Issue 73, summer 2013

Wellcome NEWS

ALL A MATTER OF TIMING

Nancy Papalopulu talks about a life of cells, science and cycles.

wellcome trust

What can we learn from the latest public views on *science?*

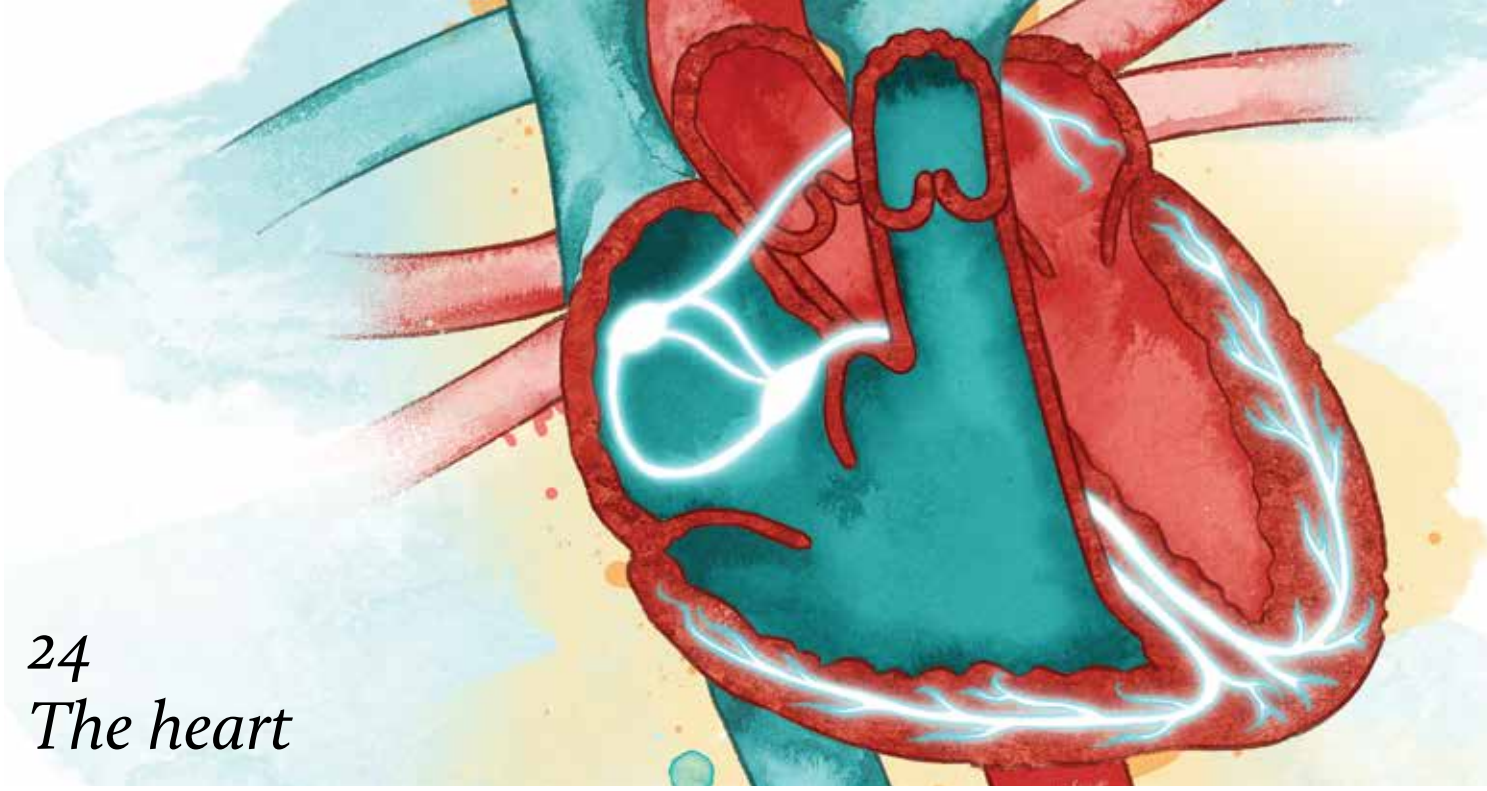
The Wellcome Trust Monitor provides fresh insights into the public's interest in, attitudes towards, and experience and knowledge of science.

This tracking survey represents the opinions of adults and young people in the UK. It aims to build a better understanding of the societal and educational context of biomedical research.

The latest results and resources are freely available online – through rich reports, datasets and eye-catching infographics. The findings will help shape science communication practice and research policy and priorities, and can be used as an academic resource.

www.wellcome.ac.uk/monitor
#WTMonitor

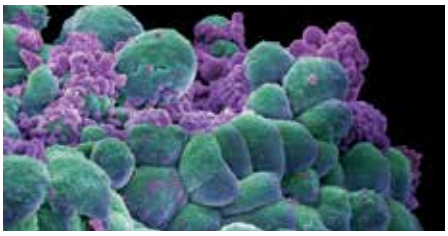
wellcome trust



24
The heart

CONTENTS

INSIDE THIS ISSUE



Wellcome NEWS

Telling the stories of the Wellcome Trust's work

Editor Chrissie Giles
Assistant Editor Tom Freeman
Writers Penny Bailey, Chrissie Giles, Michael Regnier, Emma Rhule
Design Anja Fouad
Illustrations Bret Syfert
Photography Ben Gilbert, David Sayer
Publisher Mark Henderson

Get in touch:
E wellcome.news@wellcome.ac.uk
www.wellcome.ac.uk/wellcomenews

All images, unless otherwise stated, are from the Wellcome Library. You can get copies through Wellcome Images (**wellcomeimages.org**).

Wellcome Trust
We are a global charitable foundation dedicated to achieving extraordinary improvements in human and animal health. We support the brightest minds in biomedical research and the medical humanities. Our breadth of support includes public engagement, education and the application of research to improve health. We are independent of both political and commercial interests. **www.wellcome.ac.uk**

This document was printed on material made from 25 per cent post-consumer waste & 25 per cent pre-consumer waste.

Cover: Professor Nancy Papalopulu. See page 14.

Farewell to *Wellcome News*

The way organisations communicate is changing. Smartphones, tablets and other devices mean that many more people are online much more of the time. The Wellcome Trust is adopting a 'digital first' approach, putting online at the heart of our philosophy and practice.

Being 'digital first' doesn't mean that we will eschew print entirely. Where printed materials are the most appropriate medium for a particular publication, then we will continue to produce them. However, with the shift online in mind, this issue of *Wellcome News* will be the last, as we focus our efforts on a new digital publication with wider reach and broader focus.

This new project will bring biomedical science and the medical humanities into context by telling compelling stories that explain and explore issues. It will include in-depth feature articles, graphics and film, drawing on Trust-funded research but not limited to it. Keep an eye out for the pre-launch blog, which should be live soon. On it you can follow – and influence – the course of the publication as it starts to take shape. We want your ideas about what we should cover, and how we should cover it.

Even though *Wellcome News* will not be produced any more, there are several ways you can find out about the Trust's activities and outputs.

The Wellcome Trust blog (at **blog.wellcome.ac.uk**) tells stories about life from a Wellcome Trust perspective. We welcome suggestions for posts you'd like to read, and we encourage you to share your thoughts on the stories there by commenting. You can also get in touch with us through our Twitter, Facebook and Google+ accounts.

Anyone who is supported by a Wellcome Trust grant automatically receives *Grantholders' News*, the quarterly digest of funding opportunities and deadlines, updates to grants and policies, and other Wellcome Trust news. Browse the archive at **wellc.me/ZMvbf1**.

We've loved working on *Wellcome News*, which has enjoyed several different incarnations since its launch in 1994 (read more about its first, *TRP3*, on page 32). One of the particular joys has been the opportunity to meet and interview many of the fascinating people supported by the Trust, and spend some time in their laboratories, offices and clinics.

So, we'd like to say thank you to the hundreds of people who have contributed to the magazine, in any way, over its 15 years in print. And we look forward to continuing to work with you as we pursue exciting new ways to discover and share the most fascinating, important and compelling stories in science.

Chrissie Giles, Editor, and the rest of the *Wellcome News* team.

Wellcome Collection is growing

More space, new galleries and improved facilities will result from a £17.5 million investment in Wellcome Collection over the next 12 months.

Stirling Prize-winning architects Wilkinson Eyre will transform the venue. The Wellcome Library's iconic Reading Room will become an innovative space for public engagement, and there will be a major new thematic gallery showcasing in-depth, year-long exhibitions. The creation of The Hub at Wellcome Collection will provide resources and a stimulating space for interdisciplinary research exploring medicine, health and wellbeing.

The development work begins this summer and is due for completion in summer 2014. The venue plans to remain open throughout, with a flexible programme of events and displays. **wellcomecollection.org/curioser**

Wellcome Trust appoints new Director

Jeremy Farrar, Director of the Wellcome Trust's Major Overseas Programme in Vietnam, has been named as the next Director of the Trust. He'll take up this post in October 2013.

It was 18 years to the day since Jeremy Farrar had begun working in Vietnam when his appointment as Director of the Wellcome Trust was made public in April. "I can honestly say I have loved every minute of my time in Vietnam," he says, "so it was very emotional when I was allowed to let the team know the news."

As well as his role in Vietnam, Farrar is also Professor of Tropical Medicine and Global Health at the University of Oxford, so he is no stranger to the UK and its research community. But he readily admits that the new role will be a "major change", adding: "Moving back to the UK after many years in Asia will be a culture shock, a climate shock, and will involve a very different role."

International development

Farrar was born in Singapore and travelled the world with his parents growing up, before coming to London to study medicine. His first experience of research was working for Cheryll Tickle as part of an intercalated degree in cell biology.

After qualifying, his clinical training was mostly in Edinburgh, where, inspired by Charles Warlow, he specialised in neurology and spent a year working in Melbourne, Australia. "These experiences really opened my eyes to research," he says. "That love of basic science through to pragmatic clinical research has inspired the rest of my career."

To further his training in basic science, Farrar secured a Medical Research Council Fellowship to do a PhD with John Newsom-Davis, Angela Vincent and Nick Wilcox in Oxford and at the University of California, San Francisco. "I learnt from them that you could combine a love of science and medicine, and that the people who could help bridge the gap between basic science and clinical research were going to be crucial in the future."

His own path looked set in his early 30s, but Farrar describes a 'road to Damascus' conversion: "I was giving a talk on my PhD work in Norwich. I remember looking up at the audience of British neurologists halfway through the talk and realising that I couldn't see myself remaining in neurology in Britain for the rest of my career."

The next day, quite out of the blue, he was approached about an opportunity in Vietnam. He took it, and was appointed Director of the Oxford University Clinical Research Unit in Vietnam, which is funded by the Trust and the Vietnamese government. The Unit had opened a few years earlier, in 1991, and Farrar credits much of his success there to the continued support of its original founders, Nick White, Tran Tinh Hien, Debbie Waller and Nick Day.

New direction

There are many things to keep his attention in the last few months before he takes over at the Trust, not least the emergence of the H7N9 influenza virus in China and a novel coronavirus in the Middle East. Nevertheless, Farrar says he has already noticed a few changes. "It's remarkable how many friends I seem to have suddenly gained," he says with a laugh. "But it's an honour to be in this position and I could not be more excited by the challenge and the opportunity."

He stresses that media speculation that he might move the Trust away from basic science and further towards international health and clinical research is absolutely unfounded. "I truly appreciate the value of basic science feeding in to everything that becomes clinical, public health and translational medicine. It is not a choice of one or the other."

> "I truly appreciate the value of basic science feeding in to everything that becomes clinical, public health and translational medicine."

He says his first priority as Director will be to listen: "The Trust has been superbly led by Mark Walport over the last ten years and I have never felt that the Trust needed a new Director to come and change things for change's sake. A calm period of listening and learning first is more in tune with my personality.

"I'll be exploring ways to extend existing partnerships and identify new opportunities. There is so much remarkable work going on, but still so much that needs to be done. And, crucially, all this work must be communicated in an open and engaging way, so that we can inspire the public and the next generation of young scientists.

"The great love of my professional life is asking questions, challenging dogma, trying to provide answers that matter, and inspiring others to do the same," he says, "while retaining a sense of humour and perspective. I hope I can continue to do all that as Director of the Trust."

Right royal result

The Royal Society of Edinburgh has awarded a Royal Medal to Professor Michael Ferguson from the University of Dundee, for scientific excellence. Professor Ferguson has received Wellcome Trust funding since 1988, and he studies trypanosomes, the organisms responsible for sleeping sickness. He also co-leads a drug discovery programme focused on neglected diseases, supported by a Trust Strategic Award.

Brightest brains

Congratulations to Professor Gero Miesenböck for winning The Brain Prize 2013. Director of the Centre for Neural Circuits and Behaviour in Oxford (part-funded by the Wellcome Trust), he is one of six researchers sharing the €1 million award for the invention and refinement of optogenetics. This technique uses light to control genetically modified neurons, helping to understand the brain.

Boosting research

All 32 UK medical schools have been awarded funds for activities that encourage students to pursue scientific research. These activities include research taster days, a medical science week and a mentoring scheme. The awards are made by the Academy of Medical Sciences as part of INSPIRE, a £1 million, five-year scheme supported by the Wellcome Trust.

Tip-top PhD

Dr Helen Weavers won this year's Beddington Medal for the best PhD thesis in developmental biology. She discovered that tip cells, often considered to be master regulators of organ development, act as anchors during kidney development, rather than leading growth as they do in other organs. Read more on the Wellcome Trust blog: wellc.me/18r5Tuc

New Medical History and Humanities Investigators announced

A 1946 public health notice.
Wellcome Library

The second round of our Investigator Awards in Medical History and Humanities was announced in March, with four New Investigators and seven Senior Investigators successful.

They include Oxford philosopher Dr Thomas Douglas, who will assess the role of neurointerventions in preventing crime. At the London School of Hygiene and Tropical Medicine, historian Dr Alex Mold will be exploring the changing place of the public within public health in postwar Britain.

In one of two joint Senior Investigator Awards, Professors Simon Swain (University of Warwick) and Emilie Savage-Smith (University of Oxford) will be unveiling the works of the 13th-century Syrian physician Ibn Abi Usaybi`ah with a translation and study of his book *The Best Accounts of the Classes of Physicians*, covering 1700 years of medical practice.

University of Cambridge historian Professor Sarah Franklin will be looking at the lessons to be learned from the introduction of *in vitro* fertilisation, and Professor Mark Jackson (University of Exeter) plans to investigate changing concepts of balance in modern medicine (see page 30).

Access to Nutrition Index published

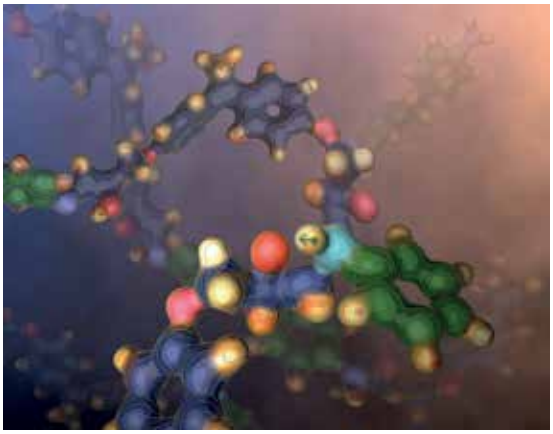
In March, the first Access to Nutrition Index was published, assessing 25 of the world's largest food and drink manufacturers on a range of measures related to their products' focus on nutrition and positive influence on consumer choice. The-best performing companies were Danone, Unilever and Nestlé, but they could still do much more to increase people's access to nutritious products.

The food industry has a vital part to play in addressing the serious global problems of obesity and undernutrition. Recognising this, and the need for an impartial way of assessing companies' commitment and actions to tackle these problems, the Wellcome Trust teamed up with the Bill and Melinda Gates Foundation in 2008 to fund the development of the Index. Our aim is not to name and shame companies, but to encourage best practice by encouraging debate and catalysing action within the industry, with the hope of changing consumer behaviour in the long term.

A follow-on Index will be published in 2015. Three Spotlight Indexes specifically assessing food manufacturers in India, Mexico and South Africa will also be published this year.

www.accesstonutrition.org/index-2013

Wellcome Images



Digital artwork of a chemical reaction. *Anna Tanczos/ Wellcome Images*

Advancing drug development

Professor Paul Wyatt and the University of Dundee Drug Discovery Unit have been awarded £6.5 million to further the development of new drugs.

New drugs to treat infectious diseases such as tuberculosis, malaria and African sleeping sickness are urgently needed in low-income countries. Developing a new drug is a lengthy process, however. In particular, there is a bottleneck at the stage known as lead optimisation: converting molecules identified in the early stages of investigation into drugs suitable for clinical testing.

The Dundee Drug Discovery Unit will establish a new centre of excellence in lead optimisation for diseases of low-income countries, funded by the Wellcome Trust and the Bill & Melinda Gates Foundation. Its initial focus will be on tuberculosis, which is responsible for over a million deaths around the world each year.

The award has been made through the Trust's Seeding Drug Discovery initiative, which was established in 2005 to facilitate early-stage small-molecule drug discovery. It is one of our first 'portfolio awards', created to allow greater flexibility in tackling diverse disease areas.

Scheme to support research on humanitarian crises

A programme to support research that will save lives in the aftermath of a humanitarian crisis – such as a flood, earthquake or civil war – was launched on 4 June by Enhancing Learning and Research for Humanitarian Assistance (ELRHA), and funded equally by the Wellcome Trust and the UK Department for International Development.

Up to £6.5 million will be available over three years for the Research for Health in Humanitarian Crises (R2HC) programme, which aims to increase the level and quality of collaborative research on recognised public health challenges in humanitarian crises occurring in low- and middle-income countries.

The programme is intended to lead to improved health outcomes and cost-effective improvements in relief efforts. Another key output will be improved ethical guidelines for those undertaking research in disaster and emergency environments, so that research projects can be approved in a timely way when, or even before, an emergency strikes.

The application process will be discussed at meetings in New Delhi and Nairobi in July. **www.elrha.org/work/R2HC**

TB setback

Results from a phase IIb clinical trial of the most advanced tuberculosis vaccine candidate, MVA85A, showed that the immune response it triggered was not enough to boost protection in young children previously given the BCG vaccine. MVA85A was originally developed by Professor Helen McShane, a Wellcome Trust Fellow at the University of Oxford. Further research will determine whether MVA85A can be improved, and whether it works in adults or in combination with other vaccines.
Tameris M et al. Lancet 2013;381(9821):1021–8.

Lofty ideals

Our criteria for forming relationships may not be as strong as we think. Researchers studied height differences in heterosexual couples from the Millennium Cohort Study. They confirmed that, in general, taller people had taller partners, and that the man was usually the taller – though not by too much. These trends were weaker than people's avowed preferences would predict, suggesting that we often compromise on traits associated with attractiveness when choosing a partner.
Stulp G et al. PloS ONE 2013;8(1):e54186.

Treating meningitis

Cryptococcal meningitis is thought to cause 625 000 deaths a year in people with HIV across the world. The recommended treatment – amphotericin B plus flucytosine – had not previously been shown to reduce mortality, but a new randomised controlled trial in Vietnam found that patients taking it survived better than those taking amphotericin B alone. No such benefit was seen with amphotericin B plus fluconazole.
Day JN et al. N Engl J Med 2013;368(14):1291–302.

Pesticides limit learning in bees

Antagain/iStockphoto

Two studies, part of the Insect Pollinators Initiative, have shown that common pesticides affect honeybees' ability to learn.

Drs Christopher Connolly and Mary Palmer from the University of Dundee and colleagues examined the effect on isolated bee brains of neonicotinoids, used on crops, and coumaphos, used in hives to kill the Varroa mite. They showed that the chemicals – in the same concentrations that are used in fields – affect the firing of neurons in areas involved in learning and memory.

Drs Geraldine Wright and Sally Williamson at Newcastle University investigated the effect of these pesticides on how honeybees learn. Using tests that mimic behaviours bees show when foraging, the researchers found that exposure to either or both of the pesticides impaired bees' learning and memory.

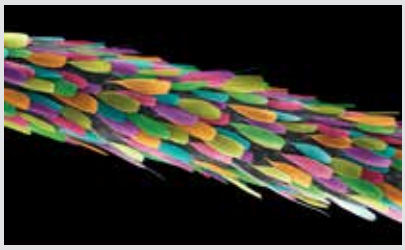
"Together, these studies highlight potential dangers to pollinators of continued exposure to pesticides that target the insect nervous system and the importance of identifying combinations of pesticides that could profoundly impact pollinator survival," said Dr Connolly.

The Insect Pollinators Initiative is funded by the Biotechnology and Biological Sciences Research Council, the Department for Environment, Food and Rural Affairs, the Natural Environment Research Council, the Scottish Government and the Wellcome Trust, under the auspices of the Living with Environmental Change partnership.

Palmer MJ et al. Cholinergic pesticides cause mushroom body neuronal inactivation in honeybees. Nat Commun 2013;4:1634.

Williamson SM, Wright GA. Exposure to multiple cholinergic pesticides impairs olfactory learning and memory in honeybees. J Exp Biol 2013 [epub].

Malaria vaccine has short-term effect



The efficacy of RTS,S, a new vaccine to tackle childhood malaria, has been shown to decline over time and with increasing malaria exposure. But despite the fall in protection, over four years, 65 cases of malaria were prevented for every 100 children vaccinated.

Researchers from the KEMRI–Wellcome Trust Research Programme in Kenya and from the University of Oxford followed 320 children who had received the vaccine as part of an earlier phase II clinical trial. This follow-up showed a fall in malaria prevention, from 44 per cent in the first year to zero by the end of year four.

Many African children are repeatedly exposed to the malaria parasite. The researchers found that the vaccine was less effective in children who were exposed to more malaria. Larger, ongoing phase III trials will provide further insights into which populations of children are likely to benefit most from the vaccine. The potential of a booster dose to sustain efficacy over time is also being assessed.

Olutu A et al. Four-year efficacy of RTS,S/ASo1E and its interaction with malaria exposure. N Engl J Med 2013;368:1111–20.

The leg of an *Anopheles* mosquito, a carrier of malaria. *Laura Holden/Wellcome Images*

Promote growth up to age two, say researchers

Research on babies born in low- and middle-income countries has shown that increasing birthweight and promoting gains in height in the first two years of life are likely to lead to improvements in height and educational outcomes, and reduce the risk of chronic disease in adulthood. But promoting rapid gains in weight relative to height gain in mid-childhood and adolescence was found to raise the risk of disease in later years.

Poor height growth in the first years of life is linked to impaired development and increased disease and mortality. Yet there are fears that 'catch-up' growth – rapid weight gain relative to height in low-birthweight children – can be harmful in later life.

In this work, an international team used data from prospective birth cohort studies based in Brazil, Guatemala, India, the Philippines and South Africa. They used conditional growth analysis to examine the long-term effects of height gain and of weight gain relative to height at different ages in childhood.

The researchers found that relative weight gain in children two years old or above was linked to higher body mass index, body fat, blood pressure and plasma glucose concentration. They call for interventions to promote height growth in infancy, rather than weight gain in school-aged children.

Adair LS et al. Associations of linear growth and relative weight gain during early life with adult health and human capital in countries of low and middle income. Lancet 2013 [epub].

UNICEF Ethiopia on Flickr

New genetic variants linked to cancer

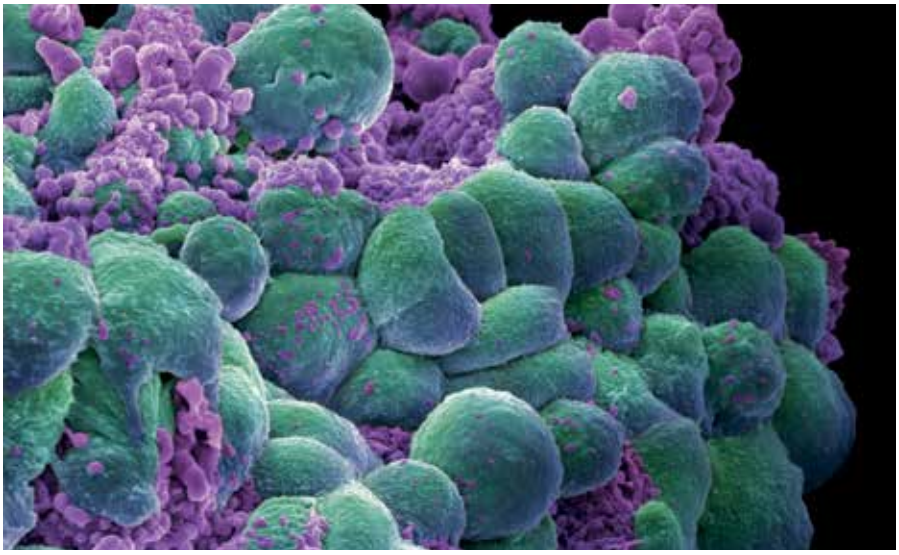
More than 80 common genetic variants have been identified as contributing to the risk of breast, ovarian or prostate cancer. Each variant has a relatively small influence on its own but someone with many of them is significantly more likely to develop cancer than someone without. The findings bring us closer to understanding heritable factors in the three most common hormone-related cancers.

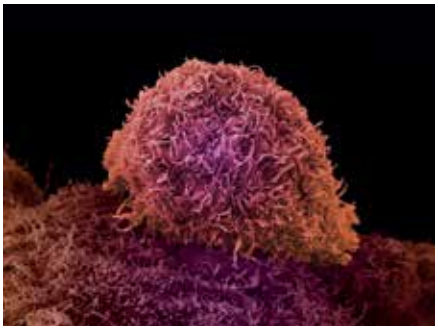
Scientists funded by the Wellcome Trust and Cancer Research UK published the research in 13 papers across five journals as part of the Collaborative Oncological Gene–environment Study (COGS). Their work assessed genetic variants called single nucleotide polymorphisms, confirming many already associated with these cancers and identifying a further 49 in breast cancer, 25 in prostate cancer and eight in ovarian cancer. Some are associated with specific subtypes of cancer, or with more aggressive disease.

Study author Professor Doug Easton, a Cancer Research UK scientist at the University of Cambridge, said: "We're on the verge of being able to use our knowledge of these genetic variations to develop tests that could complement breast cancer screening and take us a step closer to having an effective prostate cancer screening programme.

"We will be able to identify those who are at the greatest risk of getting these cancers and then target screening tests to these individuals."

www.nature.com/icogs/





Above: Prostate cancer cell.
Anne Weston, LRI, CRUK/ Wellcome Images

Left: Breast cancer cells.
Annie Cavanagh/Wellcome Images


$r = c\sqrt{n},$
$\theta = n \times 137.5^{\circ},$

DR ERINMA OCHU

HOW I GOT INTO... CITIZEN SCIENCE

Trained as a neuroscientist but with experience in television, film, public engagement and citizen science, Dr Erinma Ochu has had a remarkably varied career. She spoke to Michael Regnier about her work, which she describes as social innovation in getting the public involved in science.

I've always loved science. I was the weird kid who collected newspaper articles about genes and DNA and what the HIV virus looks like, thinking one day I might find a cure for AIDS. I planned to study genetics at university but when my A-level biology teacher told us no one knew anything about the brain, I said: "I want to study that." So I switched to neuroscience.

The most interesting aspect of my degree was my year out in industry, doing experiments every day, reading papers and figuring things out for myself. I even had a couple of papers published, albeit as a result of trying out new things in the lab in my spare time.

Curiosity – wanting to find things out, wanting to experiment – has got me where I am today. It's a driving force in my career, both in science and now engaging the public in science. As well as being fascinated by science and what is yet to be discovered, I believe that it is incredibly important that the knowledge being generated in laboratories is not just communicated but that there are opportunities for the public to engage in the practice of science. Citizen science presents the opportunity for the public to shape research questions, collect data and help analyse it.

I did a neuroscience PhD but became less sure about a lab-based career. I wanted to work in a way that was more connected with society. I told my supervisor, Professor Nancy Rothwell, and she invited me to help with preparations for her Christmas Lectures at the Royal Institution. That started me on the path from doing science to demonstrating science, and then to getting people doing science themselves.

Along the way, I worked in the film industry and the cultural sector. I've always been interested in how the mind works and how fascinated we are by storytelling, so I got into making films. It was part of the same curiosity that led me to neuroscience in the first place. Then I had another chance to work with Nancy, this time on the Manchester Beacon for Public Engagement. I brought a social innovation approach around actively engaging audiences from the digital and cultural sector and applied it to public engagement with all disciplines.

When MOSI (the Museum of Science and Industry, Manchester) wanted to do a citizen science experiment to mark the centenary of mathematician Alan Turing in 2012, I leapt at the chance. I coordinated Turing's Sunflowers, a mass participation experiment that encouraged people to grow sunflowers and count the spiral patterns in the seed heads. Lots of people joined in from all over the world and we built a community around the project.

Participation is an important way to learn how to do science. With the sunflowers experiment, I became an expert in counting these spirals in sunflowers – you start noticing more patterns and differences between them the more you do it. I really love that about citizen science: it's the chance to do science again.

Exploring the possibilities of what citizen science has to offer public engagement with biomedical research is part of what I'm exploring with my Wellcome Trust Engagement Fellowship, as is getting back into neuroscience and using storytelling. I'm taking my experiences in biomedical research, the cultural sector and public engagement, and exploring the social and scientific value created when diverse perspectives come together.

OPINION

"We need to encourage real science in schools"

DR DAVID COLTHURST, SCIENCE TEACHER

Five years ago, my wife was diagnosed with multiple sclerosis. I was a research biochemist for 15 years before becoming a science teacher, so I started thinking about whether we could do some novel research into multiple sclerosis in my school, the Simon Langton Grammar School for Boys in Kent. My idea was to investigate the role of a protein implicated in multiple sclerosis using genetically modified yeast. With the support of my school and a collaboration with researchers at the University of Kent, the Myelin Basic Protein Project (MBP²) was born.

That was the easy part; securing funding was much harder. A typical response was "You must be crazy – this is not what schools do!", until I approached the Wellcome Trust for a People Award.

The impact of the project has been dramatic. Since the project started, the number of students studying A-level biology at this school has doubled and we now have 170 students working on MBP². The opportunity to conduct original research has inspired our students, with some even designing their own projects. For instance, one student has been using DNA analysis of bee pollen from our school hives to identify the varieties of plant species the bees have visited. It has been great for our staff too. They have been able to familiarise themselves with new techniques, enabling them to teach with greater confidence.

Unfortunately, our students have found it very difficult to convert their research into a format that is recognised by exam board marking criteria. Some would argue that the reason the UK is slipping down the international league table is because our National Curriculum is too prescriptive – this is certainly a challenge we have faced. Even though we are carrying out genuine research, our model is not compatible with the mark schemes. Exams were not the reason we started this research, but it is frustrating that our students cannot get the recognition that they deserve for it. However, we are in conversation with the exam boards and the Department for Education to address this.

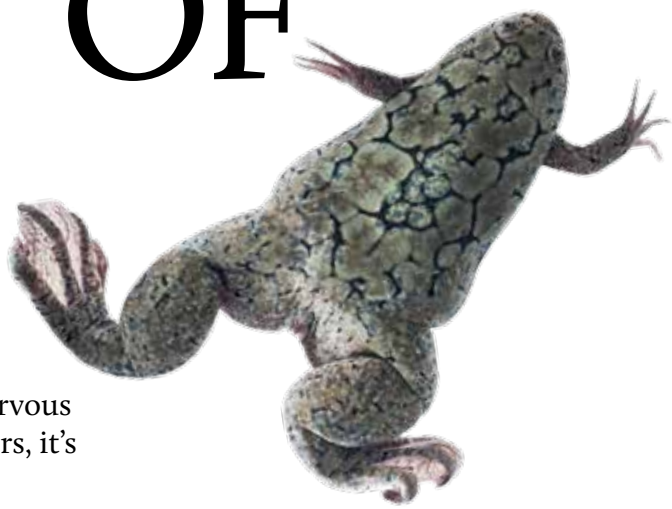
I never set out to shake up the British education system but MBP² may be a model for future change. There are now five schools around England and their university partners involved in the Authentic Biology project, each researching areas with personal significance. For example, a school in Tower Hamlets, London, has devised a project to examine the causes of diabetes among their local population, who are mainly of Bangladeshi origin and have a high prevalence of the disease.

Our original MBP² provided a template for student involvement in novel research. Our work has shown people what school students can do, that this is a way that you can motivate both staff and students and increase the number of young people applying for science subjects at university. The question is: where can it go from here?

For more, read David's post on the Wellcome Trust blog at wellc.me/V8tfjU

PROFESSOR NANCY PAPALOPULU

A BRIEF HISTORY OF TIMING



Xenopus laevis, the African clawed frog.

Professor Nancy Papalopulu studies the growth of the nervous system in frogs. As in her career, Michael Regnier discovers, it's all a question of being in the right place at the right time.

In 2006, Professor Nancy Papalopulu decided to leave the lab she had established in Cambridge ten years earlier and start pretty much from scratch with a new lab in Manchester. It was the right time, she says: "It was a good career opportunity but it was also a new challenge, which I was really ready for.

"It is very beneficial for a scientist to move. It shakes things up and stimulates people in new directions," she continues. "I would go so far as to say there is no use learning a lot in one place unless you can put it to use in another place."

Timing, location and the exchange of information are just as important for the cells Papalopulu studies. Her research follows the development of the nervous system in *Xenopus* frogs, from fertilised egg cell to embryonic brain. "We're trying to understand how cells decide to adopt a particular fate," she explains. "Where the cells come from in the embryo and their history will determine what they do, so you need to follow a cell's decisions through time."

Decisions, decisions

The history of Nancy Papalopulu's scientific career begins in high school, at Anatolia College in Thessaloniki, in Greece. She recalls one inspirational biology teacher in particular: "Mr Mastrogiannis used to tell us that one day humans would be able to grow eyes in the palm of our hands. I could not see a useful application for this but just the thought that we would understand development enough to direct it at will was absolutely fascinating and I wanted to do biology."

Decision made. But biology was not seen as a good career choice in those days and if you had the grades that she had, you were expected to choose medicine. However, she struck a deal with her parents: she would follow in her mother's footsteps and do a pharmacy degree, and if she still wanted to do biology after that, she could.

After finishing her pharmacy degree at the Aristotle University of Thessaloniki, Papalopulu duly moved to the UK to do a PhD in biology. "I had to burn the midnight oil a lot in the early years to catch up," she admits, "but I eventually got to do what I wanted."

Exciting times

She joined a new lab at the Medical Research Council's National Institute for Medical Research in Mill Hill, north London. She was Robb Krumlauf's first graduate student and he recalls her love of science and curiosity about how things worked. "I was indeed fortunate to have someone so intelligent, passionate and mature," says Krumlauf, now Scientific Director at the Stowers Institute for Medical Research in Missouri.

"We had many wonderful conversations about diverse areas of science and life in general that served to create a stimulating environment in the laboratory. I knew Nancy had a promising long-term research future in front of her and I have been very proud to see her fulfil her potential."

Papalopulu counts herself lucky too:

"Robb was very good at including us and showing us that science is a community. Mill Hill in the late Eighties was really a very exciting place to be: a number of key discoveries were made around that time, such as the mechanisms of action of morphogens and activin. I was very privileged to be a part of it, and it set me off on the best possible foot in my career."

Despite the sense of community, she became aware of a concurrent compartmentalisation within science. With Krumlauf, she was investigating the role of so-called *Hox* genes in patterning – the way that cells choose different fates depending on where they are in the embryo. Papalopulu was interested in the mechanisms of neuronal differentiation, the process by which individual cells decide whether to stop proliferating and become specialised instead. This takes place in a coordinated fashion alongside patterning, but scientists looking at the two processes did not seem to talk to each other.

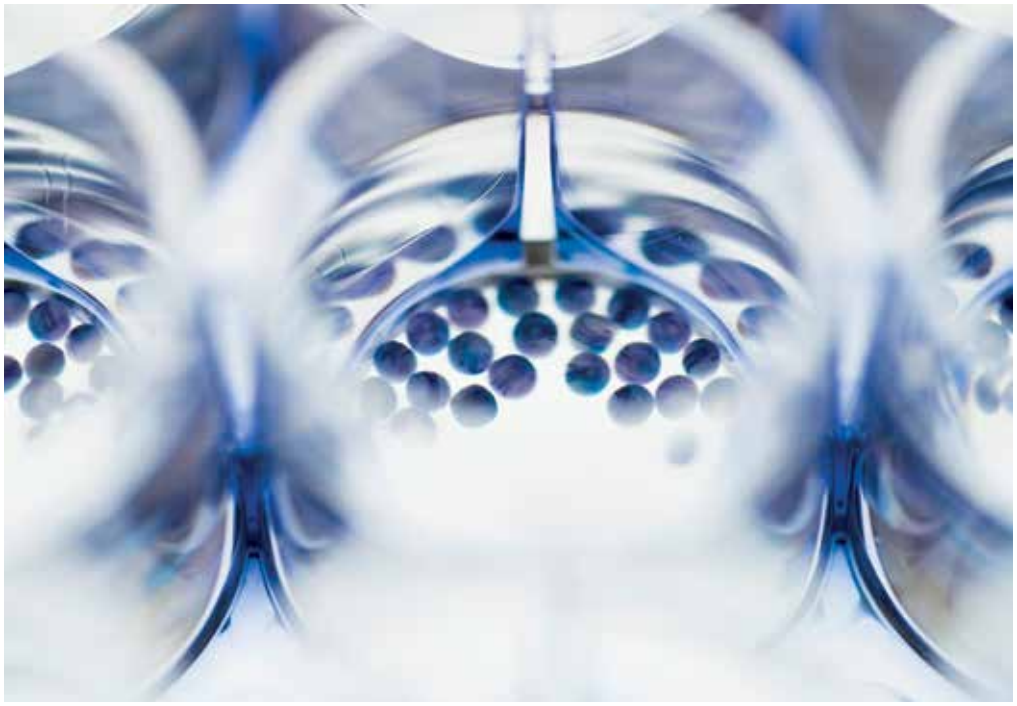
"I like to make connections," she says. "So I decided to look at how patterning influences the process of neuronal differentiation – this was the start of my fascination with timing. I moved to Chris Kintner's lab at the Salk Institute in California. My parents were not so enthusiastic initially but I was really excited about going quite far away, to another part of the world."

Finding the balance

Early in life, the nervous system begins as a group of progenitor cells. All have the potential to develop into neurons, which conduct electrical and chemical signals through the body, or glial cells, which support and regulate the neurons. However, some neural progenitors have to stay as they are, dividing to replenish the reserves for later waves of differentiation.

"If you have premature neurogenesis, you end up with fewer neurons by the end, so the nervous system does not grow to its normal size and complexity," explains Papalopulu. "On the other hand, if you have less differentiation, you also won't get enough neurons and you may develop tumours, so the balance is really important."

She says the Salk was a fantastic place to do science, albeit in a different way from Mill Hill. Eventually, though, she decided to come back to the more



> “I’m fascinated by oscillations, so I see them everywhere, but I do think science goes in peaks.”

Left: *Xenopus laevis* embryos.
Right: Nancy Papalopulu and colleagues in the lab.

“compact” environment of the UK. She set up her own lab with a Wellcome Trust Career Development Fellowship at the Wellcome Trust–Cancer Research UK Gurdon Institute in Cambridge, where she shared laboratory space with Sir John Gurdon himself.

Sir John won the 2012 Nobel Prize in Physiology or Medicine for his work showing that all animal cells contain a copy of all the genes needed to make the whole organism. The finding ignited research into cloning and, later, stem cells. It was what had made Mr Mastrogiannis dream of eyes in his hands.

Step by step

Papalopulu says she learned a lot at the Gurdon Institute, not least that serious scientists do not need to take themselves too seriously. “The Gurdon is a fun place to do science: it fosters creativity by making sure that no one is scary – a bit of self-deprecation is a great way of creating that environment.

“Most of all, what I learned from John was his ability to take a complex problem and reduce it to a series of simple questions that one can address. His clarity of thought is incredible. Some people are naturally better at it than others but as long as you enter science with open eyes and are able to take in different things from different people, you can develop these skills.”

She was looking at what makes neural progenitor cells run to different timetables. The reason seemed to be related to the cells’ sense of direction, or polarity. This being a strength of the Gurdon Institute, Papalopulu extended her research to the question of how polarity might produce heterogeneity – the different behaviour of similar cells in the same location.

All change

After nearly a decade at the Gurdon, most of which was supported by a Wellcome Trust Senior Research Fellowship, Papalopulu moved to Manchester. Still supported by the Fellowship, she had a chance to rethink and rebuild. “It was an opportunity to try new things,” she says. “And it gave me the confidence that if I could rebuild the team once, I could do it again, and that allows you to take more risks with a view to the future.”

The move went smoothly, both for Papalopulu’s young family and in terms of recruiting a new team. For example, Dr Sarah Woolner was doing postdoctoral research in the USA looking at mitotic spindle assembly during cell division. She was attracted to join the Papalopulu lab because of their work on polarity and cell fate.

“I came to visit, had a really good chat and decided with Nancy to apply for a Beit Memorial Fellowship,” Woolner recalls. “I just came to talk to her and give a talk to the lab, but we got this fellowship planned out in that time.”

Woolner now has a Wellcome Trust–Royal Society Sir Henry Dale Fellowship and is setting up her own lab upstairs from Papalopulu’s. She hopes to provide a similar style of mentorship: “Nancy let me do my own thing but I had her support and I could go to her and discuss ideas, and she made sure I got to my goals of a good paper and a good independent project. You do have to plan ahead in science – timing is very important.”

Like most principal investigators, Papalopulu does not do experiments at the bench herself any more, but she does make a point of looking at the raw data that comes out of her lab. “She will ask if you have a microscope on,” says Dr Federico Dajas-Bailador, a postdoc soon to set up his own lab in Nottingham. “Sometimes we try and finish the whole experiment before discussing it with her! But she’ll come and say, ‘Take me to the microscope room.’”

Highs and lows

“I’m always happiest looking at people’s data,” confirms Papalopulu. “It’s a source of great emotional balance. I do the admin and the grant-writing and when I need to remind myself what we’re here for, I can go and spend the day in the lab and that will make me passionate about science again.”

Her passion at the moment is

oscillation. Last year, she and colleagues published evidence of how fluctuating levels of proteins can regulate cells. Cellular levels of a protein called Hes1 rise and fall many times a day, and this was known to stop neural progenitor cells from differentiating until the levels of Hes1 dropped below a certain threshold.

They discovered that Hes1 interacts with microRNA-9, another molecule being studied in the lab, so that the production rates of the two rise and fall out of sync. However, whereas Hes1 is efficiently cleared away from the cell, microRNA-9 gradually accumulates. It is when microRNA-9 reaches a certain threshold that it becomes able to stop Hes1 production altogether, which pushes the cell into differentiation.

On a wave

This finding exemplifies a shift in our understanding of how cells work. What were once envisaged as basically linear circuits of molecular signals are instead starting to be viewed as dynamic networks. The outputs of these networks evolve as the organism develops, depending on how various parameters change.

For Papalopulu, this conceptual shift marks another exciting period in developmental biology: "This dynamic behaviour is drastically different to how we have considered development in the past," she says. "I'm fascinated by oscillations, so I see them everywhere, but I do think science goes in peaks. Something new arises, there is intense focus and after a time, we feel we understand the process very well.

"But then something new comes again, just when you thought we understood everything – and we realise we have a lot of things to understand before we know how an embryo builds itself."

Intriguingly, oscillations may also represent a mechanism for counting biological time, which could underpin most, if not all, developmental processes. "I'm beginning to suspect there is a point in everyone's career when everything from the past comes together," says Papalopulu. "I may just be entering this phase in my life. Timing, balance and progenitor heterogeneity may well come together into a single model, and that's very gratifying."

• *In May 2013, Nancy Papalopulu was elected a Fellow of the Academy of Medical Sciences.*

References

Graham A et al. The murine and Drosophila homeobox gene complexes have common features of organization and expression. Cell 1989;57(3):367–78.

Chalmers AD et al. Oriented cell divisions asymmetrically segregate aPKC and generate cell fate diversity in the early Xenopus embryo. Development 2003;130(12):2657–68.

Woolner S, Papalopulu N. Spindle position in symmetric cell divisions during epiboly is controlled by opposing and dynamic apicobasal forces. Dev Cell 2012;22(4):775–87.

Bonev B et al. MicroRNA-9 modulates Hes1 ultradian oscillations by forming a double-negative feedback loop. Cell Rep 2012;2(1):10–8.

Nancy on...

Job prospects: "I always tell undergraduates that the important thing is to find what you want to do, and if you are good at it then the job will follow. Don't decide what you want to do based on the perceived employment market."

Recruitment: "I choose people I can happily spend a lot of time talking to. If a candidate has a good CV but the conversation dies out and we are looking at our watches, that is not a good sign! The give and take of ideas is the basis of developing a good project."

Career development: "I do not know anyone who does not worry about their funding. As with biology, the key is timing: your output has to be there at the next grant assessment. It requires a lot of careful planning."

Location: "People tend to think that where they are is the centre of the universe, but if you move, you realise there is more than one centre. The idea that we just have centres of excellence and very little happening outside that is simply not true."

Patience: "My job as a mentor and supervisor is to support people when it looks like nothing is happening. There are some incredible lows in science: most of the time things don't work and people get disillusioned. But if you stay in science, you will be rewarded."

On Nancy...

"It is truly impressive how she acts as a positive role model and has not only done exceptional science, but mentored and trained a new generation of scientists."
Professor Robb Krumlauf, Papalopulu's PhD supervisor

"Nancy is a great mentor, she really focuses on making sure every member of the lab is successful and not just a few."
Dr Andy Chalmers, University of Bath, former postdoc at the Gurdon Institute

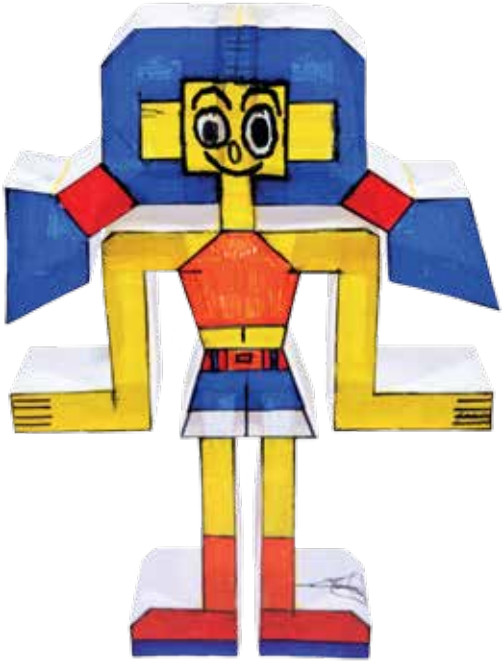
"She gave me a lot of intellectual freedom in my project but was also very helpful and supportive, particularly in terms of career development: presentations, grant-writing and making contacts are key to academic success and yet few PIs teach them to students."
Dr Boyan Bonev, Sir Henry Wellcome Postdoctoral Fellow at Harvard University, former PhD student in Manchester

"Nancy is very enthusiastic but she can also be very tough. She is not the kind of boss who will forget about you when nothing is working. She'll ask you why it is not working and how we can improve it."
Dr Federico Dajas-Bailador, postdoc in Manchester

"It's important as a woman progressing in science to have a role model. Nancy has a family, she leaves the lab on time to see them, but puts a lot of time into her research – it's good to see other women being successful and to realise you can do it."
Dr Sarah Woolner, Sir Henry Dale Fellow at the University of Manchester, former postdoc in Manchester

WELLCOME COLLECTION

SOUZOU: OUTSIDER ART FROM JAPAN



Left: clay sculpture by Shinichi Sawada.
Above: one of 20 figures from 'Girl' by Keisuke Ishino.
Below: some of the 300 obects made from twist ties by Shota Katsube.

Wellcome Collection's latest exhibition, *Souzou*, is the first major display of Japanese Outsider Art in the UK. Outsider Art – work by artists who have received little or no tuition, and are perceived to inhabit the margins of mainstream society – has had a huge rise in popularity over recent years.

'Souzou' has no direct translation in English but a dual meaning in Japanese: written one way it means creation, and in another it means imagination. Both meanings allude to a force by which new ideas are born and take shape in the world.

It is a force very evident in the 300 compelling ceramics, textiles, paintings, sculptures and drawings showcased in our exhibition – and one that raises questions about the category of Outsider Art itself. The pieces were created by 46 artists, all of whom are residents or day attendees at social welfare institutions in Japan, and all of whom have been diagnosed with a variety of cognitive, behavioural and developmental disorders or mental illnesses.

The exhibition was organised in association with Het Dolhuys, the Museum of Psychiatry in Haarlem, the Netherlands, and the Social Welfare Organisation Aiseikai in Tokyo. It runs until the end of June and will be Wellcome Collection's last major exhibition before its development project (see page 4) begins.

wellcomecollection.org/souzou

BEST OF THE BLOG

RETHINKING MENTAL HEALTH CARE

Professor Vikram Patel, a Wellcome Trust Senior Research Fellow at the London School of Hygiene and Tropical Medicine, proposes that mental health care in the world's most developed countries could learn lessons from initiatives in some of its poorest.

The conundrum of mental health care in rich countries is that, despite the apparent richness of resources, so many people with mental health problems (by one recent estimate, nearly half in the USA[1]) do not access the care which we know can enhance their chances of recovery. Likely explanations relate to the nature of mental health problems, beliefs about their causes and treatment, and the costs and inaccessibility of biomedical mental health care.

My hypothesis is that lying at the heart of these factors is the remoteness of psychiatry. Interventions are heavily medicalised, do not engage sufficiently with personal and community resources, are delivered in highly specialised, expensive settings, and use language and concepts which alienate ordinary people. In all these respects, innovations to improve access to mental health care in low-income countries might inform a rethink of the way in which rich countries provide care.

At the core of these innovations is a reassessment of who provides mental health care. There are fewer psychiatrists for the entire continent of Africa, with a population of almost a billion, than in the state of Massachusetts, with a population of less than 7 million. In such settings, the only way mental health care can be delivered is through non-specialist workers, such as training primary care doctors to provide appropriate medicines.

Recent innovations have used other types of human resources, from community health workers to lay people, to provide psychosocial interventions with impressive results[2]. They offer a range of appropriate interventions, use familiar concepts and are convenient (even offered in patients' homes or outside working hours).

Practical and simple diagnostic systems, such as the one employed by the WHO's mhGAP initiative[3], are now being widely adopted in low-income countries precisely because they are meaningful to non-specialist providers and local communities – and, I would argue, to most mental health specialists as well!

None of these ideas are unique to low-income countries, and several champions in high-income countries have worked tirelessly to improve access to mental health care by challenging the hegemony of a narrow biomedical perspective. But mental health care is still too heavily professionalised, and specialised, for the majority.

Reforming mental health care, with the goal of improving access and outcomes, requires a fundamental review of our ideas of who should provide such care to communities, and how. The innovations which are capturing the imagination of the young discipline of global mental health offer a window of hope for those who aspire to such reform[4]. As the cliché goes, health is too important to be left to health professionals alone, and this is, I would argue, even more true for mental health care.

References

1. Wang PS et al. Twelve-month use of mental health services in the United States: results from the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005;62(2):629–40.

2. Kakuma R et al. Human resources for mental health care: current situation and strategies for action. Lancet 2011;378(9803):1654–63.

3. World Health Organization. mhGAP intervention guide for mental, neurological and substance use disorders in non-specialized health settings: mental health Gap Action Programme (mhGAP). Geneva: WHO; 2010.

4. Patel V. Global mental health: from science to action. Harv Rev Psychiatry 2012;20(1):6–12.

This article was originally posted on ThInk, our blog about art, science and the brain. ThInk was created to coincide with and complement 'Wonder', a season of public events in March and April 2013 organised by the Wellcome Trust, the Barbican and the British Neuroscience Association. **thinkneuroscience.wordpress.com**

ThInk

TREATING POST-TRAUMATIC STRESS DISORDER

PROFESSOR ANKE EHLERS

Characterised by distressing flashbacks, post-traumatic stress disorder (PTSD) affects up to 8 per cent of the population at some point in their lives. Emma Rhule spoke to Professor Anke Ehlers, a Wellcome Trust Principal Research Fellow at the Institute of Psychiatry, about new treatments for PTSD.

What drew you to this research?
I am intrigued by how much psychological therapy can help people with very disabling anxiety disorders. I became fascinated by the questions of why some people develop PTSD after traumatic events, while others recover on their own, and why flashbacks appear to come 'out of the blue' and make them see, hear and feel things as if the trauma was happening again in the present.

How do you study it?
We conduct prospective studies to identify risk factors for PTSD. We also use a range of methods to investigate the nature of trauma memories and their triggers. In one recently published study, volunteers with no history of PTSD were shown narrated picture stories that were either traumatic or neutral. In between pictures, images of innocuous objects such as an onion flashed up on the screen. We later asked participants to identify blurred pictures of these objects. Objects were more readily identified if they had appeared in a traumatic context. We found similar results with people who had experienced trauma. It appears that after trauma, some people's perception of the world is fine-tuned to spotting reminders of the event.

Who is most at risk?
There is some evidence that people with a family history of anxiety or people who have experienced other traumas are at greater risk. However, a person's response during and after a traumatic event is more important. For example, we have found that people who mainly focus on sensory impressions like sounds and colours during the trauma are at an increased risk of PTSD. Certain ways of thinking about or responding to the trauma, such as dwelling on what they could have done differently, are also strong risk factors.

How is PTSD treated?
Our cognitive therapy programme helps patients identify and change unhelpful ways of thinking about the trauma. We work with them to update their trauma memories with what they know now, so that these become less threatening, and to respond to them in a more helpful way. We help patients learn to discriminate between the traumatic event and the triggers they encounter in everyday life. These often have a sensory similarity to something from the trauma. For example, after a stabbing, people may respond to any shiny object or even the reflection of light on a window, as these may remind them of the assailant's knife.

Current treatment requires 12 weekly sessions with a therapist. Randomised trials show that more than 70 per cent of patients with PTSD fully recover. We have been developing self-study modules that sufferers complete at home, allowing us to halve the number of face-to-face sessions. We are now evaluating this briefer treatment.

Can we prevent PTSD?
Jennifer Wild and I have been collaborating with the London Ambulance Service to identify predictors of psychological stress in new recruits. Our aim is ultimately to develop a training programme for emergency service workers to decrease risk factors for developing PTSD or other problems such as depression. In general, people are very resilient even to extreme stress, but no one is totally immune.

Sündermann O et al. Perceptual processing during trauma, priming and the development of intrusive memories. J Behav Ther Exp Psychiatry 2013;44:213–20.

Freeman D et al. Paranoia and post-traumatic stress disorder in the months after physical assault: a longitudinal study examining shared and differential predictors. Psychol Med 2013 [epub].

ORGAN

THE HEART

From broken hearts to the hard of heart, for centuries the heart was viewed as the seat of human emotion. Today, we know it has a central role pumping blood around the body. Emma Rhule provides a quick guide to this vital organ.

In 1628, an English physician called William Harvey published the first detailed description of the action of the heart and the flow of blood around the body. It challenged many of his contemporaries, who believed that the lungs were responsible for moving blood through the body. Of course, now we know he was right.

Harvey was also right when he hypothesised that blood flows through the body in a closed circuit. In humans, this circuit is made up of two loops, known as the double circulatory system. The first, the pulmonary system, sends blood to the lungs, where it is loaded with oxygen, and brings it back to the heart. Then, the systemic circulatory system sends the oxygen-rich blood to fuel our nervous system, muscles and everything we do.

The human heart has two types of chamber. Blood enters the atria before passing into the ventricles. The thick walls of the ventricles are needed to generate enough pressure to pump blood from the heart to the farthest ends of the body.

Cardiac muscle cells have a natural rhythm, but the sinoatrial node acts as a pacemaker to ensure that they all beat in time. Diseases, drugs and genetic mutations can disturb the rhythm of the heart and lead to a loss of synchronicity, which can be fatal.

Harvey's pioneering work was founded on thousands of dissections. Modern techniques allow researchers to learn ever more about the intricacies of the heart. Blanca Rodriguez at the University of Oxford is using computer simulations to unravel what is happening when rare heart events, such as arrhythmias, occur in humans. And cardiac magnetic resonance imaging, similar to normal MRI but fine-tuned for the heart, allows clinical researchers like Reza Razavi at King's College London to visualise the living heart.

1

Sinoatrial node

Known as the heart's pacemaker, the sinoatrial node is a group of specialised heart cells that regulate the heartbeat by sending out electrical signals at regular intervals. If the rhythm is disrupted, the heart's muscle fibres will contract in a rapid, unsynchronised way – called fibrillation. Defibrillators, often seen in medical dramas, are used to stop the chaotic heartbeat and allow the sinoatrial node to regain control.

2

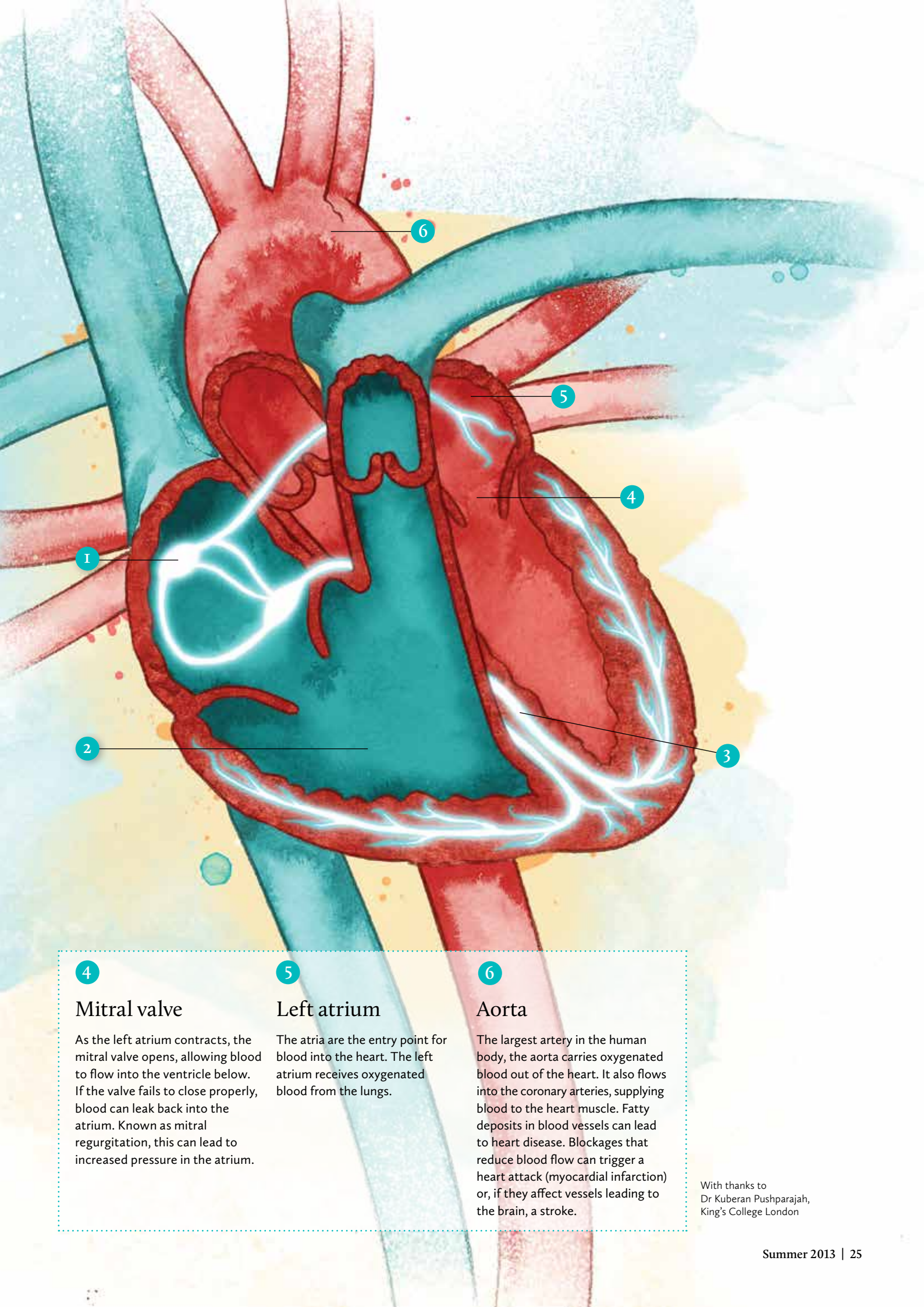
Right ventricle

One of two large chambers responsible for pumping blood around the body. The right ventricle pumps oxygen-poor (deoxygenated) blood to the lungs.

3

Bundle of His

Part of the heart's electrical wiring system, the bundle of His transmits electrical impulses generated by the sinoatrial node through the ventricle walls.



4

Mitral valve

As the left atrium contracts, the mitral valve opens, allowing blood to flow into the ventricle below. If the valve fails to close properly, blood can leak back into the atrium. Known as mitral regurgitation, this can lead to increased pressure in the atrium.

5

Left atrium

The atria are the entry point for blood into the heart. The left atrium receives oxygenated blood from the lungs.

6

Aorta

The largest artery in the human body, the aorta carries oxygenated blood out of the heart. It also flows into the coronary arteries, supplying blood to the heart muscle. Fatty deposits in blood vessels can lead to heart disease. Blockages that reduce blood flow can trigger a heart attack (myocardial infarction) or, if they affect vessels leading to the brain, a stroke.

With thanks to
Dr Kuberan Pushparajah,
King's College London

THE WALPORT YEARS

THE TEN-BILLION-POUND MAN?

Earlier this year, Sir Mark Walport stepped down as Director of the Wellcome Trust and took up his new role as the UK government's Chief Scientific Advisor. We asked leading figures from science, the humanities, media and the arts to reflect on his achievements over the past ten years. By Michael Regnier. Interviews by Barry Gibb.

In 2006, a bundle of dirty old manuscripts showed up in an auction house. They turned out to be by Robert Hooke, one of the great original minds of the 17th-century Royal Society. Lisa Jardine, Professor of Renaissance Studies, and Lord Rees, the then President of the Royal Society, came to the Wellcome Trust to ask its Director, Sir Mark Walport, for help in purchasing the papers for the nation.

"Mark looked us in the eye," Jardine recalls, "and said, 'Half a million? We can do that.'"

"The way Wellcome helped save the Robert Hooke papers was a tremendous thing to do, a very imaginative gesture," says Lord Sainsbury, who was the UK's Minister for Science and Innovation from 1998 to 2006. "Mark has shown incredible leadership at the Wellcome Trust, both in terms of maintaining extraordinarily high standards in the research, but also making certain that it works well as an organisation."

On Sir Mark's last day in the Director's office, the Wellcome Trust announced that its total charitable spend to date had passed £10 billion. Over half was spent between 2003 and 2013, the decade in which Sir Mark was in charge, which means he outspent all three previous Directors put together. But on his first day, he had initially been faced with the need to cut spending.

People person

In 2003, the world economy had been going through a slowdown, and difficult decisions were the order of the day, both within the Trust and in its funding. From the start, however, Sir Mark focused on improving the quality of support for people, even if he couldn't immediately increase the quantity.

'Supporting the brightest minds' became part of the Trust's mantra and it meant providing increasingly effective support for people to do excellent research. The culmination of this approach was the Trust's Investigator Awards, introduced in 2011, which extended the level of support of fellowships to researchers employed in universities and other research institutions.

The move away from funding specific projects and programmes of research in favour of giving researchers longer, more flexible support was one of the defining policies of Sir Mark's leadership. As the Trust is a major funder of medical research, such significant changes were controversial within the research community. However, Sir Mark is a highly respected member of that community and, even if he didn't persuade everyone that he was right, he communicated his reasons with passion and precision.

Although not the first Director to recognise the value of collaboration, Sir Mark was especially keen to build on existing partnerships and forge new ones. He knew that the Trust could not be successful if it tried to operate in isolation.

Leaders of organisations that worked with the Trust appreciated his approach. Nobel laureate Harold Varmus, currently Director of the US National Cancer Institute, says: "From my perspective as someone who has run some parallel institutions, Mark has done an extraordinary job in his ten years at the Trust. He has also been very attentive to the context in which the Trust operates, especially interactions with other countries, other agencies and with an awareness of the importance of science to society."

Research matters

Sir Mark became Director of the Trust in the same year that the gold-standard human genome was published. He cannot take credit for the Trust's involvement in the Human Genome Project, which began several years earlier at what became the Wellcome Trust Sanger Institute, but he can share a lot of credit for ensuring the Trust recognised the potential of genomics and continued to catalyse and promote research in this area.

As well as making a huge contribution in genetics and genomics, the Trust has facilitated many achievements in neuroscience, infectious diseases and basic biology. Its

support for neuroimaging has helped transform the way we understand the brain over the last decade, while Trust-funded researchers in South-east Asia have played a leading role in developing, implementing and monitoring new treatments for malaria. The Trust has also supported large, ambitious research facilities such as UK Biobank and the Francis Crick Institute.

Since 2003, there has been a notable expansion in the Trust's work beyond research. Sir Mark oversaw new initiatives in education and public engagement with science, including the foundation of the National Science Learning Centre to support teachers, and the introduction of the Wellcome Trust Book Prize to encourage literary authors to tackle medical issues.

Thanks to public-facing activities like these, people are more aware of the Trust and what it does. And it has done more to engage the public with science and medicine in general – not least at its own venue, Wellcome Collection, which opened in 2007.

"There is a particular kind of exhibition which is a Wellcome exhibition, about a certain kind of idea," says Neil MacGregor, Director of the British Museum. "Wellcome Collection is now one of the major exhibition venues of London. That's a great achievement, and I know it is only a very small part of the grand 'genome' of Mark's career at the Trust but for the museum community, it is a very important part."

In the media, too, the Trust has developed a more open attitude, led by Sir Mark's example. Fiona Fox, Director of the Science Media Centre, says: "Science has lots of leaders who are quite faceless; Mark Walport is not that kind of leader. He is bold, courageous, brave, principled, outspoken, and he is known as a leader of the scientific community."

The Trust under Sir Mark has also looked to its responsibilities in the local community. Journalist and broadcaster Jon Snow chairs a project running a day centre for vulnerable young people in Camden. "Mark ensured that neighbourhood outreach extended to us," he says. "We have benefited from visits from Wellcome staff and funding through the Trust's 'good neighbours' scheme. Mark has positioned the Wellcome Trust in the community in a way it simply wasn't before."

Leaving a mark

Sir Mark succeeded Sir John Beddington as the UK government's Chief Scientific Advisor on 1 April 2013. He is now the personal advisor on science, technology and policy matters to the Prime Minister and the Cabinet, and leads a network of scientific advisors across all government departments.

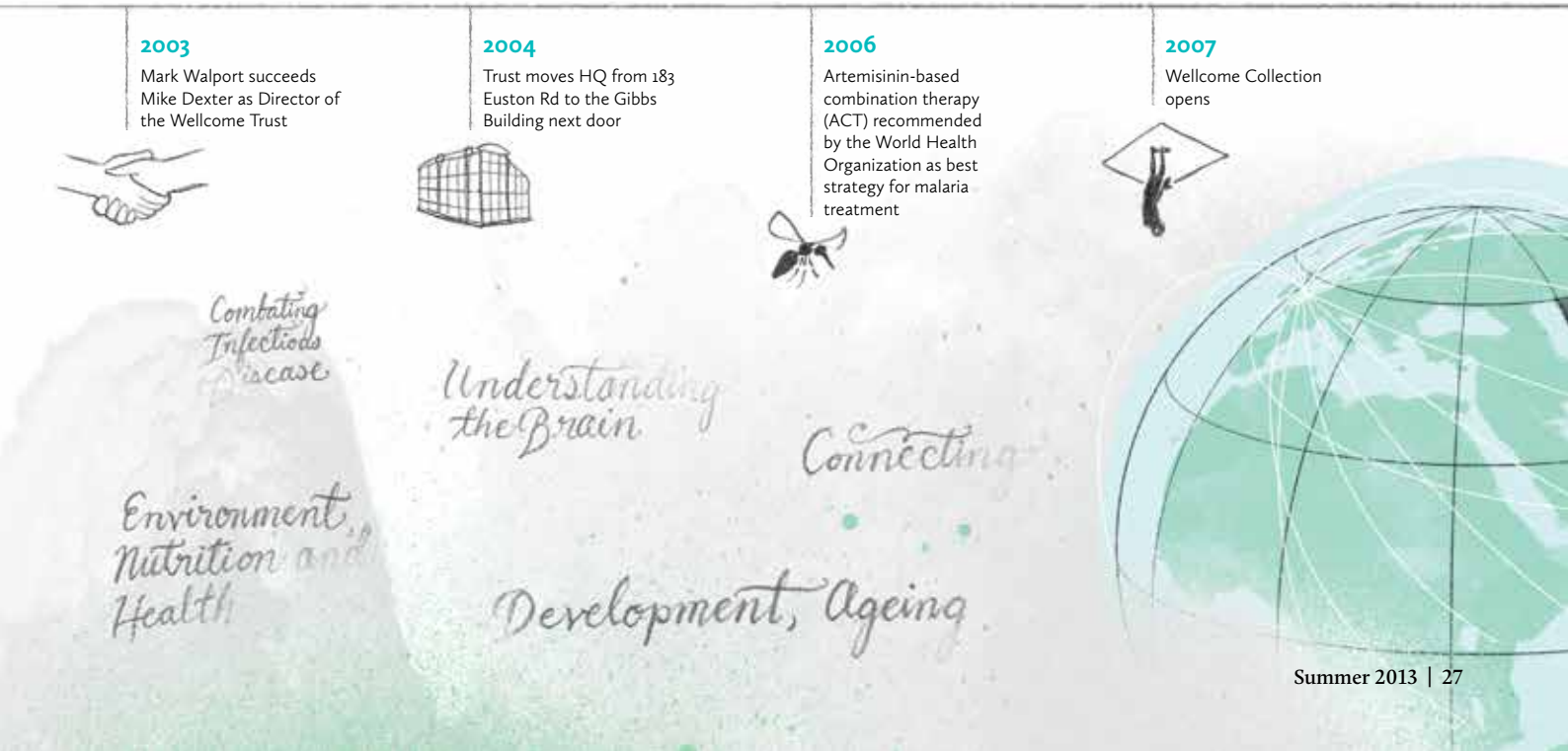
"The Wellcome Trust's loss is the people's gain," says Snow. "I think Mark will be a very good chief scientist, not because he is such a good scientist, but because he can actually communicate it and that will be a rare quality."

"I think he will make a great government chief scientist," adds Lord Sainsbury. "He may find it's a bit more difficult getting money out of the Treasury rather than giving it away, but I think he will do that with all the skill and leadership he's shown at the Wellcome Trust."

> "He has also been very attentive to the context in which the Trust operates, especially interactions with other countries, other agencies and with an awareness of the importance of science to society."
>
> **Harold Varmus**

On the following page, Sir Mark Walport shares his own thoughts on ten years at the Wellcome Trust.

continued →



A fond farewell

Headlines are tricky things. On the one hand, just a tiny number of words frequently influence whether an article is read; on the other, they can misleadingly encapsulate the contents and bias how it is read. So it was with a thoughtful and generous article by Fergus Walsh on the BBC website, entitled 'The man who gives away £600m a year'. There is no doubt that this headline was extremely effective, as the article was viewed over 480 000 times. But I don't think that those who receive funding from the Wellcome Trust believe they have been 'given' the money – and everyone involved in the peer-review process knows the extent of the due diligence behind every funding decision.

The main role of the Director is to influence the Trust's strategy and to work with many partners to maximise the impact of our extraordinary endowment and our other assets. Among those other assets, I would highlight three. The first is our staff – talented and creative people whose energy and devotion make the Trust run so effectively. Second, we have an exceptional group of Governors, who provide the support and challenge that is essential to the running of any substantial organisation. And third, we have the amazing collections and library founded by Sir Henry Wellcome, which provide the substrate for Wellcome Collection.

People enquiring about the Trust have often asked: "What keeps you awake at night?" The answer is always the same: our financial asset, our endowment, which is crucial to achieving our mission. I am pleased to pay a public tribute to Danny Truell, our Chief Investment Officer, the investment team and our advisors on our Investment Committee. They have collectively been responsible for my untroubled sleep as Director! Little did I think, arriving in 2003 following a major fall in the value of the endowment, that ten years later it would have increased by about £6 billion on top of our spend of over £5bn in support of our mission.

It has been an enormous privilege to lead the Trust. I would like to take this opportunity to say thank you to my colleagues and to our many partners, particularly those we fund, who enable us to achieve our mission of extraordinary improvements in human and animal health.

One of the best parts of the job was to visit scientists and learn of their exciting discoveries. It was always a humbling experience to visit the Major Overseas Programmes in Asia and Africa, and to appreciate their direct contributions to improving the health of some of the poorest people in the world. It has also been an amazing opportunity to chair the board of the Sanger Institute, which is spearheading the translation of results from the Human Genome Project and the sequencing of many pathogen genomes into improvements in health.

I have moved from Director of the Wellcome Trust, with independence and large financial assets, to UK government Chief Scientific Advisor, with an advisory role and minimal financial assets. But I hope that ten years at the Trust is rather good preparation. In his 1954 book *Government and Science*, Don K Price wrote: "The foundation officials themselves, always on the look out for new intellectual developments that may contribute to public affairs, thus make a great contribution in the long run to public policy." And, he noted, "they have exercised even greater influence on government almost absent-mindedly, by their support of scientific and technical programs".

I have worked closely with governments during my time at the Trust – on science and education policy and on data sharing and national infrastructure through membership of the Council of Science and Technology. I look forward to working closely with the scientific community in the public and private sectors to provide the best advice to the government on all aspects of science, engineering, technology and social science, supporting development of the best public policy.

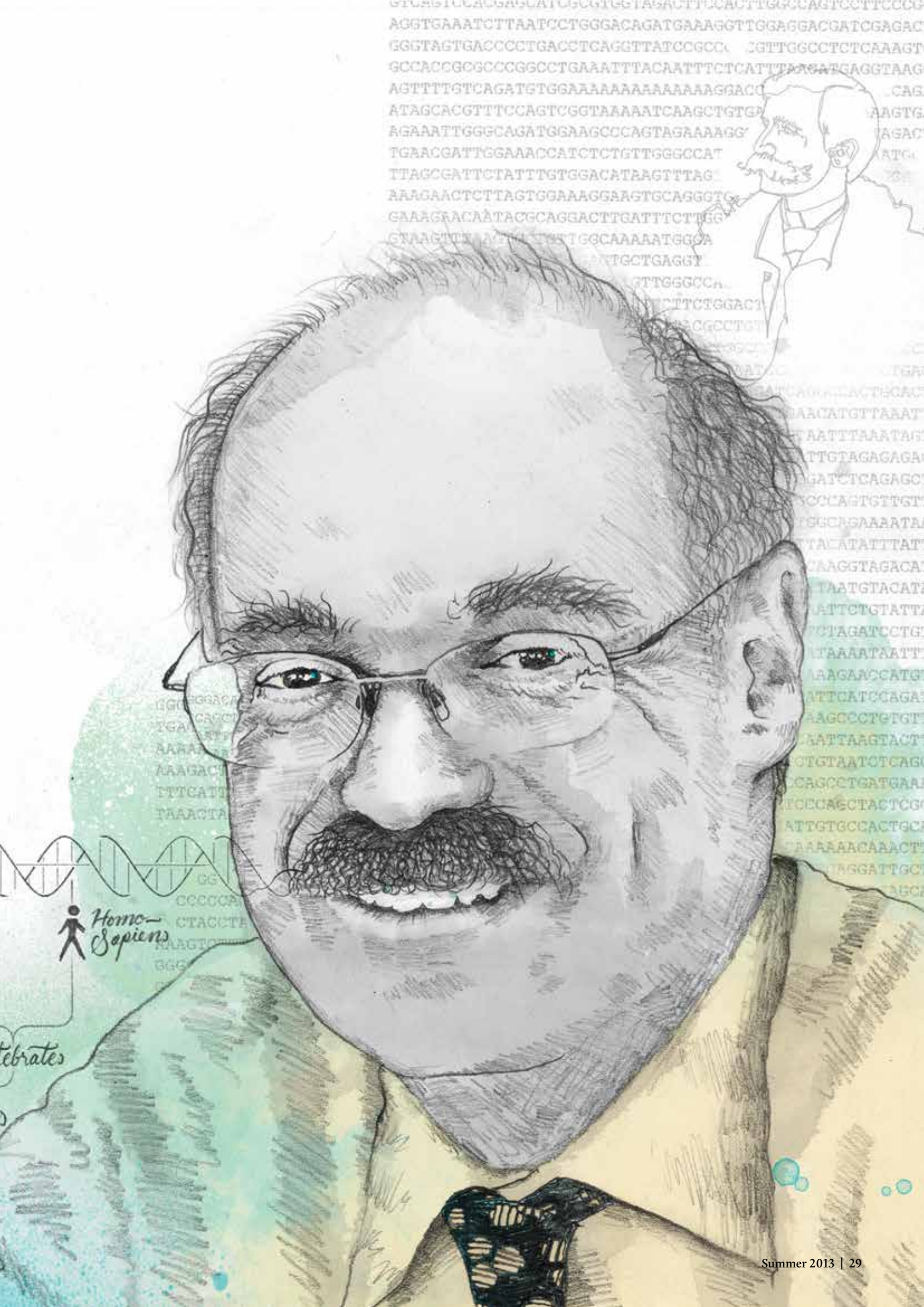
Sir Mark Walport

2009
Mark Walport knighted for services to medical research

2011
Trust celebrates 75th anniversary

2012
UK Biobank opens with data and samples from 500 000 volunteers available for research

2013
Trust's total spend to date surpasses £10bn; Sir Mark leaves the Trust to become the UK government's new Chief Scientific Advisor


Homo-
Sapiens

PROFESSOR MARK JACKSON

IN SEARCH OF STRESS

With degrees in immunology and medicine, historian Mark Jackson researches topics as diverse as his background. He tells Emma Rhule about his new book, *The Age of Stress*, and his Wellcome Trust Senior Investigator Award to explore the concept of balance.

Mark Jackson's views on stress changed after his house was flooded.

In January 2011, Professor Mark Jackson and his family came home from their Christmas holiday. A pipe had burst and for three days, water had been running through their house. Little was spared. Books, clothes, computers – all destroyed. In total, nearly three-quarters of the Jackson family home was ruined. They had no choice but to move out of the house for seven months while repairs took place.

Up to that point, Jackson had been sceptical of the idea of stress as the 'modern plague'. "If you'd have asked me 20 years ago if I thought that stress existed, I'd have said no," he admits. Fast-forward to 2013 and Jackson's latest book, *The Age of Stress: Science and the search for stability*, has been published. "Ask me now," he says, "and experience tells me we get stressed and it can make us ill."

So how did a man who didn't really believe in the idea of stress come to be writing a book about it? "In 2006 I wrote a book on the history of allergy. One of the things that came out was that many allergists after the Second World War were using stress as a way to explain certain patterns of allergic disease," Jackson says.

He came across the work of Hans Selye, considered by many to be the father of stress research. And yet, Jackson found very little written about him. "I was able to find a couple of papers about Selye in French and a few overview articles, but no clear historical study of Selye's place in the history of medicine and his work on stress."

From the 1930s onwards, Selye pioneered the popularisation of the term 'stress' in a medical context. Before this, what we would now think of as stress was variously referred to as fatigue, apathy or neurasthenia. Stress had occasionally been used but there was no consistent single term. Selye also introduced a distinction between eustress and distress – positive and negative stress – and the idea that everyone needs a bit of stress in their lives.

Stress to impress

"Hans Selye used to say that 'when you are not stressed you are dead'," says Jackson. Indeed, in the years after World War II, some doctors believed that a lack of stress was making people ill. There was a feeling that people needed some real stress to be added into their lives in order to stimulate and encourage them.

During the 1980s, the idea that stress could be beneficial and promote productivity led to an increased commercialisation of stress, with books such as Peter Hansen's *The Joy of Stress* teaching techniques for harnessing it. At the same time, pharmaceutical companies promoted sedatives and tranquilisers to vanquish it entirely. By the time Jackson was starting to think about writing the book, he says, "this was headline news, the 'epidemic' of modern stress".

What Jackson considers troubling is the shift towards 'executive stress' and the way it has skewed the debate. "In the Thatcher individualist era, being 'stressed' was, and still is, a marker of success. People forgot about the socioeconomic factors, such as poverty, poor housing and inadequate access to healthcare, that are still life's major stressors."

On balance

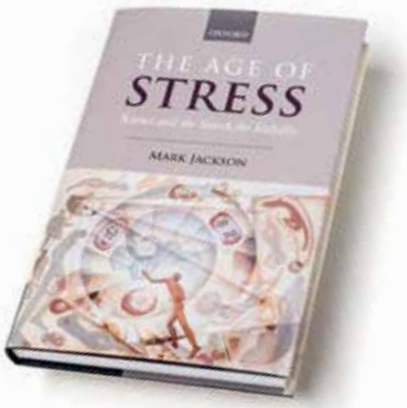
By the time he came to finish his book, Jackson had concluded: "Stress is something that we have to live with and find ways to deal with; it is multifaceted, complex and, ultimately, unavoidable." Indeed, attempting to lead a stress-free life is itself stressful. It was from this idea of the search for stability that Jackson's interest in the concept of balance, the subject of his recent Wellcome Trust Senior Investigator Award, emerged.

"Part of *The Age of Stress* looks at the way that people are struggling to control the world around them. There are all these debates about how to maintain control under stressful circumstances, with a big focus on achieving equilibrium through physiological and psychological balance."

Yet what really intrigues him is what he describes as the tension in Western medicine: "Balance is embedded as a holistic concept – a balanced diet, work–life balance. Most of Western medicine is moving towards a biomedical reductionist approach, yet we still keep hold of this notion of balance. Why?"

When asked about his vision for the next five years, Jackson says: "When I left medicine in 1997 one of my ambitions was that at some point in my career I would try to integrate the humanities back into science and medicine.

"I think we make too much of the division between the arts and the sciences. I don't think there is much difference between what I did in the lab, what I did in the clinic and what I do as a humanities researcher. We are interested in knowledge – what's the difference? We are all in the same boat."



Win a copy!

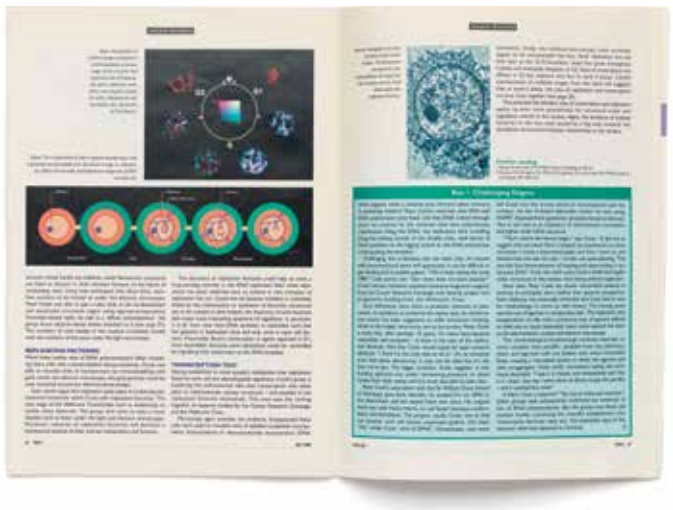
Thanks to Oxford University Press we have two copies of Mark Jackson's book to give away.

Just tell us: In which year did Hans Selye first publish *The Stress of Life*?

Email your answer to **wellcome.news@wellcome.ac.uk** with the subject line 'Stress competition'. One entry only per person. Competition closes 17.00 GMT, 26 July 2013, after which two correct entries will be randomly selected. The winners will be notified by email by 2 September 2013 and announced on the Wellcome Trust blog.

WELLCOME TRUST PUBLICATION

TRP3



Wish us luck as you wave us goodbye! To mark the last-ever *Wellcome News*, Chrissie Giles flicks through the first issue of its earlier incarnation, *TRP3*.

What is it?

The first issue of *TRP3*, the esoteric original title of *Wellcome News*.

Why is it so special?

It was the Wellcome Trust's first quarterly publication, dedicated to communicating how the Trust spent its money on research and what grantholders were achieving with their awards.

TRP3 issue 1 included articles on the newly constructed Wellcome Trust Centre for Human Genetics in Oxford, the potential of foresight as a tool for funding agencies, and a piece by Max Perutz on his efforts to deduce the alpha-helix structure of proteins. There was also a £25 prize for anyone who could explain how the publication's name was derived.

The tricksy title is related to amino acid nomenclature (of course!) and is basically a fancy way of abbreviating 'Wellcome Trust'. If your biochemistry is a little rusty, 'Trp' is the three-letter code for tryptophan (also known as 'W'), and '3' is how scientists pronounce 'Thr' – the three-letter code for threonine (also known as 'T'). The name lasted ten issues, before changing to *Wellcome News*.

Can I see it?

Copies of *TRP3* (and any of the 63 subsequent issues of *Wellcome News*) can be seen by anyone at the Wellcome Library, on request.

Want to know more?

Find out more at **encore.wellcome.ac.uk/iii/encore/record/C__Rb1660253**

Mark Neville

APPLIANCE OF SCIENCE

"Art can help people visualise, debate and use science"

MARK NEVILLE, PHOTOGRAPHER

Photography can sometimes be passive, creating a record without enough thought about how it operates in the world. I try to push the boundaries of what a photograph can do beyond sitting on a gallery wall – sometimes that includes communicating science.

I went to Corby a few years ago to document its curiously Scottish culture. In the 1930s, a Scottish steel company built a new mill in Corby and brought a lot of workers from Glasgow to staff it. The mill has since closed but the town retained a strong Scottish community – you'll find Irn-Bru and whisky-flavoured tea in the shops, and people speak with a dialect that is almost Glaswegian.

As well as driving the town's growth, the steelworks left a dangerous legacy that would come to redefine Corby. In 2009 an infamously contentious High Court case began, as the families of local children with birth defects tried to prove a link to the way Corby Borough Council dealt with toxic waste left in the steelworks when it closed down.

The families eventually won their case, which encompassed medical science, obstetrics, waste management and environmental science. I interviewed many of the specialist witnesses at the same time that I was photographing the community. I made portraits of the children with missing or deformed limbs but it was equally important to portray the whole community because, in fact, the case affected everyone.

I got a grant from the Wellcome Trust for a book called *Deeds Not Words*, which combined my photographs with text about the technical aspects of the case. The book was not sold but sent free to every local council in the UK.

Corby was a breakthrough case that brought hard science to bear where before, the evidence had been vague – but not all the findings were to be published. It was unthinkable to me that this information would not reach the people who deal with toxic waste and land reclamation on a daily basis. The book was to arm them: to inform their work and help persuade their colleagues that this job needs to be done properly.

I got some moving emails back, but nothing seemed to be changing. So curator David Campany and I approached the Photographers' Gallery about putting on an exhibition of photographs from the book to act as a platform for debate. The Wellcome Trust is supporting a symposium on social documentary photography and its relationship with biomedical issues, while a second symposium is aimed at policy makers.

It's about raising awareness and taking some responsibility for our environment. Science often deals with abstract ideas, but biomedical science is all about people. *Deeds Not Words* is my attempt to anchor science in something real – the photographs help us to visualise the science, and to talk about it in a meaningful way.

***Deeds Not Words* is at the Photographers' Gallery in London from 2 August to 29 September 2013.**

www.markneville.co.uk/works/deeds-not-words | thephotographersgallery.org.uk/2013-programme

DIARY
Courses, conferences and workshops

At the Wellcome Trust Genome Campus, Hinxton, unless otherwise specified. For more, see **www.wellcome.ac.uk/advancedcourses** and **www.wellcome.ac.uk/conferences**

The Genomics of Common Diseases 2013
Conference, 7–10 September 2013, Keble College, Oxford

Cancer Pharmacogenomics and Targeted Therapies
Conference, 15–17 September

Mouse Molecular Genetics
Conference, 18–21 September

Mitochondrial Disease: Translating biology into new treatments
Conference, 2–4 October

Infectious Disease Genomics and Global Health
Conference, 16–18 October

Regenerative Medicine: From Biology to Therapy
Conference, 30 October–1 November

Epigenomics of Common Diseases
Conference, 7–10 November

Molecular Pathology and Diagnosis of Cancer
Course, 10–15 November

Proteomics Bioinformatics
Workshop, 11–15 November

Functional Genomics and Systems Biology 2013
Conference, 21–23 November

Genome-wide Approaches with Fission Yeast
Course, 7–14 December

Fundamentals of Clinical Genomics 2014
Workshop, 14–17 January 2014

Mouse Models of Disease: Using pathology techniques to enhance phenotyping outcomes
Conference, 5–7 February 2014

Alzheimer's Disease in Down Syndrome: From molecules to cognition
Conference, 27–29 March 2014

Chromatin: From nucleosomes to chromosomes
Conference, 30 April–2 May 2014

Wellcome Collection events and exhibitions

Euston Road, London. **wellcomecollection.org**

Thinking with the Body
Exhibition, 19 September–27 October

Medicine Man and **Medicine Now**
Permanent exhibitions

Event listings
See website for details

VISIT SOON
WE'RE FREE

Slink to London

to find amphibian ancestors, chromosomes made from socks, a shrunken head and more

wellcomecollection.org

Exhibitions | Events | Library | Event Spaces | Café | Bookshop
183 Euston Road, London NW1 2BE

wellcome collection

wellcomecollection.org

The free destination for the incurably curious