500th baby joins bone study

Creating a research legacy from London 2012

Opinion: Meeting global challenges
Professor Peter Piot on why the UK should continue to invest in research in developing countries
At a time when we are determined to get the most out of the science that we fund, both in terms of delivering benefits to patients and ensuring a return on investment, it might appear that the focus of the MRC lies solely on translational research. But this could not be further from the truth. We have a strong and continuing commitment to basic research. In the past few years we have maintained a spend of more than £400 million per year on basic science, and continued to fund three-year project grants and early-career fellowships — many in basic sciences — with 113 and 97 respectively awarded in the 2010/11 financial year.

Without this discovery science, there can be no translation: the pipeline of improvements in the prevention, diagnosis and management of disease will run dry, and here at the MRC we are well aware of that.

In this issue of Network you can read about some of the latest discoveries in basic research such as the development of new genetic polymers at the MRC Laboratory of Molecular Biology and the discovery of a potential new tumour suppressor gene in simple water-dwelling worms at the University of Nottingham. These are just some examples of the kinds of work that MRC-funded scientists are doing at the outer limits of human knowledge.

Sir John Savill
MRC Chief Executive
Science Minister launches new imaging centre

Science Minister David Willetts formally launched Imanova, a new state-of-the-art imaging centre co-owned by the MRC, at a showcase event in London on 15 May.

Imanova is a pioneering public-private collaboration formed by the MRC, King’s College London, University College London and Imperial College London. It aims to become an internationally renowned imaging centre and partner of choice for industry looking to use its world-class facilities.

Kevin Cox, Chief Executive of Imanova, explained: “This is a novel collaboration, both between leading academic institutions and between academia and industry. Our aim is to accelerate the translation of great science into clinically and commercially relevant products and services.”

With both PET and MRI scanning on the same site, researchers will be able to image not only the activity of a medicine in the body but also its effect on the body systems being studied. As a result, it will be possible to see from an early stage if an investigational medicine is working effectively, and discontinue development if it is not. So not only are the new facilities providing a catalyst for translational research; they’re also offering the potential to shorten drug development times.

John Savill said: “One of my top strategic objectives is to promote mutually beneficial interactions between industry and the MRC-funded research community. I am also keen to see the MRC facilitate collaborations between universities. I have no doubt that Imanova will become a magnet for partnerships in high quality research across the UK, adding value to imaging facilities right across the country.”

David Willetts MP, Minister for Universities and Science, highlighted the Government’s support for the project: “The Government’s life sciences strategy underlined the importance of collaboration between the research base and industry as a means of driving growth and innovation. Imanova is an excellent example of this. It brings together leading academics and businesses to accelerate drug discovery and development, and is also attracting overseas investment.”

Researchers can still settle in UK

The UK Government has set new rules for migrant workers which mean that people on work permits classed as PhD-level can continue to apply for indefinite leave to remain in the country, irrespective of their level of income. This includes those working in research support posts. Home Secretary Theresa May said that this will “maintain the UK’s position as a hub for the world’s best scientists and researchers”.

The MRC, with other research councils, has argued for this exemption to ensure that the UK continues to attract, recruit and retain the best talent from across the world in order to deliver scientific programmes.

Separately, the Government has announced that the annual immigration cap for highly skilled workers from outside the EU will remain at 20,700 for the next two years.

Additionally, PhD-level jobs will no longer need to be advertised in Jobcentres and employers may hire the best applicant for such jobs, whether or not they are resident workers.

For more information see the home office website www.ukba.homeoffice.gov.uk/visas-immigration/working

MRC employees can also contact Linda Holliday, deputy HR director: linda.holliday@headoffice.mrc.ac.uk
An MRC study on the safety of an emergency treatment for children in shock has won the BMJ’s research paper of the year award.

When children go into shock from severe infection they are given fluids rapidly through a drip into a vein (fluid resuscitation). But the study found that in African children this procedure did not save lives. Providing fluids slowly was shown to be safer and more effective in aiding recovery.

Fluid resuscitation is the standard approach to treating shock in developed nations, but until the MRC trial it was unclear whether it could be safely used for African children. The findings challenged World Health Organization (WHO) guidelines on the treatment of African children with fever and shock caused by malaria, sepsis and other infections.

The BMJ award recognises “original research that has the potential to contribute significantly to improving health and health care”. There has been international recognition for the trial’s investigators, who were led by Imperial College London’s Professor Kathryn Maitland. Thanks to the trial’s findings it is hoped that thousands of deaths a year will be averted from the inappropriate use of fluid.

Commenting on their success, Professor Maitland said: “We are very honoured to receive this award. The teams at the hospitals dedicated two years to ensuring delivery of a robust trial which had an unexpected and important result which will certainly influence how African children are managed in future. The FEAST trial demonstrates that high quality trials can be conducted in Africa, and means that three lives in every 100 severely ill children will be saved if the results are implemented.”

Shock can occur after traumatic injuries, burns and severe infections and happens when the body restricts the blood flow to the vital organs in an attempt to stave off death. It affects around 10 per cent of children admitted to African hospitals, many of whom die within hours of admission. The trial, known as FEAST, was conducted in Kenya, Tanzania and Uganda and involved over 3,000 children.
Several MRC units and centres took their science out to the public this spring as part of National Science and Engineering Week.

MRC Lifecourse Epidemiology Unit staff took part in the University of Southampton’s Science Week, showcasing their new ‘Model, measure and move muscles’ activity. Visitors were able to have their grip strength measured and plotted on a graph to show how muscle strength differs as we age, and how their grip compared with others of the same age and sex.

Enthusiastic Oxford-based scientists created model flu viruses for visitors to the Oxfordshire Science Festival, which is sponsored by the MRC.

The fun continued at the Big Bang Fair in Birmingham, which attracted a record 50,000 people this year. Visitors got a taster of the MRC’s diverse range of work, learning about DNA, mitochondria and what it’s like to hear with a cochlear implant. MRC workshops on DNA damage, cancer and drug toxicity allowed for more in depth discussion with smaller groups.

Talking about why she got involved, volunteer Heather Gilbert from the MRC Institute of Hearing Research, said: “In science you have to be confident enough to talk about your research and I think this helps with your communication skills, but mainly I do it because I enjoy it. I find it really rewarding trying to make what I do accessible to people at all levels from 7-year-olds to 70-year-olds.”

Regional Big Bang fairs are taking place around the country over the summer. For more information, visit: [www.thebigbangfair.co.uk/nearme](http://www.thebigbangfair.co.uk/nearme)
February saw the birth of Rowen Hall, the 500th baby to join an MRC-funded study looking into maternal vitamin D supplements and bone health.

The Maternal Vitamin D Osteoporosis Study (MAVIDOS) is a clinical trial looking at whether giving women vitamin D supplements throughout pregnancy will lead to improved bone development in the baby compared with mothers given placebo. It began in 2008 and is led by Dr Nicholas Harvey from the MRC Lifecourse Epidemiology Unit in Southampton.

Rowen’s mother took a daily supplement (either vitamin D or placebo) after joining the study at her 12-week scan. When Rowen was born he had a dual-energy X-ray absorptiometry (DXA) scan to assess his bone density and he will have a follow-up scan at age four.

Previous work from the Southampton researchers has shown that pregnant women who are poorly nourished, who smoke or have low vitamin D levels are likely to have children with reduced bone mass in childhood. The stronger a child’s bones are very early in life, the less likely they are to be at risk of osteoporosis and broken bones in older age.

Low levels of vitamin D are common in the population, so MAVIDOS could ultimately provide critical information to inform the national strategy on optimal vitamin D supplementation in pregnancy.

www.mrc.soton.ac.uk
MPs visit MRC facilities

MPs have recently been visiting MRC facilities in their constituencies to learn more about how animals are used in scientific research. The visits come ahead of the transposition into UK law, by January 2013, of a new EU directive on the protection of animals used for scientific purposes.

Labour MP Paul Blomfield toured the MRC Centre for Developmental and Biomedical Genetics in Sheffield in April to learn about the centre’s important research in zebrafish.

Uniquely, zebrafish embryos are transparent. Their genes can easily be manipulated and their proteins can be labeled with fluorescent dye, allowing scientists to observe components of body systems in both health and disease. Such research is being used to identify genes and pathways that underlie a wide range of human diseases.

In London, Conservative MP Matthew Offord visited the MRC National Institute for Medical Research (NIMR). Staff gave Mr Offord a virtual tour of the institute’s animal facilities and showed him its aquarium which houses fish and frog animal models. Scientists explained their world-leading research, including efforts to identify new genes which play a role in male fertility.

Promising new asthma drug in the pipeline

A new drug with origins in MRC-funded work has shown promise for protecting patients with severe asthma from viral infections like the common cold, which can lead to worsening symptoms.

The drug, SNG001 (inhaled interferon beta), was assessed in asthma patients who had caught a cold. In those with severe, difficult-to-treat asthma, symptoms did not worsen during the critical first week of infection; fewer patients had exacerbations in asthma symptoms and they lost less lung function than those given placebo.

SNG001 is being developed by Synairgen plc. The company was co-founded by Stephen Holgate, an MRC Professor and former chair of the MRC Population and Systems Medicine Board, along with colleagues at Southampton University.

His ongoing MRC-funded work has increased understanding of how common cold viruses cause asthma exacerbations by exploiting a deficiency in asthma patients’ ability to produce interferon beta – a component of the immune system. This helped to highlight it as a drug target.

Professor Holgate said that the findings indicated that by boosting asthmatics’ viral defences rather than trying to target the viruses themselves, the adverse effects of infection can be effectively limited in this high-risk group of patients. He added: “This is a really promising breakthrough for the future treatment of asthma and one of the most exciting developments that I have seen in years.”
New five-year plan for UK regenerative medicine launched

Four UK research councils and the Government’s Technology Strategy Board have unveiled a new five-year strategy for UK regenerative medicine research, which includes £75m of investment in translational science.

The strategy takes stock of current capability in the UK and the knowledge gaps and translational barriers which must be overcome if the UK is to remain at the forefront of global regenerative medicine. It sets out clear objectives and a delivery plan focused on translating new biological understanding into benefits for both patients and the economy.

Dr Rob Buckle, the MRC’s head of regenerative medicine, said: “Regenerative medicine has the potential to revolutionise patient care in years to come and UK scientists are at the forefront of this rapidly evolving field. But without continued investment and careful planning, this privileged position could be at risk.

“The strategy provides a coherent framework for research and development activity in this area over the next five years to ensure that we build upon our existing strengths to deliver the regenerative therapies of the future.”

Download the strategy at: www.mrc.ac.uk/Ourresearch/ResearchInitiatives/RegenerativeMedicine

£25m funding for early-stage translation research

A key part of the new strategy is a recently-launched £25m new cross-Council funding programme, the UK Regenerative Medicine Platform (UKRMP).

Working closely with the £50m Technology Strategy Board Cell Therapy Catapult Centre, the platform will address the technical and scientific challenges associated with translating promising scientific discoveries in this area towards clinical impact. It will build on existing investment in centres of excellence in disciplines such as stem cell biology, medical imaging and manufacturing science. It will focus on early-stage translation to complement the Catapult Centre, which will work in the later stages of product development and delivery of cell therapies to the clinic.

Together the UKRMP and Catapult will help the UK regenerative medicine community operate as a single, globally competitive cluster.

For more information and details of how to apply, see: www.mrc.ac.uk/Fundingopportunities/Calls/UKRMP. Deadline for receipt of expressions of interest is 20 June 2012.
£180m Biomedical Catalyst now open

The £180m Biomedical Catalyst, jointly managed by the MRC and the Technology Strategy Board, opened for applications this spring.

The funding is available to small and medium-sized enterprises (SMEs) and academics, and aims to achieve commercial success for medical research breakthroughs. It will accept promising ideas that demonstrate significant healthcare and economic potential, and will support the development of technologies emerging from partnerships between clinicians, academics and industry.

Full details are at www.innovateuk.org/content/competition/biomedical-catalyst.ashx

A matter for debate

Six schools pitted their wits against each other this spring in the East regional final of an MRC-sponsored debating competition.

The Debating Matters competition, organised by think tank The Institute of Ideas, is open to 16 to 19 year olds and offers an accessible and engaging format for debating contemporary issues.

Teenage students argued for and against motions such as whether a system of presumed consent should be introduced for organ donation, attempting to persuade the audience and judges to side with their point of view. Queens’ School in Bushey were this year’s winning team and will go on to compete in the national final in July.

One of the judges, Professor Sheila Bird from the MRC Biostatistics Unit, said: “Debating Matters is a marvellous preparation for any walk of life but especially so for the sciences, including statistical science, the law and humanities. Judging Debating Matters puts me on my mettle as I try to make points as pithily and tellingly, as do those whom I have the honour and pleasure to judge!”

Fiorella Volonnino, a member of the winning team, said: “The whole process of research, reading and discussing these topics with others forces you to question your own values. You develop yourself, question yourself and that’s a really great process to go through.”

Seeking input on the Gateway to Research

The UK Research Councils, helped by Wikipedia founder Jimmy Wales, have engaged on a new project to build a Gateway to Research portal which will enable everyone (including members of the public and industry partners) to easily find information on the research we fund and the papers we publish.

Development of the Gateway to Research is underway, with an intended launch date in late 2013. In order to develop the site in a way that will be of most use to potential industrial partners, the MRC is looking for volunteers from small-to-medium-sized enterprises or industry who are willing to commit a few hours of their time over the next 18 months to help make the new platform as accessible as possible. Participation will involve reviewing early design and testing prototypes, as well as providing ideas and advice on what users want to be able to find on the Gateway.

For information, contact geraldine.clement-stoneham@headoffice.mrc.ac.uk

One of the Debating Matters regional finalists: Lorna Finlay, from Roundwood Park School, Harpenden.
Professor Robin Ali is an MRC-funded scientist working at the forefront of not one, but two, fields of regenerative medicine: gene and stem cell therapy. In the second part of our series on regenerative medicine Katherine Nightingale visited the Institute of Ophthalmology at University College London to learn more about Robin’s work.

The eye is fertile ground for developing new therapies. a feature that Professor Robin Ali is taking full advantage of. Not content with a thriving gene therapy programme, he took up the challenge of entering the world of stem cell therapy in 2004 when the MRC was funding researchers to move in from other fields.

Robin’s research focuses on therapies for retinal disorders, mainly those that affect the light-sensitive ‘photoreceptor’ cells of the eye. Many of these are rare, single-gene disorders that cause vision loss over time — and which currently have no treatments.

Lucky for Robin, “the properties of the eye lend it to experimental interventions,” he says. It is fairly straightforward to operate on, and the progress of a therapy — improved retinal sensitivity, for example — can be easily monitored. The eye is also somewhat protected from the body’s immune system, so there is less of an inflammatory response to introduced genes or cells.

The genetic approach

Gene therapy involves using viral vectors to deliver the correct copies of genes into cells that have a defective copy. Viral vectors are viruses which have had their disease-causing genes removed, used by molecular biologists as vehicles to deliver genetic material into cells. Much of Robin’s 18 years in gene therapy research has involved perfecting the vectors that deliver the gene, making sure that they target the right cells, for example, and that the gene is switched on at the right level.

Once the vectors had been developed, it was a question of testing the therapies in mouse models of the human diseases. His team has shown that gene therapy improves vision in around 10 different single-gene disorders in mice. So now it’s time to turn their attention to people.

“There’s little more we can learn by treating another mouse. The most exciting science now is in patients and seeing just how effectively the technology can work in people,” says Robin.

In 2007, Robin and his colleagues conducted the world’s first clinical trial of a gene therapy for retinal disease, treating 12 patients for Leber’s congenital amaurosis, in which children are born with no night vision and gradually lose central vision.

The results showed that gene therapy improved night vision but didn’t affect central vision. The MRC is now funding Robin and his team to improve their viral vector in the hope of being able to sustain central vision too. Alongside this, Robin’s group is applying for regulatory approval to begin clinical trials in other types of retinal degeneration.
He is also interested in gene therapies where the delivered gene codes for a therapeutic molecule, such as molecules that suppress the growth of new blood vessels. These could therefore treat conditions such as age-related macular degeneration, in which blood vessels grow abnormally.

**Transplanting cells**

Gene therapy will be useful for patients who still have remaining retinal cells, but Robin is also developing stem cell therapies to replace cells that have already been lost.

This research focuses on two main areas: perfecting the transplantation of retinal precursor cells into mice — and humans — and developing ways of growing a good supply of these from human embryonic stem cells (hESCs). Robin explains that hESCs are the best source because they don’t need much encouragement to become retinal precursors and have a natural propensity to do so. In contrast, adult cells are restricted and “are difficult to push down a retinal lineage”, he says.

So far, Robin and his colleagues have focused on transplanting rod light-sensitive photoreceptor cells rather than cones, because rods are more abundant in the eye and their precursors are easier to produce when differentiating from stem cells.

But getting better at transplanting cones will be key in humans, says Robin, because it is a small number of cones that mediate visual acuity. With a new MRC programme grant, Robin’s group are now investigating ways to improve cone transplantation in mice.

Robin, along with colleagues at Moorfields Eye Hospital in London, has also recently been involved in the first injection of hESC-derived retinal cells into a patient in Europe. The trial will involve 12 patients with Stargardt disease, a degenerative retinal disease, who will receive hESC-derived retinal pigment epithelium cells — cells which sustain the light-sensing photoreceptors.

The trial is focused on looking at safety rather than whether the transplants improve vision, says Robin. “We’re interested in asking basic questions about safety and delivery, the mechanics of injecting the cells, whether we can visualise them in the eye ... We’re unlikely to see any clinical benefit with patients at this stage of disease.”

But he’s still hopeful that the stem cell therapy will help patients one day. “Every now and then there’s just a sudden discovery that comes out of nowhere that just propels things forwards and that’s what’s exciting. Never say never in this field, it’s full of surprises.”
Brain uses ‘predictive text’ to recognise words

MRC research suggests that the brain recognises spoken words at a lightning speed of 50 milliseconds: twice as fast as previous estimates. Scientists at the MRC Cognition and Brain Sciences Unit (CBSU) led by Dr Lucy MacGregor used a brain scan called magnetoencephalography to measure the speed at which volunteers’ brains distinguished between the word, ‘lake’ and a nonsense word, ‘lape’.

Separately, CBSU colleagues led by Dr Matt Davis showed that a part of the brain called the superior temporal gyrus achieves this incredible processing speed using a ‘predictive text’ style knowledge of familiar words to work out which speech sounds will be heard next.

Matt explained: “Having heard the syllable ‘form…’ rather than trying to guess whether the word is ‘formal’, ‘formidable’ or ‘formula’, the brain predicts which sounds would come next if each of these words were said. By predicting which sounds will be heard, the brain can then respond to incoming speech incredibly quickly – recognising a familiar word a split-second after the critical sounds have been heard.”

The scientists plan to test the speed of speech analysis in patients who have impaired language function following a stroke, and to look at how prediction might help to make sense of speech sounds that are difficult to hear, such as picking out speech from background noise in a crowded room.

Published at www.nature.com/ncomms, February 2012 and www.cell.com/current-biology, March 2012

The worm has turned... to fight cancer

Scientists funded by the MRC and BBSRC at the University of Nottingham have identified a gene in a simple water-dwelling worm that might play an important role in the development of cancer.

Removal of the SMG-1 gene in planarian worms caused their normal cell division to go out of control, leading to lethal, tumour-like growths. The research suggests that SMG-1 may act as a ‘brake’ on growth which, if confirmed in humans, could be exploited to develop new treatments for cancer and other conditions related to ageing.

The researchers think that SMG-1 acts by suppressing a signalling pathway inside cells which is known to drive the development of many human cancers and conditions related to ageing.

Lead scientist Dr Aziz Aboobaker explained: “We’ve discovered that the SMG-1 gene and the mTOR signalling pathway, a well-known regulator of animal growth, act in harmony to exert tight control over growth and regeneration in planarians. Crucially, if this control is removed we see hyperactive cell division and the formation of tumours, which eventually kill the worms. This suggests that SMG-1 is a potential tumour suppressor gene we were previously unaware of.”

The next step will be to look for mutations in SMG-1 in cancer patients and to investigate whether these mutations cause the gene to be faulty and cause the abnormal cell growth seen in cancers.

Published at www.plosgenetics.org, March 2012
Reducing side-effects for prostate cancer patients

Using sound waves to selectively treat individual cancer sites could offer men with prostate cancer a treatment with far fewer side-effects than conventional therapy, an MRC-funded trial has shown.

The trial is the first to use an experimental treatment called high-intensity focused ultrasound (HiFiU) to treat areas of cancer as small as a grain of rice. The researchers first used MRI and mapping biopsies to pinpoint the exact location of the cancers. Then they targeted these areas with HiFiU, which causes tissue to vibrate and heat to around 80 degrees, killing the cancer cells.

Common side effects of conventional treatment – either radiotherapy, or surgery to remove the whole prostate - include urinary incontinence and erectile dysfunction. However, results showed that 12 months after treatment, none of the 41 men in the trial had incontinence problems and just one in 10 suffered from poor erections. Ninety-five per cent of the men were also cancer-free.

Dr Hashim Ahmed, who led the study at University College London Hospitals NHS Foundation Trust and University College London, is encouraged by the results:

“We’re optimistic that men diagnosed with prostate cancer may soon be able to undergo a day case surgical procedure, which can be safely repeated once or twice, to treat their condition with very few side-effects. That could mean a significant improvement in their quality of life.”

The next step will be to carry out a larger trial to see if the treatment is as effective as conventional therapy for keeping prostate cancer at bay in the medium- and long-term.

Published at [www.thelancet.com/journals/lanonc](http://www.thelancet.com/journals/lanonc), April 2012

Re-designing the molecules of life

Scientists at the MRC Laboratory of Molecular Biology have created the first man-made molecules that are capable of storing and replicating genetic information, paving the way for new therapies and diagnostics.

An international team led by Professor Philipp Holliger used sophisticated protein engineering techniques to adapt the enzymes that make and copy DNA in all forms of life, from plants to people. They managed to establish six new genetic systems based on synthetic nucleic acids. These had the same coding molecules (bases) as DNA but the ribose linkages between them (the outer parts of the DNA double helix) were replaced by quite different structures.

The technique could be used to develop nucleic acids, called aptamers, which could be used to diagnose, analyse or treat diseases such as cancer and inflammatory conditions. Aptamer therapies would have an advantage over current drugs because they would not only be able to bind to the target molecule in a very specific way but would also penetrate tissue more deeply because of their small size. They are also more stable than their DNA or RNA counterparts, have lower toxicity, do not cause an immune system reaction, and can be chemically modified to improve their absorption and break-down by the body.

The findings have important implications for our understanding of how life formed on earth, because they show that the storage of genetic information does not have to be limited to RNA and DNA molecules. The scientists suggest that life as we know it may have emerged simply because there was an abundance of the building blocks which make up RNA and DNA around on the early Earth.

Published at [www.sciencemag.org](http://www.sciencemag.org), April 2012
30 years of stellar statistics: farewell to Professor Spiegelhalter

“Stellar” and “possibly the only serious intellectual to ever emerge from North Devon” were among fond and esteemed descriptions of Professor David Spiegelhalter FRS made by his colleagues and peers as he left the MRC Biostatistics Unit in Cambridge (BSU) after three decades.

Over his career David has provided expert evidence for high-profile inquiries, such as those set up to investigate the deaths of 29 babies undergoing heart surgery at the Bristol Royal Infirmary in the late 1980s, and on the general practitioner turned serial killer Dr Harold Shipman. He has also advised the Healthcare Commission on the use of statistical methods in helping to guide hospital inspections; the theme of his most recent paper read before the RSS.

An OBE and Fellow of the Royal Society, David’s statistical expertise has won him numerous awards. His passion for education has led him to work with universities and schools to inspire young people about statistics. As Professor of the Public Understanding of Risk he produced a popular Youtube video, Professor Risk, which has been watched over 70,000 times. The video shows how statistics can be used to face up to life’s major risks, asking questions such as: are bacon sandwiches really that dangerous?

David said: “It has been a great privilege to work for the MRC for such a long time. Over the past 30 years, the MRC has been very supportive of my work and has let me do the research I wanted to do, even if it was not always what I said I would do at the previous five yearly review! I owe my scientific career to the MRC.”

David left in March to work full time as Cambridge University’s Winton Professor for the Public Understanding of Risk, a job he formerly did part-time alongside his work at BSU. His departure marks the end of an era for the unit.

Statisticians love a statistic, and perhaps the most telling one about David is that he is one of only three statisticians since the end of World War II to have been invited to read ten or more papers before the prestigious Royal Statistical Society (RSS). His biostatistics research has covered everything from ways of measuring the complexity of modelling using the concept of Bayesian probability, to work on simplifying quality of life assessments.

At a dinner held in David’s honour at Queens’ College, Cambridge his colleagues, co-authors and guests contributed anecdotes themed around his ‘biostatistical life’ – one for each year he had worked for the MRC.

David’s undergraduate studies and doctoral thesis were supervised by Professor Sir Adrian Smith. Sir Adrian noted that even at a young age, David was “well ahead of the game in seeing the connection between Bayesian learning and Artificial Intelligence.”

For nearly two decades, David has led the development of software for the Bayesian analysis of complex statistical models, WINBUGS, which has enabled the widespread application of Bayesian statistical methods in medicine and beyond. Fittingly, his farewell cake was made in the shape of the WINBUGS logo, and decorated with the appropriate algebraic symbols.
New MRC directors in Dundee and Cambridge

Professor Dario Alessi has been appointed Director of the MRC Protein Phosphorylation Unit (PPU) at the University of Dundee. He succeeds Professor Sir Philip Cohen, who stepped down in April, and was formerly Deputy-Director.

Under Dario’s direction, the unit’s future remit will be expanded to study the role of an emerging form of cell biology called ubiquitylation. Remarking on his appointment, Dario said: “Sir Philip will be a hard act to follow, but I am looking forward to the extraordinary opportunities that lie ahead. This is an exhilarating time in phosphorylation and ubiquitylation research and my main aim will be to position the unit as a focal point for collaboration between life scientists, pharmaceutical companies and clinicians.”

In Cambridge, Italian clinician scientist Dr Massimo Zeviani has been appointed Director of the MRC Mitochondrial Biology Unit (MBU). He will succeed Professor Sir John Walker in December.

Massimo currently directs the Unit of Molecular Neurogenetics at the Carlo Besta National Neurological Institute in Milan. He commented: “My main goal is to merge the wealth of expertise developed at the MBU on mitochondrial biology with mitochondrial medicine, so as to make progress in understanding the mechanisms of mitochondrial dysfunction leading to disease and hopefully develop effective treatments. This is an attractive challenge and an extraordinary opportunity for me.”

Prizes, awards and honours

Dr Helen Fisher has won the British Psychological Society’s Award for Outstanding Doctoral Research Contributions to Psychology 2011 for her PhD on the potential relationship between child abuse and later psychotic illness. The work, undertaken at King’s College London, was co-funded by the MRC and the Economic and Social Research Council.

Professor Sheila Bird of the MRC Biostatistics Unit has been elected to the fellowship of the Royal Society of Edinburgh. The honour is a tribute to Sheila’s many years’ work on study design, statistical reporting standards and survival analyses.

Professor Ian MacLennan, Emeritus Professor of Immunology at the MRC/University of Birmingham Centre for Immune Regulation, has been elected to the fellowship of the Royal Society. Ian has made several landmark contributions to immunology, especially our understanding of antibody production.

A prestigious Dutch neuroscience prize, the $150,000 Dr A H Heineken Prize for Cognitive Science, has been awarded to Professor John Duncan, assistant director of the MRC Cognition and Brain Sciences Unit in Cambridge, for his research into the neurological basis of behaviour and intelligence.

Professor Péter Somogyi, Director of the MRC Anatomical Neuropharmacology Unit in Oxford, has been co-awarded the first ever €1 million Brain Prize by the Grete Lundbeck European Brain Research Foundation, for his outstanding analysis of the brain circuits involved in memory.

Péter shares the prize with former MRC scientist Professor Tamás Freund and Rutgers University’s Professor György Buzsáki.
The MRC Tropical Epidemiology Group (TEG) at the London School of Hygiene and Tropical Medicine has made an important contribution to many discoveries in tropical medicine, including findings on the big three killers – malaria, HIV and tuberculosis. As the group celebrates its 40th birthday, we look at the impact of its pioneering work.

**1972**
Professor Patrick Hamilton is awarded a £12,000 annual budget to set up the TEG to provide expertise in epidemiology and statistical analysis for diseases which devastate the world’s tropical regions. Three years later, the group successfully applies to the MRC for funding: support which will continue for the next four decades.

**1987**
The group pioneers a type of trial design called the ‘stepped wedge’ for a major study with the MRC unit in The Gambia to measure the impact of hepatitis B vaccination (HBV). Findings show that HBV significantly reduces the chance of people passing on the infection, reducing incidence of liver cancer. This paves the way for HBV vaccination programmes to be successfully established across the world.

**1995**
The landmark ‘Mwanza trial’ is carried out in Tanzania, showing that improved management of sexually transmitted diseases at clinics reduces the incidence of HIV infection in the community by 42 per cent.

**1996**
Insecticide-impregnated bed nets are shown to reduce child mortality by 20 per cent in a trial in Northern Ghana. This is one of four trials overseen by TEG for the World Health Organization.
The TEG is involved in a study of Haemophilus influenza type b (Hib) vaccine which shows that it dramatically cuts incidence of meningitis in children in The Gambia and reduces pneumonia by 21 per cent. These studies lead to national introduction of the vaccine and Hib disease is almost eliminated.

2000

A strong association between lack of male circumcision and HIV infection in sub-Saharan Africa is found, following a systematic review by the TEG. This underpins later research confirming that circumcision provides up to 60 per cent protection against HIV.

2005

The MRC TEG Fellowship scheme is launched, providing support for one African statistician per year to take the MSc in Medical Statistics at the LSHTM. Today, fellows who have completed the training are all employed as medical statisticians in Africa or are undertaking further research training.

2006

The group collaborates on research on various drug regimens for seasonal malaria chemoprevention (SMC), which involves giving all people in a community a monthly dose of an effective antimalarial drug during the season of highest malaria risk. This contributes to the World Health Organization’s recent recommendation to SMC for children under five in areas of highly seasonal malaria transmission across the Sahel.

2009

A trial carried out with the MRC Unit in Uganda shows that treating HIV patients at home is cost-effective compared to clinic-based care. Home-based HIV care could enable improved and equitable access to HIV treatment, especially in areas with poor infrastructure.

2010

Negative trial results also play an important role in shaping policy. A trial of the vaginal microbicide, PRO 2000, carried out with the MRC Clinical Trials Unit, the MRC unit in Uganda and others, shows that there is no evidence that it reduces the risk of HIV infection in women. This provides definitive evidence that the product doesn’t work, preventing any further resources being put into this line of attack on HIV.

2012 and beyond

A recent exciting development for the group has been securing a $38m award from the US National Institutes for Health for a new HIV trial in Zambia and South Africa. The PopART trial will test the theory that if a whole community is encouraged to test for HIV, with those infected offered immediate antiretroviral treatment, this may lead to dramatic reductions in HIV incidence, perhaps even eliminating the disease entirely in these areas.

Of the TEG’s future, Dr Helen Weiss, who took on its leadership earlier this year, says: “As funding becomes ever tighter, the emphasis will be on rigorously evaluating both how effective and how cost-effective interventions are, so that limited resources can be allocated as efficiently as possible.

“The impact of non-communicable diseases such as hypertension, diabetes and mental illnesses is increasingly being recognised, especially in growing urban centres in developing countries. These will require innovative approaches to prevention and control and we look forward to tackling these new challenges in the coming decades.”
Matthew Murray, MRC Cancer Cell Unit

Matthew is an MRC Clinical Research Training Fellow in Cambridge, combining his skills as a doctor with research that could improve the diagnosis and follow-up of rare childhood cancers.

Career in brief
• Studied medicine at Cambridge University
• Specialised in paediatric oncology
• Current job: Clinical Research Training Fellow at the MRC Cancer Cell Unit, Cambridge
• Career highlight: recently chosen as Young Investigator of the Year 2012 by the Royal College of Paediatrics and Child Health and the children’s cancer charity SPArKS

I must have been about 12 when I decided I wanted to do paediatrics. I remember seeing programmes on TV about neonatal units and children’s wards and decided that’s what I wanted to do.

In my early teens I went through a period of self-doubt and considered doing plant sciences instead. That way, I thought, if I made any mistakes then the worst thing that would happen would be the demise of a plant! Fortunately I got over those anxieties and went on to study medicine and then specialised in paediatrics.

I’d always wanted to do research but there hadn’t been any opportunities until the end of my clinical training, when I was introduced to Professor Nick Coleman and he invited me to get involved in his cancer research project.

I’m studying the genetic changes that occur in a relatively rare group of cancers called malignant germ cell tumours. In normal development, germ cells go on to become the egg-producing cells of the ovary or sperm-producing cells of the testes. Sometimes, these germ cells become abnormal and/or go astray and end up in the wrong place in the body. Normally these abnormal or ‘lost’ cells self-destruct, but in certain situations they survive and go on to form germ cell tumours of the gonads (ovaries or testes) or other places such as the brain or chest.

Because of this, these are a very diverse group of tumours, affecting both sexes at all ages. Until recently, there didn’t appear to be any common genetic abnormalities shared between them. So we’ve been carrying out profiling of microRNAs - very short pieces of genetic code - in malignant germ cell tumours. This has allowed us to identify common abnormalities for the first time.

At first I was juggling the research with work as a locum consultant and was on-call at evenings and weekends. So getting this three-year MRC fellowship to underpin the research has been absolutely critical to the success of this work.

I’ve been lucky enough to experience some genuinely exciting moments of discovery on this project. One example is when we studied blood samples from patients at the time of germ cell tumour diagnosis and found very high levels of the same microRNAs that were increased in the patient’s tumours. We followed blood levels of these microRNAs during treatment and into clinical remission, and saw them fall to normal. That’s when we knew we’d found the first specific, universal blood-based marker for malignant germ cell tumours that we could investigate more widely for clinical use.

In the future I’m hopeful we’ll be able to offer a universal blood test marker as a safer and more accurate way to diagnose germ cell tumour patients and follow them up during and after treatment. We are also aiming to use tumour biology to identify ‘high risk’ patients in whom we need to maximise cure and ‘low risk’ groups in whom we can minimise long-term damage from the cancer drugs we currently use.

My day-to-day work tends to be a mixture of ‘wet’ lab work – for example, performing tissue culture experiments or using a technique called polymerase chain reaction (PCR) to determine RNA levels – and spending time at the computer carrying out analysis of data, writing up findings and submitting grant applications for further funding.

Essentially my hours are nine until six. But then after I’ve gone home, seen my children and helped put them to bed, I tend to continue with manuscript drafts or work on presentations, often until quite late. So I put in a lot of hours, but I’ve also got a lot out of it.
What I really like about doing laboratory research is that there’s the potential to benefit many people through any findings or breakthroughs that you make. As a clinician, although you make a big difference to individual patients and their families, the scope to do that is more limited.

One of the most rewarding aspects of paediatric oncology is the long-term relationship that you build up with children and their families. Although I spend most of my time on research, I still attend weekly multidisciplinary team meetings at the hospital. That’s the most time-effective way of me keeping up-to-date with the paediatric oncology patients while continuing my own professional development.

I think I’d find it difficult to go back to clinical practice without any involvement in laboratory research. So now that I’ve almost completed my PhD I’m delighted to have secured a position as an Academic Consultant in Paediatric Oncology here in Cambridge that will allow me to split my time between research and clinical work. For me, that’s the perfect job.

As told to Sarah Harrop

A meeting of minds

More than 100 MRC fellows gathered at BMA House in London in May to exchange ideas on topics as diverse as work-life balance, entrepreneurial research ideas and future MRC strategy.

The MRC Fellows’ Symposium is designed to give MRC fellows an insight into the workings of the organisation, an opportunity to meet members of senior management, Council and funding groups, and the chance to mix with peers in both similar and different areas of research.

Read all about the event at www.mrc.ac.uk/Sciencesociety/Events/Reportpreviousevent
LMB awarded £49m for brain research

The world-renowned MRC Laboratory of Molecular Biology (LMB) in Cambridge has been awarded £49m over the next five years to examine the biology of the brain at a molecular level.

A major part of the investment (£29m) is intended to accelerate researchers’ understanding of the basic biological processes that lead to devastating neurodegenerative diseases such as dementia.

The neuroscience funding, a 50 per cent increase on previous years, includes support for cellular neurobiology, one of the LMB’s major initiatives supported through their most recent five-yearly review. This will build on current strengths and look at how neurological processes, such as synaptic activity, affect simple behaviours. Around a quarter of the £49m will focus on mechanisms of neurodegeneration, with much of the remainder providing vital underpinning basic research in cellular neuroscience.

The LMB will receive nearly £170m core funding support from the MRC over the next five years to pursue its overarching mission of understand biological processes at the molecular level, including the challenge to close the gap between structural and cell biology. Separately, an additional £4.5m has been invested in a state-of-the-art Titan Krios electron microscope, the first in the UK, which will allow visualisation of large protein complexes in unprecedented detail.

Simultaneously, the Cell Biology Division at LMB will increase its focus on the processes affecting cellular damage and ageing, and a new Centre for Chemical and Synthetic Biology, headed by Dr Jason Chin, will be established within the LMB. The Centre will focus on the exploitation of novel chemistry to develop new tools to explore biological processes in health and disease, and create new approaches to therapy.

The LMB will move to new £200m facilities in Cambridge in the autumn after 50 years on its current site – a period during which 13 of the institute’s scientists have been awarded Nobel prizes, either singly or as joint winners.

Green light for NIMR to continue the good work

The MRC National Institute for Medical Research (NIMR) in London has been commended for its internationally-competitive research and awarded a further five years’ core funding: a sum of £199.8m.

The MRC’s Council highlighted four key areas of NIMR’s research as being of critical importance to the MRC’s overall strategy: infections and immunity; integrated structural biology of disease; developmental neuroscience; and physiology and metabolism. It recommended that these areas be secured over at least the next ten years with investment in new programmes.

Members noted that the new programmes offered an opportunity to support early career researchers. They commended NIMR’s Director, Professor Jim Smith, on his strong leadership during a period of significant uncertainty for the Institute; research teams currently based at NIMR will move to the new Francis Crick Institute in central London in 2015.

Professor Smith said: “The outcome of the Institute review was very positive. I am delighted that our world-class research and support services have been recognised in this way, and the outcome augurs well for our move to The Crick.”

For the latest information on MRC funding opportunities, visit www.mrc.ac.uk/fundingopportunities
Creating a research legacy from London 2012

As the last of the athletes leave the Olympics Athletes’ Village this summer clutching their medals and savouring their memories of London 2012, researchers part-funded by the MRC will move in to start a new research project.

Dr Chris Owen, of St George’s University of London, is leading research to discover whether physical activity levels will increase among families moving in to new social and affordable housing in the Athletes’ Village in 2013.

The specific provision of this housing all at once rather than in a piecemeal fashion offers scientists a rare opportunity to examine whether, and how, the built environment affects physical activity patterns and body size in adults and children moving into the area.

Low levels of physical activity in the UK population pose a serious threat to our future health, contributing to the rising tide of cardiovascular disease, obesity and diabetes. The need to get both children and adults to move more is now recognised in health policy recommendations, and where people live is thought to have a key impact on health.

Among other factors they will look at the convenience of facilities such as cycle tracks and walkways and how perceptions of the local built environment can influence its use. Residents’ physical activity will be compared with those living outside the village.

Dr Owen explains: “We hope that this ‘natural experiment’ will add to the evidence to underpin policy on whether environmental changes thought to benefit residents of social housing actually do. While the short time scale of the intervention is unique, the findings will be generalisable, informing future design of residential developments that are destined to take place elsewhere.”

The work is one of 19 projects funded under the fourth tranche of the MRC-led National Prevention Research Initiative (NPRI), a joint funding consortium of 16 UK government departments, research councils and major medical charities.

For more information on NPRI visit www.mrc.ac.uk/npri
Meeting global challenges

In times of austerity, should the MRC and other UK funders continue to invest in medical research in developing countries? Peter Piot argues that as well as a moral responsibility, there are vital scientific, economic and political interests at stake.

The heart of the MRC’s mission is to improve human health through world-class medical research. That mission doesn’t stop at Dover; diseases don’t respect national borders. The history of illness and infection is the history of human development, globalisation and migration. In profound ways - evolutionary, immunological and cultural - we are shaped by our health and illnesses.

At medical school in the early 1970s, my tutors advised me against specialising in infectious disease because, according to them, all the major problems had been solved. But barely a year into my first job in a microbiology lab in Antwerp, we received a battered flask from Zaire containing blood samples from the victims of a lethal outbreak of a mysterious haemorrhagic fever - and succeeded in isolating the Ebola virus. A few years later, the AIDS epidemic forced me to confront the extreme complexities of health and disease, and of the politics and bureaucracies of international cooperation.

Both epidemics show the enormous potential and real limitations of science to solve today’s health problems. Researchers rapidly elucidated the workings of the HIV retrovirus, and developed life-saving drugs. But it required a massive international effort to slow the spread of AIDS and make treatment available to those who most need it - and we still haven’t developed a vaccine.

The world is becoming a ‘global village’, and it is crucial for the health of Britain’s increasingly diverse and widely travelling population that our health services have access to the most up-to-date research on diseases worldwide. Recently this has been exemplified by headlines on malaria, non-communicable diseases such as cancer and diabetes, and preparedness for the London 2012 Olympics. In this context, a global outlook and involvement is vital to sustain the excellence and relevance of the UK’s biomedical research base.

The UK is a world leader in such research, and the MRC is an important and influential funder and driver of research worldwide. The MRC units in The Gambia and Uganda have led efforts to understand and combat diseases from sickle-cell anaemia to HIV. This work has been sustained over many decades, and makes a vital difference on the ground – see page 16 for some examples.

Such activity has become multinational in scope and multi-agency in character – for example the MRC is a founding partner of the Global Alliance for Chronic Diseases. Such international research collaborations bring real benefits, both for the UK and for developing countries. They also build capacity and develop skills: for example the MRC/DfID African Research Leader scheme helps strengthen research leadership across sub-Saharan Africa.

I would also argue that a healthier world is in our economic and political interests. The MRC’s international programmes and units are very cost-effective, for example the current MRC/DfID agreement is worth £45m over five years. This sum is tiny in the context of health spending, but vital in funding key projects and sustaining the UK’s position in the global health community. This also brings great - although sometimes intangible - returns in the form of goodwill and influence: ‘health diplomacy’ can be a powerful driver of international cooperation.

But there is a deeper economic and moral argument, which derives as much from religious traditions and modern science as from Adam Smith. In a globalised world, the wellbeing of people and nations is fundamentally interdependent. When war and pestilence rule, everyone suffers: something I have experienced working in countries ruled by dictators and riven with conflict. In contrast, healthy and prosperous populations are not only happier, but make much better trading partners. I think the Government understands this well, and has made a commitment to protecting international development budgets despite the economic climate.

As scientists and clinicians, we feel a strong moral responsibility to help people, and today our responsibility is global. Investment in research is vital to saving lives, alleviating suffering and contributing to peace and prosperity. But we can’t assume everyone thinks the same, or that anything will happen without communicating the value of global health research and informed advocacy.

My experience at UNAIDS taught me that it takes a lot of energy and dedication to build coalitions that actually get things done on the scale that is needed. At a time of fiscal constraint, it is of course important to invest our funds and effort as wisely as possible. But it is all the more important that we work together to communicate our vision and the value of our work to mobilise the resources required to sustain our achievements so far and meet the serious challenges ahead.

These are global challenges, and the UK has a significant part to play in meeting them. Health is a fundamental human right for all. We must recognise this and sustain our commitment to research beyond our national boundaries.
Peter Piot is Director of the London School of Hygiene & Tropical Medicine and Professor of Global Health, and currently chairs the MRC Global Health Group. He was formerly Under Secretary General of the United Nations and founding Executive Director of UNAIDS.