Secrets of our first seven days

Behind the picture: the first TV doctor
Dementia research institute established across the UK

The UK Dementia Research Institute (UK DRI) has announced five centres that are joining its headquarters at University College London (UCL), laying the foundations for an eventual 400-strong community of researchers.

Centres are being established across the UK at The University of Cambridge, Cardiff University, The University of Edinburgh, Imperial College London and King’s College London.

The centres will soon begin work on 27 research projects, from a £55m investment. These will provide answers to some of the most pressing questions about dementias, and kick-start the work of the UK DRI.

By focusing on the nuts and bolts of neurodegenerative brain diseases, the institute will reinvigorate the discovery of new drugs for dementia. UK DRI researchers will look at the problem from all angles, such as finding ways to manipulate the brain’s natural defence mechanisms, and unravelling the roles of metabolism, sleep, bacteria in the gut and much more.

UK DRI Director Professor Bart De Strooper said: “The shared vision between the centres to truly understand dementias and how they progress will be at the heart of the UK DRI’s success. We selected the centres based on scientific excellence, evidence of strong leadership, the alignment of goals with the institute as a whole, and the ability to grow and collaborate as the institute gathers pace.”

New plan for mental health research

The MRC has launched an updated research strategy to improve our understanding of the underlying causes of mental illness and to speed up the development of new treatments through laboratory science.

Mental health issues, such as anxiety and depression, are estimated to affect around one in six people at any time in the UK, costing the economy an estimated £70-£100bn a year.

The new strategy has a particular focus on:

- Looking at mental health and illness over our whole lifespan with special emphasis on youth and adolescence, because of the impact of early life experiences on lifelong mental health.
- Harnessing data from patients and the NHS and using the latest informatics technology and expertise.
- A big new investment in global mental health. This will fund scientists to develop our understanding of the interactions between biology, environment, culture, cognition and experiences during youth that contribute to mental health disorders in people worldwide.

Read more at: mrc.io/2p3tWPY
New institute to drive national data research

Professor Andrew Morris, a leading health data research expert, has been appointed director of a new health and biomedical informatics research institute.

Health Data Research UK (HDR UK) will, in a world first, bring together on a national scale laboratory, clinic and population data science research to improve health.

Drawing on the power of the NHS and associated health and biomedical data in the UK, HDR UK will develop and apply sophisticated informatics approaches needed to address the most pressing health research challenges.

Professor Morris commented: “The UK has world renowned data resources and research capabilities. As the volume and complexity of health data increases, there is an extraordinary opportunity to harness advances in mathematics, statistics and computer science to develop the medical science of tomorrow. HDR UK will enable us to remain at the forefront of this new field of health research.”

HDR UK is a joint investment led by the MRC, together with the UK health departments of England, Scotland and Wales; the Engineering and Physical Sciences Research Council; the Economic and Social Research Council; British Heart Foundation; and Wellcome.

Find out more at: mrc.io/2quiFqm

More for your money

The MRC’s new Economic Impact Report shows the positive impact on health, society and the economy of investing in medical research.

MRC funding for research is part of an investment of £3.4bn by the Research Councils UK in 2015/16.

As well as examples of how the MRC benefits the economy and society, the report is packed with stories of how our research is helping to save lives and improve health. Some examples are below:

**MRC-funded research is helping to contain the Zika outbreak in South America using technology from Oxford Nanopore Technology, a company that started as an MRC spin-out a decade ago.**

**A new form of an antibiotic resistance gene was discovered in bacteria in China by MRC scientists in 2015. As a result, the Chinese Government rapidly moved to ban supplements of the antibiotic colistin from animal feed, to prevent resistance developing to this ‘last resort’ drug.**

**Collectively the MRC, Cancer Research UK, Wellcome, University College London, Imperial College London and King’s College London have raised £650m to build and run The Francis Crick Institute: the largest biomedical research institute under one roof in Europe.**

Read the report at: mrc.io/2r39hcp
Science busking at the Crick

Scientists from the Francis Crick Institute practised their ‘science busking’ skills at the first Crick Late in May. Here, Irene Reguilon is carrying out a Mystery Object busk with members of the public (including actor Reece Shearsmith) who are trying to guess the purpose of a series of random objects taken from the lab.

Although the phrase might conjure images of scientists desperately pipetting to entertain bored commuters, science busking is all about scientists approaching people at events and festivals to show them intriguing and entertaining science demonstrations.

Visitors to the evening public engagement event also got the chance to find out why fruit flies are used as model organisms, compare tea towels to proteins, and chat about the science of the everyday.

The Francis Crick Institute recruited 18 new science buskers from across the organisation and its partners in April. They will be in action again at the MRC Festival of Medical Research, with the Crick Discovery Day on 17 June.

Become an MRC Festival citizen scientist

At this year’s MRC Festival of Medical Research, running from 17-25 June, we’re inviting the public not only to find out about life-changing MRC research taking place near where they live, but to also take part in our public participation and citizen science projects online.

Sometimes our scientists need help completing a research project; there may be lots of data to categorise or analyse – as in our Worm Watch Lab project – or they may need your help collecting data. Some projects, such as A Century of Amplified Sound, might also ask you to provide personal data.

The 2017 Festival project will ask you to collect and share data about factors that might affect your mental wellbeing. Find out about our upcoming and previous projects at: mrc.io/2rKabuY

Would you like to win an award of £1,500 by telling us why your research matters?

Enter the 2017 Max Perutz Science Writing Award to give it a go:

- In 800 words describe your research to a non-scientific audience
- Competition opened Tuesday 2 May 2017 and closes 5pm Tuesday 4 July 2017
- Shortlisted entrants will be invited to a masterclass and an awards ceremony in central London

Find out how to enter: mrc.ac.uk/maxperutz
maxperutzaward@headoffice.mrc.ac.uk
@The_MRC #maxp17
facebook.com/mrccomms
What exactly is gene editing? Why is it important in medical research?

Last year, developmental biologist Dr Kathy Niakan got the first ever licence to carry out gene editing in very early human embryos using a new technique called CRISPR-Cas9. She explains all.

Tell us about your research and what you’re trying to find out?

Our lab, at The Francis Crick Institute in London, is really interested in understanding how human embryos develop during the first seven days of development.

We all start off as a fertilised egg, which then divides to form two cells, then four cells, eight cells and so on until it forms a structure called a blastocyst at around day six. At some point around the eight cell stage we think that some of these cells are being set aside. These few cells divide to produce about 20 clumps of cells which go on to become the embryo, while the vast majority of the other cells will be set aside to form the placenta and yolk sac.

What fascinates us is, how does this happen? From this group of cells which all had an equal chance of becoming either an embryo or placenta and yolk sac, how are these cells set aside? They’ve all inherited the same DNA blueprint, it’s just that they are reading that DNA differently.

So we want to know what is the key gene that ‘flips the switch’ and decides their fate?

Interesting stuff – but how might that ultimately help people?

Well, first of all, it has importance for stem cells. If we could better understand how these 20 clumps of cells are set aside to form the embryo that could allow us to significantly improve upon methods for maintaining these cells indefinitely in a petri dish – as a type of stem cell called human embryonic stem cells (hESCs). Such cells would be truly ‘pluripotent’ ie could go on to form any cell in the body. That has a huge array of potential applications for research and for health, for example growing nerve cells to study Parkinson’s disease or making insulin-secreting cells to treat diabetes.

The other reason why it’s so important is for improving the success rate for in vitro fertilisation (IVF). Currently only about 40% of IVF embryos make it to the blastocyst stage. Typically only half of those blastocysts will implant into the uterus, and not all of those will result in a live birth – so for a woman going through a cycle of treatment there’s less than a 20% chance of a successful pregnancy.

If we can understand more about the molecular processes going on in the blastocyst we might be able to find biomarkers to pick out the embryos with the highest probability of survival and thereby boost IVF success rates.

So what is CRISPR-Cas9 gene editing and how are you using it in your research?

CRISPR-Cas9 is often been described as a pair of ‘molecular scissors’ to cut strands of DNA in a very precise way. The technique consists of making a ‘guide RNA’, a molecule that’s complementary to a particular section of DNA (for example a gene), that we want to target.

The guide RNA finds the chosen section of DNA and directs the Cas9 enzyme to cut the strand of DNA. The DNA repair mechanisms that exist in all of our cells can be error prone, and, while trying to repair the cut to the DNA, it inactivates (or ‘knocks out’) the gene we’re interested in.

In our research we want to use CRISPR-Cas9 to ‘knock out’ a gene called Oct4, which we suspect is important in allocating the cells that go on to become the embryo.

If we are able to remove the Oct4 gene at the one-cell stage and then allow that embryo to develop up until day seven, we’ll be able to test whether the blastocyst will still develop without Oct4. If it does, we can find out whether those 20 cells are normal or affected negatively in some way.

Why did you pick Oct4?

Lots of previous research has shown that Oct4 works to keep human embryonic stem cells pluripotent. It’s the most likely gene to have a very overt, obvious effect on the embryo so it seemed like a good candidate to test whether using CRISPR-Cas9 is effective or not. Basically we wanted to pick a gene where it would be very obvious to us that our methods were working.

But haven’t scientists already been able to alter DNA for a long time? What’s special about CRISPR-Cas9?

It’s effect can be seen really quickly and the probability of actually being able to ‘knock out’ the function of a given gene is much higher. Other methods for gene editing exist, for example something called homologous recombination.
But those methods are just orders of magnitude less efficient. With CRISPR-Cas9 we would need to use far fewer embryos to be confident that we’d actually affected Oct4 function, and I think it’s really important that we don’t waste human embryos using inefficient methods.

It’s just an amazing system. It’s transforming pretty much every field in basic biology.

Why do you need to use human embryos? Couldn’t you have used animal embryos instead?

We should never underestimate the difference between early human embryo development and that of other organisms. Research data show that there are fundamental differences in the timing of gene expression between human and animal embryos, for example. It would have been so easy for us if the genes and when they are expressed during early development was the same in humans and in established animal models like mice, but that’s not the case. The only way to discover the true picture of what’s going on is to study human embryos.

It’s been a year since you were granted the licence. What have you done so far?

We can’t justify using any human embryos until we are absolutely sure about the methodologies. For example we weren’t clear on how to design the right guide RNA, so we’ve spent the better half of a year optimising that, methodically testing every single possible guide RNA in human embryonic stem cells. We were also uncertain about how to inject the guide RNA into a one-cell embryo so we’ve been working with lots of very generous people across the world who have pioneered this technique in other contexts, who shared with us their pre-published data. We just want to start from scratch and make no assumptions.

So that’s all done before we even go near a human embryo. From the start we’ve agreed that if any of these pre-embryo studies at all raised a red flag, then we won’t proceed. Because it’s not justified.

Is there a risk that use of CRISPR/Cas9 in human embryos could open the door to the creation of so-called ‘designer babies’ where people get to, for example, pick the eye and hair colour of a child?

No. Here in the UK there is so much oversight from the regulators of what scientists who’ve been granted licences are doing. The Human Embryology and Fertilisation Authority regularly come to our lab to inspect our work. And there is a very clear boundary is between what is legally permitted and what is not. It’s not possible to cross that line. It would be a criminal offence.

The only way that gene editing could move in any other direction is if society agrees to that, and if the laws were changed.

Further reading:

Future of regenerative medicine looks bright

New multimillion funding for the UK Regenerative Medicine Platform (UKRMP) will help get new therapies to patients faster.

Regenerative medicine has already led to many medical advances, including growth of new skin for burns and the treatment of iron deficiency. But it has the potential to go much further, as new products offer treatments with long-term benefits or even cures.

The three partners of the funding initiative – the MRC, Engineering and Physical Sciences Research Council and Biotecistry and Biological Sciences Research Council – have committed £17m over five years.

Dr Rob Buckle, UKRMP Director and MRC Chief Science Officer said: “The UKRMP has been pivotal in nurturing this increasingly promising field of research. It has done this by bringing different scientific disciplines and teams together to help bridge the conceptual gap between scientific discovery and efforts to bring new therapeutic products to the clinic market. This will help realise the ultimate goal of making new, safe and effective regenerative therapies available to the clinic and to the patient.”

Read more at: ukrmp.org.uk
**LATEST DISCOVERIES**

**Old drugs, new dementia treatments?**

A team of MRC scientists have discovered that two existing drugs can stop neurodegeneration – the death of brain cells – in mice.

The drugs caused minimal side effects in the mice and as one of the drugs, trazodone, is already licensed for use in humans, it is ready for clinical trials.

Previously, the team had found that the accumulation of malformed proteins in mice resulted in a natural defence mechanism being activated, “switching off” the vital production of new proteins in brain cells. The researchers then looked for ways to restore healthy protein production and so prevent further degeneration.

The MRC Toxicology Unit’s Professor Giovanna Mallucci, who led the research, said: “We know that trazodone is safe to use in humans, so a clinical trial is now possible to test whether the protective effects of the drug we found in mice also apply to people in the early stages of Alzheimer’s disease and other dementias. We could know in two to three years whether this approach can slow down disease progression.”

Published online at: academic.oup.com/brain, 20 April 2017.

**‘Mini-brain’ discovery could help soothe pain**

Nerve cell structures found throughout the body may be able to control pain, new research suggests, pointing the way to development of new pain relief drugs with fewer side effects.

The scientists who made the finding, at Hebei Medical University in China and the University of Leeds, believe it challenges our understanding that pain is controlled solely by the brain and spinal cord, known as the ‘central nervous system’. Current pain relief drugs are targeted at the central nervous system but side effects can include addiction and drowsiness.

The team studied how rats and mice reacted to stimulation with warmth and touching a solid object. Results showed that peripheral nerves (which are found throughout the body) could interpret information they were sensing using specialised nerve cell structures, before it passes to the brain.

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Professor Nikita Gamper, who led the research at both universities, said: “Further research is needed to understand exactly how it operates, but we have no reason to believe that the same nerve arrangements would not exist in humans.”

Published online at: www.jci.org, 4 April 2017.

**Drug halts hot flushes**

Women plagued by frequent hot flushes during menopause could cut the number of flushes by almost three-quarters, thanks to a new drug compound.

In a trial carried out at Imperial College London and co-funded by the MRC and the National Institute for Health Research, researchers found that women who suffer seven or more hot flushes a day could reduce the number by as much as 73%, as well as reducing their severity and impact.

The team hopes that this successful early-stage study could provide hope for women who are affected by flushes and for whom hormone replacement therapy (HRT) is either unsuitable or not preferred by the patient due to safety concerns.

Professor Waljit Dhillo, from the Department of Medicine at Imperial, said: “If a woman is having more than seven flushes a day and the drug is getting rid of three-quarters of them, that’s pretty life-changing. These are exciting findings which could be practice-changing. The plan now is to find out if the compound can be as safe and effective over the long term in a larger group of patients.”


**Bats reveal virus history**

Traces of an ancient virus that causes a rare kind of human leukaemia exist in modern-day bats, MRC-funded research has found.

The discovery of viral DNA fragments in the genetic code of Bent-winged bats fills the last gap in the historical record of a viral family scientists call Deltaretroviruses. It provides evidence that these viruses are 20 to 45 million years old and have long infected mammals. The complete history will now help scientists to figure out how humans and other mammals defend themselves against the virus.

Deltaretroviruses include those that cause Adult T Cell Leukaemia/Lymphoma (ATLL). Worldwide up to 20 million people are thought to carry a virus capable of causing ATLL. It is rare for a person living in the UK to catch a Deltaretrovirus and most people who do pick up the infection will not develop leukaemia.

Dr Robert Gifford of the MRC – University of Glasgow Centre for Virus Research said: “Our discovery fills the last gap in the fossil record of retroviruses. Understanding the history of these viruses will help scientists learn more about how they affect people and animals now and in the future.”

Published online at: www.pnas.org, 7 March 2017.
**Autism tool may help babies**

Research into a video-feedback tool developed for parents of babies at risk of autism suggests it could reduce the severity of symptoms as the child grows.

The early intervention tool is the first to be developed for babies who have an older sibling with autism and so an increased genetic risk of developing the condition themselves.

Of the 54 families who took part in the study, 28 had six or more visits from a therapist who used video feedback to help parents understand and respond to their baby’s individual communication style between 9 and 14 months old.

The study found that infants from families who had video therapy showed improvement in early behaviours associated with autism, compared to those who did not.

Although encouraging, the MRC-funded authors caution the small number of participants means the results cannot be conclusive.

Jon Spiers, CEO of autism charity Autistica said: “Parents often sense their child is developing differently very early on, yet getting a diagnosis of autism can take years. Being able to deliver an intervention during this uncertain period would be a promising step forward for many thousands of families.”

Published online at: www.nature.com/ng, 24 April 2017.

**Early puberty, higher cancer risk**

The largest-ever genetic study of puberty timing has found 389 independent genetic signals that influence transition from child to adult; four times the number previously known. The study also found a causal link between early puberty timing and cancer risk in later life.

Timing of puberty varies widely and is influenced by factors like body weight, but it was not clear until now whether it has direct effects on disease risks.

By looking at genetic data from more than 360,000 people, researchers found that even when weight is taken into consideration, early puberty is linked to higher risks of breast, ovary and prostate cancers.

Dr John Perry of the MRC Epidemiology Unit at the University of Cambridge explains: “Our study shows a clear link between early puberty timing and a person’s risk of developing cancer. This could be explained by greater exposure to sex hormones throughout life in a person who reaches puberty earlier than others. We now need to do more work to understand what the mechanisms are and how we could use this knowledge to prevent cancer and other related diseases in later life.”

**One-off test cuts bowel cancer risk**

A one-off bowel screening test reduces the risk of developing bowel cancer by more than one-third and could save thousands of lives.

The bowel scope test uses a tiny camera, attached to a thin flexible tube, to examine the lower part of the large bowel. It can spot small growths, called polyps, on the bowel wall so they can be removed straight away. If polyps are left untreated they may become cancerous.

The researchers, funded through the MRC and National Institute for Health Research Efficacy and Mechanism Evaluation Programme, and by Cancer Research UK, found that the test prevented more than half of potential bowel cancers from developing in that area and two thirds of deaths were avoided.

It is the longest study ever done on the effectiveness of the test, following more than 170,000 people for 17 years on average and testing more than 40,000.

The test will be rolled out across England over the next three years, for people aged 55.

Published online at: www.thelancet.com, 21 February 2017.

**GPs trial ‘sponge on a string’ cancer test**

A simple, low-cost test for early stage oesophageal cancer, developed with MRC funding, is now being trialled at 150 GP surgeries across the UK.

The cytosponge test consists of a small sponge inside a capsule attached to a string, which is swallowed with water. It expands inside the stomach into a mesh which is pulled back up the gullet, collecting cells from the lining of the oesophagus that can be analysed with a molecular test for cancer. It was developed at the MRC Cancer Cell Unit at the University of Cambridge by Professor Rebecca Fitzgerald’s team.

The trial, being run by Cancer Research UK, will find out if the test can increase the number of diagnoses of Barrett’s Oesophagus, a condition which carries an increased risk of developing oesophageal cancer.

Dr Fitzgerald explains: “The cytosponge costs just a fraction of the traditional endoscopy examination, is more comfortable for patients and can be used easily in the GP surgery. Furthermore, the molecular test may be more specific at predicting cancer risk than standard biopsies.”

If the test is shown to be cost effective and well accepted by patients it is expected to be adopted as a standard test on the NHS.


Published online at: www.mrc.ac.uk/cytosponge

Find out more at: mrc.ac.uk/cytosponge
Behind the picture: the first TV doctor

Nowadays few people would dispute that it’s important for people to know about medical matters, but that wasn’t always the case. As our Max Perutz Science Writing Award opens to MRC-funded PhD students, Katherine Nightingale looks back at Charles Fletcher, MRC researcher and physician, whose strong belief in medical communication led him to become the first ‘TV doctor’ in the 1950s.

You don’t notice it at first – your eye is drawn instead to the strangely bandaged faces of the people to the left of the image. But there, together with the IV stand, scissors and scrubs, is not a piece of surgical equipment but a 1950s television camera and lights.

What’s it doing there? Filming a medical drama? Broadcasting the television news live from a hospital? Not quite. Instead it’s the filming of Your Life in Their Hands, a controversial medical documentary which began in 1958.

The programme beamed discussions of treatments – and, on occasion, actual operations – into the nation’s homes. The aim was to inform the public about medical conditions and demonstrate modern medical treatments, with the first series of 10 episodes including topics as diverse as radiotherapy and treatment for head injuries.

It was presented by Charles Fletcher, a doctor and epidemiologist whose career was intertwined with the MRC from its early stages. He also happened to be the son of our first chief executive – then known as secretary – Sir Walter Morley Fletcher.

Charles’s long and varied career put him centre stage in a remarkable number of significant events in medical history. As a house officer at the Radcliffe Infirmary in Oxford in 1941 he gave the first injection of penicillin to a patient. His tenure as head of the MRC Pneumoconiosis Research Unit in Cardiff between 1945 and 1952 led research which discovered how pneumoconiosis could be prevented in miners. And in 1962 he edited the Royal College of Physicians’ seminal report on the dangers of smoking for health.

His life away from science was equally varied. Educated at Eton and Trinity College, Cambridge, he rowed in the winning Cambridge boat in the 1933 boat race, dabbled in amateur dramas during his medical education, and sang in a choir.

A radical thinker
But it’s his passion for medical communication that we’re interested in here. Despite his privileged upbringing, Charles was something of a radical thinker – a supporter of the NHS (at a time when many doctors were not) and a member of the Socialist Medical Association. He was a strong believer in people having knowledge of medicine and their own health, in sharp contrast to the paternalism many of his colleagues would have practised.

For example, at the time it was commonplace for doctors not to reveal diagnoses to patients, a fact that seems startling today. Nowadays we’re used to doctors as presenters on television programmes explaining the latest research and techniques. Charles began advising on, and presenting, one-off and short-run documentaries during the 1950s, becoming the first presenter of Your Life in Their Hands in 1956.

Perhaps drawing upon his interest in the theatre, Charles was a confident and reassuring screen presence. The technology to record video wasn’t yet available, so he would hand over to doctors explaining diseases and procedures live, and to patients talking about their illnesses, in hospitals around the country.

The secret code
The show had a largely positive response from the public and the press. But it drew criticism from doctors, including accusations that Charles was seeking personal publicity as well as “destroying the mystique of medicine” by pulling back the curtain on a world that many health professionals were content to keep hidden from patients.

“They said it was improper, that it would cause hypochondria and frighten people,” Charles told the British Journal of Addiction in 1992. “Here was somebody breaching the secret code that doctors thought was their own.”

His involvement in the programme even put his career at risk, with his then boss suggesting he would not be put forward for promotion if he continued. “But I felt I couldn’t leave it mid-stream. I thought its benefits were going to be greater than any harm it might do,” he said.

The programme has periodically returned to our screens, including a long run in the 1980s with Professor Lord Robert Winston as presenter.

Charles remained interested in communication in the latter part of his career, being awarded a Rock-Carling Fellowship in 1972 on ‘communication in medicine’ and the public understanding of medical care. Find out more about our Max Perutz Science Writing Award on page 7.

Further reading
Your Life in Their Hands, The Lancet, 2006
Conversation with Charles Fletcher, British Journal of Addiction, 1992
WORKING LIFE

Damian Mole combines surgery with research. He has just been awarded a prestigious MRC Senior Clinical Fellowship to find out why people who’ve had acute pancreatitis have a shortened lifespan, even after they seem to have fully recovered.

I like to pretend that I can trace my interest in surgery back to my childhood living in Greece. I used to love watching fishermen mending their nets on the beach – I’d sit there for hours. You learn the same way with surgery; you spend a lot of time in the operating theatre watching people make very delicate, skilled movements with their hands.

The first time I saw an operation was a Road to Damascus moment for me. Surgery is the only branch of medicine where you actually see physiology, anatomy, biology in action before your eyes. It’s such a privilege. It’s a great team environment and there’s such a buzz about it. I still get that feeling every time I walk into an operating theatre.

I’ve never been entirely comfortable taking anybody’s word for anything. It must be very annoying for people. It’s not that I disbelieve people, but I like to understand why things are the way they are, rather than just taking the dogma or the status quo as a done deal. That’s why I love research, you really get to see what’s ‘under the bonnet’. The excitement when you realise you’ve found out something about the natural world that only you know is unsurpassable.

I’ve been researching a disease called acute pancreatitis for nearly 20 years, since before my PhD. It’s quite common, and caused by excessive drinking, gallstones or trauma. It causes the worst abdominal pain you can possibly imagine, which is often resistant to all painkillers. On average it kills one in 20 people who get it. Around a quarter of patients get dysfunction of organs separate from the pancreas – usually the lungs or kidneys – and go into intensive care; for them the likelihood of dying is one in five.

I want to find out why people who have had acute pancreatitis tend to die younger than those who haven’t, even after they have completely recovered. By looking at national death certificate data my research team found that those who’ve recovered from acute pancreatitis die, on average, three years sooner than those who’ve had less severe pancreatitis. We want to know what is damaged or changed in the body that has this lasting effect.

My MRC senior fellowship funding, which starts this year, will allow us to recruit and study a large number of people with pancreatitis and measure lots of things about them: their anatomy, physiology and genetics. We’ll do that at the time of their pancreatitis, three months after – when they’ve recovered – and then again two years later to see what parts of their organ systems or cell types have changed.

We’re particularly looking at a process called senescence, where cells lose their ability to divide and grow, but are still alive. If the cells in an organ are senescent then it’s likely that the organ itself will become senescent and ultimately fail. If we can unpick the molecular processes behind all of this, we can develop new drugs for pancreatitis patients to prevent an early death.

People who’ve had acute pancreatitis are more likely to get other diseases such as diabetes, so we might also be able to screen for those at greatest risk and intervene before it happens. The potential savings to healthcare worldwide could run into billions of pounds.

Combining research and clinical work can be a tough balance to achieve. My MRC fellowship is critical, it makes everything happen – it pays salaries, runs labs. Most of all it gives me a solid platform to deliver this research project, so that I’m free of the perpetual cycle of applying for funding and able to fully immerse myself in the science. The fact that taxpayers’ money is invested in my research gives me a great boost.

I’m quite firm with myself about maintaining a healthy work-life balance. In the long-term your work can suffer if you don’t have outside interests. I still want to love what I do when I’m age 65 or 70. I have four daughters, two of them identical twins, and they keep us very busy. One night each week I play trumpet in a jazz band. The others are much better musicians than me, so I have to concentrate hard to keep up. When I stop, the work stress floods back in, but for those two hours I have been totally absorbed, and it feels great to know that.

If I could choose my legacy, it would be that the people I’ve trained over the years will come to love academic research as much as I do. And it would be brilliant if my research could help pancreatitis patients to live longer and healthier lives than they do now.

The patient’s story

John Lawrie, 47, is a father of two who works in IT. He had an episode of acute pancreatitis a year ago and it is still having a huge impact on his life.

His illness started with agonising pain in his abdomen that left him curled up in a ball, struggling to breathe. Tests revealed that John had hepatitis – caused by gallstones – which also had caused his pancreas to become inflamed (acute pancreatitis). He later ended up having surgery, carried out by Damian Mole, to remove his gall bladder.

Recovery has been slow. The pancreatitis hasn’t gone away and John is still on regular pain relief medication. While struggling to recover he has also been diagnosed with diabetes, caused by the damage to his pancreas.

“That level of pain I experienced – there’s nothing that comes close to it,” explains John. “Any research that helps to aid recovery from pancreatitis has to be a good thing. A year on, I’m still feeling the effects of that day.”

Career in brief:
• Medicine degree, University of Birmingham
• PhD on pancreatitis-associated organ failure, Queen’s University of Belfast
• Clinical Lecturer, Clinician Scientist Fellow, then Senior Lecturer and Consultant Surgeon, MRC Centre for Inflammation Research, University of Edinburgh
• MRC Senior Clinical Fellowship

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• MRC Senior Clinical Fellowship

The patient’s story

John Lawrie, 47, is a father of two who works in IT. He had an episode of acute pancreatitis a year ago and it is still having a huge impact on his life.

His illness started with agonising pain in his abdomen that left him curled up in a ball, struggling to breathe. Tests revealed that John had hepatitis – caused by gallstones – which also had caused his pancreas to become inflamed (acute pancreatitis). He later ended up having surgery, carried out by Damian Mole, to remove his gall bladder.

Recovery has been slow. The pancreatitis hasn’t gone away and John is still on regular pain relief medication. While struggling to recover he has also been diagnosed with diabetes, caused by the damage to his pancreas.

“That level of pain I experienced – there’s nothing that comes close to it,” explains John. “Any research that helps to aid recovery from pancreatitis has to be a good thing. A year on, I’m still feeling the effects of that day.”

Career in brief:
• Medicine degree, University of Birmingham
• PhD on pancreatitis-associated organ failure, Queen’s University of Belfast
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71 years under the lens of medical research

Sheila Glass is one of over 5,000 people born in one week in 1946 who have been studied by scientists for their whole lives as part of the MRC-funded National Survey of Health and Development. Now aged 71, she told Sarah Harrop about what it’s been like to be one of the most studied human beings on the planet.

Known as a ‘birth cohort study’, the MRC-funded National Survey of Health and Development (NSHD) is the longest-running study of its kind in the world.

Baby boom beginnings
Originally set up to look at maternity services in post-War Britain against a backdrop of falling birth rates, ill health, poor housing conditions and unemployment, the survey later evolved into a cohort study. In such studies, researchers follow a group of people over time and this long-term assessment helps them make important links between genetics, environment, lifestyle and health.

The study’s findings have influenced policy in many areas from the importance of diet in our early years to the impact on our health as adults and made a sound best start in life. Findings from the study have shown that having one hell of a life. It makes you quite aware that your well for someone saying ‘yes’ to all of these they must be been. When I was answering questions for the mood self-reflective: “It’s made me aware of how fortunate I’ve been. When I was answering questions for the mood surveys in my 60s and I was mostly putting ‘no’, I thought well for someone saying ‘yes’ to all of these they must be having one hell of a life. It makes you quite aware that your life could have been very different.”

Of all the contributions the study has made to health and social policy, Sheila is most proud that evidence from the study contributed to the launch of the government’s Sure Start programme to give children under the age of four the best start in life. Findings from the study have shown that diet, growth and health in our early years have a major impact on our health as adults and made a sound argument for intervening at an early age.

Over the years, surveys and tests have arrived in the post which Sheila has dutifully filled out and returned. Nurses have periodically visited to do all kinds of tests and measurements – from blood pressure to lung tests involving blowing up balloons, memory and sorting tests, and measurements of grip strength and sense of smell. More recently she’s had scans of her heart, bones and brain.

“It’s been interesting as I’ve gone through the years and you can see what they were interested in studying; there was lots about hormone replacement therapy in my 40s, and then they asked about depression in your 50s and 60s and now we’re onto dementia.”

“I’ve said they can have my brain and my body when I die. My husband said: ‘Does that mean we don’t have to pay for a funeral?’”

An insight on research
Being studied for her whole life has made Sheila more self-reflective: “It’s made me aware of how fortunate I’ve been. When I was answering questions for the mood surveys in my 60s and I was mostly putting ‘no’, I thought well for someone saying ‘yes’ to all of these they must be having one hell of a life. It makes you quite aware that your life could have been very different.”

Musing on why she has continued to take part over the years, she says: “If you can do something that might add to the sum total of mankind’s knowledge, then why not? It’s an easy enough matter.”

Some findings from seven decades of the NSHD

- 2016: Study members have had a rise in wellbeing in their 70s as compared to aged 60 to 64, as tested with a series of questions about mood and mental wellbeing.
- 2014: Better performance in tests of physical capability (ie grip strength, chair rising and standing balance) in mid life was linked to higher survival rates over 13 years of follow-up. This showed the value of simple objective physical tests in helping to identify people who need more support to live a long and healthy life.
- 1999: A paper comparing children’s diet in 1950 with that in the 1990s showed that the quality and nutrient value of infant and childhood diet had declined between 1950 and 1990.
- 1984: High ability children were found not to continue into further or higher education – the so-called ‘waste of talent’ – adding to arguments for improving opportunities for children from poorer families.
Why patient involvement in research matters

A rare autoimmune condition called systemic lupus erythematosus (SLE) forced Jane Dunnage to give up work. She’s now a charity trustee and leads patient involvement for an MRC-funded trial. Here she explains why it’s so important to involve the patient voice in research.

I had to give up my job in communications about 20 years ago because of the symptoms of lupus. It was affecting my eyes and my joints, and the fatigue was extremely disabling. I found it impossible to carry on working.

But it was another four or five years before I was actually diagnosed. I became a ‘pass the parcel’ around different consultants and departments for a year. Then somebody at long last recognised the link between the wide-ranging symptoms and said, “I think you have lupus”.

Lupus is a complex autoimmune condition where cells in any part of the body can be attacked by the body’s own defences. That means it is complex to live with and causes a wide array of symptoms.

There is no cure. Therapy is complicated and sometimes based on a trial and error approach. The main aim of any medication is to try and keep the immune system from seriously affecting the major organs. Current medications carry side-effects and some patients must take lots of immunosuppressant medication.

Finding the right treatment
Research is focused on finding the right treatment for the right patient. There are four or five treatments that are used regularly, but there is no simple way of knowing which will be effective for which person.

The MRC-funded MASTERPLANS* study aims to change this. It will group people who respond well to specific therapies, then analyse their shared characteristics with the aim of guiding effective treatment for other patients. The study will look for genes, as well as chemicals and cells in the blood, urine and tissues, that may help predict how well patients will respond to lupus treatment.

It was quite revolutionary, and a great honour, to be asked to get involved in the study at an early stage. Being a rare disease, lupus affects a small population. As a LUPUS UK Trustee I got to know the clinicians and scientists involved in lupus research. Then three years ago, Ian Bruce, the Chief Investigator of the study, asked me if I would work alongside him.

We now have 18 different collaborators (14 patients and four carers) who reflect the diverse population affected by lupus – it can affect people of all ages, races and genders. Two patient collaborators sit on each of the five project committees and a working group. This means that we can support each other and ensure a patient voice if somebody’s not well enough to participate.

We’ve put together a range of opportunities for patients and carers. For example, patient representatives reviewed patient information leaflets and questionnaires, made suggestions to help successful recruitment to the study, and spread the word among lupus patients at hospital open days.

Hearing patients’ voices
Patient involvement in research is vital because we can present patients’ views directly to the scientists. We can act as ambassadors to patients and try to get them interested in participating in future trials. Enrolment for the PLANs clinical study (a key part of MASTERPLANS) is underway. This study aims to understand patient responses to two treatments.

It’s still early days. But if we can make this model of patient involvement work, there could be opportunities to replicate it for other illnesses.

We know that as individuals we may not benefit personally from the research. However we hope that the knowledge gleaned will clarify appropriate and effective treatments for patients in the future.

Anything we can do for future patients is important. Just to make some of those huge hurdles a bit flatter – so that lupus is not as devastating an experience, particularly for young people.

“Patient involvement in research is vital; we can present patients’ views directly to the scientists.”

*Maximising SLE Therapeutic Potential by Application of Novel and Systematic Approaches

Find out more on the MASTERPLANS study website: www.lupusmasterplans.org
**YOUR FEEDBACK**

*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. To share your views email network@headoffice.mrc.ac.uk

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