

WellcomeNews



ISSUE 63 JUNE 2010

Now we are ten

Celebrating a decade of research from the human genome sequence

Doctor, doctor
Meet a Trust
Clinical Fellow

Café culture
School science cafés

Great Scott
Wellcome's role
in Scott's epic
final expedition

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The Wellcome Trust

We are a global charity 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

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The sequencing of the human genome ranks among the great scientific achievements of the last 100 years, and we are extremely proud of the Wellcome Trust's fundamental role in this iconic project. Now, in the tenth anniversary year of the working draft sequence, the project's success is beyond doubt.

The first impact of the genome sequence was to enable genetic analysis on a gigantic, genome-wide scale that was previously inconceivable. Human genetic variation is being described in ever greater detail through global collaborations such as the SNP Consortium, the International HapMap Project, the mapping of copy number variation and the 1000 Genomes Project. Meanwhile, genome-wide association studies, such as the Wellcome Trust Case Control Consortium, and large-scale sequencing programmes, such as the Cancer Genome Project, are revealing how inherited variations or mutations affect health and disease.

As explored in this issue, the decisions to support such large projects were not easy in fields in which technologies were still emerging. We had the courage to back these ambitious undertakings because they were led by outstanding scientists; the results speak for themselves.

These major studies are in many ways just the beginning: they tell us which genes are involved, but not how they work. The challenge is to understand the complex biological effects of genetic variation. To take a personal example, related to my own research into the complement system and rheumatic and renal disease, I was excited that one of the first discoveries from the HapMap Project was that inherited variation in the complement regulatory protein factor H was associated with an important cause of blindness in elderly people: age-related macular degeneration. Large-scale

sequencing later showed that mutations in a gene related to factor H are associated with a newly described form of glomerulonephritis, a kidney disorder – work led by Matthew Pickering, a Wellcome Trust Senior Research Fellow, and his collaborators. These studies raise further important questions about how variation in complement regulation causes eye and kidney inflammation.

Genome-wide association studies are transforming our understanding of the genetic basis of common diseases such as diabetes. Until about four years ago, perhaps one variant per year causing increased susceptibility would be found. Now there are many hundreds of such discoveries each year. While it would be naive to expect findings about disease mechanisms to lead to instant predictive, diagnostic or therapeutic outcomes, the real value of these associations lies in how they reveal the pathways underlying the development of diseases. A better understanding of a condition's causes is essential for the creation of new drugs and strategies to treat or prevent it.

Also, importantly, advances in genomics are not restricted to human sequences, but are transforming our understanding of infectious diseases.

It is imperative over the next decade to turn this increasingly detailed knowledge into new ways of helping patients. 'Maximising the health benefits of genetics and genomics' is one of the Trust's five challenges for 2010–20 and, in partnership with the UK Department of Health, we have created the Health Innovation Challenge Fund, which this year made £20 million available for translating genetic discoveries into clinical practice.

The Cancer Genome Project, seeking the mutations that drive the development of common cancers, is the most advanced large-scale genomic study in turning genetic discoveries into new treatments. There are already drugs undergoing clinical trials as a result of this global partnership. We are proud to have been such a major part of the Human Genome Project, and will continue to ensure that our funding supports outstanding scientists to drive forward genetics and genomics at an ever-increasing pace.

Sir Mark Walport
Director of the Wellcome Trust

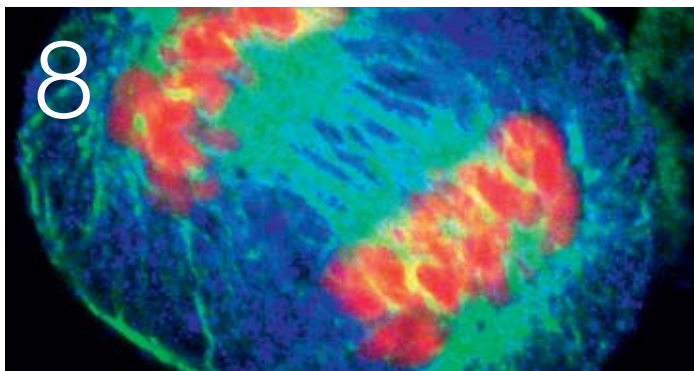
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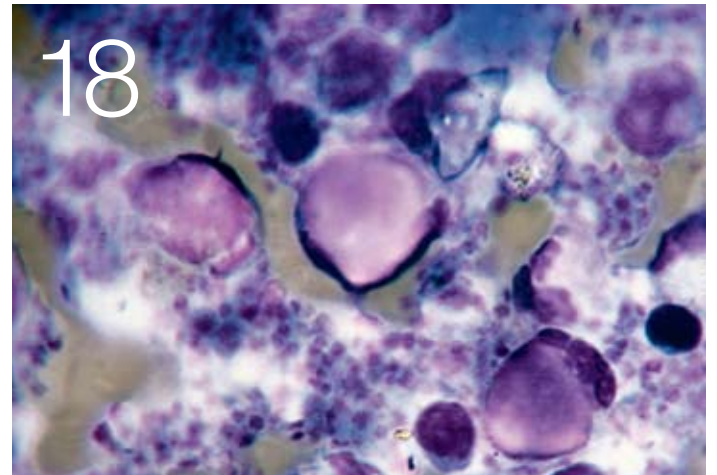
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Mike Stratton named new Sanger Director



Professor Mike Stratton is the new Director of the Wellcome Trust Sanger Institute (above). Deputy Director there since 2007, he heads the Cancer Genome Project and is a leader of the International Cancer Genome Consortium.

"It is a truly extraordinary challenge and great privilege to be appointed Director of the Sanger Institute," said Professor Stratton. "The Institute is currently on the crest of a wave of discoveries in revealing how genetic variation in human beings and in infectious agents cause disease. I aim to build ambitiously on the Institute's current leadership in large-scale analysis of genomes and experimental studies in model organisms to develop cellular systems that will explore human biology and to provide transformative insights into how diseases develop.

"In ten to 20 years' time it is conceivable

that we will all have our genomes sequenced as a routine. Our Institute will make a major contribution to understanding what these sequences mean and will also be a leading voice and activist in society's consideration of how they should be used in order to achieve our collective central mission, improving human health."

Sir Mark Walport, Director of the Trust, said: "On behalf of the Wellcome Trust, I would like to congratulate Mike Stratton on his appointment. Mike is an exceptional scientist who has made major discoveries about the genetic mechanisms of cancer."



Read an interview with the Sanger Institute's previous Director, Allan Bradley, on page 5, and more on Prof. Stratton's work on page 11.

Young people enjoy science, survey shows



The first Wellcome Trust Monitor survey on attitudes to medical research reveals unanimous public support for research and shows that, contrary to popular belief, 81 per cent of young people find science lessons interesting.

Almost all respondents thought that

medical research should be supported and encouraged, even if a lot of public money would need to be invested, though support was significantly higher for clinical research than for basic research. The survey showed that young people look favourably at science as a possible career choice: 44 per cent said they were interested in pursuing a career in science, with medicine, forensic science and engineering the most popular choices.

"There has been a big push towards improving young people's experiences of science both inside and outside the classroom. It could be that these activities are beginning to pay off," said Professor Derek Bell, Trust Head of Education.

www.wellcome.ac.uk/monitor

Book Prize panel announced

The judging panel for the 2010 Wellcome Trust Book Prize will be chaired by Clive Anderson, comedy writer, presenter and former barrister.

Panel members are:

Maggie Gee, writer and former Man Booker judge; A C Grayling, writer, professor and former Man Booker judge; Michael Neve, medical historian; and Alice Roberts, anatomist, anthropologist, presenter and author. The shortlist will be announced at the Times Cheltenham Literature Festival in October, and the winner will be named in November. www.wellcomebookprize.org



Wellcome Library on loan



Items from the Wellcome Library's vast collection are contributing to some fascinating exhibitions around the country. *China Through the Lens of John Thomson 1868–1872* will visit Hartlepool in late 2010 and the Burrell Collection in Glasgow in 2011, having already exhibited at the Merseyside Maritime Museum in Liverpool and touring China last year. It features 150 photographs selected from 688 glass negatives by the Victorian traveller John Thomson (1837–1921), from Sir Henry Wellcome's collection. The portraits record Thomson's travels in China, Indochina and Cyprus in the 1860s and 1870s. They offer a fascinating insight into his subjects and majestic landscapes, yet were for the most part unpublished in his lifetime.

Meanwhile, the National Gallery in London is exhibiting 'Acts of Mercy' (above; 14 July–17 October) by Frederick Cayley Robinson, one of the most distinctive yet elusive British painters of the early 20th century. Purchased by the Trust in 2009, the work comprises four large-scale panels in two pairs, exploring the positive forces of the human spirit in the face of destruction.

Election success for Trust researchers

The Academy of Medical Sciences has announced its 40 newly elected Fellows for 2010, who include over a dozen currently Trust-funded researchers as well as our own Head of International Activities, Dr Jimmy Whitworth.

Academy Fellows are elected for outstanding contributions to the advancement of medical science, for innovative application of scientific knowledge or for their conspicuous service to healthcare. The 2010 Fellows who currently receive Trust funding include (all Professors): Anthony Costello, Geraint Rees and William Richardson, University College London; David Newby and Mark Woolhouse, University of Edinburgh; Nicholas Craddock and Alun Davies, Cardiff University; Richard Wise, Imperial College London; Christopher

Shaw, Institute of Psychiatry, King's College London; Inderjeet Dokal, Barts and The London, Queen Mary; Alan Knox, University of Nottingham; Sheena Radford, University of Leeds; and Nazneen Rahman, Institute of Cancer Research.

Professor Sir John Bell, President of the Academy of Medical Sciences, said: "Our new Fellows illustrate the wealth of experience and diversity of talent amongst the UK's research community. I look forward to working with these skilled scientists to ensure their strengths across academia and industry are used to promote basic science discoveries, innovative healthcare and the rapid translation of research into patient benefits."

For more, see: www.acmedsci.ac.uk/p109.htm

Open (text)book on medicine

Through the open-access HINARI Programme, Trust support will give health researchers and workers in low- and middle-income countries free online access to one of the foremost textbooks of medicine. For over 35 years, the *Oxford Textbook of Medicine* has provided practical guidance on clinical management and the prevention of disease. It contains in-depth information on international medicine from 750 of the world's leading clinicians and medical scientists, covering basic

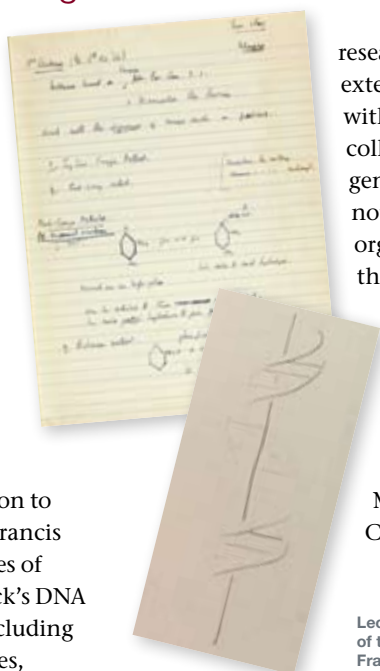
science and clinical practice, and infectious diseases. It also includes sections on the foundations, achievements and limitations of modern medicine, and global patterns of disease.

The HINARI Programme, established by World Health Organization together with major publishers, enables low- and middle-income countries to gain access to one of the world's largest collections of biomedical and health literature. www.who.int/hinari/en

Genetics archives go digital

The Modern Genetics and its Foundations project, which began in January, will digitise up to half a million images from the Wellcome Library's archival holdings. It will focus on how the science of biological inheritance developed from the later 19th century onwards, and the growing understanding of its role in human health and disease during the 20th century.

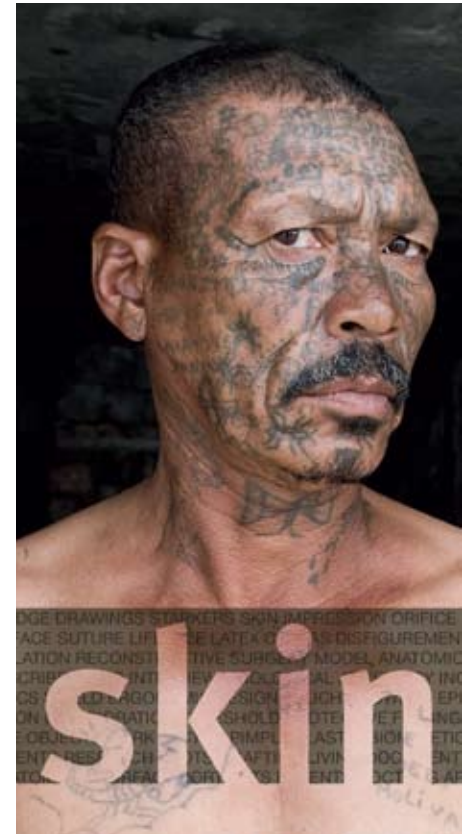
The most important collection to be digitised is the substantial Francis Crick archive – nearly 300 boxes of scientific papers spanning Crick's DNA and neurobiology research, including draft articles and books, lectures,



research notes, and extensive correspondence with Crick's scientific colleagues and the general public. Other notable people and organisations include the papers of Fred Sanger (biochemist and double Nobel Prize winner), Arthur Ernest Mourant (haematologist and geneticist) and the Medical Research Council Blood Group.

Lecture notes (1954) and sketch of the DNA double helix (1953) by Francis Crick.

Wellcome Collection reveals the naked truth



'Mr Green'. © Araminta de Clermont & Michael Hoppen Contemporary

Our skin gives us a protective layer, a sense of touch, and a highly sensitive and visible interface between our inner body and the outside world. Wellcome Collection presents the bare facts on the largest human organ this summer with new exhibition *Skin*. From historical anatomy to works by artists including Damien Hirst, Helen Chadwick and Wim Delvoye, *Skin* considers our existence within our constantly changing exterior.

The exhibition is accompanied by Skin Lab, which features artistic and interactive responses to developments in plastic surgery, scar treatments and synthetic skin technologies. The 'Skin: Exposed' symposium (16–17 July) will look at attitudes to and perceptions of nudity as they have varied across times and cultures. Chaired by writer and critic Brian Dillon, it will bring together experts from the worlds of anthropology, history of art and evolutionary science.

A series of other special events, from exhibition tours giving unique personal insights, to talks and activities around the theme of skin, will accompany the exhibition. Curated by Javier Moscoso of the Spanish National research Council, *Skin* runs from 10 June to 16 September. www.wellcomecollection.org/skin

Wellcome blogs launched

There's now another way to stay in touch with Wellcome-related activities: two new blogs.

The Wellcome Trust blog (wellcometrust.wordpress.com) covers science and biomedicine, their crossover with arts and history, and the many other activities related to our work. From new PhD students to senior researchers, museums and plays to documentaries and films, the blog will feature a variety of news, stories, event reports and behind-

the-scenes insight into the world of science from a Trust perspective.

The Wellcome Collection blog (wellcomecollection.wordpress.com) features discussion and highlights of subjects and activities of interest, in keeping with the venue's unique mix of exhibitions and events that consider what it means to be human. The blog will offer reports on what's been happening in the building and show off new content from the Wellcome Collection website.

Have you got a winning image?



The Wellcome Image Awards gallery at Wellcome Collection.

The Wellcome Image Awards celebrate the most informative, striking and technically excellent images of biomedical science acquired by Wellcome Images, the Wellcome Library's picture library. The judging for the next Awards will take place in October 2010, and the winners will be announced in February 2011, alongside a new Awards exhibition and website. All images added up until the day of judging are eligible for consideration, so to find out how to submit your images, contact Dr Laura Pastorelli on 020 7611 8347 or l.pastorelli@wellcome.ac.uk. www.wellcomeimageawards.org

Get hooked on *Big Picture: Addiction*

Addiction is a term we all use, but what exactly does it mean? *Big Picture: Addiction* explores what addiction means to different people, and examines the effects of being addicted on the minds, bodies and lives of those affected. Find out about how addictions are treated now, and join us in considering the issues that could arise in addiction in the future.

This issue is the latest in our *Big Picture* series, created for teachers, 16+ students and learners of any age. Visit www.wellcome.ac.uk/bigpicture/addiction for

extra articles, images, lesson plans, videos and more, all on the theme of addiction. You can also download PDFs or order copies of this and past issues of the magazine, including *Obesity*,

Nanotechnology and Genes, *Genomes and Health*.



Prizes and honours



Congratulations to **Professor Nick White** (above), Director of the Wellcome Trust South-east Asia Programme, and **Professor Peter Ratcliffe**, Head of the Nuffield Department of Clinical Medicine at the University of Oxford, who have been honoured in the 2010 Canada Gairdner Awards, Canada's only international science prizes.

Three Trust award holders have been named in the Cultural Leadership Programme's Women to Watch list for 2010. Congratulations to **Kate McGrath**, Director of Production company Fuel, **Laura Sillars**, Programmes Director at the Foundation for Art and Creative Technology, and **Bridget Nicholls**, Director of Festival, which celebrates the art and science of being an insect.



Well done to **Professor Janet Hemingway** (above), Director of the Liverpool School of Tropical Medicine, who has been elected to the National Academy of Sciences, one of the USA's highest scientific honours. She was elected as a foreign associate for her excellence in original scientific research, one of a maximum of 18 that may be elected annually.

A decade at Sanger

Earlier this year, Professor Allan Bradley stepped down as Director of the Wellcome Trust Sanger Institute after ten years in charge. In an interview with Mun-Keat Looi, he reflects on the Institute's changes and achievements in that time.

Reclining in a garden chair on a sunny day in Cambridge, Professor Allan Bradley looks like a satisfied man. In ten years as Director of the Sanger Institute, he has overseen some of the milestones in genomic research over the past decade: the completion of the human genome project and the first published sequences for mouse, malaria and cancer, to name just a few.

Yet his tenure began at a time of uncertainty, albeit still full of the promise of the genomics age. He took the reins from the legendary Professor Sir John Sulston in 2000, just as the Human Genome Project reached its peak. But with the announcement of the draft sequence, there were questions about what the Sanger Institute would do next. "The question was: how does an institute which essentially had just one project evolve a more holistic approach?" says Prof. Bradley.

His first, unenviable, task was to set out a new strategic plan for the Institute. His goal was to diversify its interests, essentially to transform it from a centre that sequences biology to one focused on the biology of sequences. Yet Sanger had neither the infrastructure nor personnel to do the science it aspired to.

"What we set out was essentially a ten-year programme," he says. "We needed the first five years of funding to build the physical infrastructure – animal labs for mouse work, containment units

for pathogen work, IT capacity – as well as to expand our intellectual capital by recruiting scientific leaders in a few areas."

Prof. Bradley and colleagues developed a collective vision matching the Sanger Institute's ethos as a group-led effort. And in keeping with that, they made a concerted effort to invest in the brightest young minds in key areas, who would eventually become world leaders in their fields.

"Some of our greatest successes have been in identifying young people and watching them grow to international stature as a scientist," he says, pointing to Dr Matt Hurles as an example. Hurles took on the Copy Number Variation Project, helping to establish a major new area of study in a new form of variation that wasn't fully appreciated at the time. "It shows that if you put decent resources in the hands of the right person, you can achieve a lot."

Part of Prof. Bradley's philosophy is diversification, but with focus. "The large-scale nature of our projects is a historical feature of the way Sanger operates – managerial experience, organisation, bringing lots of people to bear on a common objective. What we've been able to do is replicate that in other projects."

What is important, he says, is not just being involved in a large international project, but leading it, shaping it and making bigger contributions. He cites the International Cancer Genome Consortium as an example. For many years this was



"I wanted to transform Sanger from a centre that sequences biology to one focused on the biology of sequences"

solely a Sanger endeavour led by Prof. Mike Stratton, Dr Andy Futreal and Dr Richard Wooster. Their vision and hard work founded the field of cancer genomics, which inspired a community of cancer researchers to emulate their approach all over the world.

The Sanger Institute is now a hub of international science, an academic genome centre, with strong programmes in informatics, pathogen genetics, model organisms and human genetics. It's a far cry from 2000, or even 2006, when the Institute was mainly known purely for its sequencing.

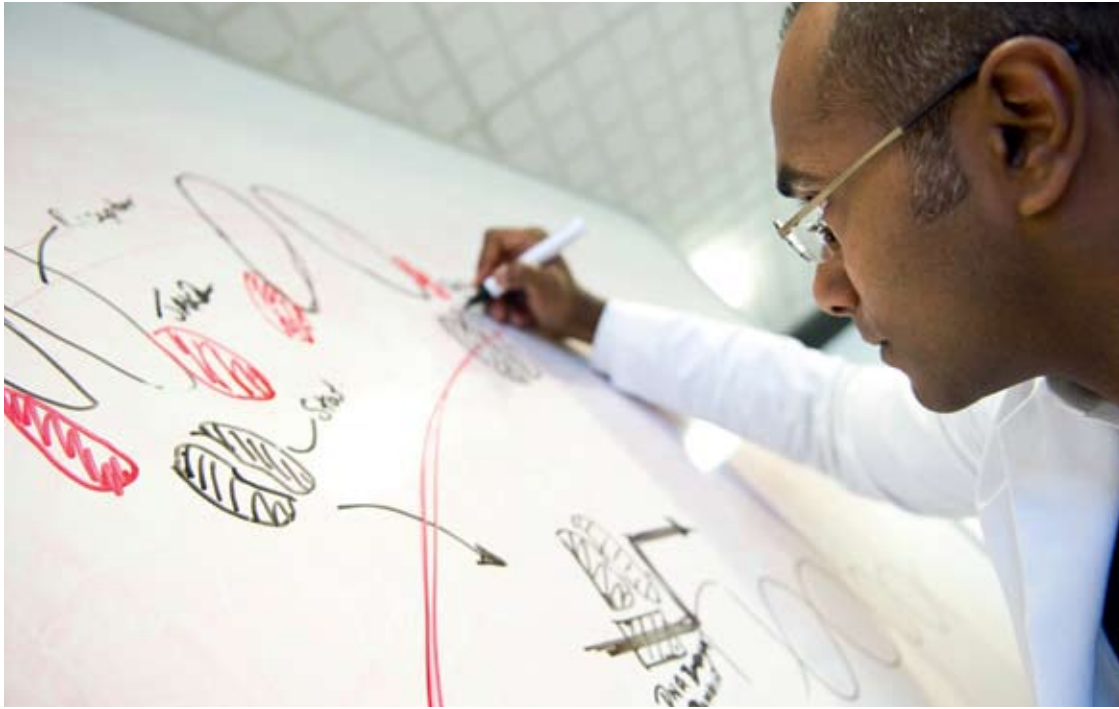
"Sanger today is regarded as an outward-looking organisation more than it was a decade ago," says Prof. Bradley. "We're proud that people look at what we're doing, access our data and resources and in many cases work directly with us to achieve their scientific objectives." More than enough reason to feel satisfied.

Ten years of discovery

- 2001 Draft human genome sequence published
- 2002 Mouse genome sequence published
- Malaria parasite genome sequence published
- BRAF* gene mutation found in 60–70 per cent of melanomas
- 2004 Gold standard human genome sequence achieved
- 2006 Copy Number Variation Project publishes first findings
- 2008 International Cancer Genome Consortium established
- 2009 Pig genome sequence published
- First cancer genomes published



Read more about the developments in genomics and genetics since the draft human genome sequence was announced in 2000 – including the stories of Professor Sir John Sulston and other scientists working at Sanger – on pages 10–13.



thing that I want to do: make a big difference by understanding how these things happen.”

Dr Dawson’s first taste of lab research came as a project on human cancer genetics using zebrafish, completed as part of his Bachelor of Medical Science degree. His involvement in clinical research continued after he qualified as a doctor, mainly in the areas of bone marrow transplantation and blood cancers.

This passion for being in the lab led him to do a PhD. Supported by a prestigious postgraduate scholarship awarded by

the General Sir John Monash Foundation, he began his research in Cambridge in 2007.

Doctor, doctor

A medical degree is a big challenge, and so is postgraduate lab research. So what drives some people to undertake both and become clinician-scientists? Chrissie Giles spoke to Dr Mark Dawson to find out.

You could say that the Wellcome Trust owes Mark Dawson. We’re in a car travelling to the Cambridge Institute for Medical Research as he recounts a painful childhood experience. Down to the final two in a primary school spelling bee in his native Australia, he was asked to spell ‘welcome’. Recalling some old Burroughs Wellcome & Co. items in his bathroom at home, he duly spelled out the double-L version. He lost.

Still, this early setback doesn’t seem to have damaged his career, or his relationship with the Trust. Recently awarded a Wellcome Trust Intermediate Clinical Fellowship, Dr Dawson also has the honour of being the first-ever recipient of a Wellcome–Beit Prize Fellowship, a sum of £25 000 provided in addition to his main award.

But what drives him and other doctors, dentists, vets and psychologists to develop a scientific career alongside their clinical work? How well does lab work sit alongside clinical responsibilities? What kind of person does it take to be a clinician-scientist?

In the blood

Dr Dawson has always had a fascination with, and desire to improve the outcomes of, blood-based cancers, including leukaemia – cancer of the white blood cells. The field of leukaemia genetics was born in the 1960s, when researchers found a key genetic change in patients with chronic myeloid leukaemia. They showed that two chromosomes exchanged parts, creating a new gene and, in turn, a new protein. In the 1990s, scientists developed a drug, imatinib (Gleevec), that blocks the activity of this protein.

“When I started as a haematology trainee, most people with chronic myeloid leukaemia had to undergo a bone marrow transplant to get a lasting remission or cure,” says Dr Dawson. Some 15 per cent of patients died from the preparation for the transplant; those that survived the transplant often endured serious consequences.

“In my time, we’ve gone from this to giving people a drug they take a couple of times a day. It’s completely transformed their lives. I thought, that’s the kind of

Back to the bench

Dr Dawson’s PhD involved research on the myeloproliferative disorders, in which the bone marrow overproduces cells. Previous work by his supervisor, Prof. Anthony Green, found that almost every patient with polycythaemia vera (one of the myeloproliferative disorders) had a mutation in the *JAK2* gene. This change results in the continuous activation of this finely regulated enzyme in people with the disease. It’s this abnormal continuous activity that drives the cancer. “Knowing that there is a single mutation present in nearly all patients with disease gave us an incredible opportunity to try and understand the disease better,” says Dr Dawson.



Researchers thought that *JAK2* acts as a mediator primarily in the cell’s cytoplasm, where it conveys messages from outside the cell to other proteins within the cytoplasm, which then enter the nucleus,

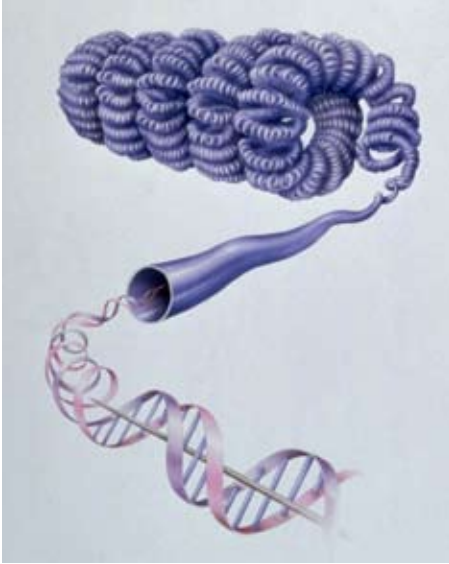


Illustration of the different levels of DNA packing, including a chromatin fibre (top) and a DNA strand (bottom). Medical Art Service, Munich

ultimately affecting how genes are transcribed (turned into RNA). In his PhD work, Dr Dawson and colleagues showed that *JAK2* is also present in the nucleus of the cell. What's more, it can add a chemical group to histones – the protein scaffolds that support DNA – changing how accessible the DNA is. This, in turn, can alter the transcription of some genes. They showed for the first time that *JAK2* can, by itself, directly influence what genes are expressed within a cell.¹

“We don't know the full implications of this yet,” says Dr Dawson, “but it does give an avenue of research that was previously unknown.”

Chromatin biology – the field concerned with chromatin, the complex of DNA and its histone protein scaffolds – is burgeoning. “I knew nothing about the field three years ago, but I've been seduced by it,” he says. “Understanding how the cell is able to regulate access to the DNA is fascinating.”

With his Intermediate Clinical Fellowship, Dr Dawson will study the role of chromatin changes in an aggressive condition called acute myeloid leukaemia. In this, and many other leukaemias, chromosomes break apart and rejoin differently. This can produce

fusion genes, which, in some cases, drive the development of cancer. But how? Some fusion genes have special properties that may be involved. “One that I'm studying has the ability to reinstate self-renewal in cells that have lost the ability, effectively making them leukaemia stem cells,” he says.

As many fusion genes are known to modify chromatin (the DNA and histone bundles), Dr Dawson is looking to understand how changes in chromatin could lead to leukaemia stem cells. The next step will then be to understand the differences between leukaemia stem cells and normal blood stem cells (from which blood cells are made), to give researchers a way to destroy the cancer stem cells but spare the normal ones.

Getting clinical

Even with all this bench work, Dr Dawson will still see patients – as an honorary haematology consultant at Addenbrooke's Hospital, he'll spend around 10 per cent of his time on clinical duties. But with a career that combines clinical responsibilities with cutting-edge research, does he see himself choosing one over the other?

“As a clinician you're working with people all the time. You're let in very personally into their lives, and you can have a profound effect on them. I very much enjoy that,” he says. “Scientific research gives you perspective into how vast the task is, and how incremental the gains are, despite years of research. But these gains are very important.

“It seems to me that medicine and science marry very well. They extract from me two very different sides of my personality, but I can't see myself losing either.”

Reference

1 Dawson MA et al. *JAK2 phosphorylates histone H3Y41 and excludes HP1alpha from chromatin. Nature* 2009;461(7265):819–22.

Mark Dawson will complete his Fellowship in two institutes: Dr Brian Huntly's lab at the Cambridge Institute for Medical Research, and Prof. Tony Kouzarides's lab at the Wellcome Trust and Cancer Research UK Gurdon Institute, Cambridge.



Mark Dawson on...

...why he chose the UK

“In the UK, it's well appreciated that clinician-scientists bring a different perspective than purely clinical or scientific researchers, and provide a bridge from bench to bedside. The opportunity that the Wellcome Trust has given me is not one I'd get at home.”

...what doing medicine brings to his scientific research

“As a clinician, the type of question I want to answer is based primarily on what is lacking clinically, which – for many blood-based cancers – is proper, targeted therapies. The only way to get these is by understanding the biology of the disease better.”

...what doing science brings to his clinical practice

“One of things we're blessed with as clinicians is instant gratification – you make someone feel a bit better and they say thank you. That's very rewarding, and is not something you get in science. Science brings a perspective of how vast the task is.”

...the one big question in leukaemia research

“How do we target leukaemia stem cells? If you think of leukaemia as a growing tree, the leukaemia stem cells are the root. Chemotherapy is like pruning the tree, but we don't actually end up killing it, because we're not targeting the roots.”

Need clinical funding?

The Trust offers support for clinicians – people qualified in medicine, dentistry, veterinary science or clinical psychology – at each stage of their career. Early-career schemes support graduates who have little or no research training, but who wish to develop a long-term career in academic medicine. Intermediate-career support includes Fellowships for MB/PhD Graduates and Intermediate Clinical Fellowships. Senior-career support includes research fellowships at the senior and principal levels. www.wellcome.ac.uk/funding

Funding

Investigator Awards: new details

In November, we announced our forthcoming Investigator Awards scheme. Further details are now available.

Wellcome Trust Investigator Awards aim to give exceptional researchers the flexibility and support they need to be innovative and to pursue bold ideas. The Awards' scale and scope will facilitate long-term planning and release Investigators from the constant pressure of the grant application cycle. The scheme extends the successful model of fellowship support to researchers in established

academic posts – that is, those who have permanent, open-ended or long-term rolling contracts of employment salaried by their university or research institution.

There are two categories: New Investigator Awards support world-class researchers who are no more than five years from appointment to their first established academic position, but who can already show that they have the ability to innovate and drive advances in their field of study.

Senior Investigator Awards support exceptional researchers who hold an

established academic position and already have an outstanding track record. They must be at the forefront of their field internationally and have a compelling long-term vision for their research.

Applications will open from 1 October 2010, with the first Awards made in May 2011. We strongly advise potential applicants to contact us, so we can review their eligibility for the scheme and provide advice as needed. www.wellcome.ac.uk/investigators

Synchrotron support secured



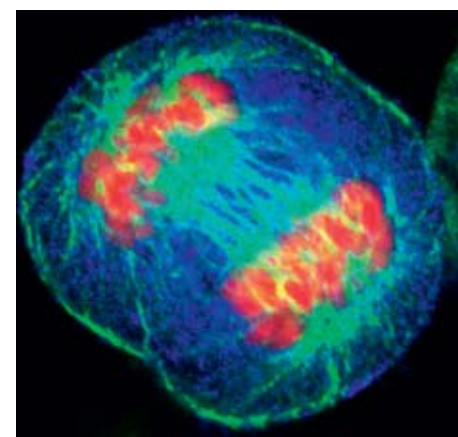
Diamond Light Source

We have announced, in partnership with the UK government, further funding to support Diamond Light Source, the UK's national synchrotron science facility (left). This, combined with other funding announced by the Science and Technology Facilities Council, means that Diamond has secured approximately £110 million for phase III of its development. This will raise the number of beamlines at Diamond to 32 by 2017, giving researchers access to new techniques and allowing the facility to continue making major contributions to the study of advanced materials, life sciences and environmental research.

Diamond currently has 17 operational beamlines with high-tech experimental

stations, which UK and international scientists use to study matter and material at the scale of atoms and molecules. Five additional beamlines will be added in phase II.

Grants to pick apart proteins



A cell in anaphase, a stage of cell division.
Matthew Daniels

We have awarded two grants to the Wellcome Trust Centre for Cell Biology at the University of Edinburgh through our Molecules, Genes and Cells funding stream. Professor Bill Earnshaw has had a programme grant associated with his Trust Principal Research Fellowship renewed. He will use a range of techniques, including live-cell imaging, to investigate the proteins that play a key role in the changes that chromosomes undergo during mitosis. To aid this and other research into protein interactions in the cell, Dr Juri Rappsilber and colleagues at the Centre have been awarded an equipment grant to purchase a next-generation mass spectrometer.

Further funding through Technology Transfer schemes

Two of our Technology Transfer funding schemes are advancing to their next stage. The Health Innovation Challenge Fund (HICF) has announced its latest theme, which will address monitoring of individuals with long-term health problems. This third call focuses on chronic diseases such as diabetes, asthma, arthritis, heart failure and dementia – which, at present, can only be controlled, not cured.



YinYing/iStockphoto

A greater shift towards self-monitoring and self-management, facilitated by medical devices and systems available today, could help. The HICF will look to support projects offering practical solutions to improving health monitoring in the home and in remote settings. Applications open in June.

www.wellcome.ac.uk/hicf

Meanwhile, the Seeding Drug Discovery initiative has been given £110 million to extend the programme for a further five years, following a review of the scheme. Since its launch in 2005, the initiative has committed over £80m to fund the early stages of drug discovery, at which work is often considered too high-risk to attract funding from commercial investors. Its successes include the completion of a phase I clinical trial of a drug to treat multidrug-resistant bacterial infections.

www.wellcome.ac.uk/sdd

Sharing stories on the NHS

A new study looking at the experiences of ordinary people and their opinions of their care over the first 60 years of the National Health Service has been published. 'Ordinary People Tell the Story' provides colourful accounts of people's encounters with the NHS in 1949, 1997 and 2008. The accounts are taken from the Mass Observation Archive, which specialises in material about everyday life in Britain.

Study authors Linda Lamont, Honorary Fellow in Contemporary History at the University of Sussex, and Fran McCabe have drawn on 60 years of comments by patients and health practitioners to make their own recommendations about the future of the NHS.

McCabe says: "The mass observation material gives us an absorbing and vivid perspective of the NHS going back to its birth. We should not forget that despite its problems, without the NHS many people, especially those without means, would not be alive today.

"People who have contributed to the Mass Observation Archive are reflective and prescient about the strengths and shortcomings of the NHS. They are aware of its complexity and discuss contentious issues around ethics and funding, sometimes suggesting solutions. Even



A World War II poster to recruit nurses and midwives.

when they have had problems using the NHS, they still hold its values to their hearts."

The study was supported by the Department of Health and a Wellcome Trust History of Medicine grant. It is available online at www.nhsnarratives.massobservationlamontandmccabe.co.uk and the Mass Observation Archive is at www.massobs.org.uk.

Populations and Public Health update

Professor Mike Begon from the University of Liverpool and colleagues have been awarded a project grant through our Populations and Public Health funding stream to study changes in numbers of the great gerbil (below), a major carrier of plague in Kazakhstan. They are using satellite imaging to look at burrows near human settlements to see whether they can predict when and where plague outbreaks will occur.

Other grants awarded include a project grant to study the pathway of care for children who died or were referred as emergency cases to a paediatric intensive care unit in South Africa. Dr Alison Ward and Professor Andrew Argent, from the Universities of Oxford and Cape Town respectively, will try to identify failures in care (without apportioning blame). Medical records will be scrutinised by an expert review panel that will make recommendations for how care could have been improved.



First Wellcome–Beit Prize awarded

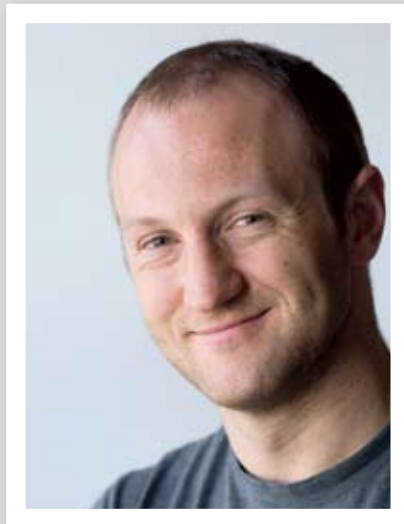
Wellcome Trust Intermediate Clinical Fellow Dr Mark Dawson from the Cambridge Institute for Medical Research is the first person to be awarded a Wellcome–Beit Prize Fellowship. You can read more about the work of Dr Dawson on pages 6–7.

The £25 000 awards are made annually to up to four selected researchers awarded Wellcome Trust Research Career Development Fellowships or Intermediate Clinical Fellowships, and are considered during the interview process for these fellowships. The awards were inaugurated in 2009 and replaced the Beit Memorial Fellowships for Medical Research. www.wellcome.ac.uk/beit

It's a rap: public engagement awards

The Rap Guide to Evolution wowed audiences and critics during Darwin200 year. Written and performed by hip-hop artist Baba Brinkman (right), the show has now been recorded as a professional studio album. Brinkman has received a People Award from us to fund 12 accompanying music videos, which will be made available for public education.

Elsewhere, Susan Norwood has received an Arts Award for *The Study of Tears*, which will explore why we cry. The project will feature video, photography and dance, as well as a documentary produced by pupils of Selly Oak Trust School, a school for students with special educational needs.



Great expectations

June 2010 marks a decade since the draft human genome sequence was announced. How much of an impact has this development had on genetics, genomics and science in general? What are the ethical and legal issues arising from this work? Chrissie Giles spoke to people who worked on the project then, and those who use the sequence and subsequent research in their work today, to find out.



Professor Sir John Sulston: “The key was tackling the whole genome”

John Sulston is among the few pioneers who, in the 1980s, began to develop the field recognised today as genomics. He and colleagues began a project to sequence the genome of the nematode, *Caenorhabditis elegans*, in 1990 – the success of which fed directly into the plans to sequence the human genome and set up the Sanger Centre (now the Wellcome Trust Sanger Institute) near Cambridge.

“I was very committed to the whole-genome approach. My philosophy, in a Douglas Adams kind of way, was that this thing is big, it’s seriously big. You’re not going to solve life by looking at a handful of genes.”

This focus on the whole genome transformed the way science is done, he argues. “As the sequence started to flow for the worm, human, fruit fly and yeast, people in sequencing labs started to get enormous amounts of correspondence from people working on other organisms who had discovered their favourite gene being matched,” he says. “There was this sense that different organisms in biology were talking to each other, and the genome work introduced a cross-fertilisation in biology that was quite novel.”

As founding director of the Sanger Centre, he was closely involved with the Human Genome Project, including in establishing the principles around data sharing. Famously agreed at a meeting in Bermuda in 1996, these conditions included that no one would take intellectual property rights over genome data, which should be made freely available within 24 hours of being produced.

For the worm community, sharing data was part and parcel of their research. Not so for those working on the human. “There were quite a few fraught political episodes,” he says. “You can get seriously rich and famous with a particular human

gene if you can lay claim to it.” Still, even when the private company Celera Genomics was set up to sequence the human genome, the public project continued, committed to releasing the data as it came.



Hatching *C. elegans*. Sanger Institute

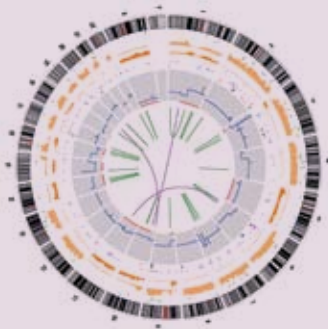
Freedom of scientific information is still part of his focus in his current role as Chair of the Institute for Science, Ethics and Innovation at the University of Manchester. “At the least we need much clearer and higher thresholds in not applying intellectual property to fundamental information. The battle’s not won, but the human genome is a tremendous demonstration of how valuable it is not to patent genes and other fundamental information.”



Professor Mike Stratton: “Recent discoveries are a remarkable testament to the power of the Human Genome Project”

A pathologist drawn into genetics in the mid-1980s, Mike Stratton spoke about the potential of the genome sequence to transform cancer treatment at the June 2000 announcement. Now Director of the Sanger Institute, how does he rate the progress so far?

In the 1990s, he was working at the Institute of Cancer Research, studying the genes that predispose to breast cancer. In 1994, he and colleagues located the second major breast cancer susceptibility gene,



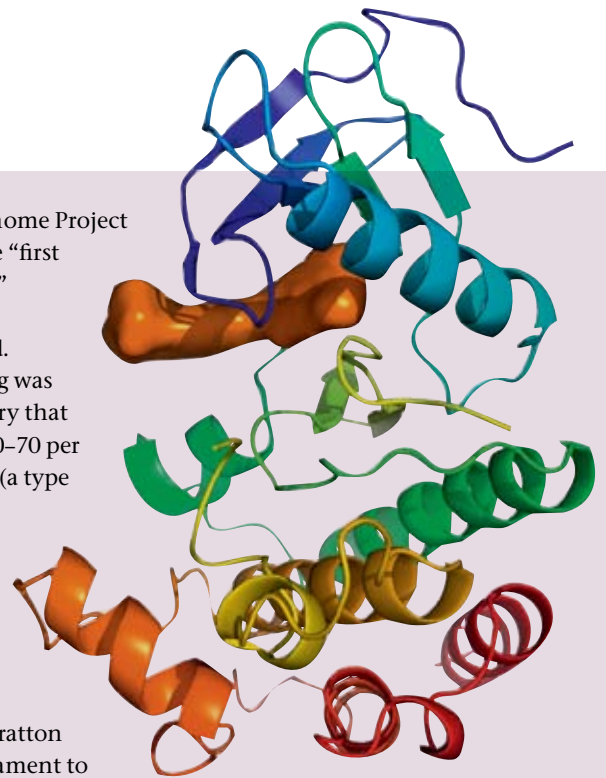
The genome of a malignant melanoma. From Pleasance ED et al. *Nature* 2009;463:191–6. © Nature 2009

BRCA2, on chromosome 13. The identification of the gene was then achieved at the Sanger Centre in 1995, with the spin-off that the first large segment of the human genome to have high-quality, finished sequence was the megabase around and including *BRCA2*.

In the lead-up to the release of the human genome sequence, he began thinking about how it might be useful in understanding the origins of cancer. “We knew that the genomes of cancer cells contain many somatically acquired abnormalities. We wanted to find these and thus identify the cancer genes involved. We saw that the now-complete normal human genome sequence would be an amazing basis to compare against cancer genomes.”

He proposed the Cancer Genome Project to the Wellcome Trust, and the “first post-genome project at Sanger” began in 2000, even before the sequence had been announced. The project’s first major finding was published in 2002: the discovery that the gene *BRAF* is mutated in 60–70 per cent of malignant melanomas (a type of skin cancer) and 10–15 per cent of colorectal cancers. Subsequent research, including a Trust-funded drug discovery programme, is today yielding drugs to block *BRAF* and thus treat melanoma, something Prof. Stratton describes as a “remarkable testament to the power of the Human Genome Project to start these lines of enquiry off”.

A fulfilment of the vision he presented at the 2000 announcement came in December 2009, when researchers at the Sanger Institute and colleagues published the first-ever complete cancer genomes. Now, researchers are working to sequence 25 000 cancer genomes, from 50 different kinds of cancer, through the International Cancer Genome Project. This will identify all the driving cancer genes and provide great



Depiction of the structure of BRAF with an inhibitor (solid orange shape) bound to it. Alfonso Zambon

insight into the processes that cause cancer.

What will this mean for treatment, ultimately? He predicts routine sequencing of cancer genomes to ensure that patients’ treatments are tailored to the mutations present. “By the end of this decade we’ll be using the genome sequence as the natural diagnostic for cancer.”



Professor Martin Bobrow: “It’s completely changed the face of biology”

Martin Bobrow, formerly a geneticist at the University of Cambridge and a Wellcome Trust Governor, was involved in the funding discussions and decisions around setting up the Sanger Centre and launching the UK part of the Human Genome Project.

What does he remember of this time? “It certainly wasn’t just another grant – it was a radical idea,” he says. He was immediately persuaded that it was “the right thing to do”, but adds that it was still a leap into the unknown. “There was quite a lot of contention as to whether it was worth investing that much money at that time, and whether the technology was going to catch up with the ideas.” Looking back, he says, it’s evident that the project worked and that the information produced was worth having.

He says that the project turned the world upside down, altering the sociology of biology and making genomics a part of every major field of biology. “Genome information is absolutely pervasive. It’s changed evolution, it’s changed all kinds of things,” he says. “Anyone who’s working on how biological systems function as physical entities sooner or later bumps up against the value of genome sequence.”



Professor Stephan Beck: “It was the opportunity of a lifetime”

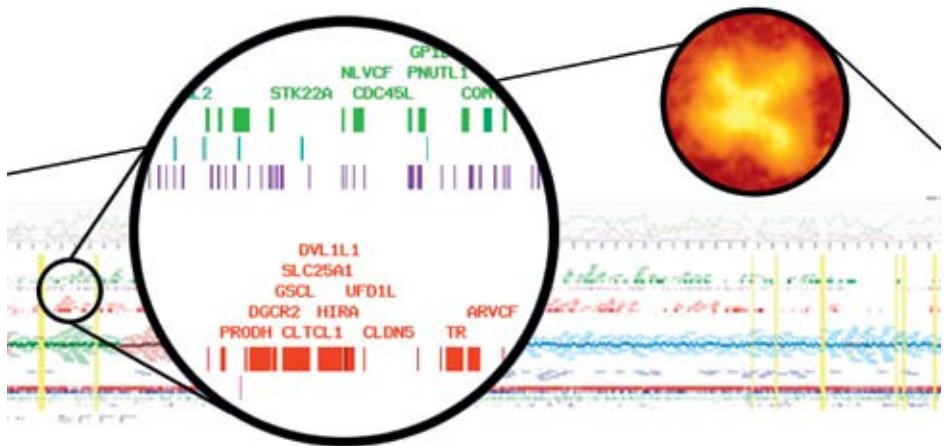
Working at the Sanger Institute from 1996 to 2007, as Head of Human Sequencing from 1998 onwards, Stephan Beck had a hands-on role in the human, mouse and zebrafish sequencing projects.

“It was clear to everyone that it was going to be an iconic project,” he says. “But there was also the sense of simply getting on with it.” This was essential, he adds, as the researchers had to do everything faster, cheaper and more efficiently week by week.

By the time the draft sequence was released in 2000, he had started the Human Epigenome Project, to look at chemical markers placed on the DNA that can show whether a gene is active or not, across the whole genome. “While the human genome sequence gives us information on where the genes and regulatory elements are, it cannot tell us how the genome is regulated.” Looking at the epigenome, he argues, would help us to understand which genes are switched on in particular cells in particular biological contexts.

Not as high-profile as the sequencing work, the epigenome work had a slow start. However, the recent launch of the International Human Epigenome Project should change this, with its plans to map 1000 epigenomes.

Now Professor of Medical Genomics at University College London, he remains on the cutting edge of research to understand how genetic and epigenetic variations relate to common diseases. “We have the same goal as when we started on the Human Genome Project: to ensure findings translate into benefit for human health. What I hope to see in the next ten years is that we understand how all the genetic and epigenetic variation in the human population causes disease,” he says. “But this doesn’t happen overnight.”



Gene map and image of chromosome 22, the first to be sequenced. Dr TJ McMaster



Dr Ewan Birney: “It was a crazy time”

Ewan Birney was completing his PhD under Richard Durbin at the Sanger Institute at the height of what he calls the “race for the genome”. Having taught himself programming as an undergraduate, he has been working in bioinformatics – using IT to analyse biological data – ever since.

He recalls some “interesting positioning” between Craig Venter’s Celera Genomics and the public project, in which there was a sense that even if the public project ‘caught up’ with

data generation, the private company had the edge on data analysis. “Making sure that we could compete in terms of presentation and analysis of the data was a key strategic driver,” he says, adding that Celera researchers were using his algorithms to analyse the genome sequence, just as he was.

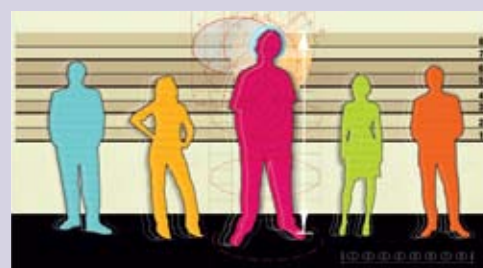
Indeed, he says that, to some, the Human Genome Project was the making of bioinformatics. “While bioinformatics had consistently been on the rise, there’s a

feeling that it really became part of mainstream molecular biology around that time,” he says.

A major part of the human sequencing project was making the information accessible and useful to researchers. As part of this, he moved next door to the European Bioinformatics Institute after he had completed his PhD, to help launch Ensembl. Ensembl is a freely available set of annotated genome databases, and now one of the most accessed websites in Europe. He also works on ENCODE, to study noncoding regions of DNA.

But what’s next for the field? There’s work to be done before genome sequencing becomes a routine part of healthcare,

he thinks, particularly as the genetic associations identified in studies have posed a conundrum. “There’s great statistical power but it’s not



Many genetic regions are known to influence height. Matthew Herring

predictive – it’s really annoying!” Why, for example, is knowing the height of a person’s brother so much better for predicting their height than studying the known genetic associations for height they carry?

The first aim is to find a way to make these genetic associations “usefully predictive”. “I’m a relentless optimist,” he says. “I’m pretty sure that we will crack some proportion of this problem over the next ten years.”



Dr Matt Hurles: “The direction of my career changed completely”

In 2000, Matt Hurles had begun a postdoc, looking for variants on the Y chromosome to trace prehistoric migration. The work he did for his PhD became obsolete and outscaled virtually overnight by the work made possible because of the sequence release.

“The first piece of the Y-chromosome sequence that came out actually completely changed the direction of my career,” he says, as it contained one of the variants he was trying to track down for population prehistory. “In trying to

investigate the molecular basis for that variant I ended up stumbling across structural variation, and how one can predict the likely location of these that might cause disease, just from the primary genome sequence.”

His work since has focused on understanding how these variants are associated with common diseases. He thinks that while we’ve learned a lot about common diseases, what we have learned hasn’t been that useful: “It’s not ten or 20 mutations for each condition having a fairly major effect in the population, it’s hundreds and thousands.”

But the success or not of the genome goes beyond understanding common diseases, he argues. “We’ve learned a fair amount about the genetic basis of rare diseases, which has led to a five-fold increase in diagnosis for patients with such conditions.” There’s also the potential to learn a huge amount more about human history, and how genomes work, including the role of non-coding sequence in health and disease.

The data produced is only one side of the sequencing’s legacy: it also catalysed the development of new technologies and applications. “Knowledge and technology go hand in hand, one catalyses the other. Thanks to the Human Genome Project, we



Genomic variation can be used to track changes across a population. *Fiona Pragoff*

now have the technology to do the blindingly obvious experiment – to sequence the genomes of patients and compare those to people that don’t have the disease.”

Will all babies have their genomes sequenced routinely in the future? *Andrejs Picjass/iStockphoto*



Daniel Vorhaus: “There are a lot of legal questions to consider”

As an undergraduate at the time, Daniel Vorhaus remembers the human sequence announcement primarily as a news event. Now an attorney at Robinson, Bradshaw & Hinson in North Carolina, USA, he focuses on legal and policy areas related to genomics and personalised medicine.

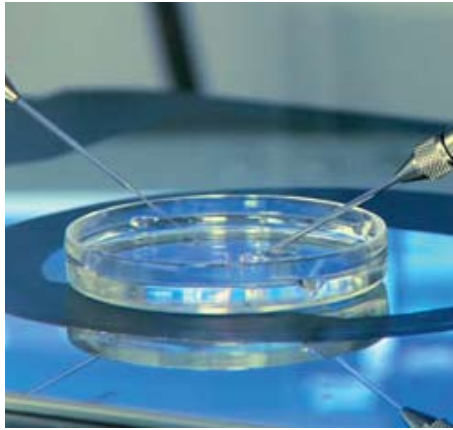
As this was an emerging field, there weren’t classes on these topics when he was at law school; for him, the really

interesting part of his job is working to try to get law and policy to catch up as closely as possible to the science. “There are gaps in how we’re dealing with genetic and genomic information and the privacy and consent issues associated with that,” he says. “This includes how genomic tools are used in medicine, and issues such as genetic discrimination and direct-to-consumer genetics tests.”

“In the next ten years, or sooner, people will be able to sequence their genomes,” he says. “Yet it’s inconceivable for most to think about what they can do with their own DNA sequence.” The answer, he thinks, will include private-sector development to make this information more accessible. “We need to help people be consumers of their own health information,” he argues, “so people can dive into this information, even when they’re healthy.”

Yohan Juliard/iStockphoto

First egg DNA transfer brings potential to stop disease



Scientists at Newcastle University have developed a pioneering technique that has the potential to help to prevent the transmission of serious inherited disorders known as mitochondrial diseases.

Mitochondria are often referred to as the cell's 'batteries' and are passed on from mother to child. One in 6500 children is born with mitochondrial mutations causing severe diseases, including

muscular weakness, blindness, fatal heart failure, liver failure, learning disability and diabetes. There are no treatments currently available. The new technique takes the genetic material from a fertilised egg that carries faulty mitochondria and transplants it into an egg with healthy mitochondria.

"A child born using this method would have correctly functioning mitochondria, but in every other respect would get all their genetic information from their father and mother," said Professor Doug Turnbull, one of the lead researchers. "What we've done is like changing the battery on a laptop. The energy supply now works properly, but none of the information on the hard drive has been changed."

- Watch a short film on this at www.youtube.com/wellcometrust

Craven L et al. Pronuclear transfer in human embryos to prevent transmission of mitochondrial DNA disease. *Nature* 2010 [Epub ahead of print].

No link between chronic fatigue and virus, study shows

Research at the Medical Research Council National Institute for Medical Research and St George's, University of London, has found no evidence of a link between chronic fatigue syndrome and a recently discovered virus. Also known as myalgic encephalomyelitis, chronic fatigue syndrome affects around 250 000 people in the UK. Its causes are not clear but a 2009 study found evidence of a retrovirus called XMRV in two-thirds of people with the condition.

The new study, which involved sampling DNA from

299 people, including 142 samples from those with chronic fatigue syndrome, failed to replicate these earlier findings. The new study supports research published earlier in 2010 that similarly could not replicate the findings.

Dr Kate Bishop, the Wellcome Trust Research Career Development Fellow who led the study, said: "We found no association between XMRV and chronic fatigue syndrome. However, chronic fatigue syndrome may encompass a spectrum of different conditions, providing a possible explanation for this discrepancy...It is important that we keep an open mind about new scientific discoveries which point to possible causes of this often very serious condition."

Groom HC et al. Absence of xenotropic murine leukaemia virus-related virus in UK patients with chronic fatigue syndrome. *Retrovirology* 2010;7(1):10.

Amanda Rohde/
iStockphoto

Reducing suicide in Sri Lanka



Suicide remains a major problem in Sri Lanka, but interventions have halved the suicide rate from 49 per 100 000 in 1995 to 23 per 100 000 in 2006. Researchers from the University of Colombo have now investigated all reported suicides in 2006 – 151 in total. Their analysis found that self-poisoning and burning were the most common methods used. Marriage problems were the most frequently cited reason (accounting for 30 per cent of the cases), with psychiatric illness accounting for just 6 per cent.

The researchers suggest that securing access and restricting availability of pesticides and drugs could help to reduce suicides further. They also call for better interventions to help people deal with anger and domestic conflict, as well as more recognition and treatment for psychiatric illness and alcoholism.

Fernando R et al. Study of suicides reported to the Coroner in Colombo, Sri Lanka. *Med Sci Law* 2010;50(1):25-8.

Wellcome News: your feedback

Thanks to all of you who completed the online survey about *Wellcome News* – we had a great response. We're looking through the results now and will be using your feedback to make some changes to the magazine over the coming issues, so keep your eyes peeled!

You don't have to wait for the next survey to share your thoughts, ideas and feedback on the magazine: email wellcome.news@wellcome.ac.uk or write to the address on the inside front cover of this issue to get in touch with the team.

A quick reminder too that all *Wellcome News* articles are available online, as well as PDFs of this and past issues. You can also subscribe online to *Wellcome News* and our other publications, to make sure you receive every issue, free, as soon as it's published. www.wellcome.ac.uk/wellcomenews

Human sleeping sickness parasite sequenced



Researchers from the Wellcome Trust Sanger Institute have unveiled a high-quality draft genome sequence for the parasite strain responsible for almost all reported cases of sleeping sickness. The chronic disease, also known as African trypanosomiasis, affects the human central nervous system and is caused by the *Trypanosoma brucei gambiense* strain (above) of *T. brucei*. Scientists had previously sequenced the *T. brucei brucei* strain, which infects cattle but is harmless to humans.

In the new study, researchers compared *T. b. gambiense* and *T. b. brucei*, looking for factors that might explain the former's ability to infect and thrive in human populations. The comparison revealed a

remarkable level of similarity between the two strains: sequences of comparable genes were, on average, 98.2 per cent identical. This suggests that *T. b. gambiense's* ability to infect humans cannot be easily explained by the addition or removal of a few genes.

"Single-letter changes in the genome; differences in the number of copies of genes; changes in how the activity of genes is regulated – all of these genetic nuances could play that crucial role in determining why *T. b. gambiense* behaves so differently," said Dr Andrew Jackson, lead author on the study.

Jackson AP et al. The genome sequence of *Trypanosoma brucei gambiense*, causative agent of chronic human African trypanosomiasis. *PLoS Negl Trop Dis* 2010;4(4):e658.

EU green light for hepatitis B rapid test

An inexpensive new test for the detection of hepatitis B virus has been given regulatory approval for use in the EU. Dr Helen Lee from Diagnostics for the Real World, who led the development of the test, said: "Our test is simple, quick, inexpensive and can survive very hot conditions for many months – all vital factors when you are working in poorer parts of the world."

Hepatitis B virus, spread through contact with infected blood or other bodily fluids, is highly infectious. Worldwide, two billion people have been infected and around 350 million people live with chronic infection. Although infection rarely kills, it can cause serious health problems and places a huge strain on healthcare resources.

The new test, developed with a Wellcome Trust Strategic Translation Award, uses dipstick technology to deliver

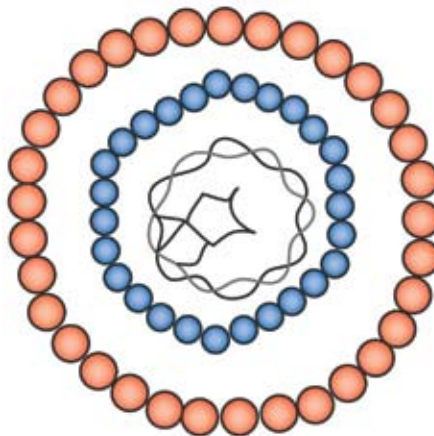


Illustration of the structure of hepatitis B virus.

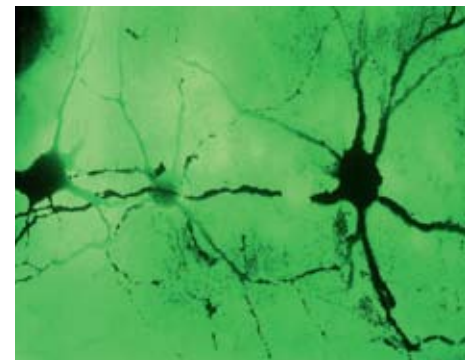
an accurate diagnosis onsite within half an hour, and can be used with minimal training. Current methods of hepatitis B diagnosis take days to weeks to get results.

Diagnostics for the Real World has already launched a rapid test for chlamydia. Other rapid tests in the pipeline include ones for HIV and influenza.

Genetic clues to basis of ALS

A pair of studies from the University of Sheffield have revealed genetic clues to the basis of amyotrophic lateral sclerosis (ALS), the neurodegenerative disease that affects physicist Stephen Hawking.

Approximately 5 per cent of ALS cases are inherited; previous studies have linked mutations in the gene *FUS/TLS* to the disorder. Professor Pamela Shaw and colleagues at Sheffield investigated the frequency of these mutations in a cohort of people with ALS from the North of England, finding mutations in 5 per cent of inherited ALS cases.



Motor neurons. Dr David Becker

In a separate study, the team looked at mutations in the gene *CHMP2B*, associated with frontotemporal dementia, which occurs in 3–10 per cent of people with ALS. Again looking at a group of patients from the North of England, their analysis found *CHMP2B* mutations in around 1 per cent of ALS cases. That figure rose to 10 per cent for those with ALS affecting mainly the lower motor neurons in their brainstem and spinal cord (ALS commonly causes injury and death to both lower motor neurons in these sites and to upper motor neurons within the motor cortex of the brain). Further evidence tracking multiple affected individuals in a family is needed to confirm the link, the researchers say.

"Accurate classification of ALS is really important to identify the best protective strategies and to optimally design human clinical trials," said Professor Shaw. "The discovery of two new genes is a step forward in classification and opens up new approaches to understanding the biological mechanisms underlying this devastating disease."

Hewitt C et al. Novel *FUS/TLS* mutations and pathology in familial and sporadic amyotrophic lateral sclerosis. *Arch Neurol* 2010;67(4):455–61.

Cox LE et al. Mutations in *CHMP2B* in lower motor neuron predominant amyotrophic lateral sclerosis (ALS). *PLoS ONE* 2010;5(3):e9872.

Classy conversations

Café Sci gives scientists a chance to escape the bench and get into schools, and gives students a chance to discuss scientific topics of their choice informally. Catherine Whitlock took a look at Cafés in the UK and Uganda to find out more about this movement.

It's early afternoon, and 40 animated students stream into the light-filled atrium at Stockley Academy, a secondary school in west London. They are gathering for Café Sci, a chance to hear about and discuss some novel, and perhaps controversial, science issues. There's no pressure to be quiet though, as informal chat is what Café Sci is all about – a chance to air their thoughts about science freely.

Stockley is one of the latest recruits to the Café Sci movement, which was launched in the UK in 2005. And the idea of taking scientists out of the lab and into schools seems to have global appeal.

Supported by the Wellcome Trust, Betty Kituyi has been hard at work setting up Café Scis in 18 schools in Uganda, East Africa. The first was held in 2009. Kituyi's background in science and education meant that she was excited at the prospect of productive discussions about science. "This is something Uganda really needs," she says. "There are lots of new technologies available, like genetically modified crops. People are concerned about these and want to know how they will affect their lives."

In Uganda, where access to computer facilities and the internet is not always possible, Café Sci's user-friendly way of interacting with science and scientists has been welcomed with open arms. "Students are learning that science does not have all the answers, but they learn what questions need to be asked," Kituyi adds.

After attending a recent Café in Uganda on black holes, the founder of the adult Café Scientifique movement, Duncan Dallas, was impressed: "Science teaching in Uganda is traditionally focused on a



one-way transmission of facts and here the students were given the freedom to talk. The discussion went on for about an hour, constantly backwards and forwards." Kituyi agrees that it's an important shift: "When I introduced Café Sci in Uganda the headteachers were so impressed that something

like this can be done outside the classroom."

There are now plans for Cafés in local languages in Uganda (see 'Speaking my language'), as well as an expansion into more schools, outside of Kampala.

Right ingredients

But what is the secret to a successful Café, whatever its location? An emphasis on student involvement

is important, meaning that students choose the topics and, in many cases, run their own Cafés. Any topic can be covered but they tend to be highly relevant, topical, controversial or all three. Students in Uganda may choose to focus on HIV/AIDS, for example, but there are also universal themes: topics such as the science of love, mobile phones and aliens are much in evidence.

The speakers are, of course, pivotal to the events. At the best-run Cafés, the speaker's talk is just a small part: discussion is the main aim. "Speakers need only to present enough information to raise questions and comment from the audience," says Dallas. Props can be a great asset. At Stockley's Café, the speaker, Jaya Nemchand, a PhD student from Brunel

Café Sci in Uganda (top and bottom) and in the UK (middle).

University, produces some hip replacement joints and artificial knees that grab the students' attention and help to illustrate the applications of her research.

Finally, the café-style environment, often with free drinks and snacks, makes both the speaker and students feel at home. In the open, welcoming space of the atrium at Stockley, free from the constraints of a classroom, students are more likely to interact.

Learning experience

In the UK, Café Sci is building strong links with the scientific community through organisations such as STEMNET and its Ambassadors scheme (www.stemnet.org.uk). Scientists – both in the UK and Uganda – welcome the opportunity to join in. Stephanie Burnett, a neuroscientist at University College London, is a regular speaker at events such as Café Sci. “It’s easy to forget how amazing your area is. It’s really interesting to talk to people who can help you grasp the bigger picture,” she says. “As a scientist you come away with a sense of renewed enthusiasm for your work.”

One Stockley student commented: “We’re learning from each Café experience what works and what doesn’t, but we like the freedom to experiment.”

That’s not hard to believe – after all, how often do students get the opportunity to decide what topic to discuss, ask the questions they like and not be assessed at any stage in the process? It seems that students and scientists alike can only gain from this kind of café culture.

Speaking my language

In Uganda, Café Sci and adult Café Scientifique events are generally held in English. But, in areas where English is not widely spoken and where internet or library facilities are not available, Cafés are held in the native language. In recognition of Café Sci’s ability to extend access to scientific and health information, Christine Munduru from the Open Society Initiative for East Africa has been awarded a Wellcome Trust International Engagement Award to run native language evening Café Scis. These are held in central village spaces where the local brew, Malwa, is served.

The goal is to discuss scientific knowledge that is of direct use to the community. Past local-language Cafés have covered health-related topics, such as malaria in pregnancy, TB and the community, and HIV testing and counselling. The scope is broader than just health, extending to topics such as fire and safety information, and fish and poultry farming. www.cafescientifique.org/uganda.htm



From top: Duncan Dallas and Betty Kituyi.

A brief history of Café Sci

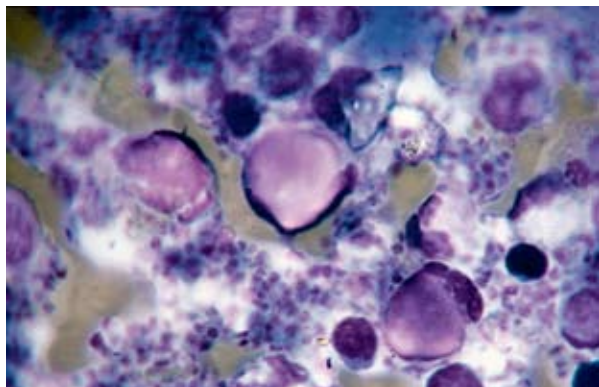
On its website, Café Scientifique is described as “a place where, for the price of a cup of coffee or a glass of wine, anyone can come to explore the latest ideas in science and technology”. It was the brainchild of Duncan Dallas, formerly head of the Leeds BBC Science Unit, who was inspired by the French Café Philosophique. In the wake of the Chernobyl disaster, BSE and GM food controversies, he saw Café Scientifique as an opportunity to foster relationships between the public and science. “Café Scientifique arose from concerns about how science is changing our world and how we relate to that as individuals and as a society,” he says.

The first Café was held in Leeds in 1998. Thanks to the work of Dallas and project director Mary Arber, there are now more than 50 running in the UK, with a strong presence in other countries around the world. They’re held in cafés, bars, theatres – anywhere outside of an academic context. Supported by funding from the Wellcome Trust, Café Scientifique was extended into UK schools in 2005, becoming Café Sci. There are now over 150 UK schools involved in the programme. www.cafescientifique.org

- Find out more on Café Sci at www.juniorcafesci.org.uk.
- Have you been involved in Café Sci? Email wellcome.news@wellcome.ac.uk and let us know your experiences.

Research

Predicting the progress of autoimmune diseases



Photomicrograph of lupus cellular infiltrates.

Researchers have identified a cellular genetic signature that predicts prognosis in two autoimmune diseases. This information may be useful for tailoring drug therapy to individual patients, potentially reducing harmful side-effects.

The research, led by Professor Kenneth Smith from the Cambridge Institute of Medical Research, looked at people with two different autoimmune diseases: inflammation of the blood vessels, known as AAV, and lupus, a disease caused by antibodies acting against the body's own tissues.

The team took blood samples from patients before treatment and isolated the different populations of immune cells, including T cells, B cells and neutrophils. By studying gene expression, they were able to get a snapshot of which cell types might be contributing to disease.

In patients with relapsing disease, a specific subgroup

of T cells called CD8+ T cells had higher levels of expression of genes involved in promoting T-cell activity, including the T-cell receptor. CD8+ T cells from these people also showed the hallmarks of having been activated already – so-called 'memory T cells' that are poised to react faster and stronger. A genetic signature of poor prognosis such as this may be useful in guiding therapy.

McKinney EF et al. A CD8+ T cell transcription signature predicts prognosis in autoimmune disease. *Nat Med* 2010 [Epub ahead of print].

Round-up

Markers to diagnose osteoarthritis

In work that we part-funded, researchers at King's College London have identified new biomarkers in the blood that could be used to diagnose osteoarthritis. The team studied the ratios of the concentration of 163 different chemicals in blood taken from women on the Twins UK register. Two ratios – valine to histidine and xleucine to histidine – have potential to be used to diagnose osteoarthritis or indicate its early stages.

Zhai G et al. *Ann Rheum Dis* 2010 [Epub ahead of print].

Cancer genome plans described

The International Cancer Genome Consortium is to decode the genomes of 500 tumours from 50 different cancer types, including blood, brain, breast, colon, kidney, liver, lung, pancreas, stomach, oral cavity and ovary cancers. The Consortium is supported by ten funding organisations from around the world, including the Wellcome Trust.

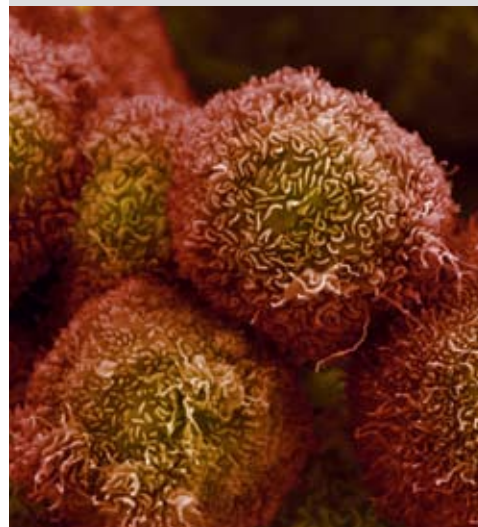
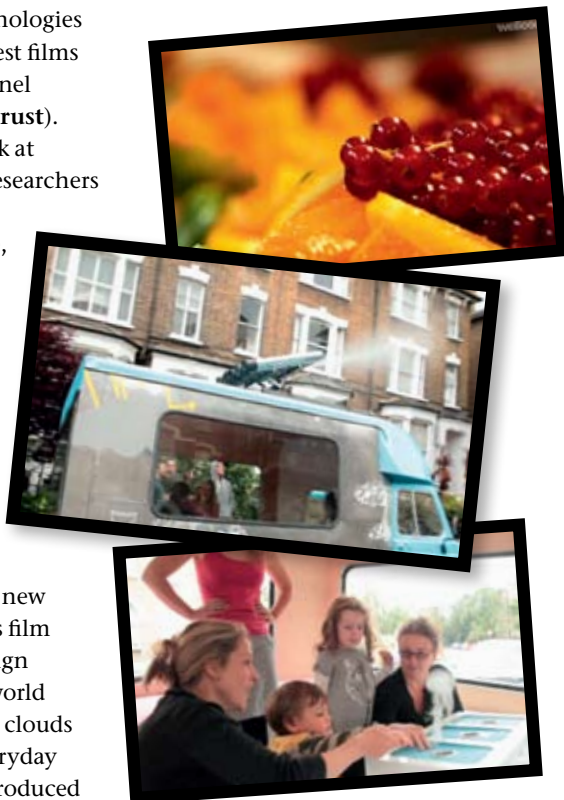
International Cancer Genome Consortium. *Nature* 2010;464(7291):993-8.

Latest Trust films live on YouTube

Fertility, food and futuristic technologies are among the subjects of the latest films to be added to our YouTube channel (www.youtube.com/wellcometrust).

Find out about pioneering work at Newcastle University, in which researchers have transferred DNA between two human eggs for the first time, bringing hope for preventing mitochondrial diseases (see page 14). Meet two research teams to examine why we feel hunger, what drives some people to eat to excess and what scientists can do about it in the film *Hungry for progress: appetite, genes and drugs*.

Lastly, explore the story behind the Wellcome Trust HQ's new window display, 'What If...?' This film takes us through three of the design projects on display, including a world in which nanotechnology allows clouds to snow ice-cream and where everyday products contain synthetically produced living components.



Pancreatic cancer cells. Anne Weston, LRI, CRUK

Diabetes signs at age ten

South Asian and African-Caribbean adults living in the UK have a higher risk of type 2 diabetes than white Europeans. Now, researchers from St George's, University of London, have shown that signs of this disease are already present in UK children of South Asian and African-Caribbean origin at age ten, bringing hope of early intervention for the disease.

Whincup PH et al. *PLoS Med* 2010;7:e1000263



Q&A: Peter Sozou

Human embryos created by *in vitro* fertilisation (IVF) can be stored for use in future fertility treatment. However, difficulties can arise if a couple create embryos together and then their relationship breaks down. With funding from a Wellcome Trust Value in People Fellowship, Dr Peter Sozou of the London School of Economics and colleagues looked at how UK law governing stored embryos might be improved to give people more flexibility over the type of agreement they can enter into.

What is the current UK legal situation?

When embryos created by IVF are stored, each member of the couple who created the embryos has the right to withdraw consent at any time before the embryos are transferred to a woman's uterus. In effect, both the woman and the man maintain a veto over using the embryos to try to produce a pregnancy, up until such time as they are used.

Why is this a problem?

Couples who have stored embryos sometimes split up, and this can lead to disagreements about what to do with their embryos. In some cases, stored embryos represent a person's only chance of becoming a biological parent – a situation that more commonly affects the woman than the man. In these cases, withdrawal of consent by the other person can have devastating consequences. We examined whether the present law, specifying a 'one-size-fits-all' agreement, can be improved to enable people to choose an alternative type of agreement when this would suit them better.

What is your alternative?

We propose giving people the option of one member of the couple voluntarily giving up their veto over the future use of the embryos. The other person would then have sole control over the embryos, so their future use would not be dependent on continuation of the relationship. This option would not replace the current form of agreement but should be available as an alternative. It would be up to the couple to decide which agreement suits them best.

What interested you about this area?

There was a widely reported case about a woman who had created embryos with her partner before undergoing cancer treatment that left her sterile. The relationship later ended and he withdrew consent for continued storage of the embryos, depriving her of the chance to have her own genetic children. The case went all the way to the Grand Chamber of the European Court of Human Rights, where the woman lost. A Wellcome Trust fellowship allowed me to explore this problem with Geraldine Hartshorne, an expert in reproductive medicine, and Sally Sheldon, a legal expert.

What other pressing issues are there?

A closely related problem is that of withdrawal of consent by donors of gametes [eggs or sperm]. Donors can withdraw consent at any time up to the time that sperm, eggs or embryos are transferred to a woman's body in fertility treatment. We found that sperm donors do withdraw consent occasionally. This has had serious consequences, including destruction of embryos that had been fertilised by the donor's sperm. In an article published in *BMJ*, we suggest a standard set of options for donors wishing to withdraw consent, and there may also be a case for restricting the circumstances under which this can take place.

Another important question is whether to use one or two embryos in a cycle of IVF treatment. Using two gives a higher chance of achieving a pregnancy but also increases the chance of a multiple birth, which can lead to complications. Because the financial costs of any complications tend, to a large degree, to fall on the public purse, there may be circumstances where a single-embryo transfer would be preferable from society's viewpoint. How to mediate this conflict is an interesting problem.

What do you do outside of work?

I probably spend more time than I should following news and current affairs. I also enjoy walking, listening to early music and eating chocolate.

Sozou PD et al. Consent agreements for cryopreserved embryos: the case for choice. *J Med Ethics* 2010;36:230-3.

Research reveals *Salmonella's* sabotage switch

Researchers have identified a 'switch' that enables *Salmonella* bacteria to sabotage host cells. The new finding could one day lead to drugs that interfere with the switch in order to combat *Salmonella* and possibly other bacterial infections.

Before *Salmonella* can establish an infection, the bacterium must first sabotage a larger human or animal host cell where it can replicate. It does this by injecting a cocktail of 'virulence' proteins into the host cell, which interfere with the cell's defences and help the bacteria to grow. The new study reveals that a



Salmonella bacteria. Janice Haney Carr/Public Health Image Library

molecular switch acts as a safety catch, holding the virulence proteins until the pH of the host cell has been recognised.

The researchers stress that the work is currently at an early stage but they hope that ultimately, it may be possible to use their findings to design better drugs or vaccines to combat *Salmonella*-related diseases, which include gastroenteritis and typhoid fever in humans, and similar diseases in livestock.

Holden D et al. pH sensing by intracellular *Salmonella* induces effector translocation. *Science* 2010 [Epub ahead of print].

Exploratory medicine

As the summer holidays near and many of us depart to warmer climes, the centenary of a chillier journey is upon us. The Wellcome Library's Ross MacFarlane tells the tale of Henry Wellcome's involvement in Scott's epic expedition to Antarctica.

On 15 July 1910, Captain Robert Falcon Scott and his fellow explorers left Cardiff on the *Terra Nova* for Antarctica, aiming to be the first men to reach the South Pole.

Famously, Scott and co. never made it back. What did survive – found next to the bodies of the explorers, eight months after their death in March 1912 – were the two medicine chests supplied for the expedition by Burroughs Wellcome & Co., the pharmaceutical company co-founded by Sir Henry Wellcome. One of these chests is on display in Wellcome Collection's *Medicine Man* gallery.

The early days of the company were also a 'golden age' of exploration, and it supplied, to many of the most famous travellers of the day, medicine chests filled with a selection of compressed 'Tabloid' products. Blieriot flew across the Channel, Stanley explored Africa, and Scott and Amundsen raced to the South Pole – all with these medicine chests as part of their essential kit. The chests were given free of charge, with explorers quick to endorse their compactness and efficiency (particularly when compared with the bulky chests filled with deteriorating medicines that the 'Tabloid' chests replaced).

But aside from Captain Scott's two chests, other Burroughs Wellcome & Co. products made their way to the South Pole. These were the photographic developing fluid supplied to the expedition's photographer, Herbert Ponting. 'Tabloid' Rytol proved a success with Ponting: in a letter preserved in the Wellcome Library, he wrote from Antarctica in October 1911 to the company, commending Rytol "to the notice of all travellers and explorers as well as amateur photographers...[it is] a



pleasure to work with chemicals put up in such an eminently practical and convenient form...It gives fine, brilliant negatives and seems to be

equally suitable for prints, plates and slides... all our developing has been done with it".

Given this endorsement, it is a reasonable suggestion that the majority – if not all – of the iconic photographs he took on the expedition came to life with Burroughs Wellcome & Co. developer. An image of Ponting developing his negatives in Antarctica, and indeed examples of his photography, were used by the company in its advertisements.

While medicine chests were supplied to the explorers of the age, Burroughs Wellcome & Co. also turned its attention to burgeoning leisure market. Special medicine chests and kits were designed and marketed to bicyclists, yachtsmen and motorists. So, when holidaying this summer – perhaps when at the doctor's being vaccinated pre-trip – spare a thought for travellers over 100 years ago and how Wellcome products, no matter the conditions, aimed to aid them on their travels.

What was inside?



Alongside own-brand dressings, plasters, lint and hypodermic needles, drugs in the medicine chest at this time included: cascara sagrada (a mild laxative, derived from the bark of the North American buckthorn tree); ipecacuanha powder (for gastric irritation, from a plant native to Brazil); Dover Powder (ipecacuanha with opium, for pain relief); quinine (for treating malaria, derived from the bark of the cinchona tree) and 'Livingstone Rousers' (named after David Livingstone and derived from rhubarb).

Above left and right: Scott's Burroughs Wellcome & Co. medicine chests. Below left and right: Adverts for 'Tabloid' Rytol featuring Herbert Ponting and one of his Antarctic photos.



Health Innovation Challenge Fund Call for proposals



Monitoring of chronic illness in the home and remote settings

The increased incidence of chronic diseases and conditions presents a huge challenge not just to the NHS but worldwide. Long-term conditions or 'chronic diseases' are those that can only be controlled and not, at present, cured. These include diabetes, asthma, arthritis, heart failure, chronic obstructive pulmonary disease, dementia and a range of disabling neurological conditions.

A greater shift towards self-monitoring and self-management could give a significant boost to patient care while reducing costs. The Health Innovation Challenge Fund (HICF), a joint £100 million funding initiative between the Wellcome Trust and the Department of Health, is currently inviting proposals for practical solutions to improve health monitoring in the home and remote settings.

UK institutions, companies, NHS Trusts and equivalent UK authorities are invited to **submit a preliminary application by 1 October 2010**. Collaboration between academia, clinicians and industry is particularly encouraged. The HICF is targeting opportunities that can deliver a healthcare outcome within a timescale of around three to five years from the date of the funding decision.

Further information and application forms are available at: www.wellcome.ac.uk/HICF



Courses, conferences and workshops



Human embryonic stem cell growing on a layer of fibroblasts. *Annie Cavanagh*

GC: Event takes place at the Wellcome Trust Genome Campus, Hinxton, Cambs.

For information on Wellcome Trust Conferences, see www.wellcome.ac.uk/conferences.

For information on Advanced Courses and Open door Workshops, see www.wellcome.ac.uk/advancedcourses.

September 2010

4–8
16th Meeting of the European Society for Pigment Cell Research
Conference **GC**

7–10
Signalling to Chromatin 2010
Conference **GC**

15–19
Genome Informatics
Conference **GC**

October

6–9
The Genomics of Common Diseases 2010
Wellcome Trust–*Nature Genetics* conference, Baylor College of Medicine, Houston, Texas, USA

17–23
Protein Interactions and Networks
Conference **GC**

27–29
Bridging the Gap on Biomedical Genetics
Conference **GC**

November

15–28
Genetic Manipulation of ES Cells
Advanced Course **GC**

28–3 Dec
Genomic Epidemiology in Africa
Advanced Course, KEMRI–Wellcome Trust Research Programme, Kilifi, Kenya

December

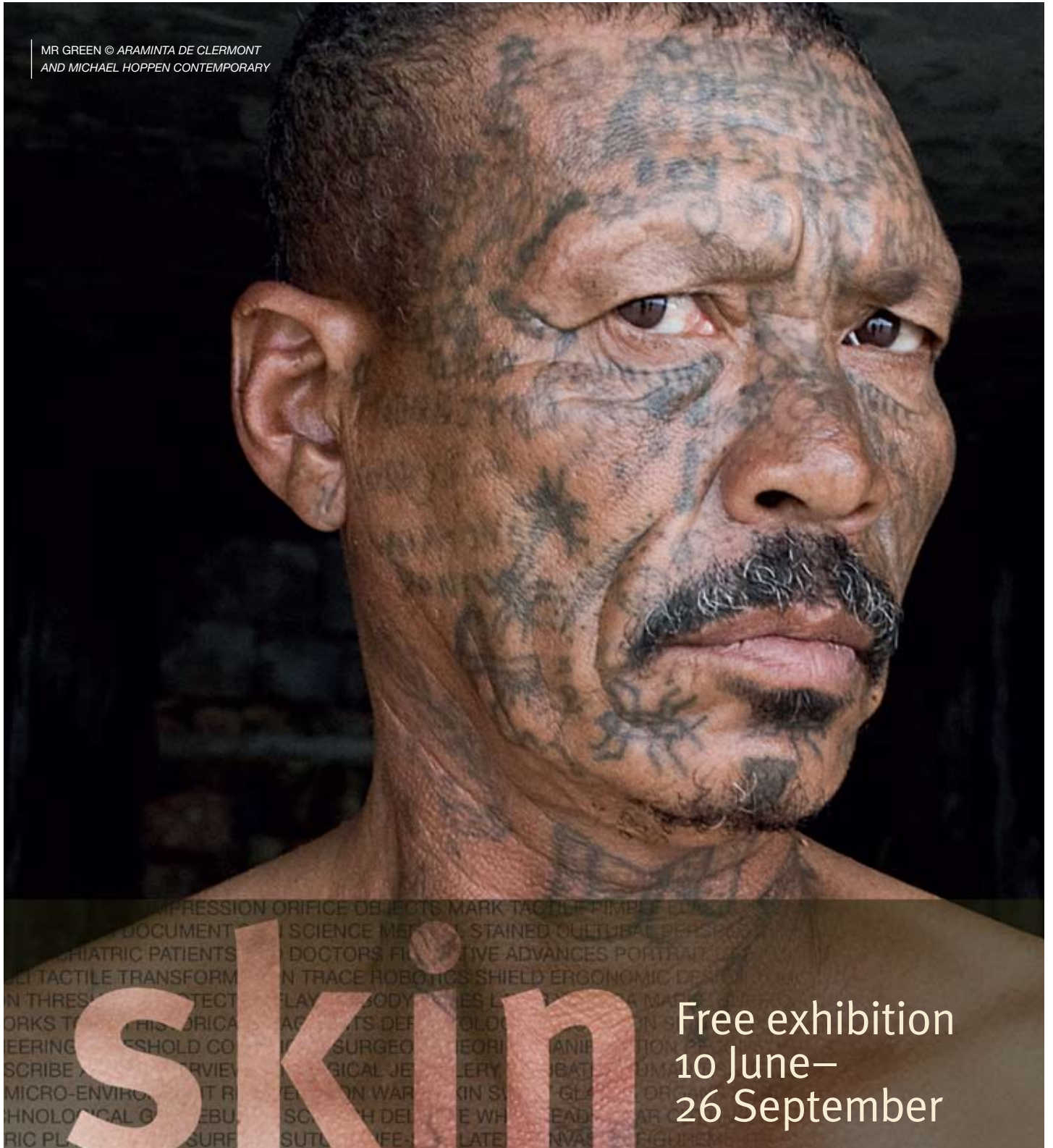
11–18
Genome-wide Approaches with Fission Yeast
Advanced Course **GC**

13–17
Proteomics Bioinformatics
Workshop **GC**

January 2011

23–28
Genomics and Clinical Microbiology
Advanced Course **GC**

MR GREEN © ARAMINTA DE CLERMONT
AND MICHAEL HOPPEN CONTEMPORARY



Free exhibition
10 June–
26 September

COLLECTION

MEDICINE MAN

Henry Wellcome's collection of curios



GALLERY

MEDICINE NOW

Science, art and personal perspectives

