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JOHN SAVILL, CHIEF EXECUTIVE

Working in partnership with other research funders is ever more important in straitened times, as discussed in this issue’s opinion piece (page 18). The MRC collaborates with others to maximise the investments we make in research. One of our most important partners in this regard is industry. After all, translation of scientific discoveries into new treatments and diagnostics is not something we can do single-handedly. We rely on the financial muscle and expertise of companies to translate our research into new treatments, devices, diagnostics and drugs that will benefit patients.

Of course, improving the economic competitiveness of the UK is also a central tenet of the MRC’s mission. In the aftermath of the economic downturn and the 2010 Spending Review, we need to take that one step further. Now, more than ever before, we must work closely with industry - not just to improve economic competitiveness of the UK, but actively to drive economic growth.

We are building on a long history of innovation and collaboration, such as the commercialisation of technology invented by scientists from the MRC Laboratory of Molecular Biology, which gave rise to the first monoclonal antibody therapies. By 2008, there were 21 monoclonal antibody drugs on the market for treating cancers and immune system disorders. Today, antibodies make up a third of new drugs for cancer, arthritis and asthma and the global antibody market is estimated to be worth $40 billion. That’s not just a one-off success story. MRC e-Val data shows us that 20 per cent of MRC researchers have had one or more productive interactions with the private sector in the last five years. Through these partnerships, MRC researchers have attracted £59.7m funding from the private sector.

Recent disinvestments by pharmaceutical companies and the struggles which smaller biotechnology companies face make alliances with the MRC increasingly attractive, too. These firms are on the look out for ways to cut costs and improve efficiency by outsourcing the costly early stages of therapeutic discovery. So the door is wide open for academic researchers looking for an industry partner.

GlaxoSmithKline, for example, is on the hunt for ‘super-collaborations’ which are long-term and, importantly, do not require the partner to match the amount of funding invested by the company.

Many of our activities are of value to pharmaceutical and biotechnology companies. We are training the next generation of excellent scientists, some of whom will take up jobs in industry, and we have resources such as the UK Brain Banks Network and the Patient Research Cohorts Initiative which we actively encourage industry to use. We have established direct links with industry through initiatives such as the MRC Industry Collaboration awards which support partnerships between academic and industry researchers.

The MRC is open for business.

John Savill

“The MRC is open for business”
Innovative MRC cancer test awarded NHS prize

A simple but highly effective test for oesophageal cancer invented by scientists at the MRC Cancer Cell Unit has been awarded an NHS Innovation Prize.

Dr Rebecca Fitzgerald and her team won the prize for developing a diagnostic test called the Cytosponge. This consists of a sponge enclosed in a capsule on the end of a piece of string which is swallowed by the patient. After the capsule has dissolved the sponge expands and can be pulled back out of the oesophagus, collecting cells on the way. The cells can then be tested using a new molecular test for a condition called Barrett’s Oesophagus which is the major risk factor for oesophageal cancer.

The NHS Innovation Prizes recognise and reward ideas that tackle some of the biggest healthcare challenges facing the NHS – such as early diagnosis of oesophageal cancer. As well as benefiting patients, the test will save the NHS money. Rather than referring patients suspected of having Barrett’s oesophagus to hospital for a costly endoscopy at a cost of £400 per patient, the Cytosponge can be used in a primary care setting and costs only £25 per investigation. If this screening test detects cancer very early then patients can be cured with endoscopy treatment, which is seven times cheaper than an operation and much less invasive for patients.

Congratulating the scientists on their prize, Secretary of State for Health Andrew Lansley said: “At a time of significant economic challenge, innovation is essential to help the NHS modernise and deliver more for less, whilst at the same time improving the quality of care for patients.”

MRC spin-out signs major deal with AstraZeneca

Heptares, a biotechnology company founded by MRC scientists, has signed a multi-million pound, four-year deal with AstraZeneca to discover and develop new drugs targeting an important family of proteins called G-protein coupled receptors (GPCRs).

GPCRs are integral components of cell membranes and help the cell to receive and respond to external signals, including those from drugs. But these receptors become highly unstable when removed from their natural cell membrane environment. To date, this has hampered scientists’ efforts to understand their structure and design medicines that work on GPCR targets.

The collaboration brings together Heptares’ GPCR expertise and its StaR® technology - which stabilises membrane proteins, allowing GPCRs to be investigated - with AstraZeneca’s capabilities in drug discovery, development and commercialisation.

The two companies will focus on several specific GPCR targets linked to the central nervous system, cardiovascular system, and metabolic and inflammatory disorders from projects in AstraZeneca’s portfolio. This research will act as the starting point for drug discovery by producing the first stabilised forms of GPCRs. AstraZeneca will have worldwide development and commercial rights to any drugs which emerge from the deal, but Heptares will receive £3.78 million up front, and potential future payments of up to £115m.

Heptares was founded in 2007 as a spin-out from the MRC Laboratory of Molecular Biology. The company was formed to take forward the pioneering work of its founding scientists, Dr Richard Henderson and Dr Chris Tate, and of a wider group of MRC scientists including Dr Gebhard Schertler, also from the Laboratory of Molecular Biology, and Dr Ed Hulme from the MRC National Institute for Medical Research in London. This is the third major drug discovery collaboration for the company this year following deals with Takeda Pharmaceutical Co and Shire Pharmaceuticals.
£3.7m invested in personalised medicines

Seven new research projects into personalised medicines – such as tumour profiling to improve cancer care and developing biomarkers for more effective drugs - are to be funded with a £3.7 million joint investment from the MRC and the government’s Technology Strategy Board (TSB).

Four of the projects will develop the use of biomarkers to predict how different groups of patients will respond to therapies for inflammatory and immune system disorders. This will help to match therapies to the relevant patient sub-groups in which they achieve the best results for alleviating symptoms, with minimal side effects.

The other three projects will work out the best ways to co-develop drugs and companion diagnostics. Research will focus on the ways in which reimbursement of costs can be distributed among the different organisations and companies involved in the development process. This should increase the number of personalised treatments that are developed, the speed of their development and their adoption by healthcare providers.

The projects will be led by five pharmaceutical and biotech companies, including AstraZeneca and GlaxoSmithKline. This is the first investment to be made through the TSB-managed Stratified Medicine Innovation Platform (SMIP), an initiative which will oversee over £50 million of government funding in personalised medicine research and development over five years. The SMIP partners are the UK health departments, the National Institute for Health and Clinical Excellence (NICE), Cancer Research UK and Arthritis Research UK.

John Jeans, former MRC chief operating officer and deputy chief executive, said: “The MRC has chosen to be a major investor in this partnership, as it provides an opportunity to enhance the competitiveness of the UK knowledge and health base in an important and innovative area. We welcome the opportunity to continue collaborating with the Technology Strategy Board and other partners in supporting the development of targeted treatments for patients.”

Government seeks input on animal research laws

A Home Office consultation on the protection of animals used for scientific purposes has been launched, seeking input on how to transpose a new EU directive into UK law. The closing date for responses is 5 September.

The new directive on research in animals (2010/63/EU), which has been eight years in the making, was published in October 2010 and will be formally adopted by all EU member states by January 2013. Its aim is to enhance the welfare of animals, facilitate modern science, harmonise regulation across Europe and cut excessive red tape.

The consultation invites expert professional advice on which parts of the current UK legislation on animal experimentation should be retained and which should be changed. By making necessary changes, the UK can continue to foster best practice and effective regulation in this area of science.

Lobby group Understanding Animal Research has coordinated discussions by the major UK bioscience organisations on the European directive, including the MRC, and is encouraging UK scientists to respond to the consultation. A background briefing about the transposition of the new directive into UK regulations is available on the Understanding Animal Research website at http://bit.ly/EUDbrief.

To view the consultation itself, visit: www.homeoffice.gov.uk/publications/about-us/consultations/transposition-protection-animals

The MRC will be responding formally to the consultation, and is actively seeking input from MRC scientists and staff responsible for animal care in developing its response at a workshop in London on Monday 18 July. For more information, email ellen.doughty@headoffice.mrc.ac.uk
Lifecourse Epidemiology Unit officially re-named

The MRC Lifecourse Epidemiology Unit (LEU) at the University of Southampton, previously known as the MRC Epidemiology Resource Centre (ERC), was formally renamed by Sir John Savill at a special ceremony in June. The renaming signals the change in its status from a resource centre to a unit.

The LEU, directed by Professor Cyrus Cooper, specialises in investigating cardiovascular, musculoskeletal and metabolic disease throughout the lifecourse, and the name change reflects the unit’s major achievements and its international standing as a strategic research leader in the field. The MRC announced the decision to change the centre to a unit following a successful five-year review, and the next five years will see investment of £14m to continue and expand the unit’s work.

The renaming ceremony was attended by local and national partners including constituency MP Dr Alan Whitehead and Professor Don Nutbeam, Vice-Chancellor of the University of Southampton.

Speaking at the event, Dr Whitehead commented: “The LEU is a tremendous asset to the city of Southampton - it has an international reputation of the highest calibre.”

Sketching out the University of Southampton’s future strategy, including its target to become one of the top ten research universities in the UK, Professor Nutbeam added: “The success of the unit is thanks to the extraordinary leadership of Cyrus Cooper and his ability to develop great potential amongst the staff.”

The ERC was established in 2003, itself a successor to the MRC Environmental Epidemiology Unit which represented a continuing intramural MRC investment in Southampton since 1979. Scientists at the unit, based principally at the University of Southampton but with an emergent programme at the University of Oxford, study the interplay of causes of disease acting at different stages throughout life.

Through an understanding of the processes at work, from before conception through to old age, population-based and high-risk preventive strategies can be developed against certain common, chronic diseases of later life. These strategies inform health policy.

The LEU will continue to maintain an internationally renowned collection of cohort studies which explore the developmental origins of health and disease: including the Hertfordshire Cohort Study and the Southampton Women’s Survey.

NEWS continued

UKCMRI takes the name of DNA pioneer

The UK Centre for Medical Research and Innovation (UKCMRI) has been re-named The Francis Crick Institute in honour of one of the UK’s greatest scientists. Sir Paul Nurse said: “Francis Crick was a superb British scientist. He embodied the qualities of collaboration, creativity and tenacity that we would like to instil within the culture of the institute to be named for him. Francis Crick led a revolution in biology and medicine, was noted for his intelligence, openness to new ideas, for switching disciplines from physics to biology, and his collaborations – not least with James Watson, Maurice Wilkins and later, Sydney Brenner.”

Last month, a report by the Science and Technology Committee highly commended the “comprehensive, ambitious and ground-breaking scientific vision” for the new institute. However, the committee also raised some concerns about its location, and the concentration of medical sciences in the ‘golden triangle’ in the south of England.

Acknowledging these concerns, MRC chief executive Sir John Savill, remarked that the Francis Crick Institute “will be a national institute for the national interest.”

“The institute is located in one of the most connected parts of the UK. This project provides opportunities for world-leading, innovative and collaborative research to flourish, and also to bring the health impacts of fundamental research to the public more quickly,” he added. “It is a key part of the MRC’s strategy to increase the impact of basic science on health, now and for decades to come, so it is reassuring to receive the backing of the Select Committee.”

The institute is founded by the MRC, Cancer Research UK, the Wellcome Trust and University College London. The building will be completed in 2015. In April, Imperial College London and King’s College London signalled their intention to join the partnership behind the institute.
MRC fellowships boosted from five to seven years

The MRC is to increase the duration of new senior non-clinical fellowships (SNCFs) from five to seven years.

MRC fellowships provide outstanding scientists with exceptional opportunities to develop their careers, by concentrating on challenging research and gaining the broader experience that is essential to a future leadership role.

The decision to lengthen the fellowships has been driven by current senior and intermediate fellows who, as part of a recent consultation, told the MRC about the challenges of establishing themselves as independent scientists. A survey of Career Development Award fellows indicated that a longer, seven-year senior fellowship would offer a highly attractive choice for them.

Sir John Savill, MRC Chief Executive, explained: “Our decision to lengthen SNCFs represents a confident investment by the MRC in some of the UK's most talented new scientists. MRC fellows are exceptionally successful.”

But he also added a word of warning: “These are personal awards and portable. So, while I encourage our fellows to take greater responsibility for shaping their careers, it is clear that some universities need to up their game in nurturing and developing their next generation of research leaders - or they risk losing them.”

Evidence shows that senior non-clinical fellows go on to have double the success rate in applying for further MRC grants than the overall competition average. Furthermore, over the past ten years, around 60 per cent have gone on to hold professorships within two years of the end of their award.

Speaking at the second annual MRC Fellows’ Symposium in May, John Savill praised the high calibre of MRC fellows: “Being an MRC fellow is a transformative personal experience which should also transform medical research. The key thing in awarding a fellowship is that it is about the person, it’s not just a grant. Our fellows can feel secure in the knowledge that they are going to do extremely well – and feeling secure is important for high risk, high gain, curiosity-driven science.”

This is just one of several new opportunities for MRC fellows: besides introducing the well-received annual MRC Fellows’ Symposium, the MRC is planning a mid-term MRC mentorship scheme for holders of the seven-year fellowship.

As Peter Dukes, Head of MRC Research Careers Awards, summarises: “We are strengthening fellows’ opportunities to make new connections within the wider MRC community.”

The first deadline for applications for the new seven-year SNCFs will be in September 2011. Applicants will normally hold a PhD/DPhil and have at least six years’ post-doctoral research experience. Applications from current MRC career development award holders are particularly welcome. The increased fellowship length will only be for new SNCFs, awarded from January 2012.

For more information, visit: www.mrc.ac.uk/Fundingopportunities/Fellowships/Seniornonclinical/MRC001826
Belfast scientist to chair Translational Research Group

Professor Patrick Johnston, dean of the School of Medicine, Dentistry and Biomedical Sciences at Queen’s University Belfast, has been appointed chair of the MRC Translational Research Group.

The Translational Research Group allocates funding for strategic research investments and makes recommendations on the implementation of strategic decisions.

Announcing the news at Queen’s University Belfast, Sir John Savill commented: “Professor Johnston’s appointment is extremely important. The role as chair of the Transitional Research Group is key to its success in the UK, which is one of our main objectives. The MRC has to deliver economic benefits from its investments and getting the right strategy to achieve that is essential. Professor Johnston is very committed to commercial translation; he has particular expertise in cancer and is clearly someone who has chosen a very receptive research environment at Queen’s.”

Successful start for SARTRE

The first Science Showcase was recently held by SARTRE, an MRC-supported translational research partnership between the Universities of Cardiff and Bristol.

SARTRE (the Severnside Alliance for Translational Research) was created in 2009, with the aim of uniting scientists from the two universities to develop new projects in translational research and provide a focal point for interactions with external partners such as bio-pharmaceutical companies.

The showcase, which was held in Newport, was an opportunity for SARTRE’s collaborators to celebrate the project’s initial successes.

SARTRE is supported by the MRC and the Welsh Government and was chosen to pilot the new MRC devolved Developmental Pathway Funding Scheme.

So far support has been given to 19 diverse research projects, from investigating technology platforms to exploring new cancer treatments, and SARTRE is currently funding around 75 scientists working in joint multi-disciplinary ventures across the two universities.

Among the groups involved in SARTRE projects are a University of Cardiff School of Dentistry team who are working on a way of safely delivering toxic antibiotics so that they distribute themselves specifically at the site of infection and a group from the University of Bristol School of Clinical Sciences who are exploring the design of new TrkA antagonists (molecules which block nerve signals) for the treatment of arthritic pain.

Professor Lars Sundstrom, director of SARTRE, commented: “This is looking good. So far about half of our smaller single milestone projects have made it to the next stage. We invested £300,000 in them and they have already brought in over £3m in further funding; this part of the experiment has definitely worked. Our larger projects are still in progress and they are hitting their milestones so we are on track for further success towards the end of next year.”

SARTRE has also been developing strategic links with the private sector and recently appointed an advisor, on secondment from pharmaceutical company Janssen, to support future collaborative working across academia and industry.
£11.5m to support new ageing research projects

From living with HIV/AIDS as an older person to art therapy for the elderly, 17 diverse research projects were recently funded with £11.5 million by the cross-council Lifelong Health and Wellbeing (LLHW) programme.

Across the UK, seven research grants of up to five years and ten pilot studies of up to two years will be supported. The research projects bring together scientists across completely different disciplines, taking a fresh approach to addressing some of the biggest challenges presented by the ageing population in the 21st century (see opposite for examples of some of the funded research).

The £11.5m funding forms the third phase of the LLHW initiative, which is led by the MRC on behalf of the BBSRC, EPSRC, ESRC and AHRC, with additional support from the UK health departments. The UK’s population is rapidly ageing. By 2034, 23 per cent of the population is projected to be aged 65 and over, and the LLHW initiative was launched in 2008 to address this challenge. Its aims are to target factors in life which impact on wellbeing in later life, identify ways to improve health and quality of life in the elderly, inform policy and increase capacity and capability in ageing-related research.

Find out more at www.mrc.ac.uk/llhw

Some of the funded projects in brief:

Managing the menopause
A grant of £1.65m has been awarded to a team led by Professor Deborah Lawlor, an epidemiologist at the University of Bristol, to investigate the effects of the menopause on health and wellbeing. By studying 2,800 women as they go through the menopause the researchers will get a detailed understanding of the effects of this major life change. This is the first time that the effects of menopause on health, social and economic outcomes, relationships with family and psychology (such as altered body image) have all been looked at together.

Ageing creatively
Professor Eric Cross, Dean of Cultural Affairs at Newcastle University, has been awarded £250,000 to lead a multidisciplinary pilot study involving researchers from the arts, sociology, psychology and medicine. Through a series of weekly two-hour sessions - involving creative writing, music and fine art – in over-55s who are not in employment, they will develop ways to measure if this can help improve wellbeing and reduce feelings of isolation. If direct creative activity is proven to be better than passive involvement, the findings could influence policy and perhaps ultimately lead to ‘arts prescriptions’ from GPs.

Deconstructing wrinkles
As we age, our tissues alter – arteries stiffen, vertebrae degenerate causing back pain, and our skin loses its elasticity and forms wrinkles. With a £260,000 grant, Professor Brian Derby and his team at the University of Manchester will use a new technique called nanoindentation to measure the mechanical properties of tissue right down to the microscopic parts from which it is composed. This will help them to better understand the tissue ageing process, inspiring new ways to alleviate these more unpleasant signs of ageing.

Taming the train
Being able to get out and about is vital for social inclusion and independence. We tend to become more dependent upon public transport as we get older – however accidents and injuries can be a hazard for older people using buses and trains. Loughborough University’s Dr Andrew Morris is leading research into the causes of accidents involving public transport vehicles and how injuries could be prevented through engineering solutions.
Nurturing tomorrow’s African research leaders

Three top-flight African scientists have recently begun research projects supported with £5m joint funding from the MRC and the Department for International Development.

The African Research Leaders Scheme is a prestigious award to support exceptional researchers. Its aim is to strengthen research leadership and capacity across sub-Saharan Africa by attracting high ability researchers and retaining them there to prevent a ‘brain drain’ to other countries.

Each of the three scientists has been funded for five years with awards of between £1 million - £2 million and will work in close partnership with a UK-based researcher, with regular visits between the two countries for seminars and mentoring.

Funded with £2m, Professor Shane Norris at the University of the Witwatersrand and Professor David Dunger at the University of Cambridge will focus on the health and wellbeing of teenage mothers and their children in South Africa, aiming to understand how early experiences can have an impact on mental health, infections and metabolic disease in early adulthood.

Another project, also funded with £2m, will aim to work out the best treatment strategies for eliminating lymphatic filariasis (commonly known as elephantiasis) which is caused by a parasitic worm infection of the immune system. The infection, which causes disfiguring inflammation of the legs and genitals, is endemic in around half of the population of Ghana. It can be treated with drugs, but it is hard to get them to the scores of infected people who need them.

Newly appointed African Research Leader Professor John Gyapong, from the University of Ghana, will work with Professor Moses Bockarie at the Liverpool School of Tropical Medicine to look at the best methods to get these drugs to people in countries with fragile healthcare systems.

The third recipient of funding is Dr Abdoulaye Diabate, a medical entomologist in Burkina Faso. Collaborating with Dr Frederick Tripet at Keele University, he has been awarded £1m to pursue an unusual new take on malaria research – studying the behaviour of the mosquitoes which carry the parasite that causes malaria.

Male mosquitoes from the Anopheles gambiae species – the main carrier of the malaria parasite in Africa – mate with female mosquitoes in a large swarm, which offers a good opportunity to kill many insects at once. Dr Diabate and colleagues will aim to find out more about how mosquitoes form swarms, and what triggers them to do it, to develop strategies for mass-killing of the insects.

They also want to discover what makes a male mosquito successful in finding a mate. This will help other researchers in the field who are trying to introduce mosquitoes into the wild population which have been genetically engineered to be resistant to the malaria parasite, rendering their bites harmless to humans. To date, these lab-bred mosquitoes have not been very good at attracting and securing a mate, so Dr Diabate’s research could help to find out why.

The second round of funding for the African Research Leaders programme will be launched later this summer. For more information, visit: www.mrc.ac.uk/Fundingopportunities/Calls

Canada-UK partnership to find new antibacterial drugs

Two teams of scientists in the UK and Canada have been awarded £4 million to speed lab research on antibiotic resistance towards clinical practice.

The research is being funded by the Canada-UK Joint Partnership on Antibiotic Resistance, a partnership between the MRC and the Canadian Institutes of Health Research (CIHR). The aim is to build on existing collaborations between the two countries by providing support for consortia tackling the problem of antibiotic resistance.

The lead UK researchers are Professor Chris Dowson of the University of Warwick and Professor Tim Walsh at the University of Cardiff, both of whom will receive £1m over four years, matched by CIHR for each Canadian lead investigator.

Professor Dowson’s research will attempt to unravel the processes which bacteria use to build key components of their cell wall, peptidoglycans. They will use these insights to develop antimicrobial drugs and identify new antimicrobial targets.

The consortium led by Professor Walsh will tackle the increase in resistance to key antibiotics used against gram negative bacteria, which cause some hospital-acquired infections. The scientists will focus on a group of enzymes these bacteria use to destroy antibiotics, called metallo-beta-lactamases. There are very few effective treatment options for gram negative bacterial infections, so new drugs could transform the outlook for patients.
## OPPORTUNITIES

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### RESEARCH PROGRAMMES

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### STUDENTS AND FELLOWSHIPS

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For updates, please check: [www.mrc.ac.uk/fundingopportunities](http://www.mrc.ac.uk/fundingopportunities)
**RESEARCH RUNDOWN**

**African trial questions WHO guidelines on children in shock**

One in ten children in Africa admitted to hospital with malaria and septicaemia are in a state of shock. Although there are effective medicines for these illnesses, these children are often already very ill when they arrive in hospital and die within hours of admission. The World Health Organization (WHO) guidelines for emergency treatment of such children are to give them fluids rapidly through a drip into a vein (fluid resuscitation) - but unexpected findings from a major MRC trial have shown that, in fact, this treatment does not save lives. The Fluid Expansion As Supportive Therapy (FEAST) trial involved over 3,000 children across Tanzania, Uganda and Kenya. Two groups of children were given fluid resuscitation of either albumin or saline in the first hour of arriving at hospital. After that, they were given fluids slowly, to replace the amounts a sick child should drink. A third group were given fluids slowly from the first hour of admission. Those given fluids slowly did better, with a 48-hour survival rate of 92.7 per cent compared with 89.4 per cent of those given fluid resuscitation. Fluid resuscitation actually caused three additional children to die out of every hundred treated. The trial was stopped early because the independent committee overseeing safety saw that fluid resuscitation was unsafe. Professor Sarah Kiguli, Chief Principal Investigator for the study in Uganda explained: “The results went against the recommendations of the WHO and the normal practice in wealthy countries, and this surprised me greatly. Finding this out before we started to encourage the use of fluid resuscitation in children with severe infections and shock across Africa was incredibly important. It will save many lives in future.”

Published online ahead of print at [www.nejm.org](http://www.nejm.org), 26 May 2011

**Antibodies show promise for both CJD and Alzheimer’s**

Two antibodies known to play a crucial role in preventing Creutzfeldt Jakob disease (CJD) could also help to prevent the onset of Alzheimer’s disease, MRC-funded research suggests. The antibodies, ICSM-18 and ICSM-35, were known to prevent production of faulty prion protein - the main cause of CJD - but studies in mice have shown that they can also block the damaging effects of amyloid beta protein, the culprit behind Alzheimer’s disease. Amyloid beta becomes attached to the surface of neurons in the brain, stopping them from communicating effectively and causing memory loss. The research, in which human amyloid beta was introduced into the brains of mice, showed that the antibodies stopped the amyloid beta from taking hold and damaging the brain. The study also confirms findings from a 2009 paper by Yale researchers which first indicated that prion protein may be involved in Alzheimer’s disease. Clinical trials of therapies based on the antibodies in CJD patients are due to begin in 2012. Professor John Collinge, director of the MRC Prion Unit at University College London, who led the study, said: “We’re thrilled that this discovery shows in mice that these two antibodies, which we are developing to treat CJD, may also have a role in treating more common forms of dementia like Alzheimer’s disease. If these antibody drugs prove to be safe in use to treat CJD, we will consider whether studies in Alzheimer’s disease should be carried out.”

The research was co-funded by the Science Foundation Ireland.

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**Good things come to those who...imagine**

New findings have shown that our imagination can play a powerful role in whether or not we make choices that benefit us in the long-term, for example giving up smoking today to avoid eventually getting lung cancer. On a subconscious level, we tend to value instant gratification more highly than waiting for a future reward – even if the future reward is bigger. But scientists from the MRC Cognition and Brain Sciences Unit and University College London have shown that if we imagine enjoying the future benefits that could stem from a choice we make, we are more likely to choose delayed gratification. Fifteen volunteers were asked either to imagine spending money, for example spending £35 in the pub in 180 days’ time, or to just estimate what they could buy with the cash. They were then asked whether they would prefer to opt for the money in 180 days, or to have £25 now. All volunteers performed both tasks several times. When they had imagined enjoying spending the money they were much more likely to choose to wait than to opt for the smaller sum of money straight away. This effect was seen to be strongest in the people who were normally less prone to consider the future consequences of their actions. Using functional magnetic resonance imaging (fMRI) – an imaging technique which shows brain activity in real time – the scientists pinpointed this imagined enjoyment of future events to an area of the brain called the medial rostral prefrontal cortex (mrPFC). Lead author Dr Roland Benoit explained: “Our ability to imagine future scenarios seems to motivate decisions in the present which will only be of benefit in the future. If we can gain a better understanding of this mechanism, we might be able to help optimise everyday decisions that have economic, environmental and public health-related consequences.”

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**‘Lean gene’ increases risk of heart disease and diabetes**

Having a leaner body does not always mean you are at a lower risk of heart disease and diabetes, according to the findings of a consortium of researchers led by the MRC. They have identified a gene that is linked with having less body fat, but also an increased risk of metabolic diseases such as type 2 diabetes and heart disease. By looking at the genomes of over 75,000 people to look for the genes that determine body fat percentage, the scientists found strong evidence that a gene called IRS1 is linked with having less body fat. A further study showed that IRS1 is linked with having unhealthy levels of cholesterol and glucose in blood. They also discovered that the gene only lowered the fat under the skin, but not the more harmful fat that surrounds the organs. Dr Ruth Loos, the lead scientist on the project from the MRC Epidemiology Unit, said: “What we’ve discovered is that a certain form of the gene keeps you lean by reducing how much fat you store under your skin. We don’t know for sure, but we can speculate that these individuals are then more predisposed to store fat elsewhere, such as in the liver and in muscle where it may interfere with normal organ function. This would increase the risk of developing metabolic disease. So we can be quite clear that not all lean people are metabolically healthy – and not all overweight people are metabolically unhealthy.”

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If you’ve ever wondered why you’re always asleep in the chair by the end of the 10 o’clock news, or why a temporary bout of insomnia leaves you forgetful and tetchy, then perhaps you need a wake-up call from Dr Pete Oliver. Network caught up with Pete at a recent Café Scientifique in Oxfordshire to find out more.

Have I got snooze for you

Pete is a post-doctoral scientist at the MRC Functional Genomics Unit (FGU) in Oxford. The FGU carries out research to understand more about muscle diseases such as Duchenne muscular dystrophy (DMD) as well as neurological disorders, mental impairment and schizophrenia. By exploring the genetic defects that cause conditions such as DMD and creating genetic models for a range of neurodegenerative disorders such as Parkinson’s disease and Huntington’s disease, effective treatments are now being developed.

Pete’s own research is carried out within Professor Dame Kay Davies’ group, in collaboration with Professor Russell Foster. His research focuses on understanding the impact of the environment - specifically sleep disturbance - on the brains of people with psychiatric illnesses such as schizophrenia and depression. He explains: “Many people will complain of a poor night’s sleep occasionally, but frequent sleep disturbance is a common feature of those diagnosed with many neurological disorders, including psychiatric disease. The aim of the work we are carrying out is to understand the pathways in the brain that link abnormal brain function with sleep patterns.”

Research has proven that sleep, or a lack of it, can affect our health significantly. Continued sleep deprivation will severely affect the hypothalamus – the part of the brain that controls language, memory, planning and sense of time. Experiments have shown that 17 hours of sustained wakefulness can lead to a reduction in performance equivalent to drinking two glasses of wine - the legal drink driving limit in the UK. You only need to observe new parents, worn down and tearful after nights of two-hourly feeds, to understand the toll that sleep deprivation can take on a person.

The impact on our cognitive function when sleep is interrupted is believed to be caused by the disruption to our circadian rhythms. Pete says: “Circadian rhythms are physical, mental and behavioural changes in the body that follow an approximate 24-hour cycle, influencing our sleep-wake behaviour, hormone release, body temperature and other vital bodily functions.”

Circadian rhythms are driven by the body’s ‘master’ clock - an amazing group of nerve cells in the hypothalamus called the suprachiasmatic nucleus, or SCN. If you’ve ever wondered why you always get sleepy at the same time each night, then you have the SCN to thank. The SCN controls the production of hormones at certain times of the day and night; including melatonin, a hormone that makes us drowsy. Pete explains: “Since it’s located just above the optic nerves, which relay information from the eyes to the brain, the SCN receives information about incoming light. When there is less light—like at night—the SCN tells the brain to make more melatonin so you get sleepy.”

There are also genetic factors to consider. Using light information from the optic nerve, the SCN helps to turn on or off the genes that control the body’s internal clocks throughout a 24-hour cycle. It is therefore likely that if there is a mistake in one of those genes, circadian rhythms will be disrupted.

Abnormal circadian rhythms can be linked not only to sleep disorders such as insomnia but also to mental health conditions such as depression, bipolar disorder and seasonal affective disorder. Poor sleep is common in neurological diseases such as Parkinson’s as well as schizophrenia, leading scientists like Pete to explore the genetic causes of this disruption.

Pete says: “Our work is beginning to demonstrate that the communication pathways and genes in the brain which influence abnormal behaviour in psychiatric disease also regulate sleep. This means that improving sleep patterns in neurological disease may positively influence the symptoms of these disorders. Importantly, this is also a cheap and potentially highly effective method of improving the quality of life for patients, their families and carers. For example, basic approaches such as using timed lighting are already being used to address abnormal sleep patterns.”

The scientific exploration of light as a treatment for psychiatric disease is both exciting and challenging. However, the potential of Pete and his colleagues’ research to produce simple and effective clinical treatments for psychiatric patients could be the wake-up call that these patients - and the NHS - are waiting for.
“Poor sleep is common in neurological diseases such as Parkinson’s as well as schizophrenia”
A spring of success for MRC scientists

Spring 2011 has seen a glut of honours for MRC researchers. The Royal Society elected several MRC scientists to its Fellowship this year. They were: Dr Steve Gamblin, a group leader at the MRC National Institute for Medical Research in London; Dr Sean Munro, a group leader at the MRC Laboratory of Molecular Biology in Cambridge; Professor Doreen Cantrell, a Wellcome Trust Principal Research Fellow at the University of Dundee and chair of the MRC Infections and Immunity Board; and Professor John Morton OBE, a cognitive psychologist at the Institute of Cognitive Neuroscience, University College London and a former director of the MRC Cognitive Development Unit.

Other new Royal Society Fellows include Professor Gerhard Matterlick, chief executive officer of Diamond Light Source Limited, the company which built and operates the synchrotron at the Harwell Science and Innovation Campus, and Professor Angela Vincent of the Nuffield Department of Clinical Sciences who has previously carried out MRC-funded research at the Weatherall Institute of Molecular Medicine.

Three MRC scientists were also elected as Fellows of the Academy of Medical Sciences in May. Professor Paul Bolam, a senior scientist and group head at the MRC Anatomical Neuropharmacology Unit in Oxford; Dr Andrew McKenzie, a senior staff scientist at the MRC Laboratory of Molecular Biology in Cambridge; and Professor Dominic Withers, a group head at the MRC Clinical Sciences Centre in London.

Several MRC scientists have been elected as new members of the Learned Society of Wales: Professor Michael Owen, director of the MRC Centre for Neuropsychiatric Genetics and Genomics in Cardiff; Professor Ole Petersen, an MRC Professor and director of the School of Biosciences at Cardiff University; Professor Julie Williams, head of neurodegeneration research at the MRC Centre for Neuropsychiatric Genetics and Genomics; and Professor Paul Morgan, recently appointed MRC Council member and dean and head of the School of Medicine at Cardiff University.

The Queen’s birthday honours list also marked out several MRC scientists and staff. Knighthoods were awarded to Dr Hugh Pelham, director of the MRC Laboratory of Molecular Biology; Dr Harry Burns, Chief Medical Officer for Scotland and a former member of the MRC’s Council; and Professor Robert Edwards, formerly a staff scientist at the MRC National Institute for Medical Research and winner of the 2010 Nobel Prize in physiology or medicine for his pioneering work in the development of in vitro fertilisation.

Professor Sally Macintyre, director of the MRC Social and Public Health Sciences Unit and MRC Council member, was made a Dame; and Lesley Caple, most recently head of Head Office Management at the MRC received an MBE. Professor Ian Kimber, who chairs both the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) and the MRC Industrial Collaborative Training and Careers Panel, was awarded an OBE.

Recognition across the pond

Professor Stephen O’Rahilly, director of the MRC Centre for Obesity and Related Metabolic Diseases in Cambridge, is one of 18 scientists from across all disciplines to become one of this year’s Foreign Associates of the National Academy of Sciences of the USA. Stephen has been distinguished by the academy for his research in metabolic and endocrine disease and for his leadership in clinical science.

Stephen is Professor of Clinical Biochemistry and Medicine at the University of Cambridge, co-director of the Institute of Metabolic Science and honorary consultant physician at Addenbrooke’s Hospital Cambridge.

Farewell to MRC deputy

John Jeans, the MRC’s chief operating officer and deputy chief executive, left the MRC on 30 June. During his tenure John took on many roles, including serving as the chair of MRC Operations Board and MRCT Board, a trustee of the MRC Pension Fund, a member of the Shared Services Centre Ltd Project Board and most recently chair of the University-Units Programme Board.

Commenting on his departure, MRC chief executive John Savill said: “During his relatively short time at the MRC John has had a big impact. I count among his many achievements restructuring the senior management team, ensuring a smooth split of MRC head office to two new locations and leading on the MRC’s involvement in the UK Centre for Medical Research and Innovation partnership. I have enjoyed the experience of working with John and have been impressed by his professionalism, his expertise in business management and his good humour.”

John will stay on as chair of the MRCT Board after his successor as chief operating officer has been appointed, and, subject to the agreement of partners, will continue to be involved in the governance of the MRC imaging consortium in London.
Boning up on osteoporosis

MRC Lifecourse Epidemiology Unit senior lecturer Dr Nicholas Harvey has been presented with a Young Investigator Award for his work on osteoporosis, or thinning of the bones. He was presented with the €2,500 award at the 2011 European Congress on Osteoporosis and Osteoarthritis in Valencia.

Nicholas’ research has shown that a mother’s diet and lifestyle during pregnancy can affect her child’s bone mass. The award recognised one of Nicholas’ research projects which looked at variations in activity of the gene RXRα at the time of birth. RXRα is involved in the action of many hormones, including vitamin D. By studying activation of the gene in umbilical cord he found that the extent to which RXRα in babies was switched on or off, through a process called methylation, was associated with the strength of their bones at age four.

The work adds to evidence that variations in maternal diet and lifestyle in pregnancy may have a lasting effect on the skeletal development of the child into older age, potentially leading to osteoporosis.

Separately, the MRC Lifecourse Epidemiology Unit’s director, Professor Cyrus Cooper, has recently been honoured with the British Society for Rheumatology’s Heberden Medal for his achievements in the field of rheumatology. Cyrus has led the Musculoskeletal Research Programme at Southampton University for 19 years, and has published over 450 research papers on osteoporosis and rheumatic disorders. His discoveries include documenting the developmental influences which contribute to the risk of osteoporosis and hip fracture in late adulthood; and demonstrating that the offspring of mothers who are deficient in vitamin D have sub-optimal bone mineral accrual (weaker bones) in childhood.

Life on earth

An MRC Laboratory of Molecular Biology (LMB) scientist’s research into the origins of life has been recognised with the prestigious Royal Society of Chemistry Tilden Prize for 2011. It has long been thought that one of the first chemical events which supported the emergence of life on earth may have been the self-assembly, through purely chemical means, of ribonucleic acid (RNA). Dr John Sutherland’s research has demonstrated a plausible method to explain how simple chemicals that existed on the early earth may have self-assembled into pyrimidine ribonucleotides – some of the building blocks which make up RNA.

A gene-ial celebration

The MRC Human Genetics Unit hosted a symposium at the Royal Society of Edinburgh in May to celebrate the scientific career of Professor Howard Cooke, who recently retired after 36 years of service with the MRC.

Howard was a group leader at the MRC Mammalian Genome Unit during a period which witnessed remarkable discoveries in chromosome biology and the first investigations of the human genome. During that time he identified the first sequences associated with the human Y chromosome and showed that there were differences in DNA sequence (polymorphisms) between individuals. He also discovered telomeres, the DNA sequence at the end of human chromosomes, and demonstrated that they are shorter in somatic cells (cells of the body) compared with the germline cells (cells involved in passing on genetic material to offspring such as sperm and egg cells).

Howard moved to the MRC Human Genetics Unit in 1987 where he went on to develop chromosome engineering based on telomere fragmentation and then mammalian artificial chromosomes.

Visionary grant

Another LMB scientist, Dr Leon Lagnado, has been awarded a prestigious grant by international funding organisation the Human Frontier Science Program (HFSP) to establish a collaboration with scientists at the University of Washington in the USA and the University of Saarland in Germany. They will investigate how nerve cells in the retina transmit visual signals across synapses, the connections between nerve cells. The retina has a special type of connection called the ribbon synapse. Using zebrafish as a model, Leon’s group has been studying how ribbon synapses respond to visual stimulation. The grant will now allow them to investigate how these synapses process visual information in the retina of mice.

Prestigious award for Edinburgh geneticist

Dr Javier Caceres, principal investigator at the MRC Human Genetics Unit in Edinburgh, is to be one of the first recipients of the Wellcome Trust’s inaugural Senior Investigator Awards. This marks Javier’s third success in 2011; earlier this year he was also elected as a fellow of the Royal Society of Edinburgh and was awarded an Honorary Professorship in the University of Edinburgh’s School of Molecular and Clinical Medicine.

The Wellcome awards support exceptional researchers addressing the most important questions about health and disease. They were presented to 27 investigators from across the UK and Brazil, and range from £1 million to £3 million. According to Wellcome Trust director Sir Mark Walport, the investigators represent some of the “very brightest minds” in biomedical science.

Javier joined the Human Genetics Unit in 1997. His laboratory focuses on the role of proteins which bind to RNA in switching genes on or off, and how alterations to the way in which RNA is processed inside the cell nucleus can contribute to human disease.
Simon Denegri was, until last month, chief executive of the Association of Medical Research Charities, and he now leads the charity Ovarian Cancer Action. As budgets are squeezed, he says, partnerships between funding bodies – such as the MRC and charities - are becoming ever more important.

Better together

All roads lead to the MRC. I am exaggerating of course, but not as much as you might think.

The MRC has an impressive story to tell about its role as a focus for research collaboration with other UK funders and partners as well as internationally. It should shout it loud, and often, in my view.

Two years ago, the Association of Medical Research Charities (AMRC) - mindful of the increasing number of partnerships and collaborations involving its 126 member charities - decided to map these links in more detail and investigate what made some more successful than others.

The project, entitled ‘Ways and Means,’ was the first formal study of collaborations between medical research charities in the United Kingdom. A report of the findings was launched at the AMRC’s AGM last year.

I encourage you to take a look. The visual map showing the partnerships that AMRC explored as part of its study is notable for the very prominent positioning of the MRC.

The picture affirmed anecdotal evidence that had previously been picked up in a survey by the AMRC and reported as part of its written submission to the House of Lords Science and Technology Committee 2009 inquiry into setting the funding priorities for science and technology research.

One member charity said that their experience of working with the MRC through clinical training fellowships was “overwhelmingly positive” and that the MRC was “very easy to work with” and “eager to collaborate”.

It wasn’t all rosy though; as you might expect - smaller charities said that they found it harder to forge a relationship, and some said they found it difficult to establish a transparent dialogue with the right people. However, the overriding sense from the survey was that
The economic situation is an added incentive for charities to forge partnerships.

…there were solid foundations from which others might learn. It was one of the initial prompts for the AMRC to undertake a more in-depth analysis with ‘Ways and Means.’

Some strong messages from those charities interviewed emerged in the analysis stemming from ‘Ways and Means’ – and I think they resonate with all of us whatever our perspective.

Collaborations enable charities to achieve more than would be possible through acting alone. Each project is unique, with no alliance quite like another. Co-funding arrangements have the potential to advance science faster, and at potentially lower costs, both overall and for individual funders. The benefits of joining forces will be reaped only if all partners are committed to improved effectiveness, efficiency and efficacy. And last but not least: collaboration is not an easy option.

The report concluded that there is a future for collaborations. It acknowledged that charities are aware of the financial changes in the sector and will have to adapt to this new environment and find ways to make their money go further. Co-funding arrangements appear to be a good and proven strategy to achieve the same if not more at reduced costs, with the added benefits of increased PR value and potentially higher quality applications.

I concur with these conclusions. The economic situation has been an important, added incentive for charities to forge partnerships of one sort or another. When the AMRC surveyed its members at the beginning of the economic downturn, about two-thirds said that they were exploring collaboration as one way to mitigate the impact of the recession. Two years later, in 2011, about a third of those charities surveyed said they had followed through on this intention.

But ‘Ways and Means’ is also clear that, although the recession has indeed been an important factor behind this behaviour, medical research charities have not lost sight of the guiding principle that ensures they bring value to their research partners, including the MRC. That is, the commitment to fund the highest quality science whatever the times. As this article goes to press, all AMRC members are being audited on their peer review policies and practices – something that you will find happening in no other country than the UK.

I say this now, not as the chief executive of the AMRC but as the chief executive of Ovarian Cancer Action, the leading charity dedicated to ovarian cancer research in the UK. Our own research centre represents a collaborative effort between Imperial College Hammersmith Hospital, the Institute of Cancer Research and the Royal Marsden Hospital. As its major funder and supporter, our vision is for the centre to become a world leader in the effort to beat ovarian cancer.

Following the Spending Review allocations earlier this year it was heartening to see the MRC come forward with implementation plans which put collaboration at the heart of the way it does business, rather than as a footnote to its strategy. One area in which I look forward to dialogue with the MRC is that of patient and public involvement in research – something I believe brings real value in good times as well as bad. As the new chair of the national advisory group INVOLVE, I look forward to closer collaboration with the MRC to strengthen its patient and public involvement in research.

Once again, my path will take me to the door of the MRC.

The AMRC’s report, Ways and Means, can be found at www.amrc.org.uk/our-members-ways--means