Opinion: How research can give patients a voice

Outfoxing the flu
Why 100 years after the deadly Spanish flu, the fight continues
As Executive Chair of the MRC my aspiration is that the UK should provide the best medical research environment in the world, with superb facilities and creative funding to support excellence throughout the country.

We need to support and encourage excellence while counteracting the belief amongst researchers that a science career is simply an unremitting series of rejections. The recently launched UK Research and Innovation (UKRI) Future Leaders Fellowships (see page opposite) are exciting opportunities for early-career researchers and innovators, and I would encourage anyone eligible to apply.

It is also essential that we support research at interfaces between fields that have not intersected previously, facilitating creativity while avoiding the temptation to micro-manage. This is a high priority for UKRI, including interdisciplinary funding schemes like the Technology Touching Life awards on page 7.

I am currently working hard to learn as much as I can about the MRC and look forward to sharing my vision for the future with you over the coming months.

Professor Fiona Watt
MRC Executive Chair
Developing future research leaders

The UK Research and Innovation (UKRI) Future Leaders Fellowship scheme aims to develop, retain, attract and sustain research and innovation talent in the UK.

Providing up to seven years of funding for at least 550 early-career researchers and innovators, the new scheme, which launched in April, will tackle difficult and novel challenges.

The fellowships can be held at any UK-based organisation currently registered as eligible to apply to the research councils (eg Higher Education Institutes, Research Council Institutes and eligible Independent Research Organisations) or Innovate UK.

Companies or other privately owned research organisations are encouraged to host UKRI Future Leaders Fellowships if they can provide an innovation and/or research environment of international standing.

There will be six calls for the fellowships, with two calls taking place each year for the next three years. Applications can be submitted in any area of research or innovation covered by the research councils and Innovate UK.

Expressions of interest for the second round are due by 4 October.

For further information visit: mrc.io/ukri-ff
£40m for new dementia research building

A landmark £40m has been awarded to the UK Dementia Research Institute (UK DRI), via the MRC, for a new iconic hub building at University College London (UCL).

The funding, which will be matched by significant capital investment by UCL, brings the total committed investment so far for the UK DRI from the MRC and its two charity partners – Alzheimer’s Society and Alzheimer’s Research UK – to £290m.

Globally someone develops dementia every three minutes and today there are around 850,000 people living with dementia in the UK. The Institute will advance the UK’s research efforts to prevent, diagnose, treat and care for those living with dementia.

The UK DRI hub at UCL will host up to 350 scientists, alongside research centres at five other universities. The total number of UK DRI researchers will grow to 700 across its six sites over the next six years.

Dr Rob Buckle, Chief Science Officer at the MRC, said: “Developing the UK Dementia Research Institute hub in partnership with UCL will bring tremendous benefits for science and for health. The new building will provide state-of-the-art facilities for research and the development of new dementia therapies, and will be located alongside neurology clinics with a dedicated space for engaging dementia patients and their families and carers.”

Read more: mrc.io/40m-uk-dri-hub

Max Perutz Science Writing Award 2018

Calling all MRC-funded PhD students!

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

Enter the 2018 Max Perutz Science Writing Award to give it a go:

- In 800 words describe your research to a non-scientific audience
- Competition closes 5pm Wednesday 4 July 2018
- Shortlisted entrants will be invited to a masterclass and an awards ceremony in central London

Find out how to enter: mrc.ukri.org/maxperutz

sciencewritingprize@mrc.ukri.org
@The_MRC #maxp18
facebook.com/mrccomms
Genome sequencing of first 50,000 UK Biobank participants

UK Biobank are embarking on a major initiative to sequence the full genomes of 50,000 UK Biobank volunteer participants.

Funded by a £30m grant from the MRC, sequencing of the whole genome will be undertaken during 2018 and 2019 by the Wellcome Sanger Institute, based in Cambridge.

UK Biobank and the MRC are taking advantage of the revolution in genetic analyses that makes large-scale sequencing possible at an ever-quickening pace.

Dr Nathan Richardson, Head of Molecular and Cellular Medicine at the MRC, said: “The UK Biobank partnership is the MRC’s largest single commitment to understanding the contribution of genetics, environment and lifestyle in maintaining good health, and complements our numerous in-depth research programmes targeting specific diseases.

“Our goal, with the support of our participants, is to ensure that the UK Biobank resource is used for the widest range of health research to bring about advances in our understanding of disease as quickly as possible.”

Read more: mrc.io/biobank-dna-sequencing

Getting involved

There are many ways you can take part in and support medical research.

Take part
You can give permission for your health information to be used in a study, donate your body, some tissue or your brain, take part in a population-based study or, if you are undergoing treatment, join a clinical trial. You may also wish to consider volunteering on our Public Panel or donating to the Medical Research Foundation to support more research for human health.

Help our researchers
Sometimes we need help from members of the public to complete a research project. Our public participation and citizen science projects would also welcome your involvement.

MRC Festival
The MRC Festival of Medical Research takes place across the UK and Africa from 14-24 June. Check out our map and lists of locations to find activities near you: mrc.ukri.org/mrcfestival

Find out more: mrc.ukri.org/about/ getting-involved

For more news from across the MRC community, visit: mrc.ukri.org/news
Investing in personalised medicine research

A five-year study has been launched to better understand childhood arthritis, a condition affecting one in 1,000 under-16 year olds in the UK.

The MRC is investing £15m into four stratified medicine projects. Stratified medicine – sometimes called personalised or precision medicine – considers genes, environment and lifestyle to deliver treatment tailored to each patient.

The CLUSTER childhood arthritis study teams up scientists from the UCL Great Ormond Street Institute of Child Health and other UK institutions to follow 5,000 children with the disease.

Currently, the standard treatment only helps around 50% of children. The other half must try different treatments until they find a therapy which works for them. Researchers hope to discover a simple biomarker test so that the right medication can be found without the standard trial and error process.

Lead researcher Professor Lucy Wedderburn said: “A biomarker test could lead to methods for accurately predicting the right treatment for the right duration, halting the worsening of symptoms, and leading to shorter time to remission. Nothing like that has been done before in this area of research.”

Three more projects funded through the Stratified Medicine Initiative:

- ReIMAGINE, to improve screening for prostate cancer
- NURTuRE, which is rethinking how new kidney disease drugs are developed and trialled
- A study on alcoholic hepatitis, aiming to help people manage their condition better.

Find out more: mrc.io/childhood-arthritis

Read about Eilean, a teenager with arthritis who’s helping researchers, on page 14.
Technology teams to solve life science challenges

Five technology research networks have been awarded £3m to unite researchers from different backgrounds in tackling life science research challenges.

Technology Touching Life is a joint initiative between the MRC, Biotechnology and Biological Sciences Research Council (BBSRC), and the Engineering and Physical Sciences Research Council (EPSRC), all part of UKRI.

By encouraging partnerships between engineers, physical scientists, and health and life science researchers, the networks hope to nurture the adventurous research needed to develop the next generation of advanced technology.

Each network focuses on a life sciences challenge where new technology could make a huge difference. These include imaging live cells within tissues and developing ‘organs-on-chips’ that mimic human body parts. The networks are national, providing opportunities for researchers across the UK to get involved as they develop.

Dr Nathan Richardson, Head of Molecular and Cellular Medicine at the MRC, said: “These Technology Touching Life networks offer an exciting opportunity to bring researchers together, across a number of disciplines, to explore the tools and technologies of the future.”

### The technology networks

**The ImagingBioPro Network** aims to develop new imaging methods to picture the complex processes in biological samples in real-time.

**3DBioNet** will explore the best ways to grow cells in 3D, to better mimic their natural state in the body.

**PhenomUK** will develop technology to collect information about the structure and function of plants, to help farmers meet the food demands of our growing population.

**Organ-on-a-chip Technologies** are aiming to grow cells within an artificial environment that mimics the human body, a potential alternative to using animals in research.

**The Integrative Biological Imaging Network** will develop new ways to take fast, high-resolution images of living cells in 3D tissues.

Read more: mrc.io/ttl-networks

Liver cells grown as a spheroid. Organ-on-a-Chip device. X-ray scanner used to visualise plant root behaviour, from seed to flowering.
With this year’s flu season over, most of us can breathe a sigh of relief. But taming a virus as notorious and unpredictable as influenza requires year-round research efforts. Carmen Chai looks back at how far we’ve come since the deadly 1918 outbreak, and what lies ahead.

It’s been labelled as one of the greatest pandemics in history. 100 years ago, the 1918 influenza virus, more commonly known as the Spanish Flu, brought the international medical community to its knees. About one in three people were infected, with estimates suggesting between 50 and 100 million people died – roughly 5% of the world’s population.

“The reason why we remember 1918 more than others, is because it was so severe in humans. It is the deadliest influenza we’ve dealt with,” says Professor Steven Riley, Professor of Infectious Disease Dynamics at the Centre for Global Infectious Disease Analysis, formerly called the MRC Centre for Outbreak Analysis and Modelling.

Falling numbers

Compare the Spanish Flu’s fatality rate to that of 2009’s H1N1. This strain killed about 1 in 10,000 infected patients. That’s 100 times less deadly than the 1918 strain, according to Steven.

The changes in both rates and absolute numbers are not solely due to changes in the virus, but in how we’ve been able to deal with the flu.

“There’s a striking difference between the Spanish Flu and subsequent pandemics. There was virtually no intervention for any infectious agent at the time,” says Professor John McCauley, Director of the Worldwide Influenza Centre at the Francis Crick Institute. John is a leading global expert
in influenza, with decades of experience researching influenza viruses.

Taming the beast

A century later, the flu research landscape has changed dramatically thanks to major milestones – some with the MRC at the helm.

One of the first major discoveries occurred in 1933 when scientists at the MRC National Institute for Medical Research (NIMR) at Mill Hill* successfully propagated the influenza virus by passing the virus from humans to ferrets, and then between infected and naïve ferrets.

Propagating the virus paved the way to studying it and finding ways to treat it. Eventually scientists found the virus could be grown in hen eggs and tissue culture. This, ultimately, provided the foundation for the dawn of mass vaccination.

To this day, the ferret remains the benchmark model for studying influenza infection.

From classification to vaccination

Now that scientists could grow and study the virus, MRC funding helped to understand the battle between the body and the virus.

As we now know, there are numerous different strains of the flu. But it all started with the realisation, in the 1940s, that there were two different groups of the virus, known as A and B. Serotyping allowed researchers to classify viruses and, eventually, find a way to beat them through vaccination.

The first flu vaccine approved for use in 1945 had not one but two different types of virus – inactivated influenza A and B. Its testing was successful and after World War II was over, the vaccine was administered to civilians.

Boosting our body’s defences

MRC-funded researchers continued on to study how our bodies fight the virus. And in the 1950s, back at the NIMR, they discovered one of the body’s defences against the virus: the family of proteins known as interferons, coined for their ability to interfere with viruses. They are antiviral substances released in response to the presence of viruses, bacteria, parasites or tumour cells, preventing a worsening infection.

John calls the discovery of interferons a ‘pivotal step’ in understanding how the body responds to virus infection. With an understanding of how the body fights – and sometimes loses to – the virus, MRC researchers were learning how to boost the immune system to fight off infection.

The birth of global flu surveillance

In 1947, the influenza laboratory of the NIMR became the World Influenza Centre of the World Health Organization. There are now 144 National Influenza Centres in 114 countries that comprise the WHO Global Influenza Surveillance and Response System.

Centres collect virus specimens, perform analyses and conduct risk assessments, sharing their data with partner institutions.
By the 1980s, scientists working on influenza began sequencing the genes of the viruses. Now ever more crucial to flu research, this allows researchers to compare circulating influenza viruses with older ones and to help identify new viruses that are likely to be predominant in the next flu season.

**A moving target**

We’ve made major strides in understanding and taming the flu. But flu vaccine production is a major concern.

“We have existing technologies to make strain-specific vaccines, we just can’t make them very quickly,” Steven says. A flu pandemic can travel around the world in less than 12 months, but it takes about four to six months for the current flu vaccine to be rolled out for use.

Because influenza viruses constantly change and mutate, vaccine composition is updated twice each year – once each for the flu season of the Northern and Southern Hemisphere. Currently, WHO experts choose which strains to include based on what’s circulating at the time and what’s likely to be dominant over the subsequent months.

While this method is effective, it’s not perfect and has led to mismatches. And Professor Sarah Gilbert, a professor of vaccinology at Oxford University, thinks we can do better.

**Building a universal flu vaccine**

With MRC funding, Sarah is developing a universal flu vaccine, to protect against all influenza A viruses.

Currently, the flu vaccine builds antibody response to the virus in the seasonal vaccine. When the virus changes its appearance, the antibodies may not be as effective in the following year.

The universal option would shift the response from antibodies to a different regiment of our immune defence forces – T-cells. T-cells can identify and combat against more than one type of influenza virus. They focus on the virus’ internal proteins, which are common for large numbers of strains.

“With a universal flu vaccine, you don’t have to worry about predictions, mismatches, stockpiling or production. If everybody in the world was vaccinated with an effective universal flu vaccine, there would be no more pandemics,” Sarah says.

“We’ve never had a vaccine soon enough to interfere with a pandemic strain. We’ve never seen the strain that caused the pandemic until it was a pandemic,” she explains.

**Covering all bases**

From John’s vantage point at the Crick, influenza’s unpredictability is its only certain feature. But that’s what captivates researchers, according to Steven.

“It’s absolutely fascinating science. There are so many different angles to study, from individual proteins, through to cells, tissues, individuals, to towns, countries, regions around the globe – there are active questions being pursued at every single level.”

*The MRC National Institute for Medical Research and Cancer Research UK’s London Research Institute became part of the Francis Crick Institute on 1 April 2015: www.crick.ac.uk

Read the full article on our MRC Insight blog: mrc.io/outfoxing-flu
New director joins MRC family

The MRC welcomes Professor Matthew Lambon Ralph as the new Director of the MRC Cognition and Brain Sciences Unit (MRC CBU)

Matthew will take up his appointment from 1 September 2018, succeeding Professor Susan Gathercole OBE who has led the MRC CBU since 2011. The unit, established in 1944, became part of the University of Cambridge’s School of Clinical Medicine in 2017.

Matthew has been Professor of Cognitive Neuroscience at The University of Manchester since 2001. He leads the university’s cross-disciplinary Neuroscience and Aphasia Unit, and is also Associate Vice-President for Research. His work combines clinical and discovery science to explore memory and language, and their multiple disorders.

www.mrc-cbu.cam.ac.uk

Superheroes vs superbugs

On 25 April, leading researchers from the MRC and UK research councils joined the Science Museum’s free, adults-only, late opening of the ‘Superbugs: The Fight for Our Lives’ exhibition.

The exhibition, sponsored by UKRI, looks at the causes and challenges of antimicrobial resistance (AMR), and why previously effective drugs are no longer winning the battle against some infections. On the night, researchers shared personal stories of how they are helping to tackle the global threat of AMR.

Professor Timothy Leighton, a researcher at the University of Southampton, said: “We’ve designed five hands-on arcade games which explain how people can change their behaviour to help stop the spread of AMR, for example through practising good hygiene. If you cannot change people’s behaviour, there’s no scientific intervention you can introduce that will really have a large societal benefit.”

PhD student Katie Smart, of the University of Warwick, used virtual reality to shrink visitors down to the size of bacterial proteins: “Virtual reality is a really good way to introduce people to how we go about discovering new antibiotics and how they work. I think it’s nice for people to learn about antibiotic resistance and see how we’re spending their taxpayer’s money.”

The Superbugs exhibition is open until Spring 2019 and can be visited by the whole family during normal museum opening hours.

Find out how UKRI is tackling AMR: mrc.io/UKRI-AMR

Read about more MRC-funded AMR research: mrc.io/AMR-research
Sight regained thanks to stem cell-based treatment

The first patients to receive a stem cell-based treatment for a common cause of sight loss have regained reading vision.

Age-related macular degeneration (AMD) is the most common cause of sight loss in the UK, leading to a rapid loss of central vision and making reading difficult for sufferers.

To replace diseased cells behind the retina, scientists created a ‘patch’ of specialised cells produced from human embryonic stem cells. Surgeons inserted the patch under the retina of the affected eye in two patients with severe wet-AMD and poor vision.

After 12 months, both patients reported improved vision – from being unable to read, to reading up to 80 words per minute using normal reading glasses.

Professor Pete Coffey, running the London Project to Cure Blindness with surgeon Professor Lyndon da Cruz, said: “This study represents real progress in regenerative medicine and opens the door to new treatment options for people with AMD. We hope this will lead to an affordable ‘off-the-shelf’ therapy that could be made available to NHS patients within the next five years.”

Published online at: www.nature.com, 19 March 2018.

Blood test could predict if drug will help breast cancer patients

A blood test could predict if a woman responds to breast cancer drug palbociclib, months earlier than current tests.

The researchers tested women with the most common kind of breast cancer, part of a clinical trial of palbociclib – a new drug approved last year for previously untreated, advanced breast cancer.

It can take up to three months to assess, using a scan, if palbociclib is working. The new blood test looks for circulating tumour DNA, shed by the cancer, in the bloodstream.

The team found they could predict if the treatment would work by comparing the amount of a gene, \(PIK3CA\), before treatment and 15 days after starting treatment. The women with a large decrease in \(PIK3CA\) were progression-free for a longer period, compared to those with a small decrease.

Professor Nicholas Turner, senior author from the Institute of Cancer Research, and the Royal Marsden NHS Foundation Trust said: “Having an early indication of how likely a treatment is to work might allow us to adapt treatment – switching some patients to an alternative drug that is more likely to benefit them.”

Published online at: www.nature.com, 1 March 2018.
Bloodless revolution in diabetes monitoring

Researchers at the University of Bath have created a non-invasive skin patch that can measure blood sugar levels without extracting a single drop of blood.

Unlike the painful and unpopular finger-prick blood test, currently used by millions of diabetics, the patch can read blood sugar levels through the skin. It uses sensors and a small electric current to draw out blood sugar from fluid between skin cells, and can take readings every 10 to 15 minutes.

After promising results in healthy human volunteers, the next step is to test the patch in people with diabetes. The team hope that the patch will become a low-cost technology that can connect to the wearer’s smartphone and help users to control their diabetes.

Professor Richard Guy, one of the study’s authors, said: “A non-invasive – that is, needle-less – method to monitor blood sugar has proven a difficult goal to attain. The monitor developed at Bath promises a truly calibration-free approach, an essential contribution in the fight to combat the ever-increasing global incidence of diabetes.”

Mouse study identifies new target for premature ageing condition

Scientists have discovered a promising treatment target in mice for a devastating genetic disorder which causes sufferers to look decades older than they are.

Hutchinson-Gilford progeria syndrome (HGPS) is a rare condition with symptoms usually associated with ageing, such as hair loss, osteoporosis, and heart disease. The average life expectancy is around 15 years.

In the study, researchers looked at mice with the same genetic fault found in people with HGPS. By slowing down an important enzyme, either by blocking it or reducing the amount made, the health of the mice improved, and they lived for longer.

This enzyme, N-acetyltransferase 10 (NAT10), does several jobs within cells including controlling cell growth. By targeting NAT10, there were less negative effects from the genetic fault across body tissues and cells.

Senior author Professor Steve Jackson from the Gurdon Institute at the University of Cambridge said: “We’re very excited by the possibility that drugs targeting NAT10 may, in future, be tested on people suffering from HGPS. I like to describe this approach as a ‘re-balancing towards the healthy state’.”

Published online at: www.nature.com, 27 April 2018.

Published online at: www.nature.com, 9 April 2018.
How research can give patients a voice

Eileen MacDonald was diagnosed with childhood arthritis when she was only a baby. 18 years on, as well as dealing with normal teenage life and managing her condition, she’s helping MRC researchers on a stratified medicine study to pick the right treatment, first time, for future patients.

It all started when I was 18 months old and I bumped my knee. My parents noticed that the swelling wouldn’t go down, and took me to our local hospital. They ran tests but the doctors couldn’t figure out what was wrong, so I was referred to the rheumatology department at Alder Hey children’s hospital, where I was diagnosed with juvenile idiopathic arthritis (JIA).

At first I was lucky. An ibuprofen derivative helped reduce the swelling, and shortly after I didn’t need any medication at all. But in my late primary school years things changed. The swelling in my knee returned and new oral steroid-based drugs caused painful side effects. I also needed regular steroid injections into my joints, under anaesthesia, for seven years.

Finding the right treatment

During my secondary school years, the arthritis moved to my other knee, both of my ankles, and my left thumb. I was prescribed an immunosuppressant medication called methotrexate which I took for two years. I hated it so much, and dreaded taking my weekly tablets as they made me feel so nauseous as a side effect. But for me to try other, newer medications, I had to try methotrexate first – for at least a year. For some people methotrexate works great, but unfortunately it didn’t for me and I was finally taken off it when it made me sick. After that I was put on an amazing drug called adalimumab, which works brilliantly for me.

Despite the effectiveness of adalimumab, one day in year 11 I had an awful pain in my ankle that didn’t go away. After a lot of hospital trips and scans, doctors discovered that I had no cartilage in my ankle joint and my bones had been grating together, resulting in a series of painful surgical interventions. After the surgeries didn’t work as hoped, my ankle joint fused itself together in an inadequate position, leaving me unable to walk properly. I’ve now been on crutches for 2 years and am waiting on a full ankle replacement.

It’s been difficult. I have had to give up things I love and sit out of things that I desperately want to do. I miss dance so much and plan to go back when my ankle is sorted, hopefully. Having to deal with this level of pain 24/7 and the fatigue is hard, especially in my A-level years and when I’m trying to be a normal teenager.
But although there are a lot of negatives, I’ve also experienced some positive things due to JIA. It has allowed me to meet some amazing people and take part in some things other people can’t – the CLUSTER study and Your Rheum group. Your Rheum is an advisory group for young people with a rheumatology condition to have their say, and help shape current adolescent and young adult rheumatology research in the UK.

**Being more than a patient**

I have the honour of being patient lead on the CLUSTER study, which is funded by the MRC. CLUSTER is a five-year project following the health trajectories of 5,000 children with JIA. The aim is to create a simple biomarker test that will lead to personalised treatment. Being patient lead has allowed me to talk to people at the frontier of research and get involved in the team as a patient representative, giving opinions and ideas. The experience and everyone I’ve met have been amazing; it’s been a wonderful opportunity.

For patients to have such a big involvement in projects like this is so important. You get to be a part of the future and the bigger picture. You feel like you’re not just a patient, you’re not just providing samples, you have a voice, you’re part of something much, much bigger.

**How research can change lives**

For the next generation of kids with childhood arthritis this research could mean they won’t have to go through what I did. They could have the right therapy handpicked for them, reducing the impact it has on their lives.

If this was available when I was diagnosed, I could have been on the best medication for me from the beginning. I may not have had all the issues I described and could be living a different life right now. That’s not the case for me. But it could be for a kid like me. This study is changing the treatments for kids with JIA and changing their lives simultaneously.

**CLUSTRER**, led by scientists at UCL and Great Ormond Street Institute of Child Health, is one of four stratified medicine projects being funded by the MRC: [mrc.io/stratified-medicine](http://mrc.io/stratified-medicine)

**Read more on page 6.**
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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Front cover image: Coloured transmission electron micrograph (TEM) of H3N2 influenza virus particles. Each virus consists of a nucleocapsid (protein coat), with a core of RNA (ribonucleic acid) genetic material, surrounded by a lipid envelope.