How doctors and researchers are using phones to improve our health

Medawar's legacy
Extending the lifespan of kidney transplants

£230m for high tech clinical research
In October, Chancellor of the Exchequer George Osborne announced the recipients of an MRC-led initiative which will change the way that clinical research is done in this country.

The £230 million Clinical Research Infrastructure Initiative (see article opposite) will bring together funding from UK Government, devolved administrations, Arthritis Research UK, the British Heart Foundation, the Wellcome Trust, Cancer Research UK, and partner universities to advance clinical research in 23 key projects at centres across the country. Many of these will involve partnerships with pharmaceutical and biotechnology companies.

It will invest in a range of revolutionary technologies aimed at identifying the causes of diseases such as cancer and dementia, and dramatically speeding up diagnosis and treatment.

The Government entrusted £150m funding to this initiative. This, together with contributions from the MRC and our funding partners, means we have been able to invest over £230m in the collaboration, which will catalyse innovation and advance our knowledge in completely new areas of clinical research.

It’s satisfying to see the geographical spread of the investment, lying as it does not only in traditional scientific powerhouses but also in strong academic research institutions and clinical structures across the country, bolstering the science base UK-wide.

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The initiative will also support University of Liverpool scientists to identify the best treatments for patients based on how they respond to drugs. They will do this using different experimental systems ranging from single cells to studies in people to careful clinical observation of patients.

Speaking in Exeter on the day of the launch, Chancellor George Osborne said: “The UK is already a world leader in science and research, which is why at Budget, I protected science spending. Today we go a step further by announcing £150 million of new investment in clinical research infrastructure. The funding will go to 23 truly innovative projects from across the UK today that represent the best of British ingenuity and scientific exploration. The Government, charities, universities and industry will be working together to advance our knowledge in combating the biggest medical challenges of our time.”

More information is available at: www.mrc.ac.uk/crri

And read our blog post on the initiative at: mrc.io/1DDUvd9
CFS/ME conference reinvigorates the field

Researchers and patient representatives alike have hailed a conference on CFS/ME (Chronic Fatigue Syndrome, Myalgic Encephalomyelitis) in September as a great success.

The UK CFS/ME Research Collaborative (CMRC) conference took place in Bristol in September and brought together more than 70 researchers and clinicians, featured presentations from MRC-funded researchers, and hosted a workshop involving around 60 patients, carers and practitioners in roundtable discussions and Q&As with researchers.

The CFS/ME Research Collaborative was formed in 2013 with the aim of providing a mechanism for CFS/ME charities, researchers and clinicians to work together to take the field forward.

Professor Stephen Holgate, Chair of the CMRC and also of the MRC’s Translational Research Group, said: “By bringing together such a diverse group of researchers, we feel confident that we’ve reinvigorated the CFS/ME research field and found some new ways to progress. We hope to use the conference as the basis of future plans for increasing the profile of, and investment in, CFS/ME research.”

Emerging themes from the conference included: the likelihood that CFS/ME probably has many causes; the need to ‘stratify’ or group patients with similar symptoms together to see whether they share common causes or markers of biological processes; the need to recognise that what causes CFS/ME might be different to what maintains it, and the need to understand that disease may not necessarily be either biological or psychological but may, in fact, be both.

Find out more about the outcomes of the conference on our blog: mrc.io/1sHdFXu

Learn more about the collaborative: mrc.io/1B96vVs

Malaria, monkeys and drones

Researchers part-funded by the MRC have been employing some unusual methods to investigate the transmission of a particular type of malaria in Malaysian Borneo.

Funded by the cross-research council Environmental and Social Ecology of Human Infectious Disease Initiative, the researchers from the London School of Hygiene and Tropical Medicine are using unmanned aerial vehicles, or drones, to collect information about forest clearance in Borneo.

They are combining this data with GPS information about the location of macaque monkeys and local people to create maps that will help them work out whether changes in forest are leading to an increase in malaria.

Cases of the malaria parasite in question, Plasmodium knowlesi, appear to have been increasing in Borneo. The parasite has historically infected macaques, and the team want to find out if it has spread to people only recently, or always caused malaria in the area. What they find out should help to inform prevention, as well as planning for local health services.

Read a post about the project on our blog: mrc.io/1CfJWzP

and find out more at mrc.io/1wovUG

Celebrating 25 years of research excellence through partnerships

November saw the MRC/UVRI Uganda Research Unit on AIDS celebrate its 25th anniversary.

With the theme ‘Celebrating 25 years of Research Excellence through Partnerships’, the celebrations took place over two days at the main campus in Entebbe and at the commissioning of a £900,000 MRC-UK/DFID-funded clinic in the capital Kampala. This site will serve as both a clinic for disadvantaged women and as a research station. The occasion was also marked with a scientific symposium, poster exhibitions and a dinner attended by local and international guests, partners and staff.

Unit director Dr Pontiano Kaleebu commended partners for their support over the years and noted that HIV – the problem which the unit was set up to address in 1989 – remained a health challenge. He added that, by taking advantage of a multidisciplinary approach and exceptional international collaborations, the unit will continue with cutting edge research in areas such as HIV as a chronic disease and the challenges of long-term anti-retroviral therapy treatment, non-communicable diseases and mental health.

Other future areas of interest for the unit will include HIV vaccine development, tuberculosis, malaria and some neglected tropical diseases.

A technique tested on dogs by MRC researchers in 2012 has helped a paralysed man whose spinal cord was severed in a knife attack to walk again.

The headline-grabbing research, which involves taking a type of stem cell called olfactory ensheathing cells (OECs) from inside the nasal cavity and transplanting them to the injured spinal cord, was first developed in rats by UCL’s Professor Geoffrey Raisman when he worked at the MRC National Institute for Medical Research.

In the recent research, carried out at UCL and Warsaw University Hospital in Poland, strips of nerve tissue were placed across the gap in the patient’s spinal cord and the OECs were injected into the spinal cord above and below the gap. The research team believes that the OECs acted as a pathway to stimulate the spinal cord cells to regenerate, using the nerve grafts as a bridge to cross the severed cord.
**NEWS**

**London clinical trials institute launched**

Clinical trials experts from across University College London have been brought together to form the Institute of Clinical Trials and Methodology (ICTM) – the largest critical mass of clinical trials expertise in Europe.

Directed by Professor Max Parmar, the institute will be associated with the MRC Clinical Trials Unit, the Comprehensive Clinical Trials Unit and two virtual members; UCL PRIMENT Clinical Trials Unit and the Cancer Research UK Clinical Trials Centre. Find out more at: [www.ucl.ac.uk/ictm](http://www.ucl.ac.uk/ictm)

**Inspiring science**

Artist Geoffrey Smith made this painting based on visits to the Mary Lyon Centre, the mouse house at MRC Harwell, for the ‘One Life, One Art’ exhibition at the Royal College of Pathologists in October.

**MRC wins animal research award**

The MRC won an award for openness in animal research from Understanding Animal Research in December.

Presenting the winners with their awards, Director of the Science Media Centre Fiona Fox described them as “the real pioneers who spoke out when others didn’t, who did it when the threat from extremists was real, who pioneered the openness agenda before anyone used those words, and most importantly, who inspired the rest of us to get to where we are today.”

**Animal testing supported where there is no alternative**

A survey published in September shows that a majority of the British public accept the use of animals in medical research ‘where there is no alternative’.

Of the 969 respondents questioned, 68 per cent agreed that they could accept the use of animals in research for medical purposes where there were no alternatives – such as using computer modelling, in vitro testing or MRI scanning. There was a small (2 per cent) decrease in the level of support since the last survey was carried out in 2012.

A report of the Ipsos MORI survey, which was commissioned by the Department for Business, Innovation and Skills, can be found at: [Mrc.io/13bqDHH](http://Mrc.io/13bqDHH)

**Measuring the impact of MRC research**

The remarkable impact that MRC research has on health, society and the UK economy is documented in a new report, Outputs, outcomes and impact of MRC research 2013/14. Showcasing some of the latest developments and gains arising from MRC-funded research – as reported by researchers – the results show that our scientists are making an international impact in delivering health gain, economic growth and changes to scientific capacity across all sectors. Download a copy at: [www.mrc.ac.uk/output13-14](http://www.mrc.ac.uk/output13-14)

**MRC recognises landmark achievement for Heptares**

Sir John Savill presented a memento to inventors from MRC spin-out company Heptares Therapeutics in November to mark key US patents being granted relating to G protein-coupled receptors (GPCRs).

Sir John praised the inventors and MRC Technology for their work to translate pioneering scientific research carried out at the MRC Laboratory of Molecular Biology (MRC LMB) and the MRC National Institute for Medical Research into new medicines targeting GPCRs; a superfamily of drug receptors linked to a wide range of human diseases.

Between 30 and 40 per cent of drugs for all conditions target GPCRs and to date Heptares has raised more than $60m in private financing.

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Mobile medicine

93 per cent of the UK population now own and use a mobile phone. Sarah Harrop finds out how mobile research is taking advantage of these pocket-sized companions to improve our health.

Smokers will tell you that the hardest part of giving up is breaking the habits and routines associated with the addiction. But imagine having a friend with you who knows all about your smoking habits and offers you advice and support whenever you’re tempted to light up. That’s the idea behind a new mobile phone app called Q Sense being developed by MRC-funded researchers at Cambridge University.

One of the lead investigators developing Q Sense, Dr Neal Lathia from the Cambridge University Computer Lab, explains: “The app will send you tailored support messages depending on what it learns about your smoking triggers. For example it might deliver advice about relieving stress for people who report high stress levels at work. Or if you regularly report smoking at work with colleagues, the app will tell you ways to cope with colleagues who aren’t quitting.”

By learning the smoker’s behaviour and using GPS to track their movements the app is able to provide personalised support to deal with the cravings after they give up. It even sends messages which are tailored support messages depending on what it learns about your smoking triggers.

M-health is the name for medicine and public health supported by mobile phones, now a burgeoning field. And with the appearance of smartphones in recent years, it has both the potential to save the NHS time and money and transform how we receive healthcare.

For example it may soon be possible for people to test themselves discretely for sexually transmitted infections (STIs) using an app and gene chip being developed by Dr Tanq Sadiq from St George’s, University of London in collaboration with experts from other universities and industry.

The UK Clinical Research Collaboration-funded team, called the eSTI2 consortium, has also built an online e-care pathway that will eventually allow people to receive their results and collect their treatment from a pharmacy without having to make an embarrassing trip to the clinic (although patients would still be able to contact a health professional if necessary). The hope is that this will encourage more people to get tested and treated; currently one in five people infected with Chlamydia never seek medical treatment.

Dr Sadiq explains: “The vision is that people would simply buy an STI test from the pharmacy in the form of a gene chip, load a urine sample onto it and have it read by the phone, all within half an hour. The phone app then interprets the data to produce the result, and sends it off electronically to a pharmacy where the patient can collect their medication.”

Testing of the e-care pathway has already begun and early trials of the phone and gene chip technologies are due to start shortly with results expected towards the end of next year.

Pocket sized tools for doctors

Contrary to what you might believe from a journey on the average commuter train, smartphones aren’t just for apps, playing angry birds or checking Facebook. Increasingly they’re also used professionally – and that includes in hospitals.

“Most doctors use smartphones pretty much every day, for looking information up, occasionally for tests, and for various medical calculations,” says Professor Alasdair MacLullich, a doctor and researcher at Edinburgh University. He’s taken advantage of this opportunity to develop a simple smartphone app to help doctors to detect delirium.

While it might sound like a Victorian malady, delirium is actually a common modern-day problem which causes great distress and is linked with dementia and even death in the elderly. But it often goes undiagnosed, because it’s hard to distinguish patients with delirium from those with dementia. With MRC funding, Alasdair has designed a smartphone app for doctors that tests patients for their ability to count slowly presented flashes of a white disc on the screen. Delirium sufferers can’t focus their attention for more than a few seconds, whereas a dementia patient usually can, even if their memory is severely impaired.

“Early detection improves patient outcomes, including the duration of the delirium and the distress associated with it, and there are knock-on effects on length of stay and other outcomes. So if we can help to increase early detection of delirium by providing a simple tool that doesn’t require a great deal of skill to use and the score means something, then I think this kit has potential for quite a lot of impact in the NHS,” says Alasdair.

He is now working with a company called Cambridge Cognition to modify and improve the app, known as DelApp. The plan is then to test in several hundred patients with a view to licensing it to a company who will launch and sell it - hopefully in around four years’ time.

Part of the allure of mobile phone technology for researchers and doctors is that it offers a simple and low cost way to empower patients to take responsibility for their own health – something that’s particularly effective in mental health.

At the University of Manchester, the MRC is funding Professor Shin Lewin and colleagues to develop an app for psychosis patients called Clintouch. By asking users a series of personalised questions about how they feel, the app gathers information on how a patient’s symptoms have changed over time which is then beamed off to their care coordinator. The idea is to detect when a patient is at risk of relapsing and head it off before it happens.

Clintouch Project Manager Dr Matt Machin explains: “One of the biggest costs to the NHS of a patient with schizophrenia is when they relapse and end up as inpatient. Psychosis patients face the challenge that treatment is only successful in the short term, so over time their symptoms come back again. Often this happens too quickly for their medical team to intervene and prevent it from happening.”

Clintouch’s developers estimate that even a five per cent reduction in re-admission rates would save an average of almost £500,000 - £1m for each NHS mental health trust.

So far, feedback from users has been promising. Matt says: “One of the things they like about it is that it empowers them to manage their condition. Besides the results of questions being uploaded for clinicians to see, patients can also see simple graphs on their own handset, and they can also privately record their own feelings and moods in a daily diary which is in the app.”
Global reach

The popularity of mobile phones isn’t confined to developed countries. Their widespread use, even in the most remote locations, could help people get faster and easier access to healthcare.

MRC Population Science Fellow Dr Chris Smith is leading a trial of MOTIF, a mobile phone voice messaging service which provides contraception support to women in far-flung villages of Cambodia. Globally there are 47,000 deaths each year from unsafe abortions, and abortion rates are highest where contraception use is lowest – so for these women, contraception can be a matter of life or death.

But, in rural Cambodia, many women are anxious about the side-effects of contraception and myths – such as the fear that condoms cause cancer, or burns – abound. Trial results are currently being gathered but health conditions these mobile solutions will be ideal.

In contrast, Peek is small, light and costs one fifteenth of the price - and it only needs one specialist to do the test rather than a whole team. Andrew is now leading a trial of Peek on 5,000 people scattered across the Rift Valley in Kenya.

So will phones play a big role in the future of healthcare? Neal Lathia thinks so: “M-health’s role is going to be very important, especially for people who are looking to manage their own health. Maybe not for the people who are looking to be empowered to take positive steps themselves in different health conditions these mobile solutions will be ideal.”

“The principle that people use smartphones and tablets is established and I see doctors using smartphones for cognitive testing and other medical testing so that it'll become normal in five to ten years or maybe sooner,” agrees Alasdair MacLullich.

And even the older generation concurs. When asked whether she minded her test being done on a phone rather than using a test kit with flashing buttons, one of Alasdair’s elderly patients told him: “It’s better that it’s on the phone because that’s the future, isn’t it?”

Some other MRC-funded M-health developments

Dr Will Whiteley at the University of Edinburgh has made the ‘FAST’ test for stroke available directly to patients by creating a free app which asks users to check someone for three main symptoms of stroke and call 999 if they are all present. Learn more at: Mrc.io/13qMWct

At the University of Leeds, a team led by Dr Janet Cade has created an app for promoting weight loss called ‘My meal mate’. The app allows people to set weight loss goals and self-monitor their daily calorie intake, using a food composition database of over 30,000 items. In a pilot trial, average weight loss of users of the app was 4.6kg (10 pounds) by 6 months. To date, the app has been downloaded over 10,000 times.

Nobel Prize for ‘inner GPS’ discovery

Former MRC scientist Professor John O’Keefe was awarded the 2014 Nobel Prize in Physiology or Medicine in October, shared with two of his former postdocs, May-Britt Moser and Edvard Moser, for their discovery of cells which make up a positioning system or ‘inner GPS’ in the brain.

While working in the MRC Cerebral Functions Research Group at University College London (UCL) in 1971, John discovered ‘place cells’ in a brain region called the hippocampus. He showed that these cells always activated when a rat was at a certain place in a room. He concluded that they formed an organised map of the rat’s activities within the room, however it wasn’t until 2005 that May-Britt and Edvard discovered the missing piece of the puzzle: how place cells map space.

The duo discovered ‘grid cells’, another type of nerve cell, which generate a coordinate system allowing for precise positioning and path-finding. With the knowledge of John’s discovery, they showed how place cells and grid cells make it possible to determine position and enable navigation. The behaviour of both types of cells helps explain how individual brain cells create a map of space, enabling us to navigate through a complex environment.

On receiving the prize, John, who is Professor of Cognitive Neuroscience and Director of the Sainsbury Wellcome Centre in Neural Circuits and Behaviour at UCL, said: “I’m thrilled to have received the Nobel Prize for work on the hippocampal place cells and their role in spatial memory and navigation. I consider myself fortunate to have received MRC backing especially in the early years, and could not have carried out my research throughout long periods of my career without it.”

John’s current research is focused on Alzheimer’s disease: “Although we didn’t know it when we first started working on the hippocampal formation, it is one of the earliest brain regions to be attacked by the disease. We think that our understanding of the rodent hippocampus will provide a good basis for studying the early stages of Alzheimer’s disease pathology and how it spreads,” he explained.
The most important chicken in medical history was a Plymouth Barred Rock Hen from New York. The chicken’s name is not recorded, but in 1911 she was brought by her owner to a young pathologist called Peyton Rous because of a large tumour growing out of her neck.

Rous subsequently performed a series of experiments so elegant it is hard to believe he didn’t know what he was looking for. He showed that the filtered extract from the tumour, containing no actual tumour cells, could cause more tumours in another chicken. Rous had discovered a type of virus, called a retrovirus, that can cause cancer.

At around the same time, in the dense tropical forests of the Congo Basin, another retrovirus managed to cross from a single chimpanzee to a single human and start a journey that would spread to 60 million people. This virus announced itself to science without fanfare: a brief report in 1981 documented five gay men from Los Angeles all with similar and unusual signs of immune system collapse, including cancers.

The paper reads with the dispassionate tone characteristic of medical case reports – the deaths of two of the men are recorded with minimal eulogy – but it was to become one of the most significant medical announcements of the century. This was how the epic narrative of the Human Immunodeficiency Virus (HIV) began in our collective psyche.

But, while the virus had been crossing species and continents, science had also been making vast strides without any idea of how important those advances would be. When the epidemic exploded across geographical and social boundaries in the 1980s we had a head start, thanks to the work that started with Peyton Rous. Because we had gained an understanding of the biology of other viruses, highly effective treatments for HIV were developed in less than 20 years from its discovery.

My research aims to contribute to this understanding of HIV biology which has so far been crucial in developing drugs. It takes place in small tubes and dishes in a lab and it’s a long way from patients and from developing treatments.

It revolves around the unanswered question of how HIV destroys the immune system. Considering that HIV is probably the most studied and understood infection in history this remains a huge gap in our knowledge.

Like all viruses HIV sits somewhere between a living organism and a collection of chemicals. It is a package of protein with a little bit of genetic code. Viruses cannot reproduce by themselves, they infect other living cells and hijack their machinery to replicate. HIV specifically infects certain vital cells in the body’s immune system and, over several years, as these cells die, the immune system weakens and patients succumb to diseases like the rare cancers and pneumonias first noticed in Los Angeles. No one knows exactly how or why these immune cells die, but some preliminary data implicates the involvement of the machinery that human cells have for repairing damaged DNA.

Superficially, the value of my research may be that it contributes to drug development which will better treat HIV infection. But justifying research by presuming the outcome is illogical almost to the point of absurdity. If I knew what was going to happen it would not be research.

I may find that I am using HIV as a tool to better understand DNA repair in human cells and this may help with treating cancer. Or the results may have no applications in HIV or cancer, but prove vital for a new epidemic as yet unimagined – just as experiments on the filtered extract of a chicken tumour have proved so directly important during the HIV epidemic.
Simple chemicals show promise for preventing heart damage

Simple chemicals found in fruits could protect vital organs from long-term damage after a heart attack or stroke, research in mice has shown.

During a heart attack or stroke, a clot can starve the heart or brain of blood and oxygen, causing irreversible damage. Further damage is caused when the clot is dislodged and blood rushes back into the heart or brain. This can later lead to heart failure.

MRC and British Heart Foundation-funded researchers have discovered that the culprit behind the damage is build-up of a substance called succinate, which forms in the body when sugar and fat are broken down to release the energy stored in food. When blood flow returns, succinate interacts with oxygen causing the release of tissue-damaging molecules.

The research also showed that such organ damage in mice and rats could be limited by administering simple chemicals when blood flow is restored. These chemicals, called malonate esters, which are found in low levels in fruits such as apples and grapes, stop the build-up of succinate and the resulting release of destructive molecules.

As well as pointing the way to new drugs for treating stroke and heart attack patients, the findings could have implications in surgery where transplanted organs suffer damage after they are connected to the transplant patient’s blood flow.

Published online at www.nature.com, 5 November 2014

New drug for boosting immunity in the elderly

A naturally occurring compound called spermidine has been shown to boost the ageing immune system in mice, suggesting a way to improve the effectiveness of vaccines such as the seasonal flu jab in elderly people.

As we age, our immune system becomes less effective at responding to new infections, and even to ones we’ve had in the past. A key factor behind this decline in immunity is that the white blood cells that coordinate the response to an infection – called T cells – lose the ability to form a ‘memory’ of the infection.

The research showed that spermidine restores the immune system’s built-in memory by boosting a cellular process called autophagy, levels of which were shown to be lower in the T cells of ageing mice.

First author of the study Daniel Puleston, a PhD student from the MRC Human Immunology Unit at Oxford University, explains: “The effect was so powerful that the treated mice mounted an even stronger T cell response to the vaccine than young mice. It’s the equivalent of a 90-year-old responding to a vaccine better than a 20-year-old, which makes this a very exciting pathway to target as a potential way of boosting vaccine protection in the elderly.”

The researchers have patented spermidine and will now see if they can use the compound, or other autophagy-enhancing drugs, to improve responses to already licensed vaccines in mice before hopefully moving on to early safety trials in humans.

Published online at http://elifesciences.org/content/3/e03706, November 2014

Positive public health impact of minimum alcohol pricing

Minimum unit pricing of alcohol in England would be up to 50 times more effective in tackling problems caused by cheap drink than the Government’s recent policy of a ban on below cost selling, according to University of Sheffield researchers.

Increasing alcohol prices is effective in reducing both consumption levels and harms. However, plans to introduce a minimum unit price for alcohol of between 40p and 50p per unit were shelved in 2013.

The MRC-funded study compared effects of the two alcohol policies on public health in England using mathematical models and General Lifestyle Survey data. Banning below-cost selling had a small effect on population health, saving approximately 14 deaths and 500 hospital admissions per year. In contrast, a 45p minimum unit price was estimated to save 634 deaths and 25,700 hospital admissions.

Professor Alan Brennan, Professor of Health Economics and Decision Modelling from the School of Health and Related Research, said: “Despite some study limitations we found that a minimum unit price of 45p would be expected to have 40-50 times larger reductions in consumption and health harms.”

Published online at www.bmj.com, October 2014

World’s first artificial enzymes created

MRC Laboratory of Molecular Biology scientists have created the world’s first enzymes made from artificial genetic material. Their synthetic enzymes, which are made from molecules that do not occur anywhere in nature, are capable of triggering chemical reactions in the lab.

The research gives new insights into the origins of life and could provide a starting point for an entirely new generation of drugs and diagnostics.

The team previously created synthetic molecules called ‘XNAs’ that can store and pass on genetic information, in a similar way to DNA. Using XNAs as building blocks, the team has now created ‘XNAsymes’, which perform simple reactions, such as cutting up or stitching together small chunks of RNA, just like naturally occurring enzymes.

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Published online at www.nature.com, November 2014
FUNDING

£30m for cutting edge research

Over £30m has been awarded to companies and universities across the UK to help develop emerging new treatments and technologies – from gene therapy to high-tech surgical dressings.

The investment, by Innovate UK and the MRC, comprises the fifth and sixth round of the Biomedical Catalyst (BMC), part of the Government’s Life Sciences Strategy. Some of the 29 supported projects include:

- ‘pH paper’ to prevent fatality through incorrect placement of feeding tubes (Edinburgh)
- Dressings with embedded clotting agents which can be left in the body (Leeds)
- A bio-engineered ‘scaffold’ to repair injured tendons (Manchester)
- Headband-mounted heart rate sensor to help resuscitate newborn babies (Derby)
- New gene therapy to tackle nerve and muscle degeneration of the fatal Huntington’s Disease (Oxford)
- A revolutionary ‘Gamma Camera’ to help diagnose and treat more cancers (Camberley, Surrey)
- Cell therapy to repair liver damage (Edinburgh)

Since opening in 2012 the BMC has supported innovation from 250 small and medium companies and universities, and attracted an additional £100m in private investment.

Minister for Life Sciences George Freeman said: “These investments demonstrate just how many businesses and universities across the country are developing life-saving treatments while adding real value and vitality to their regional economies. With Innovate UK and the MRC we are helping ensure this industry has a global reach built on solid local success.”

The BMC was set up to offer funding for development of innovative ideas that could save lives, improve treatment for patients and also provide significant UK economic impact. Any UK small or medium-sized business or academic undertaking research and development may apply to the BMC on a rolling basis, with applications assessed by independent experts.

Find out more at: www.mrc.ac.uk/biomedicalcatalyst

Experimenting on the human

Three ambitious new research programmes, which aim to deliver a step-change in our understanding of disease by using human volunteers in experimental studies have been funded as part of a £60m investment from the MRC.

The latest phase of the MRC’s Experimental Medicine Challenge will provide new insights into the biological mechanisms of Parkinson’s disease, reduced immunity in the elderly and the way the gut and brain interact to influence addictive behaviour.

By studying these conditions in people, scientists will gain a detailed understanding of how disease takes hold and progresses within the body. This may help them to identify new opportunities to intervene with medical treatments, and researchers can also use their findings from human studies to work backwards and design better experiments in the lab.

Professor Sir John Savill said: “While scientists learn a great deal from molecular, cellular and animal studies, often it’s only through in-depth human studies that we can effectively untangle complex diseases. There have been huge leaps in technologies such as high-speed genomic sequencing and lab-grown human tissue that enable us to carry out ever more sophisticated clinical studies. This will ultimately allow us to translate research into new treatments and diagnostics faster, cheaper and more safely.”

The MRC plans to commit a total of £60m to Experimental Medicine over three years.
MEDAWAR’S LEGACY

100 years on from the birth of Sir Peter Medawar - regarded as the ‘father of transplantation’ for discovering that the immune system can be coaxed to tolerate tissue grafts from another individual. - Sarah Harrop considers his legacy by speaking to MRC scientists behind one of the latest advances in transplantation research.

At the MRC Centre for Transplantation at King’s College London, Director Professor Steven Sacks is brandishing a plastic model that looks like the skeleton of a pointy-tailed prehistoric sea creature. But this is no animal. It’s a large-scale molecular model of a sophisticated new anti-inflammatory drug called Mircocept, which could extend the life of transplanted kidneys and give patients many more years of healthy life.

In the 1940s, MRC scientist Sir Peter Medawar discovered the principle of acquired immune tolerance: the ability of a living thing to overcome its natural tendency to reject a tissue graft from another individual. The discovery won him a Nobel Prize and launched a field of research looking at tackling the body’s immune response in order to overcome the problem of transplant rejection. Scientists are still working on this challenge today.

It’s now known that without controlling inflammation it will be near impossible to achieve tolerance of a transplant. Mircocept is one of the latest breakthroughs on this front as it works to ‘paint’ a kidney from the stress it goes through when it’s taken out of the donor’s body, as Steven explains.

“Many donor organs are removed through keyhole surgery and squeezing the organ through a small space pushes the blood out of it and it becomes deprived of oxygen,” he says. “And then as it comes out it’s put on ice, and its nerves are cut, obviously. All of those things are stresses to the kidney and as soon as it is connected up to the recipient’s body it becomes deprived of oxygen,” he says. “And then as it comes out it’s put on ice, and its nerves are cut, obviously. All of those things are stresses to the kidney and as soon as it is connected up to the recipient’s body it becomes deprived of oxygen.”

Inflammation, a consequence of the immune response, is bad news for a transplant because it causes tissue damage and ultimately shortens the lifespan of the organ. But Mircocept sits on the surface of kidney cells like a coat of paint and protects it from inflammation caused by a part of the immune system called complement.

Complement’s job is to attack and kill invading bacteria but in the distressed kidney it attacks and inflames kidney cells too, even if there’s no infection. Mircocept coats parts of a naturally produced substance which normally protects our cells from damage while complement is fighting off bacteria, joined onto a molecule that anchors it to the cell surface.

The drug’s inventor, Dr Richard Smith, explains how it works in practice: “Once it’s removed the organ is ‘painted’ by the drug. So the surgeon pretreats the organ with drug before transplantation. That protects it from any further damage and then it’s transplanted into the patient.”

The drug could buy surgeons and patients valuable time. Normally an organ will only be usable for a very short time after it’s removed, which can be a logistical challenge, particularly in situations when it has been donated by someone who has died unexpectedly. But in research on animals, Mircocept has been shown to extend the usability of the organ dramatically from less than an hour to overnight.

Only about half of transplanted kidneys are still functioning after 10 years in the patient and 5 to 10 per cent of transplants fail within one year. For these reasons, the demand for organs currently far outstrips the supply; so Mircocept could also help to increase the available pool of organs and save more lives, as Richard explains:

“Nowadays there’s a tendency to use donated organs that would not have formerly been used either because the donors were too old or because they were in poor health. But such is the pressure in the transplantation world that for every patient that gets an organ there’s another patient who dies on the waiting list. So if you can make an organ ‘better’, you have fewer failures in the operation and a lower chance of rejection,” he says.

A trial in over 500 patients is set to begin in early 2015 to test whether, completed with kidneys prepared for transplantation in the standard way, the addition of Mircocept allows more kidneys to function normally within the first week. Richard hopes that “with a fair wind” the drug may be available to patients within three to four years. He believes that MRC funding has been crucial to getting the drug to this stage because many companies would be put off by the complexity of carrying out a trial in transplant patients:

“Thanks to the MRC we’ve been able to bridge this gap by being able to manufacture a drug that’s really not simple to make, in the way that we want it to be done, and to carry out the clinical trials. In terms of Peter Medawar’s legacy you could say it’s the next step - or three along - of actually getting to the point of taking an advanced medicinal agent towards the market by an academic organisation. I’m sure that’s not unique, but there aren’t many examples of that that I know.”

Sir Peter Medawar: the father of transplantation

Sir Peter Medawar was director of the MRC National Institute for Medical Research from 1962 to 1972. He won the Nobel Prize in 1960 for his discovery of acquired immune tolerance. Sir Peter’s finding came from his studies of skin grafting to treat soldiers with burns in World War II. Using rabbits, he showed that the rejection of skin grafts was an immune response, and that this response could be avoided if, early on in life, animals were exposed to the tissue that would later be grafted.

You can watch a video featuring Medawar in a series of films about the pioneers of transplantation produced by the MRC Centre for Transplantation to celebrate the MRC Centenary in 2013, at mrc.io/1FK5Wy

And you can read more about the man and his research on the MRC’s website at: mrc.io/1y0ORYW

Also in the pipeline...

• Professor Martin Birchall and colleagues at the UCL Ear Institute have been awarded £2.8m through the second round of the Biomedical Catalyst (see article page 9) to allow them to carry out the world’s first clinical trial of a stem cell based voice box transplant. The ultimate goal is to produce a safe and effective therapy suitable for routine NHS use, improving quality of life for patients and carers. You can listen to an interview with Martin Birchall about progress with the trial in this issue’s MRC Talks podcast at www.mrc.ac.uk/network

• Another approach to help patients requiring organ transplants is to see whether transplantation of stem cells can stimulate damaged tissue to repair itself. Professor Stuart Forbes, at the MRC Centre for Regenerative Medicine in Edinburgh, is investigating how cells called macrophages, which are extracted from patients’ bone marrow, can be used to encourage damaged liver cells to repair themselves.

Find out more about the MRC’s regenerative medicine research at: www.mrc.ac.uk/spotlights/rm
Despite the rising profile of dementia in public discourse, the stigma associated with it remains a big problem, affecting many aspects of life for sufferers and their carers. A new report, championed by the MRC, suggests this social stigma is impeding early diagnosis, care and research into the disease, and requires society-wide action. Isabel Baker reports.

For many people, a diagnosis of dementia brings with it not only a fear of the condition itself but also a fear of how society perceives those with the disease. There’s a stigma which surrounds dementia, in the same way that HIV and even cancer were negatively branded many years ago.

Those living with dementia report discrimination, isolation, maltreatment and often outright abuse. No wonder people over the age of 55 fear being diagnosed with dementia more than any other condition and at least one in four people hide their diagnosis because of social stigma, according to data in the new report.

The impact of social stigma

Fear of being stigmatised may result in self-regulated exclusion, such as through avoiding a diagnosis, which may prevent people from planning for the future, or accessing treatments available to improve symptoms or slow down the progress of the disease.

“This report provided a unique opportunity to focus on a little-researched area that has a major impact within society,” said Professor Hugh Perry, Chair of the MRC’s Neuroscience and Mental Health Board. “We wanted to highlight what may not be widely realised – that stigma exists and that the evidence shows it is likely to worsen a person’s symptoms and quality of life through loneliness and rejection.”

The report, published by the think tank International Longevity Centre UK (ILC-UK) in collaboration with the MRC, Alzheimer’s Research UK, Alzheimer’s Society and supported by drug company Pfizer, reveals the impact that fear of dementia has on those living with the condition, their families and carers, and the research community.

“If people are too frightened to address early signs of dementia, we can’t possibly get a full picture of the disease from a research perspective, to understand how the disease first develops and how it varies from person to person,” said Hugh. “It’s clear that more needs to be done to understand the roots and causes of dementia and stamp out social stigma.”

Working together

By stimulating a conversation about stigma, the roots of it can begin to be addressed. “We hope by working together we can start to move forward and help reduce the everyday discrimination and inequalities so many people with dementia and their carers face,” said Sally-Marie Bamford, Director of Research and Strategy at ILC-UK.

As well as bringing together the views of some of the leading minds from the field of dementia and other relevant health conditions, the report includes personal experiences of dementia, from the carer to the clinical perspective. It also identifies what actions and interventions are required to reduce stigma and to promote a positive awareness of dementia across all communities.

Taking action

Getting a better picture of the early stages of dementia – part of the focus of a new powerhouse for dementia research, established by the MRC – will bring an improved perspective on what research is needed. Dementias Platform UK (DPUK) is a £53m collaboration between universities and drug companies that will create the world’s largest study group for the use in dementia research. Using health and lifestyle information from over two million people over the age of 50, as well as data from the lab, the DPUK will focus on improving early detection, treatment and ultimately the prevention of dementia.

Behavioural change

As well as investment in research, greater awareness and behavioural change within society is important. As noted by George McNamara, Head of Policy and Public Affairs at Alzheimer’s Society – beating dementia won’t just happen in a lab.

Encouraging anyone with early signs of dementia to overcome their fear or misgivings and seek support at the earliest opportunity, and improving understanding will be important, in order to make stigma a thing of the past.

The report is available from www.ilcuk.org.uk

Dementia refers to a set of symptoms that occur when the brain is damaged by certain diseases, including Alzheimer’s disease, or a series of small strokes. Symptoms include memory loss, mood changes and problems communicating and reasoning.

There are four main types of dementia: Alzheimer’s disease, vascular dementia, dementia with Lewy bodies, and frontotemporal dementia. There are also many other rarer causes of dementia, including prion diseases such as Creutzfeldt-Jakob disease.

Find out more about the MRC’s research on dementia at www.mrc.ac.uk/spotlights/dementia
MRC Senior Non-Clinical Research Fellow Dr Eva Hoffmann is trying to find why a woman’s risk of having a baby with a chromosomal disorder – such as Down syndrome – increases with age.

I started my own lab after quite a short postdoc – three years – when I was awarded my Royal Society fellowship. I undertook this at the MRC Genome Damage and Stability Centre, now embedded within the University of Sussex. I’ve been an MRC Senior Non-Clinical Research Fellow for four years and that’s really allowed me to do more blue skies research that is paying dividends now.

Research focus
I’m interested in understanding how the information encoded in our genomes and chromosomes is transmitted accurately to the next generation. For human health this is very important because there’s a high level of pregnancy loss associated particularly with a woman’s age. Today, more women over 30 are giving birth than in past generations – in the UK, women 35 and older account for around 20 per cent of all births.

We’re trying to understand which environmental and genetic factors may influence why women are so susceptible to trisomic conceptions – where the presence of an extra copy of a chromosome can cause chromosomal disorders, such as Down syndrome.

Working with clinicians, ethicists and embryologists we look directly at human eggs and embryos to find genetic factors that might have influenced the transmission of chromosomes into the mother’s egg. We also use model organisms, specifically mice and baker’s yeast, to look at genetic factors that may be similar across species.

Day-to-day work
My work is exciting and varied. I spend a quarter of my time in the lab and another quarter discussing project development. The rest is spent making sure we adhere to regulations and keeping up with the literature; we work with precious material and we’re looking across many different fields, from genetics to embryology and IVF. Quite often, I have to travel to get to material – eggs and embryos – that can’t be moved. I also visit collaborators to make sure that our protocols are aligned and we adhere to ethical and legal regulations.

I have a good work-life balance; I actively manage it and I think that’s the key. By seeing more women at the later career stages, in leadership roles and independent roles, I hope it will also filter down to the postdoc level, to show that it is possible to combine the pressures of for example having a family and having a successful research career.

The Human MeioMap Project
The MRC Fellowship has allowed me to start a bigger project, the Human MeioMap Project. It’s a global consortium of more than 50 scientists. We’re trying to map genomic and genetic changes taking place in the human germline (egg and sperm cells).

The overarching aim of the Human MeioMap Project is to try and integrate environmental effects, lifestyle choices and general ageing factors. But to do this, we first need a basic understanding of which factors affect the transmission of genetic material.

We currently focus on age-related fertility deterioration, a complex disease that affects 20 per cent of women around the world. In women the transmission of genetic material, through a process called meiosis, starts during foetal development and then stops for decades until the cell is ready to mature and be released as an egg. This ‘stop gap’ is thought to cause enormous problems.

From their mid-30s to the age of 40, up to 60 per cent of a woman’s eggs will have chromosome mistakes. By finding out what happens to chromosomes during this stop gap, we hope to understand what clinical biomarkers could be developed in order to assess whether women are at risk. We are also assessing the benefits of freezing eggs versus the clinical risks associated with egg collection, with some companies offering egg banking to young female employees this is important from a societal perspective.

We work with industrial partners, like Illumina who develop genetic tests. One of the biggest achievements of our project is bringing together stakeholders who would normally be competitors, and gaining their trust.

We are also aiming to develop tools for the clinic and the lab. An example is egg activation therapy; about a third of human eggs in the clinic fail to activate when the sperm fertilises the egg. We can activate a human egg chemically and then assess whether the activation process worked, taking the sperm and embryos out of the equation. Ethically that paves the way for a lot of different experimental approaches.

Career highlight
Doing genomics with model organisms combined with the clinical aspects, via our clinical collaborations, is a tremendous privilege. The fellowship has been a fantastic opportunity to move into a different type of research.

I’ve enjoyed interacting with so many fantastic scientists at various stages. When you look at all of the great scientists out there, they’re all passionate about their research and I think it’s incredibly important to have that passion.

Future
We’re currently trying to integrate data from eight different clinics and platforms. It is going to be a massive endeavour from an ethical, clinical, informatics and statistics perspective, but it should allow us to stratify the data and translate the science back into the clinic to help patients with their reproductive choices.

Interview by Isabel Baker
**Network** is for anyone who has an interest in the work of the MRC, including scientists, doctors and health professionals involved in medical research, government departments and parliamentarians, and university staff and students. The aim is to provide a quick, easy-to-read summary of activities across the MRC, from research news through to funding, grant schemes and policy issues, with pointers to more in-depth information on websites and in other publications.

We are keen to receive feedback on Network and suggestions for new features from our readers. So if you have any comments, please email: network@headoffice.mrc.ac.uk

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