar challenges are also found outside of the UK, but it's important to recognise that even within a country, issues will vary according to the institution and subject area. Ireland for example (where ECU has just extended Athena SWAN) has a smaller sector, less movement and more reliance on the industrial sector for career progression.

To what extent has the Charter grown since its launch in 2005?

DR: When the Charter was launched it had 10 voluntary member institutions. Now it has 120 member institutions and there are not many UK higher education institutions with STEMM departments that are not participating. In my opinion, the Charter is now seen as a standard to which most universities feel they must aspire or meet. It has almost become an issue of universities feeling they can't afford not to be successful in this area because it helps them attract staff and maintain their positions as leaders.

How do you work with institutions to encourage them to adopt its principles?

SD: Equality in science is important economically. Over 60 per cent of science undergraduates are women, but men hold 85 per cent of professor appointments. This means that we are leaking a massive proportion of potentially outstanding academic research scientists at various points in the academic career pipeline. If the UK wants to remain at the forefront of scientific research, we cannot afford to lose this supply and institutions are now realising this.

We have set up regional networks through which the member institutions can talk to each other and share good practice. At each of these meetings we answer questions about the process and give a presentation and update. In addition, we also run workshops to help with the application process. We have working groups for different areas: for research institutes not affiliated with higher education and also for medical and dental schools, to ensure that we are supporting those adequately.

What do you foresee for the development and impact of the Charter in the coming years?

DR: We need to ensure that the Charter continues to remain effective and potent. Furthermore, that it can withstand some of the challenges that are inevitable when you have a complicated and comprehensive programme that is supporting institutions to engender dramatic change. Otherwise, I hope that the Charter can grow beyond UK higher education into other sectors; possibly those allied to further education and also other jurisdictions around the world. Ultimately we want the impact to transform the environment for women in STEM subjects – both in teaching and research. That's what we believe the Charter can do, but it's challenging, and therefore we need to make sure that it continues to be effective, and demonstrably so, for everyone involved.

www.ecu.ac.uk

Equality Challenge Unit

GENDER GAP

ATHENA SWAN AWARDS:

BRONZE AWARD – recognises a solid foundation for eliminating discrimination and developing an inclusive culture that values all staff

SILVER AWARD – recognises a significant record of activity and achievement by the institution in promoting equality and in addressing challenges across the whole institution

GOLD AWARD – recognises sustained progression and achievement in promoting gender equality and to address challenges particular to the discipline

JACKIE HUNTER, CEO for the Biotechnology and Biological Sciences Research Council

With a woman at the helm, the BBSRC is working hard to promote gender equality within the research teams it funds, by tackling unconscious bias, improving equality policy and promoting the benefits of the Athena SWAN Charter

As only the second female CEO of BBSRC, you have said that you want to use your time as Chief Executive to champion equality. Can you elaborate on some of the ways in which you intend to do this?

Equality and diversity are really important in any job, and particularly in science. I hope to drive this agenda in BBSRC, and also more broadly in Research Councils UK (RCUK). I'm going out as much as I can, talking to researchers about the importance of diversity, how women can be more strategic about their careers, the importance of sponsorship and mentorship, and how issues such as unconscious bias can play a role.

BBSRC has analysed the proportion of grant applicants who are women and found it to be less than 20 per cent, and women that do apply tend to be a couple of percentage points less successful. One of my aims is to perform a root cause analysis to find out why. Understanding the root cause of differences is important for seeing what types of intervention would have the most effect.

Every year we send out letters about success rates to the top 30 institutions that receive BBSRC funding. This year we have also included the gender statistics so they can consider whether they are reflective of their pool of potential applicants. We are also going to be carrying out unconscious bias training for all our committees, appointment panels and council, and also my executive team.

When awarding funding, how does BBSRC ensure gender equality?

It comes down to looking at the panel, making sure we have a group of individuals that is ethnically diverse and gender balanced. It then comes back to unconscious bias. At the moment we're not planning on doing anything as radical as positive discrimination, but it is important to take positive steps such as unconscious bias training. I don't think I'm in a position to say that we really understand what the root causes are, and until we can do that, it's difficult to see what interventions would have the most effect, but we are committed to understand what's behind these patterns.

What do you think are the biggest obstacles that female researchers face?

A huge obstacle is the lack of sponsors – people who identify opportunities and act as your ambassador. Professor Peter Goodfellow – then Head of Research for SmithKline Beecham and previously Professor of Genetics at the University of Cambridge – recommended me for my previous BBSRC Strategy Panel role. I did that and eventually ended up on the BBSRC Council. I would not have thought of applying myself. Often, the first names that come into people's mind when they're asked

CLOSING THE

> "It's a question of diversity. If you've got a problem, you always get to a better solution if you have more than one brain working on it. It's about recognising the power of diversity and how it can add to your ability to solve problems or manage more effectively"

for recommendations for panels etc, are men. We need to prompt people to say, 'great, you've given me a man's name, now give me an equally competent woman as well'.

I think that women also need to recognise that networking is important, and more strategic about their careers and be aspirational. However, it's also about men being more diverse in their approach – less hierarchical, with more recognition of different approaches to interactions and running projects, etc.

For me it's a question of diversity. If you've got a problem, you always get to a better solution if you have more than one brain working on it. It's about recognising the power of diversity and how it can add to your ability to solve problems or manage more effectively.

How involved is BBSRC with the Athena SWAN charter?

BBSRC works with Athena SWAN; we were involved in the pilot they did with research institutions, and two of our institutes have awards – the John Innes Centre, Norwich, has a silver and the Pirbright Institute, Woking, has bronze. Athena SWAN wanted to look at how they could work with institutions rather than universities, so we are collaborating within the family of our strategically funded institutes to move them towards Athena SWAN accreditation. I've also conducted an analysis of the universities we fund, and most of them have Athena SWAN bronze awards. At the moment, adoption by an institution doesn't influence our funding decision, but that doesn't mean it won't in the future.

SOAPBOX SCIENCE

Dr Nathalie Pettorelli is a research fellow at the Zoological Society of London and **Dr Seirian Sumner** is a senior lecturer at the University of Bristol. In 2011, they founded Soapbox Science, and have since organised a series of public science communication events that aim to raise the profile of women in science. Having grown from one annual event in London, 2014 saw their reach widen to include events in Bristol, London and Swansea in the UK, and Dublin, Ireland

Can you introduce Soapbox Science and summarise what you are trying to achieve?

NP: Soapbox Science is a grassroots approach to bringing science to the masses; putting scientists at the cutting edge of their fields on soapboxes on busy urban streets to talk to the passersby about their science. The twist is that only women stand on our soapboxes, and that's because Soapbox Science aims to make a real difference to the visibility and perception of women in science.

SS: Our format was inspired by the famous Speakers' Corner in London's Hyde Park, which has been an arena of free speech for over 100 years. Speakers' Corner gave a voice to oppressed Victorian Britons, and played a

GENDER GAP

> "Soapbox Science is a grassroots approach to bringing science to the masses; putting scientists at the cutting edge of their fields on soapboxes on busy urban streets to talk to the passersby about their science"

key part in the revolution that produced the democratic culture we enjoy today. Science needs a revolution with respect to how women are treated and supported in scientific environments. Soapbox is our effort towards achieving this.

What motivated you to take action and organise the Soapbox Science communication events?

NP: 'Be the change you want to see' – there is no point blaming someone else for failing to act on something you've decided not to act on. We currently live in a world in which female scientists' achievements are less likely to be celebrated; in which female scientists earn less, are less likely to be listed as either first or last author on a paper, and are less likely to be asked to join editorial boards. Gender is clearly shaping who can do what in science today. This is something I do not accept, not only because I am a woman, but also because I train women. Soapbox is my way to push for the change I want to see.

Who are the different stakeholder groups that you hope to influence?

SS: We are targeting three different audiences: 1) the public, by aiming to give them the chance to engage directly with an active scientist – we remove any middle-man media; 2) the scientists, by giving them a very public platform from which to share their work and improve their own visibility; and 3) the next generation of women in science, by aiming to provide them with role models and to make the discussion on women in science more public, open and transparent.

Other than the Soapbox Science events, do you participate in any additional activities to promote the position of women in science?

NP: As a scientist, it's easy to promote the position of women in science on a daily basis. You can, for example, make sure that you suggest both men and women as potential speakers at international conferences, workshops or seminars; or you can top-up females' suggestions when it comes to identifying new editorial board members. Small changes can make a difference.

SS: Soapbox's effort go beyond the live events. We run a dynamic website where we host blogs about women in science – this provides a useful forum for women to air their feelings and experiences about life as a female scientist, and invaluable advice to other women (and men) on the obstacles that litter the scientific career ladder. We also run a Twitter account, which has become an important 'go-to' resource on women in science and the news associated with this topic. More locally, I am heavily in involved in the Athena SWAN award movement in my department and, like Nathalie, I try to offer support and mentorship for the female students and early career scientists I interact with on a daily basis.

www.soapboxscience.org

Twitter: @SoapboxScience

From the horse's eye

Dr Carol Hall discusses how her lifelong passion for horses and riding has led her to pursue a research career that aims to build a deeper understanding of vision in horses and, in turn, improve their training and welfare

What are the main aims of your current research?

It was almost 20 years ago that I started my research into the colour vision of horses and, since then, mine and other studies have provided considerable evidence that yellow and blue are the colours this species perceives as most colourful. My current research aims to evaluate the impact of visual features on the behaviour of the horse in both ridden and management situations. Since the environment is currently analysed from the perspective of human vision rather than that of the horse, differences in vision between horses and riders could contribute to the occurrence of behavioural problems in the horse and may result in accidents or falls in ridden work. Together with my colleagues, I am therefore attempting to find out more about what horses see in order to allow us to present their environment in a way that facilitates management and performance and improves the safety of both horse and rider.

How did you become involved in equine research?

Back in 1988, I had gained my British Horse Society Intermediate Instructor qualification and was lecturing part-time in horse behaviour. At this point, I was considering a move into research. The idea to focus on horse colour vision emerged from a discussion with a colleague – at the time, I wondered why we didn't know the answer to what seemed to be a simple question. I then approached the University of Nottingham's Psychology

Department in the UK (where I had completed my first degree) and was accepted as a research student. It took about eight years to complete the research and, during this period, I continued my lecturing role.

Could you explain why, on a personal level, your research is important to you?

I am passionate about this research because of my interest in riding and my desire to understand the world from the horse's point of view. At home, I have two Lusitanos, an Andalusian and a Shetland pony; I continuously try to improve how I train, handle and ride them. Too many people fail to appreciate how different the world around us looks to the horse and the impact that this might have on their behaviour. In some cases this may result in misinterpretation and blaming the horse for failing to behave as desired. The more we know about the horse's perspective, the easier the partnership between horse and human becomes.

How has your late entry to research affected your academic career?

To date, I believe that it has been an advantage. Indeed, my previous 'hands on' experience with horses – as well as the fact I have been involved in teaching horse management, riding and horse behaviour – is highly beneficial to my research. Additionally, I have received fantastic support from colleagues who are also inspired to find out more about horses, as well as from our students who are generally vocationally motivated. However, progress within an academic framework requires time to conduct research, publish findings and disseminate these to the wider community – and fitting this alongside my 'day job' can be challenging. Moreover, this area of research tends to be poorly funded and so it is not progressing as fast as it should. It is my strong belief that in a high-risk sport such as riding it is important to do as much as we can to reduce risks to both horse and rider. I am confident that the findings from my research will contribute to this aim.

In what ways have other colleagues or collaborators inspired or aided your work?

Many of my colleagues are involved in equestrian sport in one way or another and discussions with them ensure that my research is addressing issues that matter to the end user. In addition, my association with the International Society for Equitation Science has been a valuable source of inspiration and support. It has been hugely beneficial to have national and international collaborators in this area. We may have different approaches but we have a common aim – to improve the 'lot' of the ridden, and driven, horse. I have also maintained my links with psychology and, more recently, my rider-gaze-behaviour work has been bolstered by support from colleagues in both the psychology and sports science fields.

Horse-human harmony

In an attempt to improve the behaviour and wellbeing of ridden horses, researchers at the **School of Animal, Rural and Environmental Sciences, Nottingham Trent University**, UK, are conducting insightful research into the vision of both horse and rider

ROOTED IN THOUSANDS of years of history, the longstanding relationship between horses and humans is deeply rewarding and mutually beneficial. Indeed, people derive great pleasure from horses, and riding is one of the most popular sports in the UK. Unfortunately, indiscriminate breeding and the development of equine behavioural problems have resulted in high levels of wastage among horses. Sadly, the vast majority of this stems from human activity, often as a result of poor signals that transmit unclear messages to the horse or unknowingly reward undesirable behaviour. In order to get the most of out of these animals and optimise the horse-human partnership, it is essential to develop a more complete understanding of how the horse perceives the world and to fully appreciate the impact of human behaviour.

Motivated by a desire to improve the 'lot' of the often misunderstood horse, Dr Carol Hall has devoted the past couple of decades to exploring how horses perceive the world. As a lifelong lover of horses and the current Research Coordinator / Reader in Equitation Science at the School of Animal, Rural and Environmental Sciences at Nottingham Trent University, she is passionate about creating a more horse friendly approach to riding and training. By investigating the impact of human requirements and behaviour, Hall's research is laying the foundations for improved training methods that do not place unfair demands on the horse. To date, her studies have made fascinating insights into the welfare of ridden animals, as well as the visual ability of horses and the visual behaviour of equestrian athletes.

A VISIONARY APPROACH

Hall's research began with an investigation into equine colour vision. As an under-researched phenomenon that had previously thrown up contradictory results, she was intrigued as to why so little was known about what colours horses see."Initially, it was my aim to revisit previous colour vision studies as I was not convinced by the results," she explains. "There was a suggestion that horses could not tell the difference between yellow and white but, since my horse would ignore white road markings and freeze at yellow ones, I thought this highly unlikely." In order to assess the behavioural responses of horses to different colours, Hall analysed the hesitancy of horses to cross different coloured flooring and conducted choice tests to determine which colours horses would more readily approach. Based on methods used by Professor Karl von Frisch – a Nobel Laureate who tested wavelength discrimination in bees – she studied the extent to which horses are able to discriminate 15 different colours

KEEPING YOUR EYE ON THE RAIL: GAZE BEHAVIOUR OF HORSE RIDERS APPROACHING A JUMP

OBJECTIVES

To improve the welfare of ridden horses by improving human understanding of how they visually perceive the surrounding environment.

KEY COLLABORATORS

NTU Equestrian team:
Liz Taylor; **Cassie White**; **Dr Kelly Yarnell**; **Heather Elston**; **Sarah Tomlinson**; **Dr Sarah Redgate**; **Dr Rachel Kay**; **Anna Gregory**

NTU Psychology:
Professor David Crundall

ISES:
Professor Natalie Waran; **Dr Hayley Randle**; **Dr Charlotte Nevison**; **Professor Paul McGreevy**; **Dr Andrew McLean**; **Dr Camie Heleski**; **Uta König von Borstel, PhD**; **Marc Pierard**

PARTNERS

International Society for Equitation Science

National Equine Welfare Council

Tracksys

BioVici Ark Ltd

FUNDING

Nottingham Trent University

CONTACT

Dr Carol Hall
Principal Lecturer / School Research Coordinator / Reader in Equitation Science

School of Animal, Rural and Environmental Sciences
Nottingham Trent University
Brackenhurst Campus
Southwell
Nottinghamshire
NG25 0QF
UK

T +44 115 848 5212
E carol.hall@ntu.ac.uk

DR CAROL HALL studied Psychology at the University of Nottingham, UK, and has combined this knowledge with her experience in equestrian sports in the development of innovative taught modules. In addition to teaching and supervising undergraduate and postgraduate research projects, Hall's own research interests include equine visual perception, horse welfare, the visual behaviour of equestrian athletes and equine emotion.

AN INSPIRATIONAL SOCIETY

As a not-for-profit organisation, the International Society for Equitation Science (ISES) was formally launched in 2007 to facilitate research into the training of horses to bolster horse welfare and improve the horse-rider relationship. Since its inception, burgeoning global interest in equitation science has contributed to its rapid development among both academics and equestrian professionals. The Society now hosts a diverse, multidisciplinary membership of research, students and professionals from all over the world. Hall has been involved in the organisation since its beginnings; she has attended the majority of its annual conferences and is currently working with a group of collaborating members on a paper on recommended protocols for research in equitation science.

from varying shades of grey. The results demonstrated that all colours presented to the horses were seen as colourful to a greater or lesser extent, with yellow and blue identified as the most distinguishable colours.

Hall's foundational research on colour vision has significant implications for understanding the world from the horse's perspective. While the equine environment is currently designed with human vision in mind, horses may in fact perform better in different conditions, such as in dimmer lighting than is optimum for human sight. Additionally, key environmental features, such as jumps of certain colours and designs, could look very different to horses and humans: "Although no direct correlation between the visual features of cross-country fences and the increase in rotational falls (and subsequent injuries and fatalities) has been found," elaborates Hall."The differences in visibility for the horse and human may be a contributing factor to the occurrence of these falls."

GAUGING THE GAZE

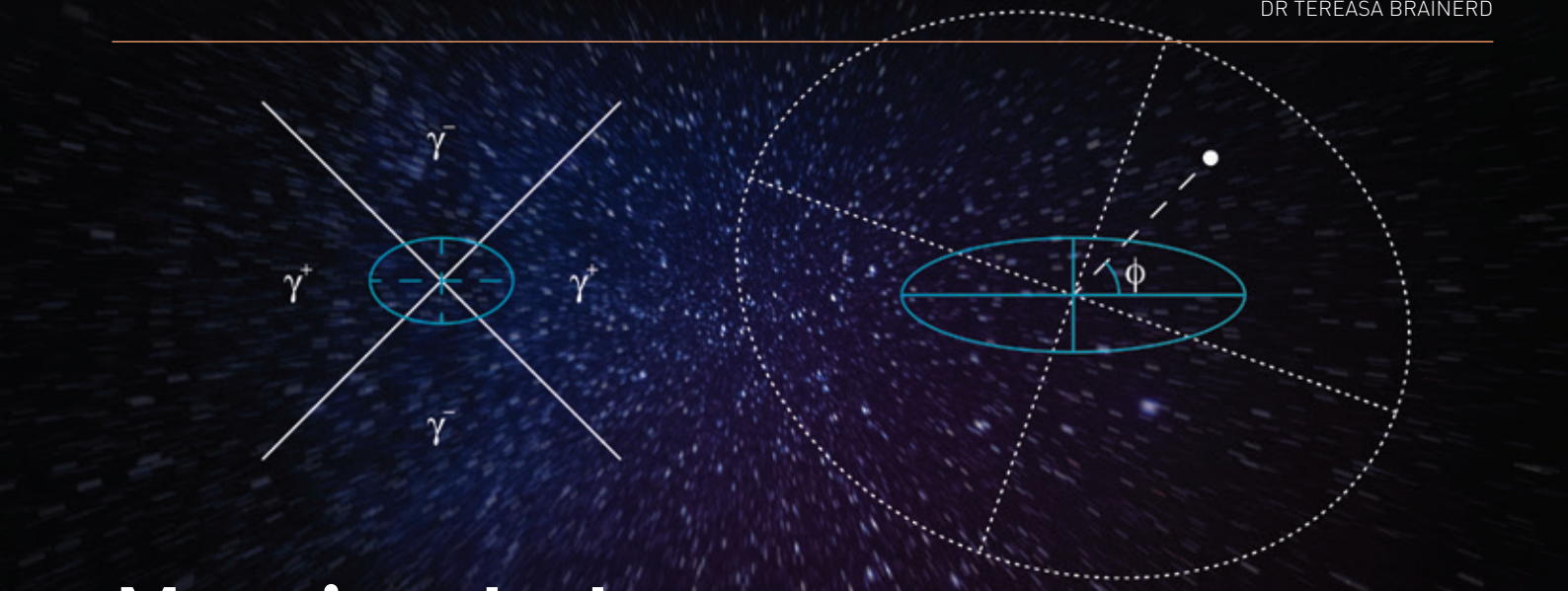
It was these differences in visual perception between horse and rider that led Hall to embark on a project that analysed the gaze behaviour of horse riders approaching a jump. While eye tracking in humans has been implemented in a number of other sports in order to identify elite visual skills, limited and cumbersome technology had previously hindered these tests in horse riding. To address these issues, Hall and her colleagues used a mobile eye-tracking device (ASL Mobile Eye) to establish the timing, frequency and duration of rider eye fixations on the jump and the percentage of time during which their point of gaze was located elsewhere. Interestingly, while no statistically significant correlations between gaze behaviour and skill scores were identified, they found that the more skilled riders tended to fix their gaze on the jump earlier and for a longer duration.

Moving forwards, the researchers are planning to use their initial data on rider gaze behaviour to determine the key features of equestrian visual skills and ascertain what differentiates elite from non-elite performers. To this end, they are currently planning to implement trials with elite riders and identify how sport-specific visual skills relate to performance. Indeed, visual training could prove to be excellent preparation for participation in equestrian sport with significant benefits for both the horse and rider. By continuing to chart the information they learn about horse vision and comparing it with human vision, Hall and her colleagues hope that their research findings could be used to develop more horse-friendly obstacles and improved training techniques for riders, thus reducing the occurrence of accidents in show jumping and cross country.

> By investigating the impact of human requirements and behaviour, Hall's research is laying the foundation for better and more informed training methods that do not place unfair demands on the horse

TOWARDS A HARMONIOUS FUTURE

Looking ahead, Hall is eager to continue forging deeper insights into how the sensory systems of horses shape their perception of the world around them. Although it is impossible to fully experience life from a horse's point of view, her studies are helping to answer complex questions about the processes that underpin horse behaviour."Having spent eight years trying – and largely succeeding – to find out at about the colour vision of horses, I am well able to appreciate that perceiving the world through the eyes of another individual, let alone another species, is far from being a simple task," she affirms. "Despite this, for those of us who ride and interact with these amazing animals, I believe there is an ethical imperative to try and look at things from their point of view and work towards improving the quality of their lives."



Mapping dark matter

Cosmological pioneer **Dr Tereasa Brainerd** shines a light on her work using weak gravitational lensing and details the challenges of making accurate measurements in cosmology

What are the main objectives behind your current research into dark matter halos?

My research aims to use weak galaxy-galaxy lensing to place constraints on the amount and distribution of dark matter around galaxies. My PhD student, Brandon Harrison, and I are making realistic Monte Carlo computer simulations of galaxy-galaxy lensing using galaxies from the Sloan Digital Sky Survey (SDSS). We embed each of the SDSS galaxies inside a cold dark matter halo, where the details of the halo parameters for each of the simulated galaxies are tied directly to the observed properties of the SDSS galaxies. We then place a population of distant source galaxies behind the theoretical SDSS galaxies, and lens the images of each of the source galaxies by all of the foreground theoretical SDSS galaxies.

In this way, we can make accurate predictions for the galaxy-galaxy lensing signal that should be observed in the real Universe. We then measure the resulting galaxy-galaxy lensing signal in the simulation, interpreting it in the same way that observational astronomers analyse observations of galaxy-galaxy lensing in the real Universe. Through this, we can explore the magnitude of systematic errors that will manifest in observational studies simply due to the way the signal is interpreted.

How did you begin studying dark matter and gravitational lensing?

As a graduate student, I studied the formation of dark matter halos using computer simulations. I was drawn to the topic because computer simulations are one of the only ways in which we can 'experiment' with the Universe. My dissertation advisor, Jens Villumsen, was visiting the California Institute of Technology (Caltech) and, through a conversation with Roger Blandford, became interested in using gravitational lensing to map the large-scale structure of the Universe. Roger and one of his students, Anne Berit Saust, had been having difficulty solving an equation that was related to gravitational lensing. One day, I went to lunch with Jens and he asked me if I would be willing to take a look at the equation. I agreed, and a few days later faxed the full solution to Roger. This initiated a collaboration between Roger, Jens, Anne and me that resulted in a landmark publication on the theory of weak lensing in relation to the large-scale structure of the Universe.

After earning my PhD, I continued to work with Roger at Caltech on aspects of weak gravitational lensing but from an observational standpoint. We placed the first upper limit on the amount of lensing by large-scale structure that exists in the Universe and published the first statistically significant detection of what has come to be known as galaxy-galaxy lensing.

Could you explain the differences between photometric and spectroscopic redshifts for galaxies?

Due to the expansion of the Universe, all galaxies outside our Local Group appear to be moving away from us, which manifests as a redshift in the spectrum. In the case of spectroscopic redshifts, a telescope and spectrograph have been used to observe the actual spectrum of galaxies. This is compared to a rest spectrum to make an accurate measurement of the galaxy's recession velocity. In photometric redshifts, the galaxies are typically observed using four or five broad filters that allow a wide range of wavelengths of light to pass through. By comparing the brightness of the galaxy as observed through all of these filters, one can estimate its redshift. Photometric redshifts are less accurate than spectroscopic redshifts, but also require much less telescope time.

How do these measurements relate to your work?

For the purposes of lensing, it all comes down to one factor: how accurately do you need to separate your foreground objects (the lenses) from your background objects (the lensed sources)? Part of my work focuses on how accurate photometric redshifts need to be in order to make precision measurements of weak gravitational lensing.

What is your input into NASA's Wide-Field Infrared Telescope (WFIRST) mission?

My work is potentially very important for the WFIRST mission, which has the goal of using weak lensing to measure the dark matter mass distribution with unprecedented accuracy. My current investigation centres on how well standard methods of converting the observed weak lensing shear into a measurement of surface mass density actually work. We are finding that the standard method leads to an error of ~25 per cent, which is unacceptably large in the 'era of precision cosmology'.

Curves in space

Members of **Boston University**'s Department of Astronomy are using a cosmological phenomenon called weak gravitational lensing to map dark matter in the Universe. Their work will provide important theoretical insights that are relevant to future space-based studies

DARK MATTER MAKES up around 85 per cent of the mass of the Universe, but remains one of the greatest mysteries of astronomy. The visible material within galaxies is observed to be moving so quickly that its mass alone is insufficient to keep the galaxies bound together by gravity. The reason that the visible material can move so quickly, yet the galaxies are not torn apart, is due to the presence of dark matter. Dark matter, which gives galaxies additional mass by providing the gravity they need to stay intact – is inherently mysterious. It does not absorb, reflect or emit light, and can only be detected from its gravitational effects. However, using the phenomenon of galaxy-galaxy lensing, it is possible to determine the quantity and distribution of dark matter around galaxies.

THE POWER TO BEND LIGHT

According to Einstein's theory of general relativity, mass causes space to curve. After being emitted by distant galaxies, particles of light – photons – travel along a straight path through the Universe, but under the influence of a large mass, such as another galaxy, the paths of the photons are bent. Because of the curvature that their mass causes, galaxies act as lenses, bending the paths of light emitted by distant objects. These astronomical gravitational lenses are similar to conventional glass lenses but have a variable index of refraction. Since the gravitational potential of the lens varies across the plane of the sky, gravitational lensing produces a similar effect to looking through the bottom of a wine glass, resulting in a distorted image.

Strong gravitational lenses produce highly distorted and magnified images, and multiple versions of each object. Conversely, weak lensing produces only mild distortions. Since the distortion is at most a few per cent, weak lensing cannot be detected using the image of a single lensed galaxy – it can only be detected by performing statistical averages over many galaxies.

GALAXY-GALAXY LENSING

Over the past 25 years, this phenomenon (weak lensing) has become a standard tool for cosmological studies. Observations of weak lensing allow cosmologists to map the amount and location of dark matter directly, and are also useful for constraining fundamental cosmological parameters independently of other methods.

Making an important mark on this field is Dr Tereasa Brainerd, who pioneered understanding in the field in the 1990s. Together with her collaborators Professor Roger Blandford and Dr Ian Smail, she demonstrated the existence of galaxy-galaxy lensing in our Universe – the effect whereby distant galaxies are systematically lensed by foreground galaxies at a weak level – and she also performed the first simulations that showed it to be a multiple deflection problem. Brainerd is presently Associate Professor and Chair of the Department of Astronomy at Boston University, USA, where she is simulating galaxy-galaxy lensing in order to infer the amount of dark matter in the Universe.

ON A MISSION

This work is funded by the NASA Astrophysics Theory Program (ATP), which supports theoretical investigations of astrophysical phenomena targeted by NASA astrophysics missions. Indeed, there is a tight link here, as Brainerd's investigations are directly related to weak lensing studies that will use data obtained by NASA's future astrophysics mission: the Wide-Field Infrared Telescope (WFIRST).

Currently the top-ranked large space mission in the New Worlds, New Horizon (NWNH) Decadal Survey of Astronomy and Astrophysics, WFIRST will obtain deep images in multiple bandpasses, and redshifts of millions of galaxies, in order to investigate the weak lensing effect known as cosmic shear. Combined, the data collected by WFIRST will represent an unprecedented weak lensing dataset, which will be used to conduct extensive studies of cosmic magnification and galaxy-galaxy lensing, as well as cosmic shear. Brainerd's theoretical investigations will be directly relevant for interpreting these future observations.

MATHEMATICAL DILEMMAS

Working with PhD student Brandon Harrison, Brainerd is testing the application of a known theoretical relation between weak lensing shear and lens surface mass density. This relation states that, for a single gravitational lens, the weak lensing shear is directly related to surface mass density through a multiplicative constant.

Weak gravitational lenses are characterised by two basic parameters:

CONVERGENCE – the magnification or demagnification of the source galaxy, without any change to its shape

SHEAR – 'tidal' forces acting across a bundle of light rays as they pass by the gravitational lens. Shear causes distortions in the images of galaxies; for example, shear due to a weak gravitational lens changes the image of a perfectly spherical galaxy into an ellipse

Pinning down this relation has presented many challenges for Brainerd: "The problem with galaxy-galaxy lensing is that you have to deal with all of the multiple deflections," she expounds. "All galaxies in the foreground are lensing all galaxies in the background, and the image of each background galaxy is affected by numerous foreground galaxies." Adding to this complexity, the multiplicative constant assumes a different value for every single lens-source pair in the sample. Thus, in a realistic dataset, it can take on multiple values.

In order to infer surface mass density from measurements of shear, observers typically estimate the multiplicative constant using an average value taken from all of the lenses in the sample. So, when observers infer the surface mass density from observations of galaxy-galaxy lensing, they are actually computing a ratio of two mean values. However, the ratio of two means is not mathematically identical to the mean of a set of ratios – a mathematical inequality, which leads to systematic error.

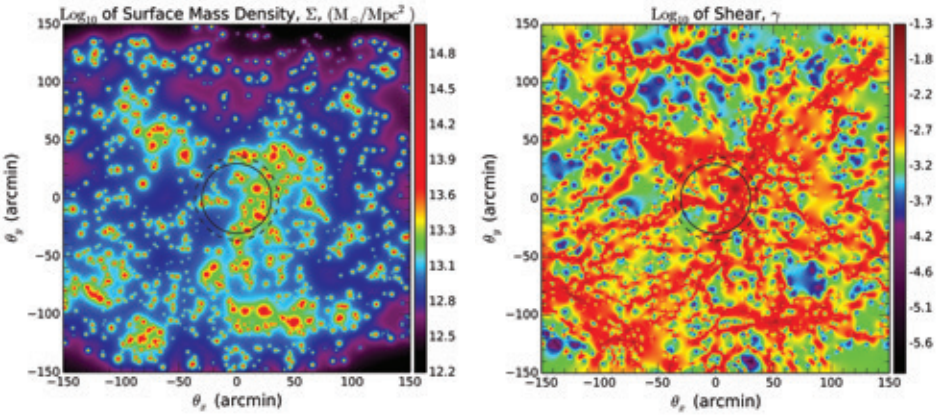
ELUCIDATING ERROR

Although still in the throes of tackling a major mathematical problem, Brainerd and Harrison have made important progress. In the past year, Harrison has successfully constructed realistic simulations of galaxy-galaxy lensing using the Sloan Digital Sky Survey (SDSS). The simulation results clearly show that the observational method for inferring lens surface mass density leads to an underestimate, which can reach 25 per cent on small angular scales.

The space-based studies of galaxy-galaxy lensing due to be carried out with both NASA's WFIRST and the European Space Agency Euclid missions aim to place much tighter constraints on dark matter mass distribution. In this context, a 25 per cent error simply due to technique will be unacceptable. This work therefore has important implications for space agencies, highlighting the need for a new standard for interpreting observations of galaxy-galaxy lensing.

FROM THEORY TO OBSERVATION

Looking beyond the project, Brainerd aims to make the transition from theory to observation, exploiting a recent investment from Boston University of US $10 million in a scientific partnership in a new 4 metre optical/near infrared telescope – the Discovery Channel Telescope (DCT). The DCT is owned by Lowell Observatory, a private astronomical research institution, and its construction was partially funded by Discovery Communications, Inc. "Over the next five to 10 years, I hope to use the DCT to make observations of gravitational lensing in order to map dark matter in the Universe, constrain the degree to which galaxies are intrinsically aligned with each other, and understand the evolution of galaxies in clusters," concludes Brainerd.



Left: The dark matter surface mass density of the lens galaxies in one of Brainerd and Harrison's simulations of galaxy-galaxy lensing, shown using a logarithmic scale. The lens galaxies have an average redshift of z = 0.2, corresponding to a distance of 2.2 billion light years from Earth. The scale size of the figure is 25 square degrees (equivalent to about 127 times the size of the full moon).

Right: The weak galaxy-galaxy lensing shear that occurs when a plane of source galaxies, all located at a redshift of z = 0.4 (corresponding to a distance of 3.7 billion light years), is lensed by the galaxies shown on the left. Again, a logarithmic scale has been used. Red regions correspond to regions of substantial amounts of weak lensing shear, and are much more 'interconnected' than the regions of high surface mass density of the lens galaxies.

SLOAN DIGITAL SKY SURVEY

SDSS provides a large spectroscopic database and an even bigger photometric database

- The size of the survey is important; the larger the sample, the more accurately the signals can be detected

SDSS enabled Brainerd and Harrison to predict the weak lensing signal under some very specific assumptions about the distribution of dark matter in the Universe – cold dark matter halos whose properties are scaled according to the observed properties of the galaxies

- The researchers are using SDSS as the basis of their computer simulations
- SDSS is the 'real-world' starting point for their simulations, used to 'assign' dark matter halos to SDSS galaxies
- Once the dark matter has been placed around each of the galaxies in the simulation, the lensing effects of their dark matter halos on a population of theoretical background galaxies are computed

INTELLIGENCE

USING WEAK GRAVITATIONAL LENSING TO CHARACTERISE DARK MATTER HALOS

OBJECTIVE

To use weak galaxy-galaxy lensing to place constraints on the amount and distribution of dark matter around galaxies.

KEY COLLABORATORS

Brandon Harrison, PhD student, Boston University, USA

FUNDING

NASA Astrophysics Theory Program – award no. NNX13AH24G.

CONTACT

Dr Tereasa Brainerd
Chair, Department of Astronomy

Boston University
Department of Astronomy
725 Commonwealth Avenue
Boston
Massachusetts 02215
USA

T +1 617 353 6646
E brainerd@bu.edu

http://bit.ly/tereasabrainerd
http://people.bu.edu/brainerd

DR TEREASA BRAINERD received her BSc (Hons) in Physics from the University of Alberta in 1987 and her PhD in Astronomy from the Ohio State University in 1992. She joined the faculty of the Department of Astronomy at Boston University in 1995, following postdoctoral research positions at the California Institute of Technology and Los Alamos National Laboratory.

Prior to becoming Chair, she served as the Director of Boston University's Institute for Astrophysical Research for six years. She has also held the positions of the Department's Director of Undergraduate Studies, Director of Graduate Studies, and Chair of the Graduate Admissions Committee. In addition to galaxy-galaxy lensing, her research interests include the use of satellite galaxies to probe the dark matter distribution around galaxies and the use of cosmic magnification to constrain the large-scale structure of dark matter in the Universe.

BOSTON UNIVERSITY

Investing in inventors

Dr Yolanda Comedy explains why policy makers must invest in inspiring, educating and supporting inventors, and how the use of Invention Ambassadors can help further innovation

What are the overarching objectives of the American Association for the Advancement of Science (AAAS)-Lemelson Invention Ambassadors Program?

The goals of the Program are to help cultivate a new and diverse generation of inventors; increase global understanding of the role of invention in creating a better quality of life, including creating new products and building new businesses; and highlight the importance of inventors and invention education in building economies and fostering innovation.

Essentially, the Program is a celebration of inventors and the way that invention changes lives, improves the economy, and is sometimes just ridiculously cool. Invention is geared towards solving problems and looking at challenges in a whole new way. The concept underlying the tagline for the AAAS-Lemelson Invention Ambassadors Program – 'Advancing the World Through the Power of Invention' – is what gets me out of the bed in the morning. There are extraordinary individuals in our world who are always thinking, 'how do I make things better?' and we need more of these people.

How did the AAAS-Lemelson Invention Ambassadors Program first come about?

Jerry Lemelson, one of the founders of The Lemelson Foundation, was one of the most prolific inventors of the 20th Century and AAAS is the publisher of *Science Magazine*, which was originally started, edited and published by one of the country's most well-known inventors, Thomas Edison. Both organisations, with our history of invention were excited by the Invention Ambassador idea of Alexander Nicholas from The Lemelson Foundation, who had previously been an AAAS Policy Fellow. Personally, I loved the idea at once – I had previously worked for both the White House and IBM on science policy issues, so I was excited about celebrating the role that invention plays in improving global quality of life. Indeed, I'm part of the science policy field because of my passion for solving world problems. Policy is often central to those efforts, as is highlighting lessons learned and what works and what needs to work better.

Why should invention be better understood, supported and highlighted?

We often overlook the role of invention in improving our quality of life. 'Innovation' has become such a buzzword that we don't think about all of the components that cause innovation to occur, but invention is a critical component. Invention and innovation impact our daily lives in so many ways, from making peanut butter sandwiches to cell phones to changing our relationship with finite resources.

What are the main responsibilities of an Invention Ambassador?

An Invention Ambassador's main responsibility is to give talks and serve on panels to discuss their role as inventors and what needs to occur to ensure that future inventors are encouraged, supported and celebrated. It is also our hope that, through the Invention Ambassadors Program, we will create a community of inventors who can support each other, learn from each other and foster ideas to establish a great cadre of future inventors.

How was the first class of Invention Ambassadors selected?

To help us kickstart this new Program, we created an incredible advisory committee of people who genuinely care about invention and innovation. The Invention Ambassadors applied or were nominated. We had a dedicated working group who read through and scored these applications, and conducted the interviews. The results of these interviews determined the inaugural Ambassadors.

By what means does the Program support the activities of the Invention Ambassadors?

Officially, our job is threefold: to appoint great Ambassadors, find and/or create worthwhile venues in which they can share their messages, and help conduct research to find important messages to share with audiences. However, we see our role as bigger than this! Since we have such an extraordinary inaugural class, our job is also to help create a community. Our inaugural Ambassadors have bonded and shared information, time, thoughts and experiences with each other. We see it as our job to help these relationships deepen and expand, and to provide moral support for these incredible inventors.

In which direction do you see the Program developing in the future?

We have opened up applications for the second class. Furthermore, while this is a pilot project, we hope to continue the Program further and initiated discussions with The Lemelson Foundation to this end. I look forward to the possibility of solving problems through invention by continuing to celebrate invention, foster dialogue and help inspire future inventors!

Dr Yolanda Comedy has written an article about invention entitled 'Invention: the Invisible Hero' which can be accessed online at **http://bit.ly/Ingentaconnect**

Ambassadors for invention

In an effort to celebrate and highlight the importance of inventors and invention, two organisations have joined forces to establish the **American Association for the Advancement of Science-Lemelson Invention Ambassadors Program**

Dr Yolanda Comedy outlines the impressive achievements of the first class of Invention Ambassadors

TACKLING THE GRAND challenges of the 21st Century increasingly requires countries to invent and innovate. To inspire a new generation of inventors, creative strategies and programmes must be devised and implemented. This is exactly the goal that has led two organisations – The Lemelson Foundation and the American Association for the Advancement of Science (AAAS) – to forge a new partnership. The partnership draws strength from AAAS and The Lemelson Foundation's missions to serve society and benefit the world. Lemelson is dedicated to inspiring and enabling the next generation of inventors, and AAAS's mission is to 'advance science, engineering, and innovation throughout the world for the benefit of all people'.

A PIONEERING PROGRAMME

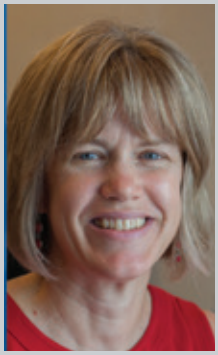
"Invention is the foundation for innovation, and its ecosystem requires two core components: culture and talent," explains Dr Yolanda Comedy, Director of the AAAS Center for Advancing Science & Engineering Capacity and a driving force behind the Program. In order to support these components, the Program simultaneously celebrates and highlights invention and inventors in an effort to garner new interest from policy makers, innovation stakeholders and the general public alike.

The premise of the Program is simple: over a three-year pilot phase, appoint 15 Invention Ambassadors to promote invention and inventors. This will be achieved by relaying important messages about the key role played by invention within the innovation ecosystem, as well as the myriad ways invention is necessary for job creation, supporting the economy and improving quality of life.

THE PROGRAM IN PRACTICE

The Program began in November 2013, and the inaugural class of seven Invention Ambassadors was ready to begin its year-long tenure in the summer of 2014. Together, the class contains a broad range of areas of expertise and backgrounds, but all of the

THE INAUGURAL INVENTION AMBASSADORS



Professor Karen Burg

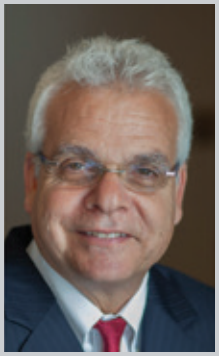
"Karen cares about helping people have an easier time in the operating room and creating better experiences for women with breast cancer. She is an engineer who knows how to make tools and designs that work but are less invasive."

Dr Rory Cooper

"Rory, who is himself in a wheelchair, thinks constantly about improving life for people with disabilities. He is passionate about inventing new devices and tools. He loves wheelchair racing and has designed chairs for people who race."

Sorin Grama

"Sorin is passionate about turning research into applications that can help the world. He moved to India with the aim of helping farmers achieve the refrigeration necessary to get their milk to market. Now, after many painstaking years, his invention is useful to many."



Dr Paul Sanberg

"Paul is an inventor with approximately 100 health-related patents, and his work has been instrumental in bringing new pharmaceutical and cellular therapeutics from bench to bedside. He also founded the prestigious National Academy of Inventors."

Steven J Sasson

"Steve invented the digital camera, which has transformed so many things – from smartphones, to using less chemicals and wasting less paper, to medical imaging. This man caused a real revolution in the way we take and share images."

Paul Stamets

"Paul is dedicated to saving the planet. He is an incredibly passionate person, who has figured out methods to protect our health, save our bee populations, create less harmful ways to rid ourselves of pests and thinks constantly of preserving the Earth and its organisms."

Dr Vinod Veedu

"Vinod and nanotechnology are both out to change so many aspects of the way we live. From nanobrushes to surf boards, Vinod is consistently inventing and improving many things around us."

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE (AAAS) - LEMELSON INVENTION AMBASSADORS PROGRAM

OBJECTIVES

- To celebrate and highlight the importance of invention and inventors
- To increase societies' understanding of the critical role of invention in improving quality of life and addressing global challenges
- To help cultivate a new and diverse generation of inventors
- To get more people excited about supporting and becoming inventors
- To increase understanding of the role of invention, inventors and invention education and the need for a robust invention ecosystem in building economies and fostering innovation

PARTNERS/FUNDING

The Lemelson Foundation

CONTACT

Dr Yolanda Comedy
Director, Center for Advancing Science and Engineering Capacity

American Association for the Advancement of Science
1200 New York Avenue NW
Washington, DC
USA

T +1 202 326 6780
E ycomedy@aaas.org

www.aaas.org/invention

https://bit.ly/LinkedInAAASLemelson

https://twitter.com/InventionAMB

http://bit.ly/PlusGoogleAAASLemelson

http://instagram.com/inventionambassadors

http://bit.ly/YouTubeAAASLemelson

YOLANDA L COMEDY is the Director of the AAAS Center for Advancing Science & Engineering Capacity, where she directs a number of programmes, including the AAAS-Lemelson Invention Ambassadors Program. Comedy works on science and technology issues and has previously worked for the White House, serving as a Senior Policy Analyst for both the President's Committee of Advisors on Science and Technology and the President's Information Technology Advisory Committee; and IBM working in strategic phillanthropy, governmental programmes and business consulting, Comedy obtained her PhD from Indiana University in Political Science.

AAAS
ADVANCING SCIENCE, SERVING SOCIETY

To view videos of selected Invention Ambassadors speaking at the Celebrate Invention event visit **http://bit.ly/CelebrateInvention**

Ambassadors are united by the fact that they are prolific inventors. Overall, the group holds a combined total of approximately 150 patents.

Upon selection, the Invention Ambassadors participated in a 'Celebrate Invention' event at the AAAS Headquarters on 1 July, 2014. "Each Ambassador in attendance spoke for 12 minutes about their inventions and their lives as inventors. The theme of their talks centred on moments of invention – that moment or those moments in which something transformative happened," recalls Comedy. "It was great – informative and inspiring."

Each inaugural Invention Ambassador will speak at two or more strategic engagement events over the course of their tenure. Comedy and her colleagues position the Ambassadors in appropriate dialogues and venues and identify and generate compelling, evidence-based messages to bolster the Ambassadors' call to arms.

HOT ON THEIR HEELS

While the first class of Invention Ambassadors continue their important work and move towards the Culminating Event in June 2015, applications and nominations for the second class of Ambassadors is already open at http://inventionambassadors.aaas.org. The new class can pick up directly where the first class left off, but Comedy hopes that the Program will begin to build a community of inventors and that previous classes will stay involved.

It is too early to predict what will become of this community of Invention Ambassadors following the pilot's completion, but it is hoped that this community of creators will have a significant impact on invention within the policy landscape in the years ahead.

DATES FOR YOUR DIARY

Invention Ambassadors will be speaking at the upcoming events:

AAAS Annual Meeting
12-16 February
San Jose, California, USA

4th Annual National Academy of Inventors Conference
19-20 March
Pasadena, California, USA

VentureWell OPEN Conference
20-21 March
Washington DC, USA

AAAS Forum on Science & Technology Policy
30 April – 1 May
Washington DC, USA

Ambassador Culminating Event
15 June
West Orange, New Jersey, USA

Robots of the future

An early interest in science fiction sparked **Dr Elizabeth Broadbent**'s lifelong fascination with robots. Here, she discusses a career that has spanned engineering and psychology, and her ambition to oversee the development of more acceptable robots

How did you become interested in human-robot interactions?

Star Wars made a big impression on me when I was small – I loved the personalities of the robots, their humour and their conscientiousness. As a teenager, I read the novels of Isaac Asimov and Harry Harrison, and I dreamed of making Giskard and Daneel, robots from Asimov's books who were so loyal and caring to humans. To this end, I started with an honours degree in Electrical and Electronic Engineering, before going on to work for a small New Zealand company called RoboTechnology. However, I was frustrated by the limitations of technology and robots at the time.

What were these limitations, and how has your career path brought you closer to overcoming them?

When I first graduated from engineering school the only robots being made were very mechanical and performed factory-type tasks. They did not interact with humans very much and were essentially just machines. This was frustrating because I wanted to make robots that could think, feel and interact with us on a personal level, and I particularly wanted to make robots that could care for people who were unwell and needed support.

To better understand how to give robots thoughts and feelings, I studied how people think and feel. I went back to university and obtained my PhD in Health Psychology. This, combined with my engineering background, sets me up well to make robots that are not only technically sound but also acceptable, which is important in ensuring people are comfortable around them. One way in which my research has furthered knowledge in this field is studying how robots' appearance, voice and behaviour affect people's reactions to them.

Could you pinpoint the key factors involved in developing robots for healthcare purposes and some of your greatest successes to date?

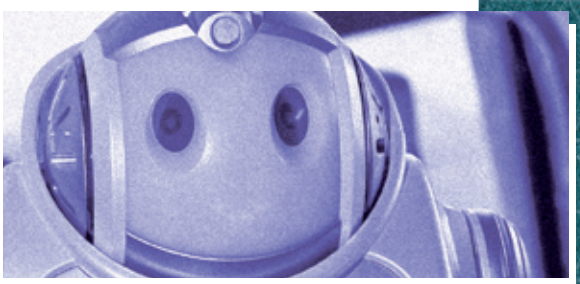
The key factors are making robots look good, simple to operate, responsive and reliable – all of which will make people more accepting of them. On top of that you need to make the robots perform a useful task. Our largest project to date involved the deployment of 35 autonomous robots at Auckland's Selwyn Village retirement community. Some of the tasks they did were to remind people to take medication; play music and memory games; take blood pressure and pulse oximetry; and use Skype in a simple way. In the four-month trial, we demonstrated that healthcare robots are feasible and acceptable for both staff and residents, and that companion robots can reduce loneliness in older people.

Another of your projects focuses on robot aesthetics. Why do you think robot features can sometimes be perceived as 'creepy', and how are you addressing this issue?

Robots can appear creepy because they do not fit into the category of human or machine. They might look human-like, but the way they move, talk or feel isn't quite right, and this can create unease. We are trying to address this issue in a few ways – first, by making robots more human-like so they do not look unnatural, and secondly, by avoiding the situation where robots look half human and half machine. They can look human-like or machine-like, but not a scary mixture of both.

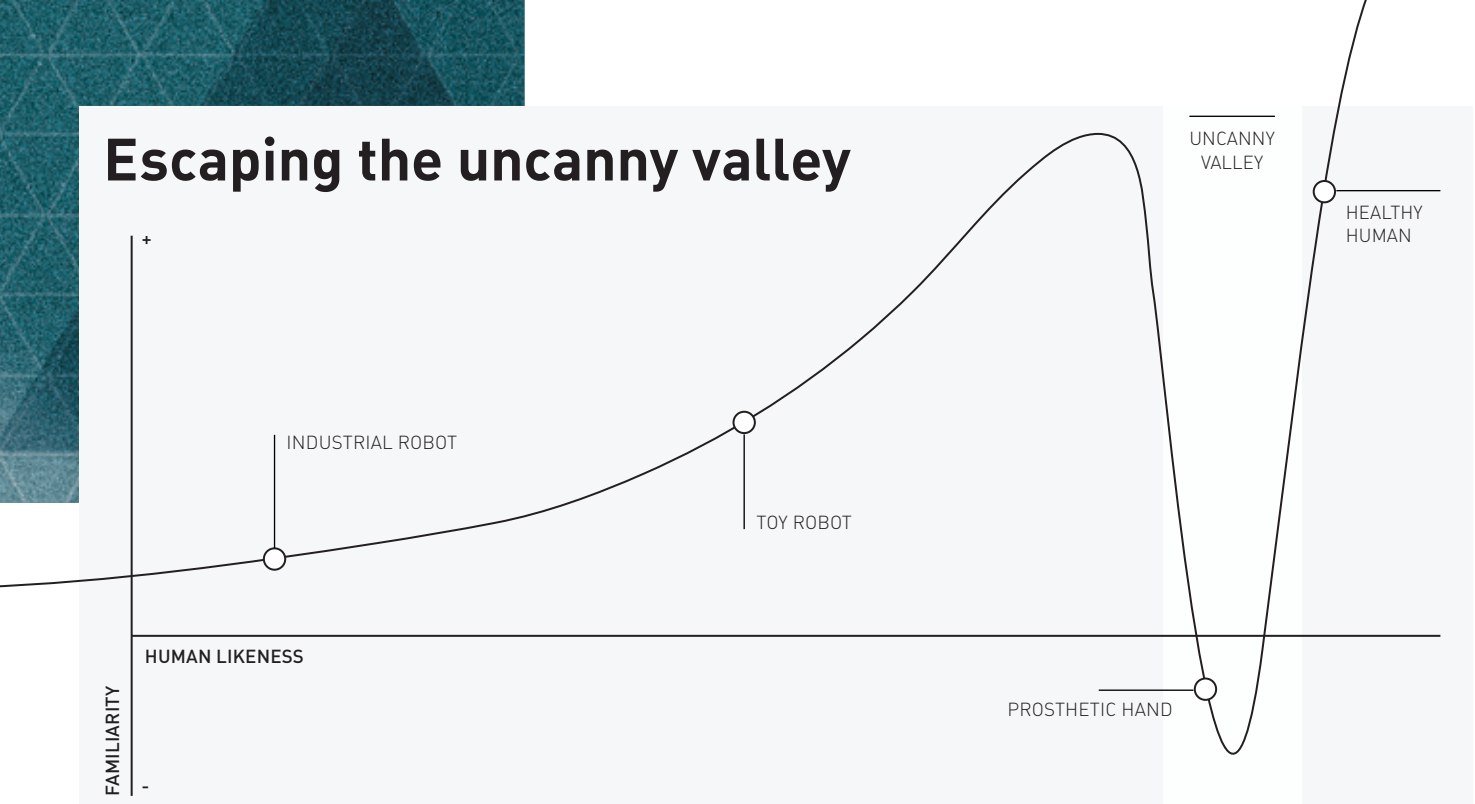
Besides healthcare, will your research have any other applications?

At present, my focus is on healthcare, but there are potential applications for robot acceptance findings in many other areas, such as in industry and domestic situations. We are poised on the brink of seeing robots in many different areas, and we need to find out more about what makes them acceptable in these applications. Most of the grant money in robotics to date has gone towards making robots more technically advanced, but more efforts need to be dedicated to investigating the factors that promote acceptance in order to see the projected robotics boom realised.



Irobi, a healthcare robot developed by the research team and Yujin Robot.

Escaping the uncanny valley



An international team based at the **University of Auckland**, New Zealand, is looking at the interface between humans and robots in a bid to make the widespread adoption of these machines in healthcare a reality

ROBOTS HAVE LONG caught the world's imagination through futuristic stories played out on screen and in literature in which they are often portrayed as the servants or helpers of mankind. Indeed, much of the modern study of robots is inspired by these works of fiction. In one sense, servile robots are already a significant presence, as they are utilised in a variety of applications ranging from factory work to military purposes. However, these robots are a far cry from the intelligent, often humanoid robots of fiction.

The silver face is seen as more 'eerie' than the human-like face.

While robotics has not yet reached the extraordinary heights of these stories, there have certainly been enormous advances in the field in recent years, with pioneering teams producing highly complex androids such as the Actroid and the HRP-4. Such projects are undoubtedly incredible feats of engineering, but the practical applications of these robots tend to be either highly idiosyncratic or non-existent. To truly realise the vision laid out in science fiction, there is a need for robots that are not only capable of interacting with humans, but also serving specific functions.

CARING ROBOTS

One area that has been flagged as suitable for the implementation of robots has been care of the elderly. Developed countries are currently facing the problem of an ageing population, a phenomenon that results in a large proportion of older people in need of care. In response to this need, several projects have focused on developing robots that provide assistance, health check-ups or company to the older generation. One such project is being undertaken at the University of Auckland, New Zealand, where an international collaboration with a number of Korean robotics institutions has been developing and testing healthcare robots for older people since 2008. Dr Elizabeth Broadbent, who leads the Human-Robot-Interaction aspect of this initiative, has brought her passion for robotics and human psychology to the table in an effort to create robots that provide tangible benefits for the elderly. Working in partnership with The Selwyn Foundation, a non-profit organisation providing residential care, retirement living and community services for older people, the team has run extensive studies to determine the functions that robots should perform, as well as people's reaction to them.

These trials proved highly successful, with robots helping everywhere from the café to the dementia care unit at the Foundation's Selwyn Village retirement community. The robots provided useful functions that ranged from playing games to giving reminders about taking medication, and the team's studies have led to further work exploring whether similar efforts can help to supplement resources in rural areas. Not content with resting on their laurels, however, the team also recognises that there is still room for improvement.

IMPROVING AESTHETICS

While the Auckland group's studies have shown that robots possess the technical capabilities to provide useful services in healthcare, Broadbent feels that there is an often overlooked hurdle when it comes to their implementation, and that is people's perception of them. In fact, the very stories inspiring so much of robotics have also proved its downfall in this respect, as they instil preconceived notions in people's minds: "Though most individuals have never interacted with a robot in real life, they have mental schemas about what robots should do, what they should look like, and what their abilities should be," points out Broadbent. "These mental schemas act like a pair of tinted glasses

Dr Broadbent and a retirement village resident interact with PARO.

PARO THE ROBOTIC SEAL

One particularly noteworthy success for the retirement village residents was PARO, a fluffy baby seal robot developed by Japanese industrial automation company AIST. A randomised controlled trial carried out by the team showed that it significantly reduced loneliness in the elderly population of the complex, serving this function even better that the resident dog.

through which people see and interpret real robots." Only by acknowledging and re-shaping these views about what robots ought to be can we use robots to their full potential.

For the researchers testing and designing these robots, there are more physical ways in which they can alter people's reactions to them. The 'uncanny valley' hypothesis refers to the tendency for things that look almost, but not exactly, like living humans to arouse a sense of unease in people – the valley in question referring to the sudden dip in a graph showing comfort level plotted against resemblance to a human being. This phenomenon presents a problem for roboticists because, although attempts to make robots appear as life-like as possible have produced some remarkable results, their lack of perfection could have a significant impact on their acceptance by the public. That being the case, what is the ideal form for a truly user-friendly robot to take?

This is a question that Broadbent and her team were keen to answer, building on their previous work with healthcare robots. They set up a trial using a Peoplebot robot to help participants take their own blood pressure while displaying one of three images on its display screen: a human-like face, silver face or no-face. The researchers hypothesised that the robot's 'face' might lead participants to subconsciously imbue it with varying degrees of personality and mind, and this might alter their response – which they were asked to rate after each exposure. The results were in keeping with the uncanny valley theory, as the silver face was least preferred, suggesting the mixture of human and machine features is to be avoided.

ON SCREEN

While the employment of robots as an integral component of people's lives may still be a long way off, recent years have seen computers and other devices become completely indispensable. Research has shown that people tend to treat these machines in an unusual way: "Humans are social creatures and we are used to interacting with other people and animals," explains Broadbent. "It appears that we automatically respond to computers and other technologies in the same ways that we interact with other people." In a natural extension of her research, Broadbent decided to examine how this attitude to other technologies compared to people's reaction to robots – specifically whether robots elicited a more positive reaction. This research is important, as robots are more expensive than computers so they need to have demonstrable advantages if they are to be rolled out in a healthcare setting.

Broadbent and her team set up a trial in which people were given either a robot – namely the loosely humanoid iRobiQ – or a computer tablet as an exercise coach. The same software was run on both devices, instructing participants to carry out some basic exercises and asking them questions. Intriguingly, people were more likely to obey the instructions when issued by the robot, and their general perceptions of it were much more positive, with many expressing the desire to interact with it again. This study presents a tantalising glimpse of the potential that widespread adoption of robots could have for healthcare.

Having implemented robots in a trial healthcare environment to great success, Broadbent and her collaborators are excited about broadening the scope of their operations, and they already have one project in the pipeline: "Our next big project is investigating whether robots can reduce hospitalisations in patients with chronic obstructive pulmonary disease," she enthuses. However, she is also dedicated to the much wider task of influencing human perceptions and behaviour around robots by experimenting with their aesthetics. Work in this area will help to bring the interactive robots of fiction one step closer to real life.

MAKING ROBOTS THAT CARE

OBJECTIVES

- To develop and trial robots for healthcare applications
- To test different robot appearances and behaviours in an effort to establish the optimum features in helper robots
- To compare human responses to robots and computers, in order to establish the value of utilising robots in settings that have previously used computers

KEY COLLABORATORS

Associate Professor Bruce MacDonald, Department of Electrical and Computer Engineering, the University of Auckland, New Zealand

Professor Ngaire Kerse, Department of General Practice and Primary Health Care, the University of Auckland, New Zealand

PARTNERS

The Selwyn Foundation

Yujin Robot

Gore Health

Counties Manukau District Health Board

FUNDING

Health Research Council of New Zealand • Korea Ministry of Knowledge and Economy (MKE) • Korea Institute for Robot Industry Advancement (KIRIA) • New Zealand Ministry of Business, Innovation and Employment

CONTACT

Dr Elizabeth Broadbent
Senior Lecturer in Health Psychology

Department of Psychological Medicine
Faculty of Medical and Health Sciences
University of Auckland
Private Bag 92019
Auckland 1142
New Zealand

T +64 9 373 7599
E e.broadbent@auckland.ac.nz

https://bit.ly/UniDirectoryAuckland

http://bit.ly/RoboticsAucklandElizabethBroadbent

http://bit.ly/ElizabethBroadbentGoogleScholar

DR ELIZABETH BROADBENT began her career with an honours degree in Electrical and Electronic Engineering, before undertaking an MSc and then PhD in Health Psychology. She is currently a senior lecturer in the Faculty of Medical and Health Sciences at the University of Auckland, where she also collaborates extensively with the School of Engineering.

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND

EUROPEAN PLATFORM OF WOMEN SCIENTISTS

Vice-President **Claudine Hermann** introduces EPWS, a Platform dedicated to the promotion of equal opportunities for female scientists

Representing more than 12,000 women scientists' concerns, needs, interests and aspirations is no easy feat! How does the European Platform of Women Scientists (EPWS) fulfil this mammoth task?

EPWS' full members are associations and networks, which in turn have individual members. Alongside these, the Platform's individual and supporting members make the complete combination, enabling us to reach Europe's 12,000 women scientists. Indeed, the greatest difficulty comes from the geographical dispersion of our European members, therefore, the role of our board of administration members is very important. We also communicate through our website, which is constantly updated, and via our newsletter and emails.

In what ways has the organisation evolved over the past decade?

The main evolution of EPWS was in 2009, when we shifted from a well-funded EU project to an association running on its members' voluntary work. In this restricted situation, the Platform continued to disseminate its messages at the EU level: we organised a lunch debate at the European Parliament in 2012 and co-organised a fringe session at the 2014 Innovation Convention with the Platform's member association, the European Women Inventors and Innovators Network (EUWIIN); produced several position papers related to the place of gender in Horizon 2020 when this programme was in discussion; and worked in close relationship with the Helsinki group (of national civil servants on Women in Science at the Directorate-General Research and Innovation).

What makes the Platform particularly unique?

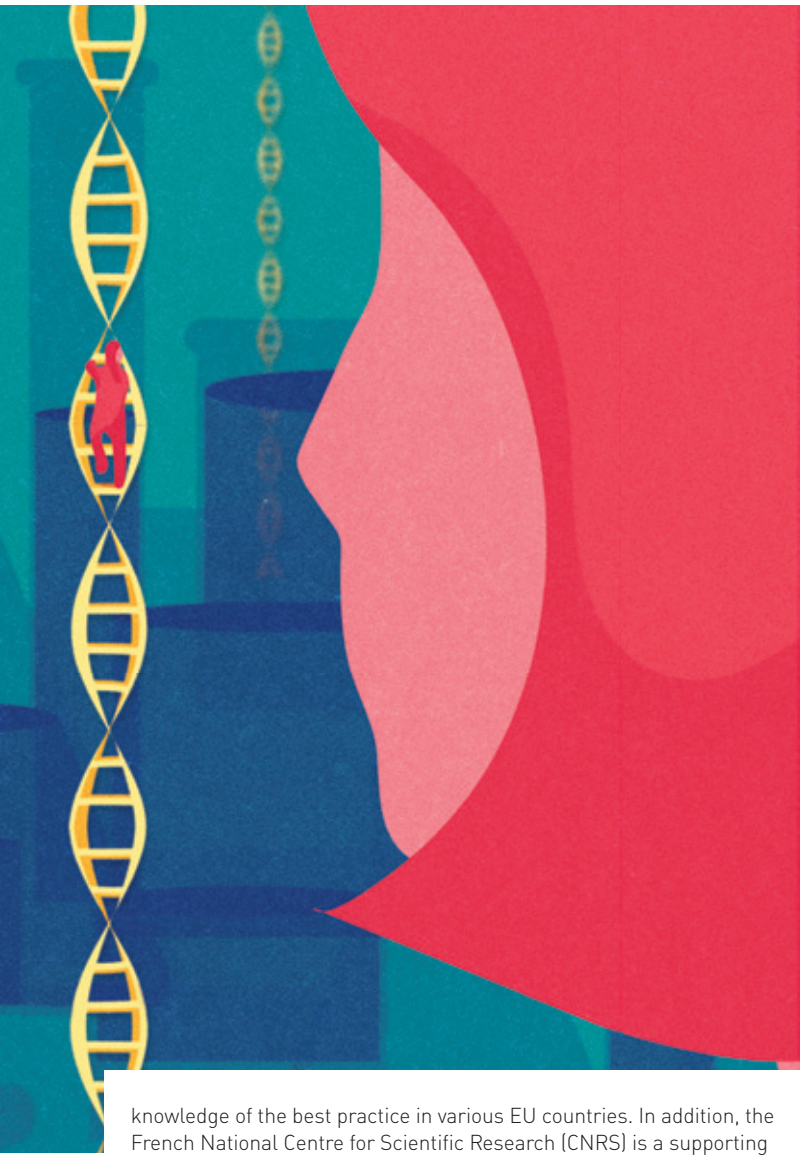
The close collaboration of EPWS' members from the many different EU countries. In spite of cultural and disciplinary differences, they have learned to trust one another and to be efficient together. This is very special and is our greatest strength.

Are you working closely with any organisations or individuals that are specifically focused around addressing the issue of gender inequality in science?

All the EPWS board members represent national associations that are working on the reduction of gender inequality in science. They are facilitating a lengthy and well-recognised discussion on this topic and are frequently asked to contribute their expertise. In France, for example, the Ministry of Higher Education and Research is asking EPWS to produce an annual benchmarking report, taking advantage of our

MARKING A MILESTONE

Incepted in 2005, the Platform has now reached its 10th anniversary. To celebrate this momentous occasion, EPWS has a number of special events on the horizon, including a conference in Germany to coincide with its Genral Assembly.



knowledge of the best practice in various EU countries. In addition, the French National Centre for Scientific Research (CNRS) is a supporting member of EPWS.

What activities is EPWS carrying out to tackle the issues of gender bias and inequality within the European R&D landscape, and to encourage more women to join the scientific community?

Apart from its position papers, EPWS took a very active part in the drafting of the recommendations following the conferences under Lithuanian (the Structural Change Promoting Gender Equality in Research Organisations Conference, Vilnius, in November 2013) and Italian (the Science, Innovation and Society: achieving Responsible Research and Innovation Conference, Rome, in November 2014) EU presidencies, for a proper consideration of gender in EU programmes. We have an important activity of disseminating gender information, which is very useful to our members at the national level.

You work closely with EPWS' President, Dr Brigitte Mühlenbruch. How do both your experiences and skills contribute to the successful running of the Platform?

Brigitte has had a long experience of EU affairs. Personally, as one of the founders of the French association 'Femmes & Sciences' (Women and Science), I know how to efficiently run a national association – a European association is more difficult due to geographic dispersion and initial cultural differences.

Our involvement and experiences have been recognised at the national level: Brigitte was honoured with the Order of Merit 1st Class of the Federal Republic of Germany, by Federal President Joachim Gauck in October 2014 in acknowledgement of her pioneering work in the promotion of women in science at national as well as European levels. As for me, I became commander of the Legion of Honor in 2011.

Are there any relevant upcoming events that you are excited about hosting or attending?

Of course, we are excited by our 2015 anniversary conference. We are also quite eager to see the assessment of the Horizon 2020 regulations regarding gender (Article 16th) – rules are a good thing, their implementation is essential to produce a change in mentalities.

Where would you like to see EPWS developing in the next five to 10 years?

We dream of an EU research area in which gender equality can be achieved and EPWS would no longer be necessary! In the next 10 years, EPWS will still need to bring the voice of EU women scientists to the EU level, making them more visible through awards, initiatives, etc. We would like to gather more associations and networks from Central and Eastern Europe, and from the private sector; and also to link our members more efficiently to help them apply for more EU projects.

CLAUDINE HERMANN DISCUSSES THE CURRENT STATUS OF EUROPEAN WOMEN SCIENTISTS

The best report on the current status of women scientists in Europe is the *She Figures* booklet, issued every third year. *She Figures 2012*, the latest publication, cites:

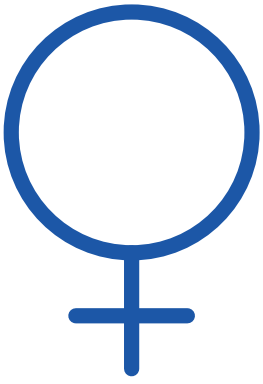
- In the EU-28 women represented 40 per cent of all researchers in the higher education sector, 40 per cent in the government sector and 19 per cent in the business enterprise sector
- The proportion of women among full professors was highest in the humanities and the social sciences, 28.4 per cent and 19.4 per cent respectively, and lowest in engineering and technology, at 7.9 per cent

epws

WWW.EPWS.ORG

EUROPEAN INSTITUTE FOR GENDER EQUALITY

Institute Director **Virginija Langbakk**, discusses how her work in addressing the gender imbalance has equipped her for this role, and EIGE's efforts to support and facilitate the establishment of equality worldwide



What contributed towards the establishment of the European Institute for Gender Equality (EIGE)?

There was an international conference in Sweden in 1999, during which the Swedish Minister for Gender Equality raised a proposal for an agency on gender equality. It took a long time to reach the decision as there were many different Member State processes involved.

Before adoption of the formal decision, the European Parliament and the Commission carried out two feasibility studies analysing the necessity to start a special agency addressing gender issues. In December 2006, the European Parliament and the Council adopted the legal document establishing the Institute.

When did your involvement in gender equality begin?

In 1997, I was working for the Swedish Association for Local and Regional Authorities, focusing more on international development and cooperation. I was given the responsibility to coordinate the work on gender equality and began developing my first projects – at the same time reading, learning, expanding the competence and collating all the necessary data and background information.

From a political perspective, we were also supporting and training women candidates in different countries, exploring the links between such areas as gender and HIV in Africa. We also looked at the importance of human resources and strategies for developing, for example, projects on water and sanitation and gender, and how to support governments in addressing these issues.

How did this engagement lead to your current position as Director of EIGE?

I didn't apply during the first round because the vacancy announcement was very much connected to managerial experience, and not so much on gender equality expertise. I wasn't keen on simply administrative/management work. During the second round, however, there seemed to be more gender equality knowledge requirements. When I applied, the questions were very mixed during the different interviews and assessments. They needed a range of expertise and managerial skills. It would have been very difficult if I hadn't worked on gender equality beforehand, as well as several other knowledge areas that were required to fulfil my position at the Institute.

How did the Gender Equality Index become connected with the European Commission (EC)'s *Strategy for Equality between Women and Men 2010–2015*?

The idea of creating the Index was first discussed and introduced in the roadmap, which guided the EC's work before the *Strategy for Equality between Women and Men 2010–2015*. First proposal of an Index was commissioned by the EC within the framework of the roadmap.

We expanded this approach for the Index, and created a new concept based on a lot of research and discussion. As our index was adopted into the Strategy, we developed it further as a robust monitoring tool, including new aspects, for example, satellite domains and issues of violence against women, and also intersecting inequalities such as age and gender, sexual orientation and gender, and disability and gender.

Can you elaborate on EIGE's methods and tools of practice?

Our methods and tools are connected through our gender mainstreaming work. In order to do this, we need to have functioning methods, understandable approaches and concrete statistics. These are all influential tools in areas where gender equality is not naturally present.

Specifically for gender mainstreaming, we are focusing on capacity building tools. This is an objective, for instance, for all military and diplomatic staff of all Member States and EU delegations in developing countries – in particular, those in conflict. There is an obligation for

staff to be trained in gender sensitivity and understanding, but the training and capacity building is insufficient and is not delivering what it should. This hinders progress in gender mainstreaming, as what can't be seen can't be measured, and therefore it is impossible to analyse the achievements.

Why is gender training a priority area for EIGE? What are the organisation's activities within this field?

Gender training is important for people who either don't agree with gender equality or are unaware of the challenges women face – some young people think that women and men are equal everywhere. So, gender training is partly about raising awareness.

The Institute focuses on its capacity for mainstreaming by processing and developing guidelines for improved use of such tools, like gender impact assessments and gender budgeting. It is fundamental to have the capacity to provide good quality training, which contributes to better gender mainstreaming.

Can you explain the steps EIGE is taking to prevent and combat gender-based violence?

Many studies have shown the depth of the gender-based violence problem. We recently launched a very important administrative data study to analyse the public sphere – mostly the services that are obliged to help and support victims of violence, including the police, judiciary, social and health services.

Our study of female genital mutilation (FGM) was the first EU-wide study to evaluate FGM prevalence. From this, we realised that even definitions of FGM differ between regions, and that practitioners do not always have the correct gender training. We now want to propose a strategic framework for our work on violence against women. This is an important step because each Member State is bound to implement a victim's directive or protection order if a victim moves from one Member State to another, and must ensure that she has the same guarantee of support. The main focus for us now is to agree on and harmonise the definitions, so that we can have a common agreement and work towards a common goal.

Intimate partner violence is also a huge problem. We recently launched another study, led by a very well-known expert on gender mainstreaming, Sylvia Walby, on our behalf. Different methods to count and assess the costs for the public services as well as for the victims (short- and long-term impact) and their children, were identified and analysed.

In addition, we are thinking of developing a 'minimum model' approach so that the Member States can conduct their own calculations. In so doing, we provide means to appeal to decision makers or redirect planning efforts by showing that conducting more early prevention not only helps prevent a victim's suffering, but also saves the budget for other priorities.

How important is the involvement of men in ameliorating the issues of gender inequality?

Men are very important; we have been discussing their involvement and engagement for many years. Men who make the decisions are not usually those who attend conferences or meetings on gender equality. It is possible they do not have time to go deeper in the area, or that concrete connection to gender equality and their everyday life is insufficiently visible; however, we must find a new approach to show this added value. At the European Parliament in Brussels in December, we had men engaging in a violence against women campaign. The Institute is trying to obtain role models for drawing young men into the debate to change attitudes towards violence against women.

EIGE is also trying to convey that we are a gender equality Institute – it's not only for women's empowerment. There are areas where men are the minority; for example, education, where women are outnumbering men, or life expectancy. We have discussed issues with the leading European men's organisations in order to join forces and work towards closing the gender gap.

eige.europa.eu

Back to basics

A detailed exploration of impulsivity and how it is influenced by visual exposure to nature is enabling **Dr Meredith S Berry** to better understand the complexities of human behaviour. Ultimately, she expects this work will promote both human and ecological health

Could you first introduce your research foci?

Much of my research is related to the factors influencing the decisions people make about a broad range of topics, including their health, the environment and money. In the case of both our health and the environment, negative consequences – such as diabetes and climate change, for example – may be relatively far in the future and probabilistic, resulting in choices that emphasise the present. Our research focuses on factors that influence future-orientated choices so that we might promote healthy, sustainable decision making that benefits humans and our ecosystems.

What inspired you to begin examining this particular area?

Numerous and pressing environmental and human health issues result from detrimental human behaviour. Studying the basic processes that influence this behaviour has allowed me to gain a better understanding of how it is associated with a wide range of important issues. Ultimately, these lines of research provide insight into how we might promote healthy human choices in a number of different areas.

How are you monitoring the effects of natural environments on impulsive decision making in a laboratory setting?

Participants view stimuli of natural environments (eg. pictures of forests, mountains and lakes) on a computer, and then we assess how they make decisions about small, immediate or larger, delayed trade-offs related to money, health and environmental outcomes. Participants in another condition view stimuli of built environments such as cities and buildings, and we also assess how they make decisions about small, immediate outcomes or larger, delayed outcomes.

What is meant by delay discounting, both generally and in regard to your research?

Delay discounting refers to the decrease in subjective value of an outcome; for example, money, when there is a delay in receiving this outcome. In other words, the subjective value of outcomes that occur in the future are less valuable than those that occur now.

Studying basic behavioural processes that contribute to impulsivity in delay discounting provides insight into behaviours associated with such pressing societal issues as drug and alcohol abuse, pathological gambling and obesity.

Could you discuss some of your most important results to date and what this has meant for the trajectory of your research on natural environments in relation to built environments?

Previous research has shown that exposure to natural as opposed to built environments increases happiness, enhances mood and restores attention. Our results are the first to suggest that exposure to natural compared to built environments may also improve how humans make decisions, and the underlying mechanism driving this result may be related to lengthened time perception.

These results highlight the broad importance of natural settings for humans – it is critical for people to be exposed to nature, especially those who live in cities and may have limited access to natural settings. We hope to continue this line of research to better understand the complex mechanisms contributing to these results.

With whom are you collaborating to conduct your research? Have you been influenced by any female role models?

I have been fortunate enough to work with numerous collaborators across departments and institutions – many of whom are excellent female role models. The conceptualisation of this work began at Utah State University with Drs Amy Odum and Kerry Jordan and continued with the help of Dr Mary Sweeney. Highlighting an important step for women, Dr Odum was recently named the first female Editor in Chief of the *Journal of the Experimental Analysis of Behavior*, a scientific journal which has published research since the 1950s.

I am also fortunate to work closely with Dr Norma Nickerson at the University of Montana, who has offered unique contributions and perspectives for this research, as well as in numerous other areas including predator conservation. Dr Nickerson, through her work as a research professor and the director of a prominent tourism institute, provides a better understanding for creating economic impetus for conservation of important natural settings and wildlife. Further, Meredith Repke and Dr Luke Conway have added a great deal of insight into our current thinking surrounding these research questions, and have been invaluable to our multidisciplinary approach.

Sustainable decisions

Researchers at **Utah State University** and the **University of Montana**, USA, have been conducting trials to determine the impact of different stimuli on decision making. Their goal is to increase future valuation of human and environmental health, thereby promoting sustainable behaviours and practices that will improve this health for decades to come

MOST HUMANS WOULD admit to having exhibited a certain level of impulsivity; for example, at some point deciding to overindulge in high fat or unhealthy food while disregarding the long-term effects of overeating. It could be argued that a certain level of impulsivity is inherent in all humans, but sometimes impulsive behaviour can be gravely reckless and is associated with damaging repercussions later down the line, both for the individual and society; exacerbating, for example, persistent societal issues such as obesity and drug addiction.

Delayed consequences have been found to have little influence on present behaviour, which is problematic as the decisions we make today impact not only our future health, but also the health of our planet. For example, poor human decisions can be linked to pressing environmental challenges such as species extinction, accelerated climate change and natural resource exploitation.

A MULTIDISCIPLINARY EXPLORATION

Previous studies have shown that exposure to scenes of the natural world improves mood and restores attention, and researchers are now beginning to build a detailed picture of the link between impulsive behaviour and exposure to natural environments. Impulsivity is a multifaceted and complex construct that encompasses a number of meanings and can be measured in different ways. This complexity is further compounded by the term's various uses. A growing body of research exploring the construct is therefore necessary.

Dr Meredith S Berry is currently based in the Department of Society and Conservation at the University of Montana, and was previously located in the Department of Psychology at Utah State University. She is working closely with collaborators Drs Amy Odum, Kerry Jordan and Mary Sweeney – also at Utah – as well as University of Montana researchers Dr Norma Nickerson, Meredith Repke and Dr Luke Conway, to determine how humans make decisions about their health, the environment and money.

A highly multidisciplinary approach has enabled the team to achieve significant headway in better understanding the factors that influence the decisions people make. Their current focus is on the effect of visual exposure to natural environments on impulsivity, with particular recent emphasis on subjective time perception.

DELAY DISCOUNTING

In a study published in *PLOS ONE* in May 2014, the researchers set out to better understand how impulsive decision making may be affected by exposure to the environment. To do this, the team measured the effect in a delay discounting task. Referring to the decline of value of a reward with increased time to its receipt, delay discounting can be used to measure impulsivity in the context of the inability to delay gratification. "For example, one might prefer to receive $40 now, rather than wait to receive $50 in one year. In this way, the value of the monetary outcome that is delayed by one year is decreased (ie. discounted)," Berry articulates.

A total of 204 participants were randomly assigned to one of three groups: natural, built or control. Individuals were shown stimuli relevant to their particular condition, with an image appearing on a computer screen for 10 seconds. Images of geometric shapes were used for the control condition, while the natural group viewed scenes of nature and the environment – mountains, for example – and the built group was exposed to images of urban landscapes.

WOLVES IN MONTANA

In another research arm closely linked to their environmental interests, Berry and Nickerson are working to understand wildlife conservation of apex predators to promote biodiversity. In this work, the opinions of Montana residents towards the economic and ecological impacts of the grey wolf are being measured through a survey. Public opinion is an influential component in wildlife management decisions and Berry believes that gauging these beliefs will contribute to legitimising management practices and facilitating long-term conservation goals.

THE NATURE OF IMPULSIVITY: VISUAL EXPOSURE TO NATURAL ENVIRONMENTS DECREASES IMPULSIVE DECISION MAKING IN A DELAY DISCOUNTING TASK

OBJECTIVE

To better understand human decisions as they relate to personal and environmental health. Specifically, to identify basic mechanisms that influence human behaviour, so that healthy sustainable choices might be promoted.

KEY COLLABORATORS

Dr Amy L Odum; **Dr Kerry E Jordan**, Utah State University, USA

Dr Norma P Nickerson, University of Montana, USA

Dr Meredith A Repke, University of Montana, USA

Dr Lucian G Conway, III, University of Montana, USA

PARTNERS

University of Montana, USA

Utah State University, USA

FUNDING

National Science Foundation (NSF)

Cambridge Center for Behavioral Studies

Institute for Tourism & Recreation Research

CONTACT

Dr Meredith Berry
Project Coordinator

545 Beverly Avenue
Missoula
Montana 59801
USA

T +1 407 595 1560
E meredith.berry@umontana.edu

www.researchgate.net/profile/Meredith_Berry

MEREDITH S BERRY received her BS in Experimental Psychology from the University of Florida, her MS in Experimental Psychology from Utah State University, and her PhD from the University of Montana in Forestry and Conservation. Her interests include the intersections of conservation, psychology and behavioural economics, as well as human and non-human animal behaviour, learning and memory.

Poor human decisions can be linked to pressing environmental challenges such as species extinction, accelerated climate change and natural resource exploitation

This visual perception was combined with a delay discounting task, which tested participants using hypothetical monetary outcomes, asking them to choose between immediate and delayed rewards. The immediate amount either increased or decreased according to the participant's response with each subsequent trial. When the immediate outcome was chosen, the amount of the subsequent immediate outcome decreased, whereas selecting the delayed outcome led to an increase in the amount of the next immediate outcome.

ALL ABOUT THE ENVIRONMENT

In a world-first, the researchers have demonstrated that exposure to natural environments is able to reduce impulsive decision making in humans, relative to built environments or geometric shapes. Berry and her colleagues identified the effects of natural versus built environments on mood, attention and time perception as possible factors that can help explain the correlation between exposure to natural environments and decreased impulsive decision making.

The researchers discounted enhanced mood as the driving mechanism for less impulsive decision making because participants were exposed to scenes of nature. Positive mood induction is proven to heighten impulsive decision making, and mood is improved in natural environments. Therefore, if mood was the primary agent impacting on the researchers' results, natural scenes would increase rather than decrease impulsive decision making, which was not the case.

Scenes of nature are thought to slow time perception, which could have decreased impulsive decision making in the natural condition. It is believed that with slowed time perception, delays may be perceived as shorter. In terms of the impact of attention on delay discounting, individuals with attention deficits are more impulsive and differences in attention could result in decreased impulsive decision making when viewing natural scenes, as viewing such scenes could increase baseline levels of attention.

A SOLID FOUNDATION

The groundbreaking data garnered by the team will form the foundations of future research exploring the broad importance of natural settings for humans. Building on this work could lead to the development of techniques to decrease impulsive, damaging human decision making, thereby promoting human and ecological health; for example, exploring the potential value of including exposure to natural environments as a treatment component for maladaptive behaviours. "I hope the applications of this work focus on integrating more nature-based treatment components for disorders associated with impulse control such as drug addiction and obesity," Berry explains. "I also hope this research adds to the impetus for conservation of pristine natural settings such as undeveloped forests. It is of paramount importance that we support and preserve natural settings that remain available to us, both for human and ecosystem health."

TIME PERCEPTION

Berry has identified an absence of research that specifically investigates the possible effects of natural environments on time perception, and therefore a deficit of work that tests the effect of natural environments on both impulsivity and time perception in one single study. In a new line of investigation that builds on the *PLOS ONE* study, the researchers are adding two measures of time perception to the experiment, asking participants to estimate how many minutes they believe have elapsed during the study, and give a scale measurement of whether or not they thought time passed quickly during the experiment. This will help establish the correlation between exposure to nature and how time is perceived.

Reading the waves

Instilled with a passion for the ocean at an early age, **Dr Cristina Forbes** uses her enthusiasm to predict storms and storm surge. Here, she describes how her love for oceanography and meteorology developed, and details her efforts to refine a national storm surge prediction model

What experiences have most shaped your fascination with oceanography and meteorology?

As a child, I sailed along the coastlines of Argentina and Uruguay, where there is a strong, violent wind event called the 'Pampero' that blows over the Argentinian Pampas grasslands. This regional storm is dangerous for unprepared sailors in the South Atlantic Ocean, so my parents taught me how to read the ocean waves and skies in order to take advantage of the best winds and be safe under extreme weather conditions. I used this knowledge to race in, and win, sailing regattas. In the process, I developed a great respect for the ocean and the weather.

These experiences drove my passion for using physics and mathematics to simulate and predict oceanic and meteorological phenomena later in life. I went on to study physical oceanography (the mathematical equations that describe waves, currents and other ocean features) in Argentina, earned the equivalent of a Master of Science degree and taught geophysical fluid dynamics and waves and tides at the Instituto Technológico de Buenos Aires (ITBA). I later earned a PhD in Meteorology and Physical Oceanography from the University of Miami in Florida, USA.

Could you highlight some of the benefits afforded by your association with the National Oceanic and Atmospheric Administration (NOAA)?

I work at the National Hurricane Center (NHC) in Miami, which is part of NOAA, and for CyberData Technologies – a minority woman-owned company certified by the US Small Business Administration that delivers support services to the US Federal Government, such as the provision of scientists and specialists in information technology for government projects. My main task is to provide operational support to the NHC during tropical cyclone events by generating storm surge guidance for the evacuation of vulnerable coastal areas. I also work on improving the National Weather Service Sea, Lake and Overland Surges from Hurricanes (SLOSH) numerical storm surge prediction model, to provide better water level and inundation forecasts and for effective evacuation planning. It is extremely rewarding to use my experience, knowledge and skills to impact society by helping to save property and lives.

Can you outline the current aims of your numerical ocean modelling?

I am presently incorporating ocean waves into our storm surge modelling system. Waves are particularly important in areas where there is steep bathymetry – an abrupt descent of the ocean floor near the coast. This innovation will enable us to provide better guidance of inundation in islands of the Caribbean, like Puerto Rico, and in the Pacific Ocean, such as the Hawaiian Islands.

Do you have further plans for using the SLOSH model? Will you be focusing your efforts in any other locations?

We will continue using the SLOSH numerical model for storm surge guidance along the US Atlantic and Gulf of Mexico coastlines during the hurricane season (1 June – 30 November). We are also using the SLOSH model to run multiple hypothetical tracks to determine the vulnerability of coastal areas to tropical cyclones of different wind speeds, storm motions, sizes and landfall locations during the off season. These results are used by local communities for long-range planning and evacuation purposes.

Are you collaborating, both nationally and internationally, to carry out your research?

I collaborate with scientists in the US and around the world. We communicate via email, telephone and electronic conferencing software, and meet in person at scientific conferences and workshops. There is an international effort sponsored by the World Meteorological Organization (WMO) in Geneva, Switzerland, to develop a storm prediction system for Hispañola (Haiti and the Dominican Republic) and other regions around the world. A couple of years ago, I was invited by WMO to serve as an expert to help develop an implementation plan for a storm surge prediction system for the Dominican Republic. It is very exciting to share ideas and discuss technical issues that will help protect the country and the world against this extremely dangerous natural hazard.

Is there a particular message you would like to impart to our readers?

As more and more people migrate to the coast, they urbanise the landscape and build structures there to protect lives and property. In spite of nature's sporadic wrath, the Earth is an extremely fragile place and we – as world citizens and its caretakers – need to adapt, be gentle, learn and understand the environment to better protect ourselves and our planet. As the Native American Cherokee Indian proverb says: "Let us walk softly on the Earth..."

Superstorm prediction

A physical oceanographer and her team at the **National Hurricane Center** in Miami, Florida, USA, are working on a national storm surge model. Using data obtained during Hurricane Sandy, they are improving the model for future events in order to help protect both people and property

HURRICANE SANDY WAS the most lethal and destructive hurricane of 2012, and the second costliest hurricane in US history. It began as a wave in the Caribbean, but quickly turned into a tropical storm in a period of just six hours, officially becoming a hurricane on 24 October. Sandy became the largest Atlantic hurricane on record, with winds spanning 1,100 miles. It killed at least 286 people across seven countries, and is estimated to have cost over US $68 billion.

Sandy, and other destructive landfalling hurricanes, are a testament to the importance of capable and reliable prediction systems. Accurate forecasts of hazardous weather can save lives, mitigate property loss and improve economic efficiency. Indeed, this is the mission of the US National Hurricane Center (NHC), part of the National Oceanic and Atmospheric Administration (NOAA).

Dr Cristina Forbes, Physical Oceanographer and Storm Surge Modeller at the NHC, is dedicated to improving predictions of extreme weather events by applying new scientific advances. After working at the University of North Carolina, where she developed real-time storm surge prediction systems for the state, she joined the Storm Surge Unit at the NHC, where she is working to make better storm surge predictions by improving the National Weather Service (NWS) Sea Lakes and Overland Surges from Hurricanes (SLOSH) model.

STORM SURGE SIMULATION

SLOSH, a numerical coastal ocean model, is used by the NWS to develop a range of storm surge prediction simulations, including real-time, historical and probabilistic simulations. Underlying the model is AutoSurge, an automated, event-triggered, storm surge prediction system. Developed by Forbes in 2010, AutoSurge eliminates labour-intensive tasks, computes storm parameters with a high level of accuracy and prevents human input error – essentially, it runs SLOSH. The system automatically generates an array of products, using the output from SLOSH to provide guidance to the Storm Surge Unit at the NHC.

The moment a tropical disturbance is identified as having the potential to develop into a tropical cyclone, AutoSurge begins to generate storm surge forecast simulations. The system then alerts the Storm Surge Specialists, sending guidance via email. In the 2012 hurricane season, AutoSurge was run in surge-only mode (without tides), and more than 1,000 numerical simulations were conducted during Hurricane Sandy.

REPRODUCING DESTRUCTION

In partnership with NWS, Forbes recently carried out a retrospective analysis of the forecasts made during Hurricane Sandy. She conducted a numerical simulation of the storm tide that flooded the US Atlantic coastline during the hurricane using SLOSH, in an effort to assess its ability to replicate the storm. "We went back, reanalysed our forecasts, and validated our numerical model results against the actual wind and ocean measurements taken during Hurricane Sandy," she explains.

As a result of subsequent upgrades to the model, SLOSH is now able to predict storm surges in an extremely accurate and rapid manner, typically taking only a couple of minutes. "This enables us to run multiple simulations to take into account the uncertainty in the tropical cyclone track and intensity predictions, and thus provide more reliable information on probable inundation (flooding) levels," adds Forbes.

To assess the ability of the upgraded model, the team used SLOSH driven by the final version of the NHC's hurricane track data to create a retrospective model simulation of the storm surge that occurred during Hurricane Sandy. Following this, they examined how water level results simulated by SLOSH compared to the actual water level measurements from NOAA tide gauges, and the extent of inundation assessed by the U.S. Geological Survey (USGS).

IMPROVED PREDICTIONS

As Forbes confirms, the results were surprisingly favourable: "The SLOSH model results compared very well with the observed water levels". Verification analyses showed that the model is capable of accurately simulating the height, timing, evolution and extent of the water driven ashore by Hurricane Sandy. The 2013 upgrades to the model, including the incorporation of astronomical tides,

Hurricane Sandy image courtesy of the Earth Observatory, NASA Goddard Space Flight Center.

STORM SURGE MODELLING IN IMPOVERISHED NATIONS

An international effort, spearheaded by the World Meteorological Organization (WMO), is aiming to develop storm surge prediction systems for impoverished nations around the world.

Dr Cristina Forbes was invited by WMO to serve as a storm surge expert to help develop an implementation plan for the Dominican Republic, a nation in desperate need of resources, to save lives during extreme events like tropical cyclones.

A workshop was held in 2011 in order to understand how a numerical storm surge prediction model can be developed and deployed for the country. As a result, a number of important institutions agreed to work together to create a national repository of geophysical data. Once this is complete, a numerical storm surge prediction model will be implemented and a grid built to simulate coastal flooding. These efforts will later be rolled out to other nations around the world. In the past year, an expanded whole-island approach, to include not only the Dominican Republic but also Haiti, was devised to help both nations during tropical cyclone events. Currently, resources are being secured to bring this project to fruition and prevent destruction and the loss of lives in these impoverished island nations.

increased the hindcast accuracy of the model, enabling forecasters to better predict the timing and degree of the water level.

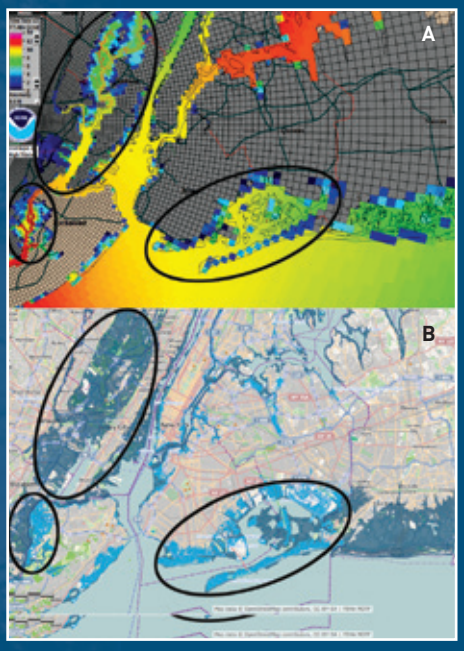
Further quantitative assessments of the simulation results – comparisons with water surface peak elevations measured at 13 NOAA tide gauge stations, by 60 USGS storm surge sensors deployed ahead of the storm and 268 high water marks collected after the storm, a total of 341 observations – showed that the simulated water levels at more than one-third of the measurement locations had under 10 per cent error. Furthermore, the model's level of efficiency means it is able to run large, automated ensembles of real time predictions in order to account for the variability of tropical cyclone forecasts. In turn, this ensures that guidance offered to the public is more reliable.

PLANNING FOR PROTECTION

The analysis, published in the *Journal of Marine Science and Engineering* in 2014, provides a baseline for the evaluation of future versions of SLOSH and for comparisons with other modelling systems – which is important as the NWS moves towards a multi-model system. Forbes comments: "The results guided us in improving the storm surge model and input data for future tropical cyclone events".

At present, Forbes is incorporating waves from the Simulating Waves Nearshore (SWAN) model – a third-generation wave model developed at Delft University of Technology in the Netherlands – into the SLOSH model. SWAN is able to compute random, short-crested, wind-generated waves in coastal regions and inland waters, and she hopes that by combining the two models she will be able to predict inundation caused by tropical cyclones in Hawaii, Puerto Rico and the Virgin Islands, before expanding to other islands in the Caribbean.

Forbes' ongoing goal, to enhance the SLOSH storm surge model, is driven by a desire to continuously improve the accuracy of predictions, and ultimately protect human life. "I will continue to conduct verifications of the water levels and inundation extent after tropical cyclone events in order to improve our entire forecasting system. So, when the next storm comes, we will have better, more accurate predictions of storm surge," she explains. By including ocean waves, the model's prediction of water levels will become more accurate, and emergency managers and government agencies will be better able to plan evacuations in their localities.



(A) SLOSH model-simulated storm tide in feet (ft) above ground level (initial water levels 0.9 ft). High – 14 ft (magenta), Low – 0 ft (dark blue).

(B) Modeling Task Force (MOTIF) field-verified Hurricane Sandy Impact Analysis graphic (courtesy of FEMA). Final high resolution storm surge extent (grey); very high resolution extent (blue) – New York City.

INTELLIGENCE

SEA, LAKE AND OVERLAND SURGES FROM HURRICANES MODEL

OBJECTIVE

To improve storm surge predictions through developing and upgrading the National Weather Service Sea, Lake and Overland Surges from Hurricanes (SLOSH) model.

KEY COLLABORATORS

Dr Cristina Forbes, Physical Oceanographer, Storm Surge Modeler, CyberData Technologies Inc., National Oceanic and Atmospheric Administration (NOAA), National Weather Service (NWS), National Hurricane Center (NHC), Technology and Science Branch

Dr Craig Mattocks, Meteorologist, Software Developer, NOAA, NWS, NHC, Technology and Science Branch

Jamie Rhome, Storm Surge Unit Lead, NOAA, NWS, NHC, Technology and Science Branch

Arthur Taylor, Physical Scientist, NOAA, NWS, Office of Science and Technology, Meteorological Development Laboratory, Evaluation Branch

PARTNERS

NOAA

Federal Emergency Management Agency (FEMA)

World Meteorological Organization (WMO)

FUNDING

NOAA

CONTACT

Dr Cristina Forbes
Principal Investigator

Storm Surge Unit – National Hurricane Center
11691 SW 17th Street
Miami, Florida 33165-2149
USA

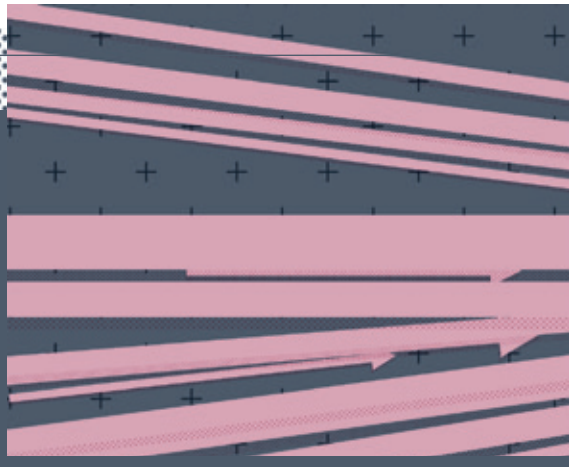
T +1 305 229 4448
E cristina.forbes@noaa.gov

www.nhc.noaa.gov
www.cyberdatainc.com

DR CRISTINA FORBES studied physical oceanography in Buenos Aires, Argentina, and subsequently earned a PhD in Meteorology and Physical Oceanography at the University of Miami, Florida. She is now working in the Storm Surge Unit at NHC as Physical Oceanographer and Storm Surge Modeller to help advance numerical storm surge prediction systems.

No filter

Dr Susanne Schmid harbours a longstanding fascination with the complex mammalian brain. Here, she explains how her research is tackling one of the major challenges in modern neuroscience: understanding how the brain processes sensory information to engender the appropriate behavioural response



Why is sensory filtering so important and what are the potential implications for an individual when this mechanism fails to function normally?

Sensory filtering is vital because the brain constantly receives sensory information from our five senses and not all of it is important. There is a lot of repetitive information that we do not need to attend to and our brains have built-in mechanisms to filter out bits that are repetitive or unimportant. These mechanisms protect the brain's resources and allow us to focus on salient information and suppress background noise. If our ability to repress this noise does not function normally then the brain is easily overloaded with information. As a result, it is difficult to focus attention and concentrate on specific aspects.

Can you summarise the symptoms of schizophrenia that are caused by a breakdown in sensory filtering?

The disruptions in sensory filtering do not only apply to schizophrenia but also to autism and a range of other mental disorders and neurodegenerative diseases. However, these symptoms are most prevalent in schizophrenia and autism. When sensory filtering does not work this impacts cognitive function, including the ability to learn, working memory and attention span. It is a matter of debate as to whether sensory filtering also plays a role in causing some of the positive symptoms of schizophrenia such as hallucinations and delusions.

To what extent do habituation and prepulse inhibition act as good measures of sensory filtering? Can you briefly explain these terms?

We measure sensory filtering in both humans and animals through a technique called the acoustic startle response, and examine the habituation and prepulse inhibition of that response. Habituation is when we attenuate our response to repetitive stimuli – a process that is deficient in patients with schizophrenia and autism. We also observe a disruption in prepulse inhibition as well, particularly in schizophrenia, but also Parkinson's and Alzheimer's disease to a lesser extent. Prepulse inhibition describes the fact that if there is a normal sensory stimulus that precedes the startle stimulus, the startle response will be greatly attenuated. The underlying concept is a little more complicated; put simply, it means that individuals with disrupted prepulse inhibition cannot focus their attention properly on something, they are more likely to become distracted and show improper behavioural responses.

Are there particularly unique or advanced methodologies that you use in your research you would like to elaborate on?

We do use some cutting-edge technologies. One of the most interesting is how we test attention and distractibility in our rats using a touchpad – similar to a tablet computer. We train the rats in boxes where we do a classical task called the Five Choice Serial Reaction Time task. During this, they initiate a trial by touching a spot at the back of the box with their noses causing a specific field on the tablet to light up 5 seconds later. They need to keep their attention focused for the 5 seconds and then touch this exact spot on the tablet. We can also give distracting noise during the attention period in order to see whether they can still maintain their focus. We do this with both normal and autistic rats. Another method we use is optogenetics. This involves novel technology in which we insert light sensitive ion channels into the synapses of cholinergic neurons and activate them by light.

You are in the process of shifting your focus from the context of schizophrenia to autism. How are the findings you have made to date, working on schizophrenia, applicable to the treatment of autism and other diseases?

Our work targets a group of symptoms that are common to both schizophrenia and autism. The reason for the shift towards autism is that it is very difficult to have a good animal model for schizophrenia because it is intrinsically a mental disorder; you can never tell if a rat is hallucinating or not. With autism, however, we have better rat models. We use a model where we give a prenatal injection of valproic acid – an antiseizure and antimigraine medication which, when taken by pregnant women, increases the risk of autism for their child – and these rats then display typical autism behaviours such as stereotypic movements, social behaviour deficits and learning disruptions.

De-cluttering the mind

Based in the Schulich School of Medicine and Dentistry at the **University of Western Ontario**, Canada, the Schmid Lab is using animal models to study the mechanisms that underpin both normal and disrupted sensory filtering

FROM THE MOMENT we wake up until the moment we go to bed, our brains are constantly bombarded with an abundance of sensory information. Derived from our senses, the overwhelming majority of this information is filtered out before we are even conscious of it. This prevents the higher cortical centres of the brain from being overloaded with irrelevant data – and it is a pre-requisite for vital cognitive functions such as attention span, memory and social interaction. Yet, the reverse is also true; any disruptions in the body's sensory filtering system have negative repercussions on higher cognitive functioning.

> The researchers in the Schmid Lab are primarily focusing on two potential treatment targets: the calcium and voltage-activated potassium ion channel and the cholinergic system

Unsurprisingly, problems with sensory filtering have long been associated with a number of mental and neurodegenerative diseases, particularly schizophrenia and autism. In the case of schizophrenia, patients are usually prescribed antipsychotic drugs; however, while these are highly effective at preventing hallucinations, they have a minimal impact on sensory filtering abilities. This means that many patients are unable to function normally at a cognitive level – and persisting memory, attention and social interaction deficits often prevent them from going back to work or from living a normal, well-adjusted life. There is, therefore, a compelling need for research that unveils the complex mechanisms of sensory filtering circuits, in turn paving the way for potential drug targets.

Drawing on their animal models of schizophrenia and autism, a team of researchers at the Schmid Lab – based in the University of Western Ontario's Schulich School of Medicine and Dentistry – are attempting to respond to this need. Led by Dr Susanne Schmid, Associate Professor of Neurobiology and Associate Chair for Research in the Department of Anatomy and Cell Biology, these researchers are making promising strides in understanding the processes that underlie both normal and disrupted sensory filtering. Using two operational measures to explore these processes – namely, habituation and prepulse inhibition – they are primarily focusing on two potential treatment targets: the calcium and voltage-activated potassium ion channel (BK channel) and the cholinergic system.

CHANNEL TARGET

As the ion channel located on the presynaptic terminal of a neuron – that is, the axon terminal where different neurons make contact – the BK channel plays a role in regulating the excitability of cells and is highly unusual in that it is expressed in a number of different neuron transmitter systems rather than just one. It represents a new and exciting field of research. While some previous work has been done on the BK channel in frogs – with results suggesting that it provides the mechanism for fine-tuning synaptic strength – very little is known about how the BK channel mechanism functions in mammals. "We know that the BK channel is expressed in many different

SPATIAL LEARNING AND MEMORY IN MICE

OBJECTIVE

To study the mechanisms underlying normal sensory filtering and sensory filtering disruptions in animal models of schizophrenia and autism.

KEY COLLABORATORS

Marco Prado; **Vania Prado**; **Jane Rylett**; **Mandar Jog**; **Matthew Hebb**; **Mike Strong**; **Raj Rajakumar**; **Stephen Ferguson**, University of Western Ontario, Canada

Catherine Rankin, University of British Columbia, Canada

John Yeomans, University of Toronto, Canada

Steward Clark, University at Buffalo, USA

Peter Ruth; **Peter Pilz**; **Marlies Knippers**, University of Tuebingen, Germany

Phillip Winn, University of St Andrews, UK

Soren-Peter Olesen, NeuroSearch A/S, Denmark

FUNDING

Canadian Institutes of Health Research

University of Western Ontario

Natural Sciences and Engineering Research Council of Canada

Ontario Brain Institute

Canadian Foundation for Innovation

Ontario Research Funds

Ontario Mental Health Foundation

CONTACT

Dr Susanne Schmid
Associate Professor for Neurobiology
Associate Chair for Research, Department of Anatomy and Cell Biology
Co-director of the Neuroscience Graduate Program

Schulich School of Medicine & Dentistry
University of Western Ontario
Medical Sciences Building, Room 470
London
Ontario N6A 5C1
Canada

T +1 519 661 2111 x 82668
E Susanne.Schmid@schulich.uwo.ca

www.theschmidlab.com

DR SUSANNE SCHMID gained her undergraduate and postgraduate degrees at the University of Tuebingen, Germany, before working as a research assistant and postdoctoral researcher at the University of Tuebingen Eye Hospital. In 2006, she moved to Canada as a guest professor at the University of Toronto, and has been at the University of Western Ontario since 2007.

neurons and that it influences synaptic strength – but the cellular molecular mechanisms in mammals have remained elusive until recently," Schmid points out. "It is a relatively new target and there are currently very few drugs that we can use to block or enhance BK channel function in our experiments."

Building on prior work that implies the BK channel fine-tunes the strength of the connection between two neurons, recent experiments conducted by Schmid and her team tested the short-term and long-term habituation of both reflexive and motivated behaviour in mice deficient for the pore-forming α-subunit of the BK channel. Interestingly, they found that the short-term habituation of reflexive behaviour was abolished in the BK knockout mice while the long-term habituation of both reflexive and motivated behaviour was unaffected by BK deficiency, thus indicating a clear distinction between the mechanisms for short-term and long-term habituation. Moreover, in another study the researchers found that mice with deficient BK channel function display impaired prepulse inhibition and spatial learning – and yet have normal working and spatial reference memory. Going forwards, an enhanced understanding of the role of the BK channel in sensory filtering will enable the development of specific drugs for improving sensory filtering and the symptoms associated with disruptions.

THE NICOTINE FACTOR

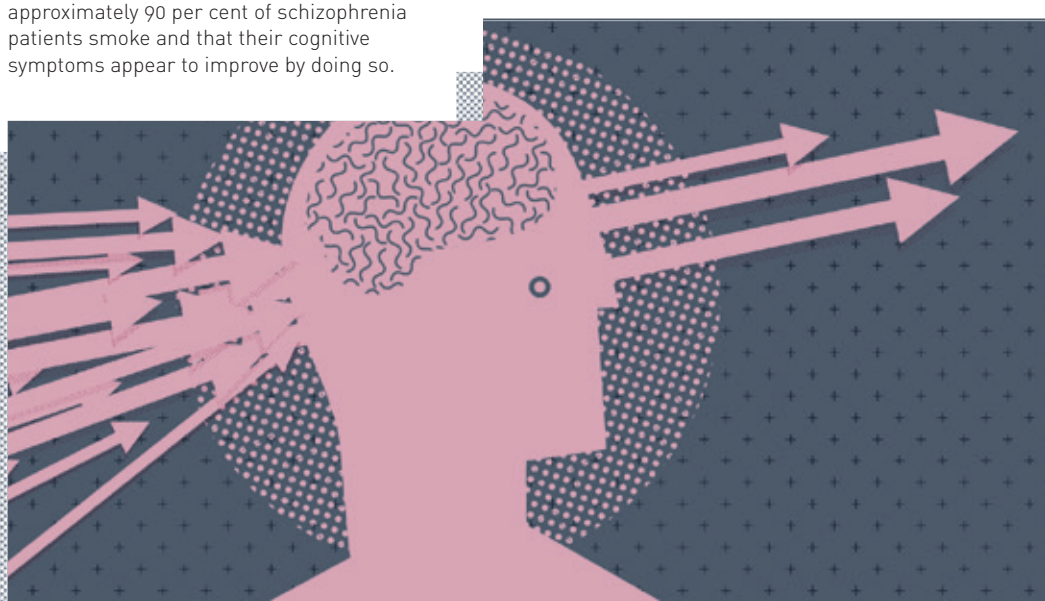
The network of nerve cells that uses acetylcholine in the transmission of nerve impulses – known as the cholinergic system – is the other key focus area in the Schmid Lab. In addition to its well-established role in higher cognitive functioning, there is strong evidence that acetylcholine is also involved in sensory filtering. Indeed, when nicotine enters the brain it attaches to acetylcholine receptors and mimics the neurotransmitter's actions. A body of research has shown that schizophrenics who smoke show substantially improved prepulse inhibition and cognitive functioning than those who do not. Similarly, nicotine administered to healthy non-smokers has also been demonstrated to enhance prepulse inhibition. In this light, it is perhaps unsurprising that approximately 90 per cent of schizophrenia patients smoke and that their cognitive symptoms appear to improve by doing so.

Based on these insights, Schmid and her colleagues are determining the function of midbrain cholinergic cell groups in cognitive function and examining their interactions with non-cholinergic cells. To this end, they are combining cutting-edge optogenetic approaches in both *in vivo* and *in vitro* experiments with behavioural and electrophysiological approaches using their animal models of habituation and prepulse inhibition of startle. The hope is that this will enable them to assess the possibility of modulating the activity of the cholinergic system through pharmaceutical or electrical interventions.

TRANSLATION AND PROGRESSION

Ultimately, the basic and preclinical research conducted in the Schmid Lab is laying the foundation for the development of medication that enhances sensory filtering and cognitive function in humans. The identification of viable drug targets for the treatment of adverse cognitive symptoms will have a significant impact on the quality of life of patients with schizophrenia and autism, as well as on other groups who are affected by sensory filtering deficits. "Although we are still a very long way away from fully understanding these disorders and diseases, drugs that improve the cognitive function are extremely valuable," Schmid asserts. "As developmental disorders, we may never be able to fully cure schizophrenia and autism – yet by treating the symptoms we can ensure that those afflicted will be able to live much more fulfilling and independent lives."

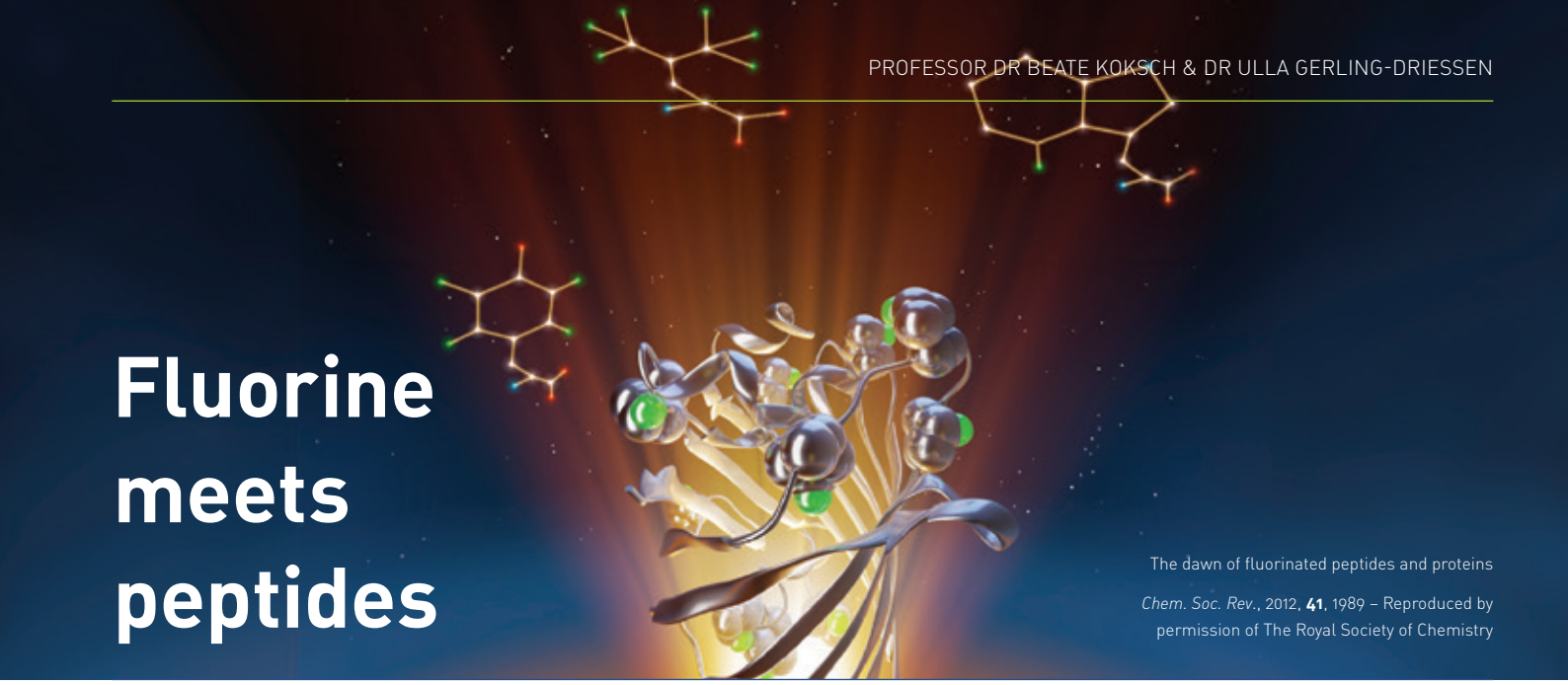
Importantly, Schmid's research could also have a wider impact on society at large: at present, health and welfare systems in Canada and elsewhere are burdened by a range of mental and neurodegenerative diseases that prevent individuals from operating at their full potential. The introduction of innovative new therapies for sensory filtering disorders represents a highly promising development for both individuals and the wider community. Until then, Schmid and her team will continue to apply their knowledge and expertise to probe the complex cellular mechanisms that are responsible for sensory filtering.



Schulich MEDICINE & DENTISTRY

Western UNIVERSITY · CANADA

Fluorine meets peptides



The dawn of fluorinated peptides and proteins

Chem. Soc. Rev., 2012, **41**, 1989 – Reproduced by permission of The Royal Society of Chemistry

Highlighting their research into fluorine, **Professor Dr Beate Koksch** and **Dr Ulla Gerling-Driessen** explain how they have applied their chemical expertise to develop novel peptide-based models that will advance understanding of protein-protein interactions and encourage the design of new drugs

Could you introduce your research on peptides and outline its main objectives?

BK: My research group specialises in the design, synthesis, characterisation and application of peptide model systems to a diverse range of problems in biomedicine, biotechnology and materials science. Peptides and proteins have many different roles in nature; they may be enzymes that perform chemical reactions in cells, structural components, transport molecules, molecular motors or storage 'warehouses' – not to mention their roles in defence and regulatory processes. Their overwhelming structural and functional diversity depends upon the physical and chemical properties of their constituent amino acids.

The introduction of fluorine into small molecules and biopolymers has a wide range of effects on their physicochemical properties, often desirable, but also unpredictable. As the chemical element with the highest electronegativity, fluorine is rather unique. The fluorine atom imparts the carbon-fluorine (C-F) bond with low polarisability, high polarity and the ability to change the behaviour of neighbouring functional groups, in a covalent or non-covalent manner. The way fluorinated amino acids influence protein stability and function, as well as peptide-protein interactions, are not easily generalised. Thus, a rational design applying fluorinated amino acids in peptide and protein engineering is currently not possible. Our group has established a research programme that aims at understanding the impact of fluorination on the properties of peptides and proteins. We have developed a set of highly versatile peptide model systems for the purpose of gaining insight into the complex interaction properties of fluorinated amino acids in the context of peptide and protein environments.

UG-D: Fluorinated amino acids can have dramatic effects on protein stability and protein-protein interactions due to the unique stereoelectronic properties of fluorine. Previous approaches to assessing their properties have mainly focused on helical systems, even though fluoro-amino acids are known to exhibit lower propensities to adopt helical structures than their hydrocarbon analogues, suggesting that fluorinated amino acids may generally be well suitable for modulating non-helical structures. Still, fluorinated amino acids have rarely been studied in amyloid forming peptides. A common application is the use of NMR-labelled fluorinated amino acids to gain insight into the mechanism of structural conversion and amyloid formation.

However, a systematic study that includes the specific properties of fluorinated amino acids as factors for peptide folding and amyloid formation was still missing. Thus, during my PhD I examined the substitution of natural amino acids within an amyloid forming model peptide by amino acids that contain different stoichiometries of fluorine in their side chains. This approach enables a systematic evaluation of the impact of fluorine on amyloid formation. I have investigated the impact of several intrinsic properties such as size, hydrophobicity and secondary structure propensities of the fluorinated amino acids on the amyloid formation process. I found that the increases in the fluorine content per side chain additively reduce the α-helix propensities while the hydrophobicity of these amino acids increases with increasing fluorine. We have shown that the fluorine content of fluorinated amino acids significantly influences the kinetics of the amyloid formation process. A strong correlation between increasing fluorine content and amyloid formation was found, which was attributed to the interplay of the intrinsic properties of the particularly incorporated fluorinated amino acids and the position that was substituted in the sequence.

What expertise do you both bring to this project? How did your collaboration come about?

BK: I studied chemistry and have a PhD in biochemistry. During my PhD studies I learned about protease-catalysed peptide synthesis and was interested in applying this technique for the incorporation of fluorinated amino acids into peptides. I soon found out that this did not work and started to study why this was the case, as the literature in this field was very limited at that time. I became fascinated by the potential of this particular class of amino acids, and began to systematically evaluate the properties of different kinds of fluorinated amino acids in the context of peptides and proteins.

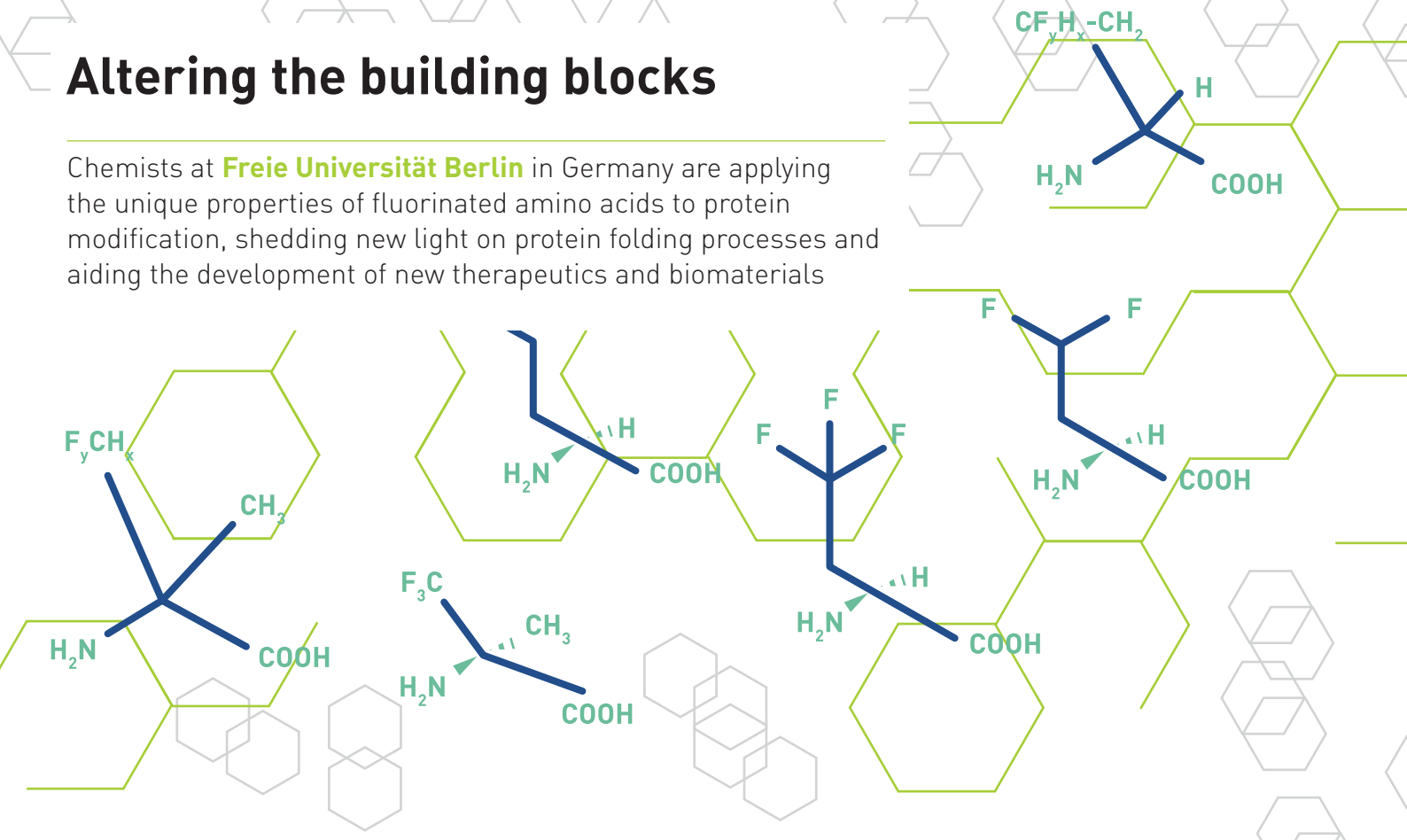
UG-D: I completed my MSc and PhD in the group of Professor Koksch and have been working in two important areas of her research: protein misfolding and fluorinated peptides.

Why is fluorine an ideal element for peptide and protein modification?

BK: Amino acid residues carrying functional groups that are orthogonal to biological systems may serve as biophysical probes for the detailed determination of structure-activity relationships, or components of tailor-made biomolecules. In particular, the incorporation of fluorine atoms has been shown to enhance protein stability *in vivo* and improve the physical properties of protein-based materials.

Altering the building blocks

Chemists at **Freie Universität Berlin** in Germany are applying the unique properties of fluorinated amino acids to protein modification, shedding new light on protein folding processes and aiding the development of new therapeutics and biomaterials



ONE OF THE four major biological macromolecules – proteins – are critical for life on Earth. In the body, proteins fulfil a huge range of functions: they act as hormones, catalysts and transporters, and provide mechanical support and storage. They are the most versatile macromolecules in living systems, and play critical roles in almost all biological processes, including immune protection, movement, nerve impulse transmission and growth, and differentiation.

Strikingly, this vast diversity is the result of just 20 amino acids, the building blocks of proteins. They provide a chemical complexity which allows proteins to perform a wide range of functions, as the amino acid sequence (primary structure) of a peptide dictates how it will fold into more elaborate 3D structures.

As protein structure dictates so many biological processes, efforts to understand it are extensive. A major contributor to these efforts is Professor Dr Beate Koksch, who leads a lab in the Institute for Chemistry and Biochemistry at the Freie Universität Berlin. Working with Koksch is postdoctoral fellow Dr Ulla Gerling-Driessen, who pursued her postgraduate studies in Koksch's group. Together with the students and co-workers in the Koksch group, they aim to understand peptide structure in order to manipulate protein structure for a number of applications. This is an important goal for several reasons: gaining insight into how primary structure is linked to folding under real-life conditions precedes the ability to inhibit disturbed folding processes, which underlie disease. Furthermore, incorporating particular amino acids in specific positions in proteins could enhance the therapeutic effect of peptide-based drugs, of which 100 were marketed in 2013 – with sales totalling over US $40 billion. However, this work also has implications outside medicine, as increasing the range of building blocks that can be used to engineer proteins, beyond the natural amino acids, has great potential for materials science.

FLUORINE INCORPORATION

The team has developed a unique method of interrogating protein structure by incorporating fluorine into amino acids. Although it rarely naturally occurs in biomolecules, fluorine has a highly beneficial effect on the pharmacokinetics and biological properties of proteins, making it a valuable element in the protein modification toolkit. The reason fluorine has such effects can be traced back to its physicochemical properties; it is the most electronegative element, and has an extremely strong bond with carbon, that is weakly polarisable.

Koksch's research programme aims to exploit these properties to understand protein structure and function, and studies fluorinated amino acids in the context of peptide and protein environment. These highly functionalised amino acids can be used as biophysical probes for detailed studies of structure-function relationships, and to construct tailored biomolecules.

However, it is not easy to predict the effect of fluoroalkyl groups in native proteins, because they combine two opposing chemical properties: polarity and hydrophobicity. Thus, in order to understand the complex molecular interactions of fluorine within polypeptides, the Koksch lab developed a number of innovative peptide-based models.

STRUCTURE CONVERSION

The ability to assume more than one stable confirmation is a feature of proteins involved in the development of neurodegenerative diseases. In many conditions, changes in protein secondary and tertiary structures cause aggregates to form. When normally soluble proteins assemble together, they form amyloid fibrils, which are resistant to degradation. When these insoluble protein aggregates, or plaques, are deposited in nerve tissue, they can cause neurodegenerative disease. Although the process has been intensely studied, how fibrils form from peptide building blocks is incompletely understood.

To narrow the knowledge gap, the Koksch lab designed model systems that allow systematic analysis of how mutations in the

FLUORINE: A POWERFUL ELEMENT

Fluorinated amino acids have garnered much attention for their ability to enhance the biophysical, chemical and biological properties of proteins

Fluorine interacts with proteins in a unique way, as the Koksch lab has shown in two recent studies:

1. Impact on proteolytic stability

The group investigated how fluorine affects proteolytic stability (resistance to proteases, enzymes that digest proteins). In a systematic study, they incorporated fluorinated amino acids into the substrates of two digestive system enzymes.

Fluorination only increased proteolytic stability in a few cases, indicating that fluorine's ability to enhance the metabolic stability of drugs should not be used as a general statement. Due to fluorine's unique properties, fluorinated amino acids can interact with proteins in a manner that is impossible for non-fluorinated analogues. These results will inform the future design of peptide-based drugs.

2. Ability to mediate protein-protein interactions

In another study, the team introduced fluoroalkyl groups into a protease inhibitor. Crystal structures of this inhibitor in complex with the protease revealed changes to the water molecules in the enzyme's binding pocket.

These changes represent a previously undescribed mechanism by which fluorine mediates peptide-protein interactions. The cooperative role of fluorine strengthens their hypothesis that fluorinated amino acids are a unique family of building blocks for protein engineering.

primary structure impact the secondary structure of proteins. Using these systems, the team is able to follow the interconversion between different secondary structures in response to environmental factors, such as pH and metal ion concentration. These model systems allow scientists to study complex issues in protein folding, such as the role of electrostatic interactions in the aggregation process, both in the context of the native environment and at the molecular level.

FINDING THE SWITCH AND FLUORINATING IT

This particular model was based on the α-helical coiled coil, a pervasive protein motif involving two strands wrapped around each other, but with additional histidine residues to create binding sites for Cu^{2+} and Zn^{2+} ions. In their investigations, the team showed that protein secondary structures can be switched via these metal ions. Furthermore, these transformations appear to be common in the early stages of neurodegenerative diseases, when the concentration of metal ions in brain tissue is naturally elevated. Moreover, the impact of interfaces, membrane environment and ionic strength on conformational changes was studied using model peptides.

In a more recent study, the impact of fluorination on structural conversion and amyloid formation was investigated. Introducing amino acids with different fluorine content in their side chain into key positions of the coiled coil motif, drastic effects on the amyloid formation process were observed which could be attributed to the altered physical and chemical properties of fluorinated amino acids.

PROTEIN-BASED DRUGS

The team's *in vitro* investigations with its peptide-based models have revealed how fluorine influences the folding and stability of proteins, elucidating the key role of fluorine-fluorine interactions on the folding process.

The researchers have successfully designed proteins whose folding can be controlled, a major achievement in peptide chemistry. Looking ahead, the team intends to combine its peptide models with emerging analytical techniques and screening methods, such as surface plasmon resonance (which enables the detection and monitoring of biomolecular interactions) and phage display technology (used to identify the interaction partners of proteins) to study the interaction patterns of a range of fluorinated residues within polypeptides. Ultimately, this will allow use of the beneficial properties of fluorinated amino acids to design peptide drugs and fluorinated protein-based materials for a range of purposes.

THE DAWN OF FLUORINATED PEPTIDES AND PROTEINS

OBJECTIVES

To understand the impact of fluorination on the properties of peptides and proteins.

KEY COLLABORATORS

Professor Dr Günter Haufe, Organic Chemistry Institute, University of Muenster, Germany • **Professor Dr Anne S Ulrich**, Karlsruhe Institute of Technology, Institute of Organic Chemistry, Germany • **Professor Ashraf Brik, PhD**, Ben-Gurion University, Israel • **Professor Dr Nediljko Budisa**, Institute of Chemistry, Technische Universität Berlin, Germany

FUNDING

German Research Foundation (DFG) (KO1976/2-2, KO1976/5-1)

DFG Research Training Group: Fluorine as Key Element

CONTACT

Professor Dr Beate Koksch
Professor of Organic Chemistry and Natural Product Chemistry

Institute of Chemistry and Biochemistry
Takustrasse 3
14195
Berlin
Germany

T +49 30 838 55344
E beate.koksch@fu-berlin.de

http://userpage.chemie.fu-berlin.de/~akkoksch

PROFESSOR DR BEATE KOKSCH studied Chemistry and Biochemistry at the University of Leipzig and pursued her postdoc while working with Professors Reza Ghadiri and Carlos Barbas III. Since 2004, she has been Professor of Organic and Natural Product Chemistry at Freie Universität Berlin. Her group studies complex folding mechanisms that occur in neurodegenerative diseases, develops new multivalent scaffolds and investigates fluorinated amino acids, peptides and proteins.

DR ULLA GERLING-DRIESSEN studied chemistry at Freie Universität Berlin and graduated in 2009 with an MSc in Chemistry under the supervision of Koksch. She pursued her PhD in the same group. Gerling-Driessen's research focused on investigating the properties and morphologies of fluorinated amyloid forming peptides. She is currently a postdoctoral fellow working with Koksch and Professor Dr Rainer Haag at Freie Universität Berlin in collaboration with the Helmholtz-Zentrum Geesthacht for biomaterial research.

Freie Universität Berlin

the last word:
Blazing the trail

An expert in neuroscience and prominent female researcher, **Baroness Susan Greenfield** discusses her experiences of gender inequality, as well as her passion for science and helping women progress in the STEM field

What attracted you to pursue a science career?

At school I was interested in philosophy and classics – my major subjects were Latin and Greek. It wasn't until university that I became frustrated with philosophy and started studying psychology. My interest in science came quite late; in school I thought the subject was all about facts and therefore didn't provide much room for originality. Whilst studying philosophy, I had questions posed like: 'What's a person?', 'what's a mind?' and 'what's consciousness?' and realised these could be answered with neuroscience. In other words, I wasn't interested in science as such but the questions science could answer.

There is an argument that men are on average more intelligent than women and therefore it is only natural for a greater number of men to hold senior positions in STEM. What are your thoughts on this hotly debated subject?

I don't think anyone would dare state something like that now. They're not more intelligent, but generally more confident – men will promote the seven out of 10 qualities they have, whereas women apologise for the three out of 10 qualities they don't. It's certainly nothing to do with intelligence because that's such a multifaceted and complex phenomenon.

I listened to a fascinating radio show about women recently. Again, the problem is that we tend to talk very quickly – I certainly do – because we are frightened we're going to get interrupted and want to squash as many words in as possible; whereas men will talk slowly and deeply and that gives them more authority.

Are we still tackling the same residual challenges in this area, or have new issues emerged in the gender paradigm?

If anything, it has become more subtle. I remember coming second after competing for a prize in the US, and my supervisor said to me: 'Don't worry, you've done well because first of all you're a foreigner and secondly you're a woman'. It's definitely more 'underground' today.

There was a recent paper on gender bias in the *Proceedings of the National Academy of Sciences of the USA* (*PNAS*). Researchers found that when the names of job applicants were changed to a male name they were more favourably reviewed (the study is available at www.pnas.org/content/109/41/16474.full) . Also, sadly, women are not as nice to other women scientists. This may be due to the perception that some women are distrustful of other women, it's hard to say because I personally don't feel that. I try to do everything I can to help women in science.

What more can be done to address the issues of female underrepresentation in STEM?

We must start early – this means attracting school girls to science, and that is not done through smoke and mirrors, bangs and whizzes that might attract a boy, but by showing how relevant it is to everyday life.

Talking about the brain more, for example, would be a covert way of discussing science because everyone's interested. People think the brain is too complex to teach at a young age, but I talk to schools, indeed sometimes to primary schools, and the pupils have been very interested. We also need to look squarely at provisions for ring-fenced funds for women – in fact, anyone who's had primary childcare.

Do you have a take home message for girls and women looking to embark on an education or a career in STEM?

I think you have to be passionate about it because it's a very insecure career path compared to other professions, often with lousy pay and long hours – but I couldn't envisage doing anything else. Alternatively, you may want to enter private sector industry or apply your science to the media, law or politics. There are many applications for people with A level or degree level science. However, I would stress that unless you really care about your field, conducting the research is going to be hard.

That being said, nothing beats seeing something happen during an experiment that no one else in the world has witnessed. It is particularly fulfilling when that result validates an idea you've had, but then equally fascinating when nature is showing you an outcome that you never could have imagined.

International INNOVATION

Disseminating science, research and technology

Download the *International Innovation* app for iPad, iPhone* and on the Google Play™ store.

Gain free access to over 200 research articles showcasing cutting-edge developments from across the spectrum of scientific disciplines.

ANDROID APP ON Google play

Download on the App Store

*iPad and iPhone are trademarks of Apple Inc.

International INNOVATION

INFECTIOUS DISEASES

A GLOBAL PROBLEM CALLING FOR AN INTERNATIONAL SOLUTION

JOIN RESEARCHERS FROM ACROSS THE GLOBE BY PUBLISHING WITH *INTERNATIONAL INNOVATION*

EXPLORE THE RANGE OF DISSEMINATION OPPORTUNITIES AVAILABLE TO YOU IN THE FORTHCOMING THEMED EDITION

TO DISCUSS YOUR INVOLVEMENT IN THE INFECTIOUS DISEASES ISSUE OF *INTERNATIONAL INNOVATION*, CONTACT:

CAROLINE HERBERT
COMMERCIAL DIRECTOR,
EMAIL: CHERBERT@RESEARCHMEDIA.EU
PHONE: +44 (0) 7946 434091

HTTP://WWW.INTERNATIONALINNOVATION.COM/HEALTHCARE

ANDROID APP ON Google play

Download on the App Store

*iPad and iPhone are trademarks of Apple Inc.