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Scientists tame the tallest mountain

Sir Edmund Hillary, who with Sherpa Tenzing Norgay was the first person to reach the top of the world’s tallest mountain, died in January aged 88. MRC research contributed to the success of the 1953 Everest expedition – accompanying Sir Edmund was MRC scientist Dr Griffith Pugh. He studied ways to combat the swollen brain, nausea, fatigue and insomnia that can afflict adventurers wanting to reach the world’s highest and most inhospitable places. Network charts the work that led to this towering achievement.

Dr Griffith Pugh was a climber as well as a scientist. It was his passion for the mountains that got him the distinguished job of working out some of the requirements for reaching the summit. Working at the Human Physiology Division at the National Institute for Medical Research (NIMR) in London, Griffith Pugh was commissioned at very short notice ahead of the expedition to study nutrition, acclimatisation, equipment and the effects of supplementary oxygen on climbers at high altitudes. The trip itself was funded by the Royal Society. Griffith Pugh studied the climbers’ body weight, changes in the acidity of their urine and nutritional problems at high altitude, and took samples of respiratory gases and blood that were sent back for analysis in England.
After Everest, Griffith Pugh remained in MRC laboratories for the rest of his career. He worked on the physiology of survival in the cold, heart and lung responses to high altitude, cross-Channel swimming and Olympic athletes’ performance. He died in 1994.

Learning from experience
Griffith Pugh helped bring professional science to endurance sport. In the days when footballers prepared for a cup final with a shot of whisky and a cigarette, his research was pioneering. The year before, and in preparation for, the famous Everest conquest, Griffith Pugh climbed Cho Oyu, the sixth highest mountain in the world. The expedition didn’t even reach four-fifths of Everest’s height – which is nearly 9 km high – and the party suffered from insufficient acclimatisation, diarrhoea and respiratory infections.

Following Griffith Pugh’s report from Cho Oyu – of which there are only eight copies in existence – the MRC formed a High Altitude Committee. It gave advice to the Joint Himalayan Committee – a group formed in 1947 with the aim of reaching the top of the mountain. Griffith Pugh worked on ways to minimise failure. He devised a programme of physiological experiments and combined the information from previous Everest expedition investigations with results from the few months of work before the team left for Everest in 1953.

A breath of fresh air
Griffith Pugh investigated the way oxygen was expended and the amount of oxygen used by members of the expedition and calculated quantities of oxygen in cylinders that would be needed.

On Cho Oyu the previous year, the researchers had discovered that the men were able to sleep comfortably all night wearing oxygen masks, which reduced fatigue during daytime work.

The researchers advised the climbers on their breathing equipment, and scientists at the MRC’s Electro-Medical Research Unit in Buckinghamshire made oxygen sets for trial on the trip. The sets that were finally used increased climbing rate and enhanced endurance and enjoyment, enabling climbers to walk for a longer time.

Griffith Pugh studied the effects of acclimatisation and identified physiological changes such as more rapid breathing and modification of the blood’s acidity by the kidneys. In further experiments he examined the effect of acclimatisation on brain function and heart rate, and on muscular exercise and climbing ability.
An army marches on its stomach
In the past, Everest climbers had relied upon local food and bulk stores from England. But with this diet there were problems of decreased appetite, dehydration, diarrhoea, cravings for particular foods and enhanced sugar need. There was also extensive weight loss because of loss of appetite. Dr Pugh was asked to plan rations, and included certain ‘luxuries’ to satisfy predicted cravings. The MRC also took advice from Dr Philip D’Arcy-Hart – a pioneer in tuberculosis treatment at NIMR – about the potential of an anti-tuberculosis drug, isoniazid, which was believed to have a side effect of boosting appetite. The research resulted in fluid and salt requirements being well met and calorie intake being much higher than in the 1952 expedition.

Griffith Pugh also worked on dehydration problems and provided advice on clothing for Everest. He recommended special light and warm high altitude boots and that tents and windproof clothing be made from a particular type of fabric and sleeping bags be specially designed.

Out in the cold
The adventures didn’t stop there for Griffith Pugh. He joined Sir Edmund again in 1957 in Antarctica, and studied the effects of cold and carbon monoxide poisoning from burning fuel in huts. On another trip, they returned to the Himalayas for nine months and studied the long-term effects of altitude. As a subject in his own experiments, Griffith Pugh rowed the English Channel to find out how swimmers avoided hypothermia. And leading up the Mexico City Olympics in 1968, he researched the effect of altitude on athletic performance – finding that although altitude increased times for long-distance events, it enhanced the ability to sprint.

Scientists tame the tallest mountains >> CONTINUED

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Update from the MRC Chief Executive

In the previous article you’ll have read about some of the
exciting changes being made
to the way health research is
managed in the UK. To make
sure the MRC has the agility to take
these plans forward, we’ve also made
some changes to our own structures
for making decisions about funding
and strategic direction.

Restructuring of the MRC research boards has begun
and a new executive role is planned for board chairs.
The Health Services and Public Health Research Board
is processing its last applications and plans are in place
for redistributing board portfolios. We are also working
to strengthen public health research across all boards, to
ensure it is firmly embedded across our entire portfolio.

Plans for the new Strategy Board and overview groups
are continuing apace. The Strategy Board is already
up-and-running and held its first meeting at the end of
January. The board is developing the overall strategic
plans for the MRC, to ensure that we can respond to the
demands of the current and future research environment.
It will also advise on budgets for the research boards and
make direct awards out of a new strategic fund.

We are creating four overview groups to oversee
global health, population sciences, translational research
and training and careers. Over the next couple of
months we’ll finalise the precise remit of these groups
and appoint chairs.

All of these changes will strengthen our decision-
making. They will help us to work more effectively with
the National Institute for Health Research and other
partners. This, in turn, will ensure we maintain funding
for the highest quality research, from fundamental
science right through to population and clinical studies.

As we work on the finer details of these plans and put
all the new structures in place, we’ll keep you updated
as often as we can. Keep an eye on the MRC website
and look out for the May/June issue of Network.

Sir Leszek Borysiewicz

of research translation,” explains the MRC’s Chief
Executive Sir Leszek Borysiewicz.

He’s pleased with the developing relationship:
“Together under OSCHR, we’ve looked at the
barriers to progressing research so that it’s turned
into benefits for people more quickly.” Part of this
is by nurturing partnerships between clinicians,
basic scientists and industry.

Another central task is to ensure a more
strategically coherent approach to research
which makes it easier for scientists to understand
research priorities and therefore secure funding
for translation. Sir Leszek explains: “This will lead
to new ways to diagnose illness, develop new
treatments, better devices, the best prevention
strategies – and crucially ensure that people see
these benefits as quickly as possible.” The single
strategy wants to see research of the highest
quality carried out by the best scientists using
the best facilities.

Sir David Cooksey’s review commended the
efforts of Professor Davies and NIHR (established
in April 2006) to foster a culture of research in
the NHS through the strategy Best Research for
Best Health. And she is upbeat about progress
so far: “We started almost two years ago a
three-year transition, taking the money that was
historically allocated to hospitals (yet did not bear
any relationship to research outputs, relevance
quality or any markers like that) to reinvest it
transparently in more research, but peer reviewed,
and in starting to build research networks”
(see box below).

CONTINUED >> next page

The NIHR clinical research networks were set
up to ensure patients and clinicians could reap
benefits from taking part in research and to
support high quality clinical trials and other well
designed evaluative studies. They cover areas
including cancer, dementias and neurodegenerative
diseases, diabetes, medicines for children, mental
health and stroke. “They are already boosting the
numbers taking part in clinical trials, improving
their speed, quality and coordination, and
strengthening NHS links with industry,” according
to a progress report from NIHR, Transforming
Health Research, published in January.

Sir Leszek Borysiewicz
The MRC and NIHR want to avoid unnecessary upheaval for researchers. Each organisation will take lead roles for areas of research. In some areas the lead will administer funding for both organisations while in others the lead role will cover strategy and coordination only. In clinical trials, which both organisations have historically supported, NIHR has been given responsibility. Funding will therefore, in future, be managed by NIHR on behalf of the MRC. In the same way, the MRC is now the lead organisation for methodology and NIHR’s investment in methodology research will therefore be managed by the MRC on behalf of NIHR.

AREAS OF JOINT WORKING:

**Discovery and exploratory medicine**
The MRC has been awarded extra funding to expand the discovery and translation of fundamental laboratory and clinical research and early clinical studies of potential new interventions.

**Public health research**
NIHR will take responsibility for strategic coordination of research into obesity; and infection. The MRC will coordinate ageing and lifelong health; and addiction and mental health.

**Clinical trials and evaluation**
NIHR will fund and manage programmes for large-scale clinical trials and ways to evaluate interventions. The MRC will continue to support large clinical trials through the Efficacy and Mechanisms Evaluation programme, which will be managed by NIHR on the MRC’s behalf.

**Global health**
The MRC will lead on global health research and will continue to support trials in global health. Such trials will be funded by the MRC and managed by NIHR on its behalf.

**Research methodology**
To speed the translation of research into better health and patient benefit, a methodology research programme, led by the MRC, will look at better ways of doing research.

**Human capital**
Recruiting, training, retaining and developing a world class health research workforce requires a coordinated strategic approach, which NIHR will lead on.

More details on funding can be found at [www.mrc.ac.uk/opportunities](http://www.mrc.ac.uk/opportunities) and [www.nihr.ac.uk](http://www.nihr.ac.uk).

Over the past few months the MRC and NIHR have been developing a plan for health research coordination, as Professor Davies describes: “I think we’ve worked very effectively together to come through to a shared strategic plan which accommodates both of our strategies – signed off under different governance arrangements – and yet helps us to work across the previous divides.” The areas include public health, human capital, global health, methodology and e-health (see box).

Sir Leszek is equally confident: “In the future, the MRC will be responsible for delivering fundamental research while NIHR will focus on applied research. But we’ll both have shared responsibility for translating research into patient benefit – and this will be overseen by the Translational Medicine Board to ensure we’re delivering. But we want to make sure that scientists always have a clear idea of where to go for funding.”

The strategic plan reflects the Cooksey view that there should be a much clearer allocation of responsibilities between the MRC and NIHR. Each organisation will look to its own research strengths as Sir Leszek explains: “What we’ve always made clear is that fundamental research in the lab and clinic coupled with NIHR’s expanded support for applied research will lead to innovation and improved health. OSCHR, and the structures it created, such as the Translational Medicine Board, are helping us to achieve that vision.”

You can hear a full interview with Professor Sally Davies at [www.mrc.ac.uk/NewsViewsAndEvents/podcasts](http://www.mrc.ac.uk/NewsViewsAndEvents/podcasts).
Molecular biology training in East Africa

The Infection and Immunity Division at UCL in collaboration with Kilimanjaro Christian Medical Centre, has been awarded funding to run a short course in molecular biology for scientists in East Africa. The course will help to increase the numbers of scientists and clinicians in biomedical research, an important priority in Africa.

The two-year programme, jointly funded by the Wellcome Trust, the MRC and the British Council, together with commercial support from Applied Biosystems and Corbett Research, will train staff in molecular tools for respiratory microbiology for a number of new and ongoing projects across East Africa.

Dr Tim McHugh of UCL, who is running the programme, said: “We first developed this course in 1997 for colleagues at the Kilimanjaro Christian Medical Centre. It provides an introduction or refresher to scientists and clinicians who, by virtue of their age or career path, have missed out on recent developments in the use of molecular tools in diagnosis and epidemiology of infections.”

New awards to boost vaccines research

The MRC is investing £3.5 million in six new projects which have the potential to prevent diseases ranging from flu to malaria to cervical cancer.

A review of the MRC’s vaccine work last year showed the organisation was very good at research into how vaccines work in cells and at testing them in large groups of people. But the review found that more work needed to be done to fill gaps in between – turning promising discoveries into clinical products and the first tests in humans. Chaired by Professor Felicity Cutts of the London School of Hygiene and Tropical Medicine and then at the World Health Organization, the review panel recommended that the MRC put out a rapid call for proposals in translational vaccine research.

Professor Adrian Hill of Oxford University has been awarded a grant for the development of a malaria vaccine. A successful vaccine could protect many of the more than two billion people who are exposed to this deadly parasite every year. At the National Institute for Biological Standards and Control, Dr Simon Beddows will study immune responses to vaccines against human papilloma virus, which causes around two-thirds of cervical cancer. This work will shed light on the best use of these vaccines and the design of future ones.

Professor Peter Beverley of Oxford University is working on a test to predict the effectiveness of various new TB-booster vaccines – this will help decide which should go on to clinical trials. Dr Tim Brooks of the Health Protection Agency is working to improve animal models of flu to make testing vaccines and drugs simpler and safer.

Meanwhile Dr Katie Flanagan at the MRC Laboratories in The Gambia has been awarded a grant to use biomarkers – biological indicators of health or disease – to investigate how common vaccines interact with each other and what causes their side effects. This is especially important given the role of immunisation in protecting children from a wide range of killer infections. And finally, Dr Caroline Trotter of the University of Bristol will lead a study to improve surveillance of the effectiveness of meningococcal type A vaccine in parts of Africa and so maximise its impact.
Showcase pilots dragon’s den
The MRC and MRC Technology’s quarterly showcases are helping to develop the next generation of healthcare products by showing off MRC science to industry and introducing researchers to potential industry partners. Since the first neurosciences event in December 2006, showcases have been held for each MRC research board. And a £3 million funding scheme has been set up to encourage joint research, with the first applications funded last year and more projects in the pipeline.

The second neurosciences showcase was held on 26 and 27 February, featuring topics like neuroimaging, disease targets and brain banking. It tried a new approach, with a ‘dragon’s den’ style session that allowed six MRC scientists to pitch their ideas directly to a panel of industry representatives. Each scientist gave a five-minute presentation, which was followed by five minutes of questions from the industry ‘dragons’. The session was designed to answer previous criticisms that scientists at the showcases didn’t always have an opportunity to talk directly to the industry representatives, and to make the scientists think about how to sell their ideas.

Astrid Limb, of the UCL Institute of Ophthalmology, was judged the scientist who gave the best pitch. She said: “I viewed the session as an opportunity to show the industry representatives how our recently discovered ‘Müller stem cells’ could be applied to the design of human cell therapies to restore vision. Development of these therapies requires extensive resources and infrastructure, and so I thought this would be a chance to seek support from industrial partners to help us develop this technology.”

Innovative medicines initiative to launch in April
Plans for the Innovative Medicines Initiative (IMI), a new partnership between the European Commission and the European Federation of Pharmaceutical Industries, are well underway, with the scheme due to launch in April.

The initiative presents a unique opportunity for European public and private sector research organisations to work together. Funded projects will aim to improve the mechanisms for bringing new medicines to market by addressing safety and effectiveness issues as well as advancing training and knowledge management. The European Commission and European pharmaceutical companies will each award €1 billion of research funding to academic institutions, small and medium-sized businesses, patient groups, regulators and not-for-profit organisations during the 10-year life of the scheme. The first IMI call for proposals in April will seek expressions of interest by July this year, with funded projects due to begin in 2009.

The MRC is working to promote the programme to UK researchers. It has £50,000 available to assist UK participants with costs such as travel and accommodation while they prepare expressions of interest. To find out more, visit www.mrc.ac.uk/applyingforagrant/internationalopportunities.

MRC and GSK to identify new therapeutic targets
The MRC and GlaxoSmithKline (GSK) have announced a jointly funded programme to identify and validate genes associated with common human diseases. A key aim of the programme will be to translate these observations into new drug targets and biomarkers (biological indicators) of disease.

Each organisation will invest £1 million in the programme over the next three years, which will bring together academic and industrial expertise and resources and enable sharing of large databases and sample collections.

To mark the creation of the partnership, two major awards have already been announced. The first is to be led by Professor Peter McGuffin at the MRC Social, Genetic and Developmental Psychiatry Centre in London. It will support research into depression where the genetic basis is complicated and the underlying mechanisms not well understood. And led by Professor Nick Wareham at the MRC Epidemiology Unit in Cambridge, the second project will study large population-based cohorts to identify new gene variants associated with obesity and related metabolic disorders.
New centres of excellence to address public health

The MRC has contributed to a £20 million project to set up five centres of excellence in public health.

The centres, based in Newcastle, Cardiff, Belfast, Cambridge and Nottingham, aim to strengthen research into complex issues like obesity, smoking and health inequality. Each centre will receive up to £5 million over the next five years to create new academic posts and develop training and career development programmes. They will bring together leading scientific experts from a range of disciplines with healthcare professionals and policy makers to tackle issues which are likely to have a significant impact on the health of the nation. The initiative is led by the UK Clinical Research Collaboration, with support from several charities, research councils and government funders.

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<tr>
<th>CENTRE</th>
<th>DIRECTOR</th>
<th>LOCATION</th>
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<tr>
<td>Diet and Physical Activity Public Health Research Centre</td>
<td>Professor Nick Wareham</td>
<td>University of Cambridge</td>
<td>University of East Anglia, MRC Social and Public Health Sciences Unit (Glasgow), MRC Biostatistics Unit, Epidemiology Unit, Dunn Human Nutrition Unit and Collaborative Centre for Human Nutrition Research (all Cambridge)</td>
</tr>
<tr>
<td>Centre for Translational Research in Public Health</td>
<td>Professor Martin White</td>
<td>Newcastle University</td>
<td>Durham University, Northumbria University, Sunderland University, Teesside University</td>
</tr>
<tr>
<td>Centre for the Development and Evaluation of Complex Interventions for Public Health Improvement</td>
<td>Professor Laurence Moore</td>
<td>Cardiff University</td>
<td>Swansea University, Bristol University</td>
</tr>
<tr>
<td>UKCRC Northern Ireland Centre of Excellence for Public Health Research</td>
<td>Professor Frank Kee</td>
<td>Queens University Belfast</td>
<td>Institute of Public Health in Ireland</td>
</tr>
<tr>
<td>The UK Centre for Tobacco Control Studies</td>
<td>Professor John Britton</td>
<td>University of Nottingham</td>
<td>A strategic partnership between seven of the leading tobacco control and policy research groups in the UK: Nottingham; Bath; Edinburgh; Birmingham; Stirling; Queen Mary, University of London; and UCL (University College London)</td>
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Defeating diabetes

Research published in January suggested that most people with diabetes would benefit from taking statins, even if they don’t yet have symptoms of heart disease or high cholesterol levels. Jointly funded by the MRC, the British Heart Foundation and the National Heart Foundation in Australia, the research is just one of a myriad of studies related to diabetes that’s seen in the news all the time.

Diabetes and, in particular, type 2 diabetes which is mostly caused by obesity, is big news. According to the charity Diabetes UK, one in 20 people in this country will soon have the disease, which costs the NHS £13.7 million every day. This is why MRC scientists are carrying out research aimed at tackling it from several different angles.

Molecular and behavioural insights

One route is to study the molecular mechanisms that lead from obesity to diabetes. By genetically manipulating mice, Dr Antonio Vidal-Puig, an MRC researcher at the University of Cambridge, has found a mechanism in fat cells that delays the onset of obesity-associated diabetes.
A genetic component

Researchers studying families, adopted people and adopted twins have confirmed that heritable factors are likely to be responsible for a significant proportion of the differences between people in their body mass index. The genetic mutations found so far all affect hunger and involve appetite control in the brain rather than the speed that the body burns up food.

A search for genes linked to type 2 diabetes among nearly 40,000 people revealed a gene called FTO. This gene is associated with early onset and severe obesity. The 16 per cent of adults who had two copies of this gene weighed about three kilograms more and had a substantially increased risk of obesity compared with those without the gene. The FTO gene’s association with obesity was confirmed by MRC researcher Professor Philippe Froguel at Imperial College London.

Exploring dietary habits

At MRC Human Nutrition Research in Cambridge, Dr Susan Jebb leads a team studying the specific dietary factors which increase the risk of overeating. Their research has shown that humans have a weak innate ability to recognise foods with a high energy density and to reduce the bulk of food eaten to maintain energy balance. For example, fast food generally has a high energy density, and people tend to consume similar volumes of this with little reference to calorie content. The team showed that an energy-dense, low fibre, high fat dietary pattern at five and seven years increases fatness in later childhood. They are continuing to explore the impact of changes in dietary habits on the risk of obesity and related metabolic diseases.

A LONG HISTORY OF OBESITY RESEARCH

Many scientists believe the obesity epidemic in Western society was triggered at the end of the Second World War, when technology began to take the place of physical effort and industrial farming led to cheap and processed foods. As the decades passed, eating became cheaper, quicker and more convenient.

MRC scientists have been investigating obesity for more than two decades. They have studied and clarified the details of energy balance, and identified the social, environmental, genetic and parental factors that influence it. They have also developed ideas for treatments and evaluated their impact.

In the 1980s, people did not understand what caused weight gain. Professor Andrew Prentice, at the MRC Dunn Nutrition Unit in Cambridge, worked with Dr Andy Coward to develop a way to measure how much energy a person expends. The ‘doubly-labelled water method’ uses a harmless tracer that tracks the amount of carbon dioxide produced by the body as a by-product of energy generation. They showed that it is the simple imbalance between energy into the body (through the food choices we make) and energy out (mainly through physical activity) which is the cause. Their research showed that, despite belief to the contrary, obese people do not have a slower metabolism or burn energy any less quickly than thin people.

Subsequent work by the same team brought attention to the importance of low levels of physical activity, based on the rise in second car ownership, the increase in labour-saving devices, more hours of TV watched and the reduced numbers of people employed in manufacturing and farming.

The question of whether the body has any control over appetite has been debated by scientists for many years. In 1962, Dr James Neel proposed the ‘Thrifty Gene Hypothesis’, which suggests that humans evolved genes for efficient food collection and fat deposition to survive periods of famine and, now that food is continuously available, these genes are disadvantageous because they make us obese in preparation for a famine that never comes.
Dr Tim Chico spends three days in his lab and two days in the clinic. In his lab, he studies the blood vessels of zebrafish and watches blood cells underneath transparent skin, trying to understand what affects their flow and testing drugs that change this. In the clinic he treats patients with atherosclerosis – a condition arising from blocked blood vessels and altered blood flow. Blocked vessels are the cause of most heart attacks and strokes.

Tim is not the only scientist at the Centre for Developmental and Biomedical Genetics (CDBG) in Sheffield who swings between the lab and the clinic. The centre houses a mixture of clinicians and basic scientists, all keen to collaborate and learn from each other. Turning discoveries about how the body works into new ways to treat and prevent disease is viewed as an essential part of the process. This is a fertile environment – as Professor Philip Ingham, Director of the centre (pictured), explained: “The exciting thing is the opportunity for clinician scientists to work side by side with developmental geneticists – these close interactions are helping us establish novel disease models which, in turn, have great potential for the discovery of new therapeutic agents.”

**Early insights**

The centre has been dynamic from its inception. Six years ago, the MRC received an application for a centre development grant from a small group of basic research scientists at the University of Sheffield, led by Philip. But this was a group with a difference. Fuelled by Philip’s vision and leadership, the researchers were hosting clinical researchers in their labs and had set up joint PhD studentships and collaborations between scientists working on all stages of the translational research spectrum.
Now, the centre boasts an annual income of more than £2 million and has grown its number of principal investigators to 24. Constant communication between its staff is key. “We enjoy having the clinicians around. And they like being able to understand model systems and how organ systems and organisms function normally,” said Professor Marysia Placzek, a basic scientist and Deputy Director of the centre.

Model centre

Scientists at the CDBG use animal models, such as zebrafish – a tropical fish from the minnow family – the fruit fly Drosophila and chicks to study normal and aberrant cellular mechanisms. These help to identify genes that underlie human disease – neurodegenerative, cardiovascular and musculoskeletal disease, as well as cancer – and can be used in drug discovery.

“Developmental genetic analysis of model organisms has revealed much about the genes that underlie our own development as well as the diseases that afflict us,” said Philip Ingham. His own landmark discoveries include the characterisation of a biological signal that acts as a key regulator of animal development and also underlies a number of human cancers. A major focus of Philip’s current research is understanding how this signal controls growth in the developing embryo, which may yield new leads for tumour therapies.

The scientists at the CBDG appreciate the importance of basic research, but are also very aware of what their work might lead to. Marysia Placzek’s lab, for example, uses chick embryos to study a part of the brain called the hypothalamus, which is thought in humans to be involved in regulating and maintaining normal functions, including behaviour.

CONTINUED >> next page
Dr Vincent Cunliffe, one of the founding members of the centre, recruited from the biotechnology sector by Philip Ingham, researches genes associated with neurological disorders, such as Hereditary Spastic Paraplegia – an inherited disorder characterised by progressive weakness and stiffness of the legs – and Huntington’s disease. He looks at the zebrafish’s equivalent of the human genes that are thought to cause these conditions in order to unravel the underlying biology. He also examines the regulation of genes associated with cancer in the fish, and works with neurologists who have found the equivalent genes in humans that are responsible for prostate cancer.

In the bones
Another basic scientist, Dr Henry Roehl, investigates bone and cartilage conditions. This includes a cellular mechanism in zebrafish that is similar to a mechanism responsible for skeletal defects in humans. For example, he examines bone cells that cannot stack properly, which causes a human condition called Hereditary Multiple Exostoses, which affects one in 50,000 of the population and results in a short stature and tumours in cartilage. Henry hosts a clinician in his lab who is working on tooth development and runs a repository of bone samples in Leiden, the Netherlands.

Zebrafish are also the model for work in Dr Freek van Eeden’s lab, who is interested in Von Hippel-Lindau, a disease that involves the abnormal growth of blood vessels in some parts of the body, and affects one in 36,000 people. There is a mutation of a gene in zebrafish that is equivalent to the human version.

From pisces to person
Work on fish is directly relevant to consultant clinicians who see patients in the hospital. Professor Moira Whyte, the clinical co-Director of the centre, and Dr Steve Renshaw study inflammatory diseases, which are widespread and life-threatening with few available treatments. Steve explained: “The zebrafish has the same building blocks of the immune system as humans.”

These mechanisms can be manipulated genetically or with drugs in the fish, with the aim of eventually designing therapeutic drugs to treat the human conditions. In the clinic, Steve and Moira see patients with chronic obstructive pulmonary disease, asthma and other lung diseases, and their observations feed back into ideas for research that they carry out in the lab.

Similarly, Tim Chico’s observations in people give him ideas for his zebrafish work. Studies from his patients have highlighted the important role of inflammation in atherosclerosis and heart attacks. This has led the team to start looking at the interplay between inflammatory cells and the blood vessels in zebrafish to try to understand why inflammatory cells may be the basis for arterial disease.

A flying success
The fruit fly, also known as Drosophila, is another model used at the centre. Dr David Strutt focuses on fly eyes and their structure. “We are trying to understand what the genes do in Drosophila.”

Dr Alex Whitworth looks at the molecular mechanisms of Parkinson’s Disease and other neurological disorders.
MouseBook

MouseBook is a new database that will help MRC scientists to find information on mouse models generated at the MRC’s units in Harwell.

Mouse models are used to understand the genetic basis of disease and for the development of new drugs and other therapies. Scientists at Harwell carry out research across a wide range of human health areas, including congenital heart disease, neuromuscular disorders, diabetes, deafness, osteoporosis and osteoarthritis. Conceived and developed by staff at the Mammalian Genetics Unit (MGU) and Mary Lyon Centre, Mousebook will help to share the wealth of primary data generated at Harwell with data about individual mouse genes, whole genomes and physical characteristics from a number of other databases.

Professor Steve Brown, Director of the MGU, said: “MouseBook is a great step forward in opening up our scientific data and services to the wider research community. Harwell’s mission is to deliver to academia and industry the tools for systematic characterisation of mouse models of human disease. These models help us to understand the molecular causes of disease and provide pre-clinical models to foster translational research and the development of new ways to treat disease. MouseBook is an important part of this endeavour.”

To access Mousebook and to find out more about the data sources it will link to, visit www.mousebook.org.
Professor Brian Worthington, 1938–2007
A leader in British radiology who made significant contributions to magnetic resonance research, Professor Brian Worthington died in December aged 69.

Brian Stewart Worthington qualified in medicine in 1963 in London and completed a radiology residency at London Hospital, obtaining a Fellowship of the Royal College of Radiologists in 1969. He then moved to Nottingham where he was appointed to a newly created post in neuroradiology. Professor Worthington served nearly two decades as professor and head of the Department of Academic Radiology at the Queen's Medical Centre at Nottingham University, and was professor emeritus since 1998. In addition to his early pioneering work with magnetic resonance, Dr Worthington later contributed greatly to defining the role of ultra-high speed echoplanar imaging in clinical practice.

With more than 400 scientific and clinical papers to his name, Professor Worthington served on the editorial boards for several journals and was a fellow of the International Society for Magnetic Resonance in Medicine and an honorary member of the Radiological Society of North America. He won several awards and accolades throughout his career and in 1998 was made a fellow of the Royal Society, a rare honour for a radiologist. Among his immense contributions to UK science, Professor Worthington served on the MRC’s Molecular and Cellular Medicine Board between 1996 and 2000.

Professor Bryan Jennett, 1926–2008
Professor William Bryan Jennett died in January. He was an influential neurosurgeon who transformed the care of people with head injuries. His main interests were in the mechanisms of acute brain damage and the long-term consequences of head injury.

Bryan Jennet finished top of his class at Liverpool Medical School and went on to further training in Cardiff, lecturing in Manchester and two years as a Rockefeller Fellow at UCLA. He then returned to the UK and took up a post in Glasgow combining clinical work with research. He jointly led an MRC cerebral circulation research group, which brought about an international brain injury databank that is still in use today. In 1972 Professor Jennett coined the term ‘vegetative state’ and later created the legendary Glasgow Coma Scale and Glasgow Outcome Scale, which are used to describe the depth of a coma and assess the likely outcome of a head injury. Among Professor Jennett’s many honours, he served as president of both clinical neurosciences at the Royal Society of Medicine and of Headway, the national head injury patients’ group. He received a CBE in 1992 and, in 2007, was the first recipient of the Medal of the Society of British Neurological Surgeons.

Professor Norman Bleehen, 1930–2008
Professor Norman Bleehen, who directed the MRC Unit of Clinical Oncology and Radiotherapeutics for two decades and served on the MRC Cell Board and numerous MRC committees and working parties, died in February.

Norman Montague Bleehen studied at Middlesex Hospital Medical School and Oxford and became an MRC research student in 1951. Following house appointments and time as a medical specialist in the army in Germany, he returned to take up an academic position at Oxford, before completing specialist training in oncology. From 1969 to 1975 Professor Bleehen was a consultant advisor to the Chief Medical Officer and in 1975 he became a Cancer Research Campaign Professor of Clinical Oncology and director of the, now-closed, MRC Unit of Clinical Oncology and Radiotherapeutics. He served on boards and councils for the Imperial Cancer Research Fund, the British Institute of Radiology and the International Society of Radiation Oncology, edited several scientific journals and received accolades including a CBE in 1994. He was a fellow of St John’s College, Cambridge, since 1976.
Weighing the impact of MRC research

The MRC is strengthening its evaluation of research, following the approval in December of an evaluation strategy.

The research councils are expected to demonstrate that they provide support for research in the best way to create an excellent science base, and in ways that benefit health, quality of life and the economy.

In December, the MRC’s Council approved an evaluation strategy which outlines how the organisation will strengthen the evaluation of research funding and policy decisions as well as the impact of MRC research. This work involves collaboration across the MRC, and with external partners such as the National Institute for Health Research and Research Councils UK (RCUK).

Feedback from researchers on their achievements has always been crucial to the MRC in making the case for continued investment in medical research. The evaluation programme will continue and improve on this process by collecting comprehensive data on the quality, progress, and impact of MRC work. RCUK has a long-term vision to gather data about research outputs and outcomes from all its researchers, using a single online system, linked to a single route for applying for research council funding.

Research councils are committed to reducing the administrative burden placed on researchers in providing information on research outputs and outcomes. Steps to achieve this include coordinating separate schemes that currently exist across the councils, implementing more efficient systems to collect data and ensuring the data provided by researchers is used effectively.

Ian Viney, head of evaluation for the MRC said: “The MRC’s new evaluation programme will help ensure that we are better able to demonstrate the importance of MRC work by early in 2009. Early changes will involve collection of output and outcome data via an online form, which will replace separate annual requests to MRC researchers for information on publications and achievements.”

To find out more, contact Ian Viney: email ian.viney@headoffice.mrc.ac.uk or phone 020 7670 5450.

There are four main elements to the MRC’s evaluation programme:
• Improving the data held about the research portfolio, specifically information on research outputs and outcomes.
• Introducing evaluation planning for all new funding initiatives.
• Ensuring that evaluation data is used in the MRC’s policy-making.
• Developing evaluation methodology to better meet the MRC’s needs, including assessing the economic impact of medical research.
Award-winning pictures of science
Three images captured by MRC scientists won 2008 Wellcome Trust Image Awards. An 11.5 day-old mouse embryo (pictured) captured by Dr James Sharpe of the MRC Human Genetics Unit in Edinburgh used optical projection tomography, a new imaging technique that allows scientists to study the internal structures of organisms. Dr Venki Ramakrishnan of the MRC Laboratory of Molecular Biology in Cambridge was the second MRC winner, with his image of a molecular model of a ribosome. Ribosomes translate the code carried from DNA on messenger RNA to build molecules of protein inside the cell. And Kate Sullivan, of the National Institute for Medical Research in London, created an image of a cross section through a seminiferous tubule, a long tightly coiled tube in the testes in which sperm is produced. The winning images can be viewed at the Wellcome Collection website at http://images.wellcome.ac.uk.

Malnutrition fuels community poverty cycle
An international team has shown that under-nutrition in mothers and children can have a life-long effect on the health and prospects of the child and even affect future generations. The scientists looked at data from research in Brazil, Guatemala, India, the Philippines and South Africa and showed that under-nutrition was closely linked to shorter adult height, less schooling and reduced economic productivity. Lower birth weight and under-nutrition in early childhood were risk factors for high glucose concentrations, blood pressure and heart disease in later life, suggesting that malnutrition in the womb could not be reversed by access to more food at a later stage in life. Critically, the research also showed that poorer life outcomes were also often passed from one generation to the next, with the offspring of undernourished mothers also displaying low birth weight. Professor Caroline Fall at the MRC Epidemiology Resource Centre in Southampton, is one of the authors of the research and predominantly studies malnutrition in India. She’s now spearheading a large-scale intervention trial in Mumbai, looking at the impact of better diet on mother and offspring by recruiting young women before they become pregnant and providing them with a high-energy daily dietary supplement. “The damage suffered as a result of mother and child under-nutrition leads to permanent physical and mental impairment and also harms future generations. Populations who are severely affected by stunting and the negative health and life impacts of under-nutrition in early life will be less able to grasp opportunities to climb out of poverty,” said Professor Fall.

The Lancet 2008; 371: 340–357
Hormone limits malarial brain damage
Research at the MRC’s unit in The Gambia has found that high levels of erythropoietin (Epo) – a hormone produced in response to anaemia – may help protect children from long-term brain damage due to severe malaria. When the malaria parasite moves into the brain, a condition known as cerebral malaria, it becomes even more deadly, killing almost one in five affected children. Neurological problems affecting vision, speech and movement are common among those who survive. When it gets into the brain, the malaria parasite sticks to blood vessels and blocks them. This reduces the oxygen supply to brain tissue and destroys nerve cells, causing the brain damage associated with cerebral malaria. Epo is made in response to low oxygen levels in the blood and encourages the production of new red blood cells. It has been shown to help protect nerve cells in the brain from long-term damage. This led the team to hypothesise that high levels of Epo could prevent lasting damage in children with cerebral malaria – which they confirmed by comparing levels in children who developed brain damage with those who didn’t. One of the research leaders, Dr Climent Casals-Pascual, said: “These results are very encouraging and clearly indicate the potential of erythropoietin as a therapy for cerebral malaria. It suggests it could be used in addition to standard therapy to improve outcome.”

Proceedings of the National Academy of Sciences 2008; Epub ahead of print

Infecting mice with cold virus offers treatment hope
Scientists have been able to recreate rhinovirus infection, the culprit behind most common colds, in a mouse for the first time. Discovered 50 years ago, rhinoviruses only usually infect humans and chimpanzees. There is currently no effective treatment for the virus, which can lead to more serious illnesses such as pneumonia and can worsen asthma in susceptible people. Professor Sebastian Johnston of Imperial College London, who led the research, said: “Until now it has not been possible to study rhinovirus infection in small animals. This has been a major obstacle to new treatments.” The scientists discovered that rhinovirus can’t get into mouse cells because it can’t bind to their receptors. So they modified the mouse receptors to make them more like the human ones, and found that the virus could then infect the cells of the modified mice. Professor Johnston said: “These mouse models should provide a major boost to research efforts to develop new treatments for the common cold, as well as for more potentially fatal illnesses.” The research was co-funded by the MRC, Asthma UK and GlaxoSmithKline.

Nature Medicine 2008; 14: 199–204
Refinement of the use of chronic implants in animal research

The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) and the Wellcome Trust are hosting a workshop on 1 October to highlight scientific and technological advances which have implications for refinement of the use of chronic implants in animal research. It’s hoped that the workshop will lead to improvements in animal welfare and more efficient research. To find out more, visit www.nc3rs.org.uk/chronicimplantsworkshop or email enquiries@nc3rs.org.uk. To attend, you need to register by 1 September.

More red tape cut

A new system to iron out the drawn out process of getting permission to carry out research was launched at the end of January. IRAS will make it easier to apply to carry out health research in the UK.

Applying for research approval often involves grappling with a bewildering array of forms. But the new Integrated Research Application System (IRAS) will put seven review bodies’ application forms in one place. The new system means researchers won’t have to duplicate data because once information has been entered, the system will fill in the different application forms relevant to the research proposal.

The project is led by the National Research Ethics Service (NRES) under the umbrella of the UK Clinical Research Collaboration. Dr Janet Wisely, Director of NRES said that consulting widely with researchers will be vital in the next few months before IRAS becomes compulsory: “It is important to us that researchers have the opportunity to use this system widely and give us feedback on all aspects, especially whether it is helpful to them and how it could potentially be more useful.”

IRAS is supported by the NHS R&D Forum, the major regulatory and governance bodies, the UK health departments, the UK Clinical Research Network, the Forum of NHS Wales for R&D Management in Health and Social Care and research funders. Find out more at www.ukcrc.org/activities/regulationandgovernance/streamliningapplications-iras.aspx.
Professor Mark Pepys of the Centre for Amyloidosis and Acute Phase Proteins at UCL has been awarded the 2008 Ernst Chain Prize for “exceptional work on the acute-phase proteins and their clinical and pathophysiological significance”. Amyloidosis is a disorder of protein folding and has been implicated in diseases including Alzheimer’s and diabetes. The Ernst Chain Prize was established in honour of Sir Ernst Chain, who received a Nobel Prize in 1945 alongside Sir Alexander Fleming and Lord Howard Florey for the discovery of penicillin. It is given annually to a scientist who has made an original and substantive contribution to the field of science which has furthered, or is likely to further, understanding or management of human diseases.

Professor Alan McNeilly of the Human Reproductive Sciences Unit in Edinburgh has been awarded prestigious medals from two UK societies. He was awarded the Dale Medal of the Society for Endocrinology, the society’s highest accolade. He also received the Marshall Medal from the Society for Reproduction and Fertility. This is the Society’s premier honour and is awarded to an outstanding contributor to the study of fertility and reproduction. Professor McNeilly said: “I’ve never considered my research as work – it’s always been fun. The best part for me is working with clinicians to help inform their clinical practice. To do that we need to understand how the brain controls the ovary and how, from that, you get healthy babies.”

Congratulations to the first group of MRC staff who have completed the externally accredited introductory diploma in management. The achievement was celebrated at an award ceremony at MRC Head Office on 22 February. Professor Simon Denny of the University of Northampton (which runs the course) presented the awards, and said that the MRC group had achieved the highest marks in the shortest time since the course began. Recipients of the diploma were Anthony Wright of Human Nutrition Research in Cambridge, Drs Pamela Brown and Kurt Sales from the Human Reproductive Sciences Unit in Edinburgh, Tamsin d’Estrube of the General Practice Research Framework in London and Sean Maher from MRC Head Office in London. Also awarded the qualification but not in attendance were Claire MacEvilly of Human Nutrition Research in Cambridge, Graham Reed of London’s Clinical Sciences Centre and Judith Adams from the Mary Lyon Centre in Harwell.

Max Perutz science writing competition

Closing date: 2 May 2008

If you are an MRC PhD student with an interest in communicating your science to a wider audience, then this competition is for you. First prize is £1000 and the winning entry will be published in The Guardian. For more information, see www.mrc.ac.uk/newsandevents/maxperutzaward.
The secrets of healthy ageing

As Abraham Lincoln once said, “In the end, it’s not the years in your life that count, it’s the life in your years.” Ageing is a lifelong process, but when does it begin, what causes it, and will medical research ever combat it? Join Professor Cyrus Cooper, director of the MRC Epidemiology Unit, and other scientists to explore the issues of ageing. The event coincides with the Scottish launch of the new MRC/BBSRC Lifelong Health and Wellbeing exhibition, which will be on show after the talks. The event will be held on 1 April at 6pm at the Royal College of Physicians in Edinburgh. For information and booking visit www.sciencefestival.co.uk.

How hormones rule our lives

Delve deeper into how hormones in our body, environmental factors and lifestyle choices can affect our health and that of our children. From obesity to infertility, the evidence is all around us. Come to the National Museum of Scotland in Edinburgh on 2 April at 6pm to hear Professor Richard Sharpe of the MRC Human Reproductive Sciences Unit. Find out more and book a place at www.sciencefestival.co.uk.

The art-science divide: where does brain science fit in?

On 16 April at 6–8pm, Professor Graham Collingridge, Director of the MRC Centre for Synaptic Plasticity in Bristol, Professor Dame Nancy Rothwell of the University of Manchester, Dr Mark Lythgoe of the UCL Institute for Child Health and scientist-turned artist Dr Lizzie Burns will discuss how art can bring meaning to complex neurological concepts. To be held at Whitworth Gallery in Manchester, the discussion will be followed by an informal reception and tour of a small exhibition of Dr Burns’ artwork.

SET for exhibition

Three of the MRC’s most eminent women scientists have received Women of Outstanding Achievement Awards from the UK Resource Centre (UKRC) for Women in Science, Engineering and Technology (SET).

Professor Dame Kay Davies, of the MRC Functional Genetics Unit at the University of Oxford, was selected in the category of SET Discovery and Professor Uta Frith, of the Institute of Cognitive Neurosciences at UCL, received her award for Discovery, Innovation and Entrepreneurship. Professor Dame Nancy Rothwell, from the University of Manchester, was chosen in the category Communication of SET with a Contribution to Society.

All three are part of a contemporary photographic collection that will be exhibited at the Royal Society and around the country. The portraits have been commissioned by the UKRC, which was established in 2004 as part of a Government strategy. Funded by the Department for Innovation, Universities and Skills, the centre provides advice and services and encourages discussion about ways to address the under-representation of women in SET.

Of her inclusion in the exhibition, Professor Davies said: “I was delighted to hear the news of the award. I hope it will inspire other young female scientists to follow science as a career.”

As well as displays at the Royal Society and BA Festival of Science, the exhibition tours the country. It grows in size each year to create an inspiring legacy for future generations. To find out more, visit www.ukrc4setwomen.org.
A new play is helping thousands of school children and students to explore the social, moral and scientific questions raised by stem cell research. ‘Nobody Lives Forever’ has begun a national tour of UK schools and colleges. The play has been written by Judith Johnson for the Y Touring Theatre Company, in partnership with the Association of Medical Research Charities.

Y Touring plays are shown to young audiences, who then debate the issues involved, as Simon Wilde, the MRC’s external communications manager explained: “The play’s main audience of students and young adults is traditionally a difficult group to reach. Y Touring has a reputation for skilfully using theatre to convey and explore often complex scientific issues. The actors, who are well briefed, return to the stage after the performance to talk about the issues raised. The MRC’s decision to provide funding, along with the Department of Health, to develop and present this play is based on Y Touring’s excellent history in discussing difficult topics.” The company has visted at least 19 schools in London and in October will embark on an eight-week national tour.