

# ANNUAL REPORT & FINANCIAL STATEMENTS

The Francis Crick Institute Limited  
A company limited by shares

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# AN INSTITUTE FOR DISCOVERY

Our commitment to excellence, our emphasis on multidisciplinary research, our focus on young and emerging talent and our novel ways of partnership working are some of the factors that set the Crick apart.



## Who we are

The Francis Crick Institute is a biomedical discovery institute dedicated to understanding the fundamental biology underlying health and disease. Our work is helping to build an understanding of why disease develops and to translate discoveries into new ways to prevent, diagnose and treat illnesses such as cancer, heart disease, stroke, infections and neurodegenerative diseases.

## CHAIRMAN'S LETTER

2

## DIRECTOR'S INTRODUCTION

3

## TRUSTEES' REPORT

(INCORPORATING THE STRATEGIC REPORT  
AND DIRECTORS' REPORT)

4

## INDEPENDENT AUDITOR'S REPORT

47

## CONSOLIDATED STATEMENT OF FINANCIAL ACTIVITIES

49

## BALANCE SHEETS

50

## CONSOLIDATED CASH FLOW STATEMENT

51

## NOTES TO THE FINANCIAL STATEMENTS

52

## Our vision

**Our vision is to be a world-leading multidisciplinary biomedical research institute.**

We bring together outstanding scientists from all disciplines and carry out research that will help improve lives and strengthen the economy.

## Our strategy

**At the heart of the Crick is a commitment to the highest quality science.**

We have five strategic priorities:

- Pursue discovery without boundaries.
- Create future science leaders.
- Collaborate creatively to advance UK science and innovation.
- Accelerate translation for health and wealth.
- Engage and inspire the public.

## Our founding partners



**Imperial College  
London**



## What's inside

### Creative collaboration 28

Sophisticated microscopy is being used to image biological processes in atomic detail.



### Engage and inspire the public 34

The latest Crick exhibition showcases a series of collaborations between scientists and artists.



## CHAIRMAN'S LETTER



“

We have a clear strategy  
and high levels of  
confidence in our future.

As I reach the end of my first year as Chairman of the Crick, I am very encouraged with the progress that is being made.

We have a clear strategy and high levels of confidence in our future; we are on track with our plans and have made some significant achievements across all of our strategic objectives, some of which are highlighted in the Trustees' Report that follows.

Sir Paul Nurse, Director of the Crick, and members of his executive team will shortly be meeting with the Crick's core funders to assess progress with establishing the Crick, and we look forward to providing them with assurance that the set-up, governance structures and strategic direction are progressing as expected. The core funding from the Medical Research Council, Cancer Research UK and the Wellcome Trust remains fundamental to the Crick's future.

The aims of the Crick are long term, and we are still at the early stages of development, but I am confident that the team is focussed on what needs to be done to ensure that the Crick makes a significant contribution to the United Kingdom and to the rest of the world. High quality biomedical research is already being carried out at the Crick, and a dozen young talented Group Leaders have been recruited in the first 18 months of operations in the new building.

During the year, the evolution of the Board has continued. I would like to thank my predecessor, Sir David Cooksey, and the other Trustees who retired during the year (Dr Lynne Gailey, Professor Doreen Cantrell, Professor Peter Gruss, Sir Harpal Kumar and Philip Yea, who also chaired our Audit and Risk Committee) for their contribution through a vital stage in the Crick's early development and welcome Iain Foulkes, Professor Fiona Watt and two independent Trustees, Dame Ottoline Leyser and Brian Gilvary, who now chairs our Audit and Risk Committee. We expect during the next few months to further enhance the Board with the addition of two additional independent Trustees.

Above all, I would like to thank our researchers and operational staff for all their efforts in helping to make the Crick a world-leading multidisciplinary research institute.

**Lord Browne of Madingley**  
Chairman

## DIRECTOR'S INTRODUCTION

Our first full year in the Crick has seen us make significant advances, and we can look forward to broadening our research endeavour in the years to come, says Director Paul Nurse.

Welcome to our annual report and financial statements for 2017/18, which focuses on our science, our people and our facilities as we work towards our goal of being a truly world-class institute.

Crick scientists have made a number of important findings this year, increasing our understanding of the biological processes underlying human health and disease. Many of the most significant advances can be found in the Research Highlights section on pages 8 to 23.

We welcomed the first three early-career group leaders to be recruited into our programme for training future science leaders. Silvia Santos, Lucia Prieto-Godino and Pontus Skoglund are early-career scientists who are now establishing research groups at the Crick (see page 25). Four more group leaders have been recruited this year. They will stay with us for up to 12 years, benefiting from the support, facilities and opportunities for collaboration available here. At the end of this period, they will take their established groups elsewhere, to establish a network of connections throughout the world. These are key parts of our national role.

### Looking forward

Central to the Crick's approach is that the best science is done where there are no boundaries between disciplines. We have been working with our university partners to appoint researchers to lead new groups in the physical sciences, which brings an interdisciplinary aspect that is crucial for today's biomedical research. Four researchers will arrive at the Crick over the next few months. We are also improving clinical links, providing more research training for clinicians and building closer collaborations with partner institutions on the medical implications of our research. As this report demonstrates, it has been a year of significant advances, and we can look forward to broadening our research endeavour in the years to come. We are working to optimise our facilities, to support excellent science and to inspire the public with the latest science and its potential. Our aim is to make the Crick one of the most exciting places to be in biological and biomedical research.

**Sir Paul Nurse**  
Director of the Francis Crick Institute

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Central to the Crick's approach is that the best science is done where there are no boundaries between disciplines.



# TRUSTEES' REPORT (INCORPORATING THE STRATEGIC REPORT AND DIRECTORS' REPORT)

The Francis Crick Institute aims to improve lives through greater understanding of the biology underlying human health. We have made significant progress against our five strategic priorities in the past year, reflecting our commitment to the highest quality science.

## PROGRESS AGAINST OUR STRATEGY

*Cells in an early zebrafish embryo know how to form distinct layers thanks to a network of signals (see p.19).*

# 01

## Pursue discovery without boundaries

Our approach to biological and biomedical research is to foster excellence, break down barriers between disciplines and work across institutions.

- Four researchers at the Crick were elected Fellows of the Royal Society, Academy of Medical Sciences and the American Association for the Advancement of Science, reflecting their outstanding contributions to their fields.

### 36 For more information

- Research highlights from last year included new insights into how tumours evolve and evade treatment, the use of genome editing to understand the role of a key gene in human embryo development and a step forward in our picture of the network of nerve cells that help maintain a healthy gut.

### 8 to 23 For more information

- Our Scientific Advisory Board held its first meeting in November 2017. The Board offers advice on implementing the Crick's scientific strategy and consists of eminent scientists from around the world, many of whom have led research institutes and helped formulate science policy.
- Lucia Prieto-Godino, Silvia Santos and Pontus Skoglund arrived at the Crick to establish new research groups following the 2017 recruitment of early career group leaders in biomedicine. A further eight group leaders have been appointed in 2018 and will arrive in the coming year. A total of 700-800 applications were received for the positions.

### 25 For more information

- There were 21 university research groups working at the Crick at the end of 2017/18, bringing their expertise and forming new collaborations. This follows another successful call last year for researchers at UCL, Imperial and King's to apply for these positions, with more to come this year.

### 28 For more information

# 02

## Create future science leaders



**Postdoc to Principal Investigator**  
The Crick Postdoc to PI programme provides training and support for postdocs interested in moving on to establish their own research groups. This includes practising chalk talks (above), an important part of applying for an independent research position.

The scientific training we provide aims at developing research excellence, dynamism and multidisciplinary activity, expanding the talent pool for biomedical science across the UK.

- Our training and development programmes for PhD students, postdoctoral fellows and laboratory research scientists are now well developed. There are training courses on presenting and writing about research, programming and use of scientific software. We've introduced careers talks, work placements for PhD students and undergraduate teaching opportunities for postdocs.

- The Crick signed up to the Technician Commitment, an initiative across the sector to ensure visibility, recognition, career development and sustainability for technicians working in higher education and research.

- We hosted the inaugural symposium of Equality, Diversity and Inclusion in Science and Health Research (EDIS), a new network formed by the Crick, Wellcome and GSK to make these issues a priority in research organisations.

# PROGRESS AGAINST OUR STRATEGY CONTINUED

03

## Collaborate creatively to advance UK science

The Crick promotes novel forms of partnership with its founders and the broader scientific community.

- We launched a joint recruitment call with our three university partners for early-career group leaders in the physical sciences. The aim was to recruit chemists, physicists, mathematicians, computer scientists or engineers who wanted to apply their research to biomedicine. Four applicants will take up their positions during 2018. They will spend six years at the Crick before moving to an established position at UCL, Imperial or King's.
- The Crick African Network is a new partnership with five institutes in Africa. It received a five-year £6 million government grant to establish a fellowship programme that will train African researchers to tackle infectious diseases in their home countries.
- A new cryo-electron microscope is to be installed at the Crick alongside two similar machines thanks to funding from Wellcome. It will be owned and used by a consortium of London universities – Imperial, the Institute for Cancer Research, King's and Queen Mary University of London – making this technique available to researchers across the city.

**31** For more information



**Collaborating with African scientists**  
The Crick African Network has held several workshops in Africa, like this one in Ghana, building research skills and supporting the best African scientists in tackling infectious disease.



# 04

## Accelerate translation for health and wealth

We conduct discovery science that is open to translation, turning advances in understanding into new ways to prevent, diagnose and treat disease to improve lives and strengthen the economy.

- A new spin-out company called Ervaxx has been created to develop cancer vaccines. Based on research on human endogenous retrovirus in George Kassiotis' lab, the company has backing from investment group SV Health Investors.

— Researchers from AstraZeneca and the Crick are collaborating on early-stage research that could translate into new treatments and health innovations in the future, thanks to a five-year research agreement that was signed last year. This adds to our existing partnership with GSK, where joint projects are already delivering new insights into the underlying biology of disease.

### 32 For more information

- We are building closer links with partner institutions on the medical implications of our research. We also launched a new postdoctoral clinical fellowship scheme, complementing existing PhD level opportunities at the Crick for clinicians wishing to gain from a full training in basic science.

# 05

## Engage and inspire the public

Our public, education and community programmes engage people in our science and encourage dialogue about biomedical research.

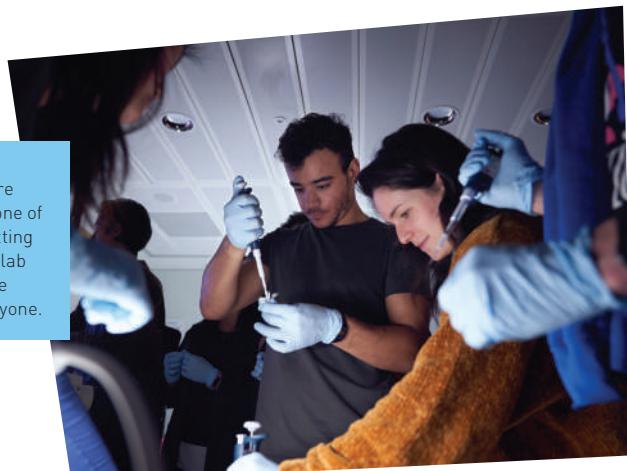
- Our exhibition, *Deconstructing patterns: art and science in conversation*, opened in the Manby Gallery in February 2018. In the first month, we welcomed over 2,000 visitors to the exhibition.

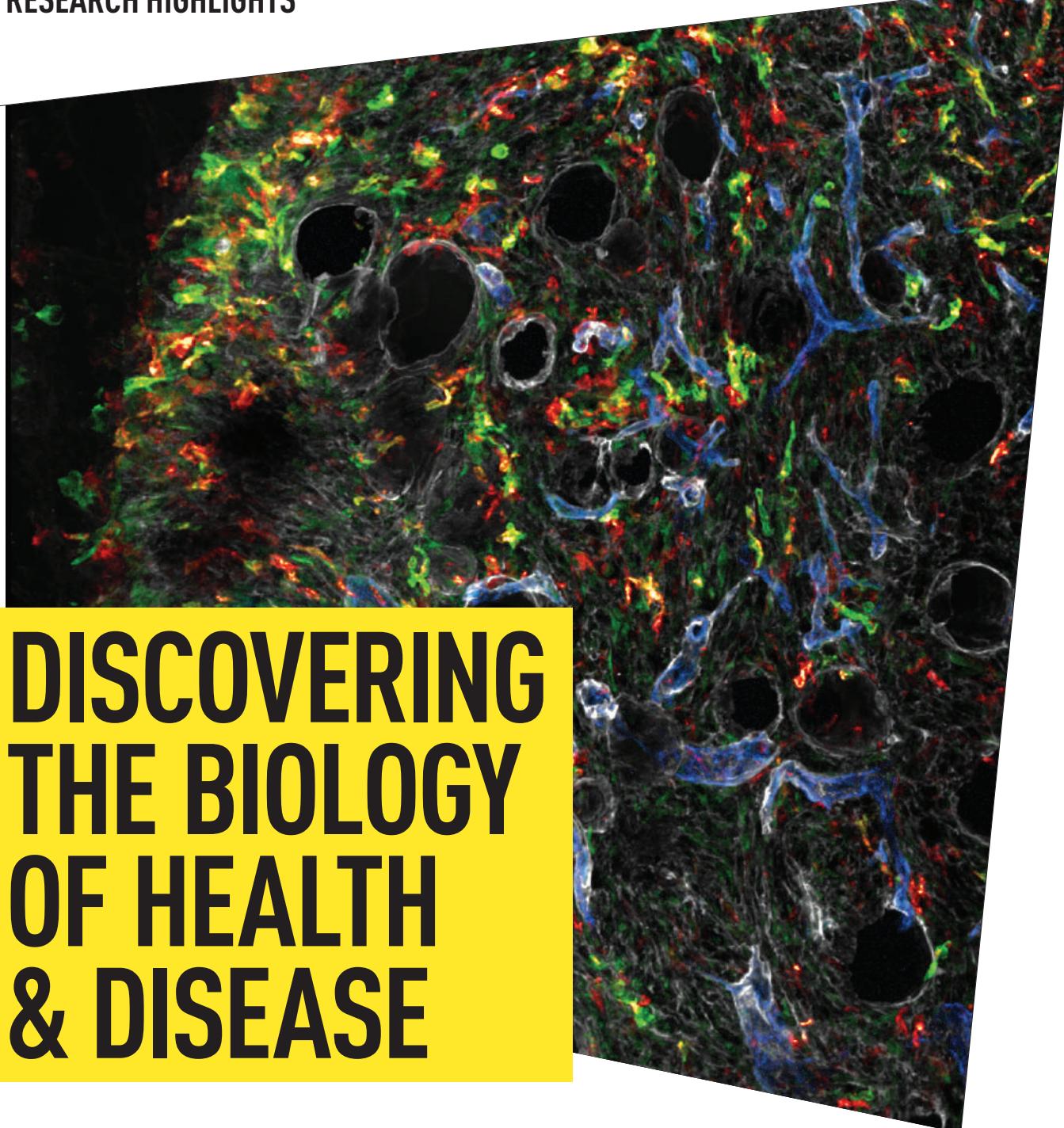
### 34 For more information

- Two Crick Late evening events and a Discovery Day for families were held at the Crick, part of a full programme of public events. Thousands of people got involved with the demonstrations and activities across the three events.
- Greg Clark, Secretary of State for Business, chose the Crick as the location to launch the UK government's Industrial Strategy.
- A local group of young filmmakers worked closely with Nate Goehring's lab in a collaboration with Holborn Community Association. The result is a film that offers a metaphor for the lab's research on growth and development.

#### The Crick Late events

People had the chance to explore many areas of our research at one of our Crick Late events. From getting hands-on with state-of-the-art lab equipment to inspiring talks, the events offer something for everyone.





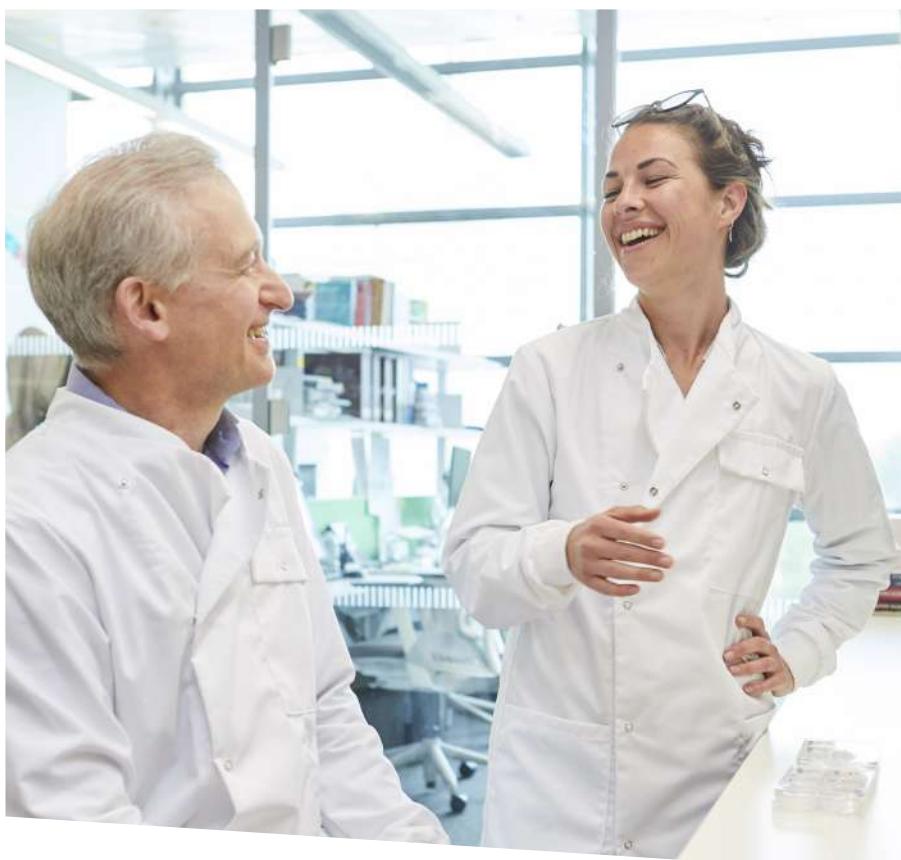
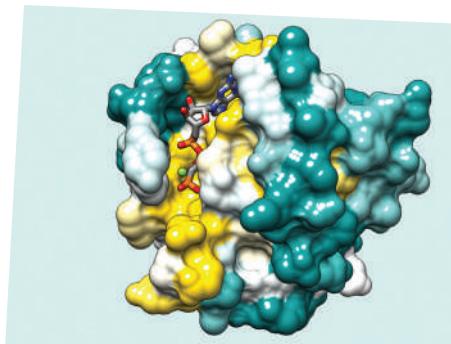
# DISCOVERING THE BIOLOGY OF HEALTH & DISEASE

Our scientists made a number of significant findings last year, showing the breadth of research undertaken at the Crick and demonstrating how our research is advancing the understanding of health and disease.

*A mouse tumour (grey/white areas) being infiltrated by cDC1 immune cells (yellow), triggering anti-cancer responses (see p.14).*

Julian Downward lab

# Cancer-causing mutation suppresses immune system



Mutations in *Ras* genes – which drive 25% of human cancers by causing tumour cells to grow, multiply and spread – can also protect cancer cells from the immune system.

Research, by a team from the Francis Crick Institute and Institute of Cancer Research (ICR) in London, shows that mutated *Ras* genes can suppress the immune system around tumours by increasing levels of a protein called PD-L1. Small amounts of PD-L1 exist naturally in the body to prevent the immune system from attacking healthy cells, but cancer cells can exploit this to protect themselves.

"Understanding how different mutations protect cancer cells from the immune system will help us to offer patients more precise and effective treatments," explains Matthew Coelho, a former postdoc at the Crick who was part of the team that led the work.

## Developing better treatments

Antibodies that target PD-L1 proteins are currently used in the clinic, but it is hard to determine which patients might respond best to the therapy. By revealing the causal link between *Ras* and PD-L1 levels, the study offers new possibilities for combination therapies using different drugs.

"Our study highlights the fundamental role that *Ras* mutations play throughout the different stages of cancer," says Julian Downward, Group Leader at the Francis Crick Institute and Head of the Lung Cancer Group at the ICR. It was already known that *Ras* mutations played a key role in starting around a quarter of all human cancers, causing cancer cells to grow, multiply and spread. "We now know that they also help to protect the cancer cells from our immune systems, making them more difficult to treat," he says. "Understanding the mechanisms behind this will help us to develop better treatments in future, for example boosting immunotherapy approaches with drugs that disrupt cancer's defences."

*Immunity* (2017) 47, 1083

*Ras* protein (top). Julian Downward and postdoc Sophie de Carne Tresseron, members of the research team (bottom).

## RESEARCH HIGHLIGHTS

CONTINUED

Scientists at the Francis Crick Institute and UCL have found that unstable chromosomes within lung tumours increase the risk of cancer returning after surgery. They have used this new knowledge to determine the risk of relapse up to a year before the cancer returns.

"For the first time we've revealed new insights into how tumours evolve and evade treatment, a leading cause of cancer death," says Charles Swanton, the lead researcher on the Cancer Research UK-funded TRACERx lung cancer study.

The team analysed tumours from 100 patients with non-small cell lung cancer (NSCLC). They found that patients with a high proportion of unstable chromosomes in their tumour were over four times more likely to have their cancer return, or die from their disease, within two years.

### Blood test

The researchers then investigated whether this genetic diversity could be tracked clinically. By looking for tumour DNA in blood samples taken from 24 patients after surgery for NSCLC, they accurately identified more than 90 per cent of those people destined to relapse – up to a year before clinical imaging could confirm the disease's return.

Christopher Abbosh of the UCL Cancer Institute, who led the work with Nicolai Birkbak and Gareth Wilson at the Crick, said: "Using circulating tumour DNA we can identify patients to treat even if they have no clinical signs of disease, and also monitor how well therapies are working. This represents new hope for combating lung cancer relapse following surgery, which occurs in up to half of all patients."

The TRACERx study involves more than 225 researchers and clinicians based at 19 centres across the country and is supported by Cancer Research UK, the Francis Crick Institute, UCL Cancer Institute, University College London Hospitals Biomedical Research Centre, the Royal Society, Achilles Therapeutics, illumina, Natera and the Rosetrees Trust.

Nature (2017) 545, 446

*Tumour DNA circulating in a patient's blood may be able to predict whether their lung cancer will come back after surgery.*

Charlie Swanton lab

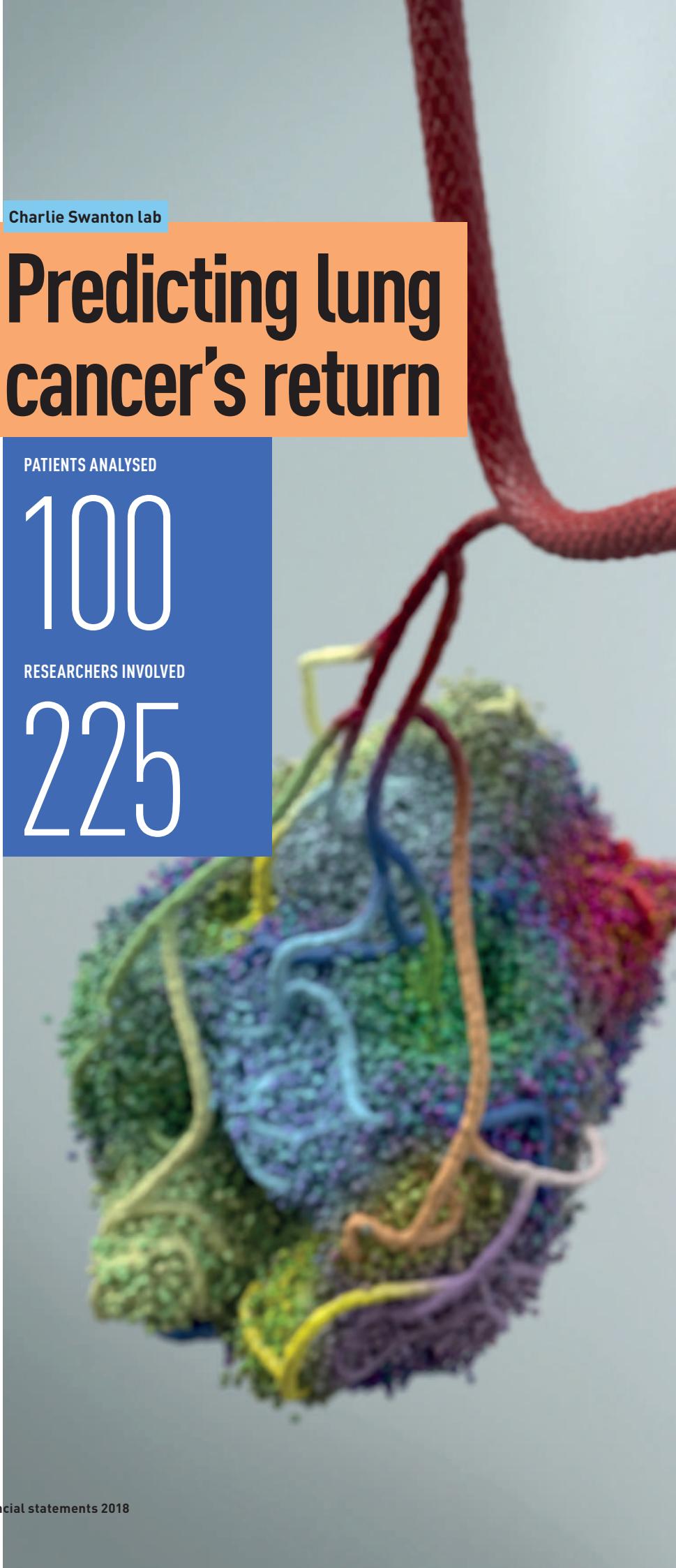
# Predicting lung cancer's return

PATIENTS ANALYSED

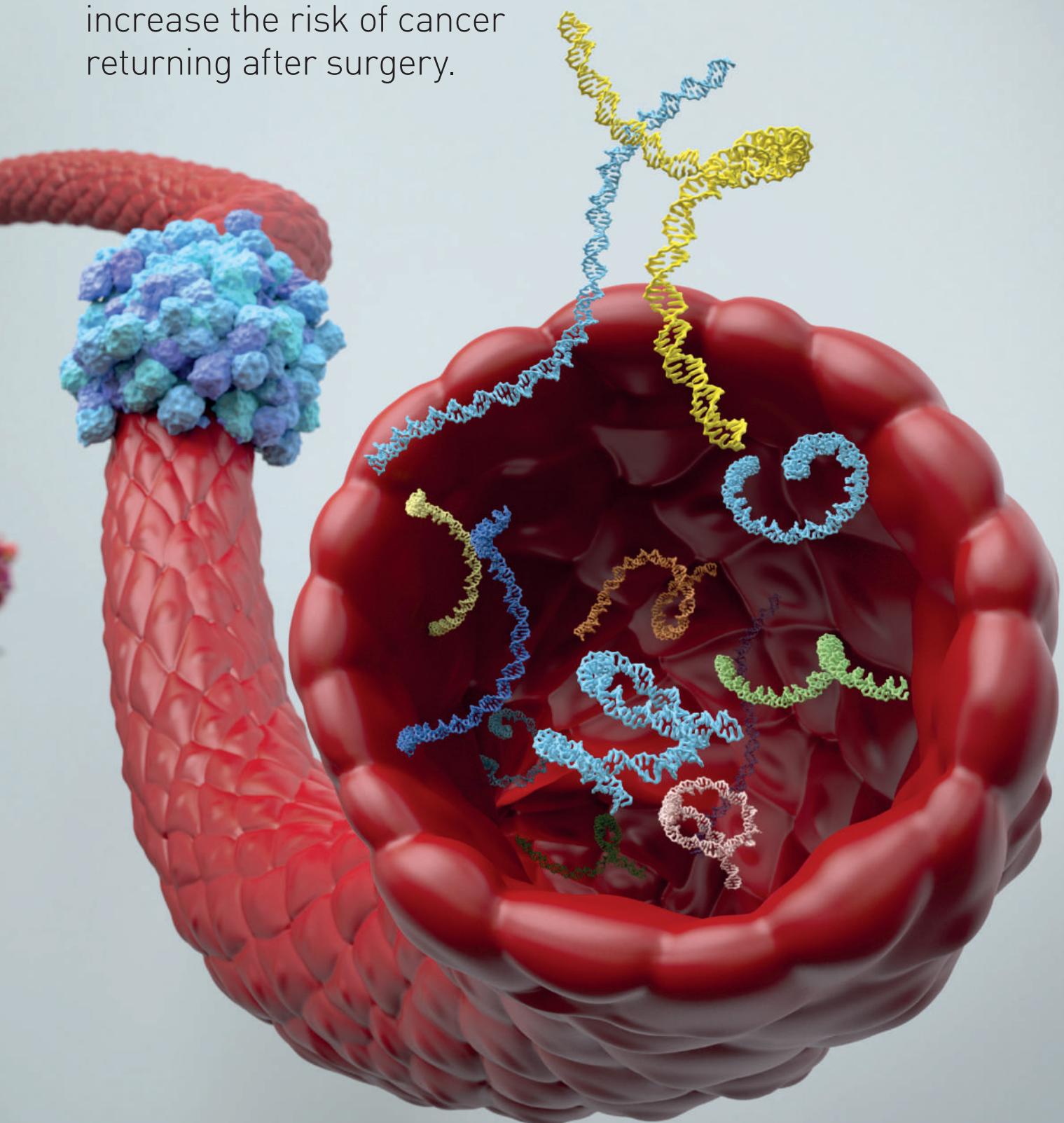
100

RESEARCHERS INVOLVED

225



Scientists at the Francis Crick Institute and UCL have found that unstable chromosomes within lung tumours increase the risk of cancer returning after surgery.



Kathy Niakan lab

# New understanding of human embryo development

Researchers have used genome editing technology to reveal the role of a key gene in human embryos in the first few days of development.

“

We were surprised to see just how crucial this gene is for human embryo development, but we need to continue our work to confirm its role.

Norah Fogarty

This is the first time that genome editing has been used to study gene function in human embryos, which could help scientists to better understand the biology of our early development.

The Crick team used genome editing techniques to stop a key gene from producing a protein called OCT4, which normally becomes active in the first few days of human embryo development.

### Crucial gene

After an egg is fertilised, it divides until at about five days it forms a ball of around 100 cells called the ‘blastocyst’. The study found that human embryos need OCT4 to correctly form a blastocyst.

“We were surprised to see just how crucial this gene is for human embryo development, but we need to continue our work to confirm its role,” says first author Norah Fogarty. “Other research methods, including studies in mice, suggested a later and more focused role for OCT4, so our results highlight the need for human embryo research.”

Kathy Niakan, who led the research, adds: “If we knew the key genes that embryos need to develop successfully, we could improve IVF treatments and understand some causes of pregnancy failure. However, it may take many years to achieve such an understanding, our study is just the first step.”

### Lessons for stem cell biology

The team spent over a year optimising their techniques using mouse embryos and human embryonic stem cells before starting work on human embryos. To inactivate OCT4, they used an editing technique called CRISPR/Cas9 to change the DNA of 41 human embryos. After seven days, embryo development was stopped and the embryos were analysed.

As well as human embryo development, OCT4 is thought to be important in stem cell biology. ‘Pluripotent’ stem cells can become any other type of cell, and they can be derived from embryos or created from adult cells, such as skin cells. Learning more about how different genes cause cells to become and remain pluripotent could help us to produce and use stem cells more reliably.

The embryos used in the study were donated by couples who had undergone IVF treatment. The study was done under a research licence and strict regulatory oversight from the Human Fertilisation and Embryology Authority (HFEA), the UK Government’s independent regulator overseeing infertility treatment and research.

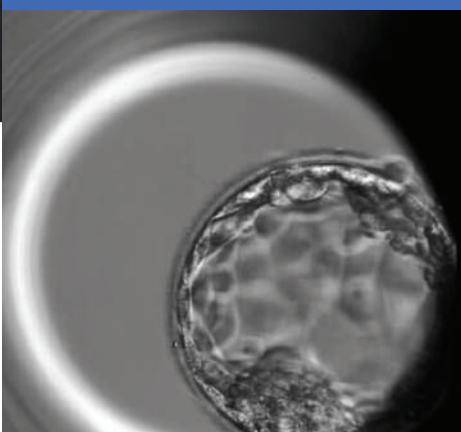
Nature (2017) 550, 67

*Kathy Niakan (overleaf, main image). Human embryos form a blastocyst (overleaf, bottom left) after about seven days, unless OCT4 is inactivated (overleaf, bottom right)*



A HUMAN EMBRYO FORMS  
A BLASTOCYST AFTER

5 DAYS  
IT CONSISTS OF AROUND  
100 CELLS



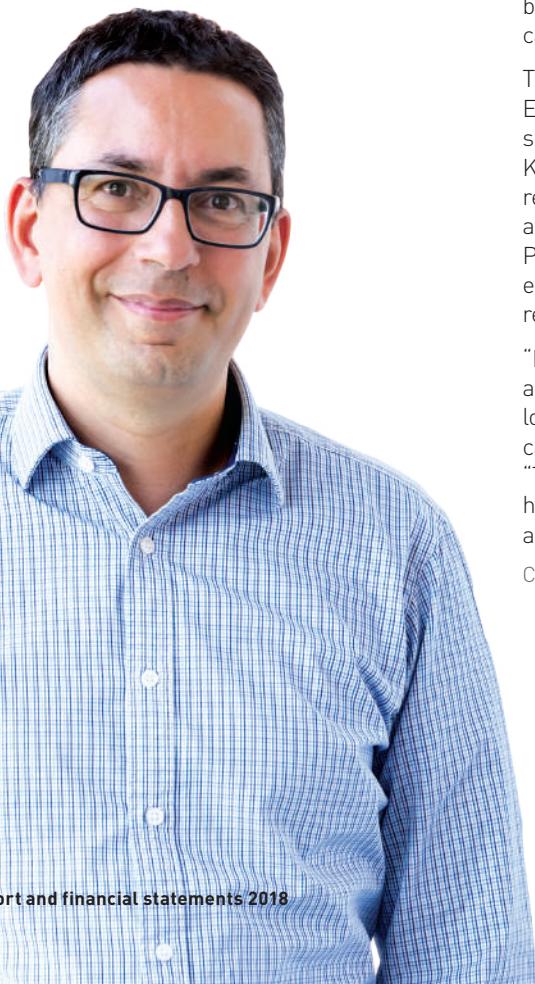
Caetano Reis e Sousa lab

# Chemical attraction could improve cancer immunotherapy

“

Now that we know better how this key anti-cancer response works, we can look at identifying other ways in which cancers get around it.

**Caetano Reis e Sousa**



Better immunotherapies for cancer patients could be developed using chemicals that attract specialised immune cells toward tumours, research suggests.

Scientists at the Francis Crick Institute have discovered that immune cells called Natural Killer cells accumulate in tumours and release chemicals that attract specialised dendritic cells (cDC1) – white blood cells known for triggering anti-cancer immune responses – to the tumour.

Genes associated with Natural Killer cells and cDC1 correlated with cancer patient survival in a dataset of over 2,500 patients with skin, breast, neck and lung cancers. A similar correlation was seen in an independent group of breast cancer patients, with a particularly positive outcome for women with triple negative breast cancer, which typically has a poor prognosis.

### Opportunity for new treatments

“Our findings have given us a renewed appreciation of the importance of Natural Killer cells and cDC1 in the immune response against cancer,” says Caetano Reis e Sousa, who led the study. “Attracting more cDC1 to tumours could be the basis of a new immunotherapy for cancer patients.”

The team also showed that prostaglandin E2 (PGE<sub>2</sub>), a molecule produced by some cancer cells, suppresses Natural Killer cell activity and reduces the responsiveness of cDC1 to the chemical attractants. This suggests that blocking PGE<sub>2</sub> with drugs might help boost the effectiveness of immunotherapies by restoring cDC1 levels in tumours.

“Now that we know better how this key anti-cancer response works, we can look at identifying other ways in which cancers get around it,” says Caetano. “This understanding will ultimately help us to develop new immunotherapy approaches to help more patients.”

Cell (2018) 172, 1022

Jean Langhorne lab

# Genes linked to malaria parasites' persistence

The ability of malaria parasites to persist in the body for years is linked to the expression of a set of genes from the *pir* gene family, scientists from the Crick and the Wellcome Sanger Institute have found.

The researchers showed in a mouse study that as few as 1 in 10 of the parasites that initially appear in the blood express this set of *pir* genes. But almost all the parasites found persisting in the body weeks later express the genes, and can be a source of further spread of the disease.

Malaria is caused by parasites which are passed between people by mosquitoes. The body's immune system will eventually destroy most of the malaria parasites, but some will continue to reside dormant in the body year after year without causing any symptoms.

The team hopes that a better understanding of the *pir* gene family will make it possible to destroy this reservoir of parasites that allows ongoing transmission of malaria.

Jean Langhorne, who led the work at the Crick, says: "Understanding how certain parasites go on to establish chronic infection and determining how a particular set of *pir* genes are involved may provide us with a means to prevent chronic infection which could be applicable to all types of malaria in humans."

Nature Microbiology (2017) 2, 16276

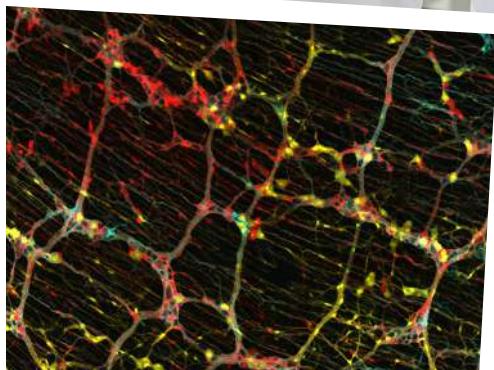
Deirdre Cunningham, Irene Tumwine and Sarah Manni (left-right) in the Jean Langhorne lab.



## RESEARCH HIGHLIGHTS CONTINUED

Vassilis Pachnis lab

# Architecture of our 'second brain'



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We uncovered a set of rules that control the organisation of the 'second brain'.

Reena Lasrado

Scientists have made an important step in understanding the organisation of nerve cells embedded within the gut that control its function. The discovery could give insight into the occurrence of common gastrointestinal diseases, including irritable bowel syndrome and chronic constipation.

The researchers have revealed how the enteric nervous system – a chaotic network of half a billion nerve cells and many more supporting cells inside the gut wall – is formed during mouse development.

Often known as the 'second brain' for its vast number of neurons and complex connectivity, the enteric nervous system has a crucial role in maintaining a healthy gut.

"The neural networks of the gut are responsible for well organised and stereotypic functions such as secretion of enzymes that break down food, movement of food along the gut, communication with immune cells and bacteria, and the relay of information to the brain," says Vassilis Pachnis, Group Leader at the Francis Crick Institute.

Using genetic tools, the team labelled developing cells of the enteric nervous system with unique colours and followed their descendants through development and into the adult animal. By examining the type of cells produced by single progenitors, they could understand their properties.

"We uncovered a set of rules that underpin the organisation of the 'second brain' not just along a single gut layer but across the 3D space of the gut wall," says first author Reena Lasrado.

The research was led by the Crick in collaboration with the University of Leuven, Stanford University, the Hubrecht Institute and the Quadram Institute Bioscience.

Science (2017) 356, 722

Vassilis Pachnis and Reena Lasrado (top).  
Multicoloured families of cells in the gut wall (below).

James Turner lab

# Cause of infertility side-stepped in mice



Scientists have created healthy offspring from genetically infertile male mice, offering a potential new approach to tackling a common genetic cause of human infertility.

Our sex is determined by the X and Y chromosomes. Usually, girls have two X chromosomes (XX) and boys have one X and one Y (XY), but approximately 1 in 500 boys are born with an extra X or Y. Having three rather than two sex chromosomes can disrupt formation of mature sperm and cause infertility.

#### Extra chromosome removed

Researchers at the Crick found a way to remove the extra sex chromosome to produce fertile offspring. If the findings can be safely transferred into humans, it might eventually be possible for infertile men with Klinefelter syndrome (XXY) or Double Y syndrome (XYY) to have children through assisted reproduction using this technique.

Working with researchers at Kyoto University, the team took small pieces of ear tissue from XXY and XYY mice, cultured some of the cells and turned them into stem cells. They noticed that in the process, some of the cells lost the extra sex chromosome.

#### Stem cell development

By guiding the stem cells to become cells with the potential to become sperm and reintroducing them to a male mouse to mature, they could use assisted reproduction to create healthy, fertile offspring.

However, the researchers caution that more work is needed before this approach could ever be used in humans as it is currently not possible to make mature human sperm outside the body.

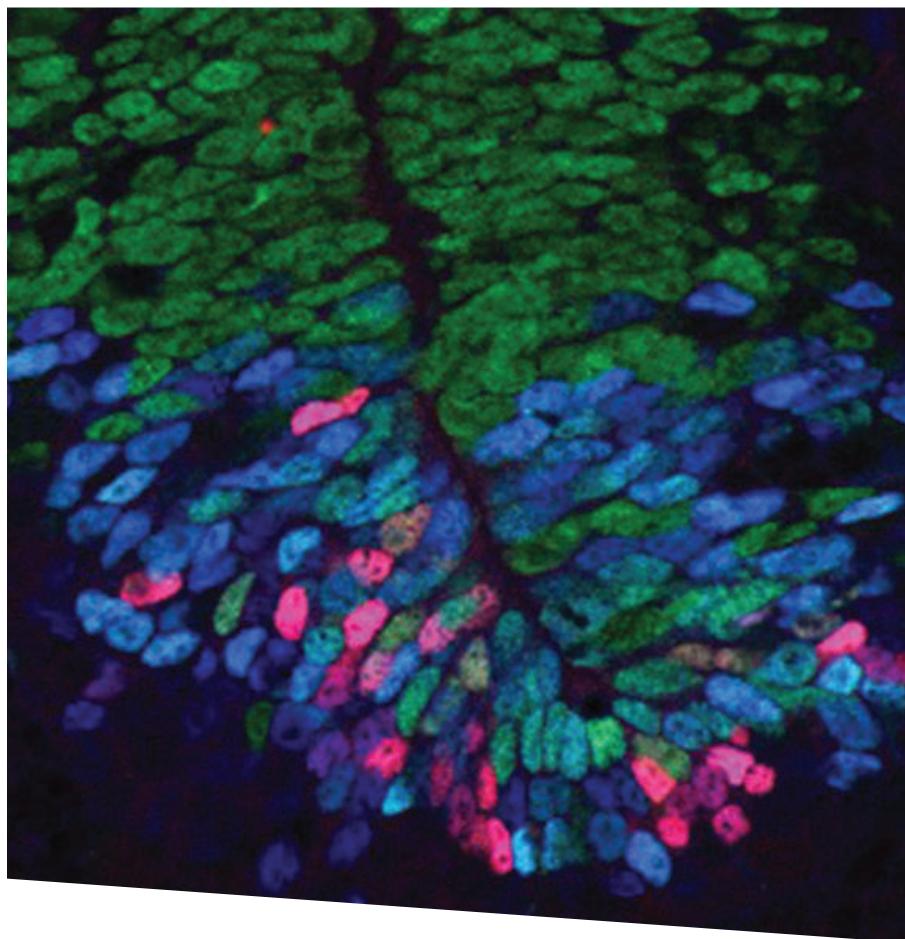
Science (2017) 357, 932

Takayuki Hirota and James Turner (top), part of the research team that produced healthy mouse pups (bottom) from infertile male mice.

## RESEARCH HIGHLIGHTS CONTINUED

James Briscoe lab

# Mechanism for spinal cord development discovered



Scientists have uncovered how nerve cells in the spinal cord are organised in precise patterns during embryo development – a finding that could give insight into regenerative medicine.

As embryos grow and develop they need the right cell types to end up in the right places inside forming organs. This is particularly important in the spinal cord, where different nerve cell types must be accurately positioned so that circuits can assemble properly to control muscle movement.

### Two signals control gene activity

Researchers at the Francis Crick Institute, the Institute of Science and Technology in Austria and the Ecole Polytechnique Fédérale de Lausanne in Switzerland have found that cells destined to become nerve cells in developing mouse embryos use two different signals spreading from opposite sides of the spinal cord – the back and belly side – to measure their position accurately. Based on this map, they turn into the appropriate nerve cell type.

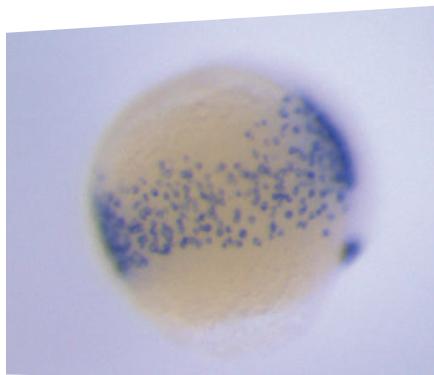
The team of biologists, physicists and engineers found that the strengths of the two signals originating from the back and belly sides of the body affect gene activity in developing nerve cells. Based on this gene activity in early development, the cells turn into the appropriate nerve cell type for that position in the spinal cord.

"We have shed light on the long-standing question of how developing tissues produce the right cells in the right place in the right numbers," says James Briscoe, Group Leader at the Crick. "In the long run this will help inform the use of stem cells in approaches such as tissue engineering and regenerative medicine. However, there is still much more to learn and we need to continue developing these interdisciplinary collaborations to further our biological understanding."

Science (2017) 356, 137

*A developing spinal cord shows precise patterns of gene activity. The red, blue and green identify different types of cells.*

# A new layer of complexity in embryo development



New insights into how cells know what they should become in the zebrafish embryo have been revealed by Caroline Hill's lab at the Crick.

In vertebrates, a growing embryo begins as a simple ball of cells. All the cells look alike and have the potential to form any part of the body.

"It's a fascinating question," says Group Leader Caroline Hill. "How does a single fertilised egg go on to form a human body with all the different organs in the right place and the right size?"

An important early step sees a transformation of the embryo into three

distinct layers: the ectoderm (where cells go on to form the skin and nervous system), mesoderm (blood and muscles) and endoderm (gut, pancreas and other internal organs).

Levels of a single protein called Nodal were thought to be responsible for determining where cells in the zebrafish embryo become endoderm and mesoderm. Nodal is present in different amounts across the early embryo, at high concentration where the endoderm forms and lower where the mesoderm forms.

"We knew this didn't fit the entire picture," says Andrew Economou, a postdoc in Caroline's lab, "because Nodal signalling didn't extend across all of the future mesoderm."

## Network of signals

Andrew, working with another postdoc in the lab, Thijs van Boxtel, has shown that a more complex signalling network governs the process. This gives tight control over where the division between endoderm and mesoderm occurs. A second factor called Fgf extends the signal to become mesoderm, to all the cells in the layer; while a third protein drowns out the Fgf signal where the endoderm needs to be.

The understanding gained may be important for using stem cells in medicine in the future. If you know what prompts cells to become a certain type, you may be able to come up with cell therapies to replace lost function. For example, generating insulin-producing cells for the pancreas could one day help treat diabetes.

*Developmental Cell* (2018) 44, 179

*Caroline Hill and Andrew Economou. Cells destined to become endoderm (blue) spread around the developing zebrafish embryo (bottom).*

## RESEARCH HIGHLIGHTS CONTINUED

Frank Uhlmann lab

# Two DNAs wedded with this ring

Crucial processes in our cells such as separating chromosomes in cell division, DNA repair and switching genes on and reading them out all require DNA molecules to be brought together in an organised way.

All organisms, from bacteria to humans, have rings of proteins that encircle DNA and are important in organising and packaging the long DNA molecules within cells.

But until now it remained unknown how the protein rings loop together two DNA molecules to allow processes such as chromosome separation to happen correctly. Frank Uhlmann and his former postdoc Yasuto Murayama, now with his own lab at the National Institute of Genetics in Japan, have shown how this happens in yeast with a protein ring called cohesin. The advance relies on Yasuto's success in recreating the binding of cohesin onto DNA in the test tube.

### Molecular carabiners

Frank compares cohesin to the metal rings used in mountaineering called 'carabiners' which open up to clip onto a rope then use a slider to lock them on. "In binding one rope, you haven't achieved anything," he explains. "When you open up the carabiner and lock it onto a second rope as well, that's when you can go climbing."



Frank and Yasuto have shown that after binding one DNA molecule, the cohesin ring opens and binds a second. But the second DNA is single-, not double-stranded. DNA replication then occurs and makes the single-stranded DNA into double-stranded DNA.

"This was a total surprise. At first we couldn't believe it. But this is how it works. Cohesin binds single-stranded DNA. It's a really important mechanism," says Frank.

Cell (2018) 172, 465

*Molecular model of a cohesin ring. Credit: Martin Singleton, Francis Crick Institute.*



This was a total surprise. Cohesin binds single-stranded DNA. It's a really important mechanism.

**Frank Uhlmann**

John Diffley lab

# Unravelling how DNA gets copied

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It's a big job. You can't just start at one end and copy the three billion letters in the human genome.

John Diffley



How molecular machinery gets loaded onto DNA ready to create new copies of our genetic data has been revealed by Crick scientists.

New copies of our DNA are needed every time our cells divide, and it's the structure of DNA that allows this replication. The two strands in the DNA double helix are first unwound before each acts as a template for a new strand. The result is two new DNA molecules with the same genetic information copied in both.

Seeing the link between structure and replication is one thing. Understanding how a cell ensures complete control over the whole process is another.

"It's a big job. You can't just start at one end and copy the three billion letters in the human genome," says John Diffley, Group Leader at the Crick. "You start at tens of thousands of sites along the DNA, otherwise it would take forever."

## Controlled unwinding

Replication has to start at all 50,000 sites at the same time, once and only once in each cell division. The control needs to be extraordinary: the error rate has to be less than 1 in 100 million or it is lethal for the cell. One main point of control is the initial unwinding of the DNA helix. This is done by a cellular enzyme called a DNA helicase.

John, and fellow Crick researcher Gideon Coster, have shown how helicases get loaded onto DNA. Two helicases pointing in different directions get clipped onto the double helix at the start sites of replication before setting off in opposite directions, unwinding the DNA. While the study was done in yeast, we know that similar proteins carry out the same role in humans.

## A piece of the puzzle

They found that one helicase is loaded on at one replication site. However, unexpectedly, the other is loaded at a distant, previously unrecognised site. It then tracks along the DNA to join its partner and gets ready for action.

John explains: "It's a piece of the puzzle of how our genomes are replicated, a process that tends to become misregulated in cancer. We now want to look at whether helicase loading shows differences in cancer cells."

Science (2017) 357, 314

John Diffley, and with Gideon Coster (inset).

Simon Boulton lab

# Telomerase's dark side discovered



An enzyme called telomerase is crucial for maintaining the ends of chromosomes as our cells grow, divide and age over time.

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In order to translate science effectively into new treatments, you need to understand how systems work at this detailed mechanistic level.

**Simon Boulton**

Simon Boulton's group at the Crick has discovered a surprising activity of telomerase. It's surprising because it leads to the opposite outcome: the rapid loss of telomeres, a key structure that normally protects chromosome ends.

This 'telomere catastrophe' was known to occur when a protein called RTEL1 was missing. RTEL1 normally helps unwind a DNA loop present at the end of chromosomes to allow telomerase to do its maintenance job. Simon and his team wondered if getting rid of both telomerase and RTEL1 would accelerate the telomere crisis.

Confounding all expectations, they found that knocking out both RTEL1 and telomerase in mice rescued the situation. The telomere was maintained as normal.

"It was astonishing," says Simon. "It suggested that telomerase was actually toxic in cells lacking RTEL1. But why was unclear."

Carefully reconstructing what was going on, they found that in the absence of RTEL1's DNA loop unwinding activity, telomerase was blocking telomeres from being copied ahead of cell division. To relieve the blockage, cells had no other choice but to cut off the whole telomere.

Removing telomerase meant that telomere copying never got blocked and there was no catastrophe, explaining the rescue Simon's team had seen. It also reveals the biology at the root of the devastating rare genetic disorder Hoyeraal-Hreidarsson syndrome which is caused by RTEL1 mutations.

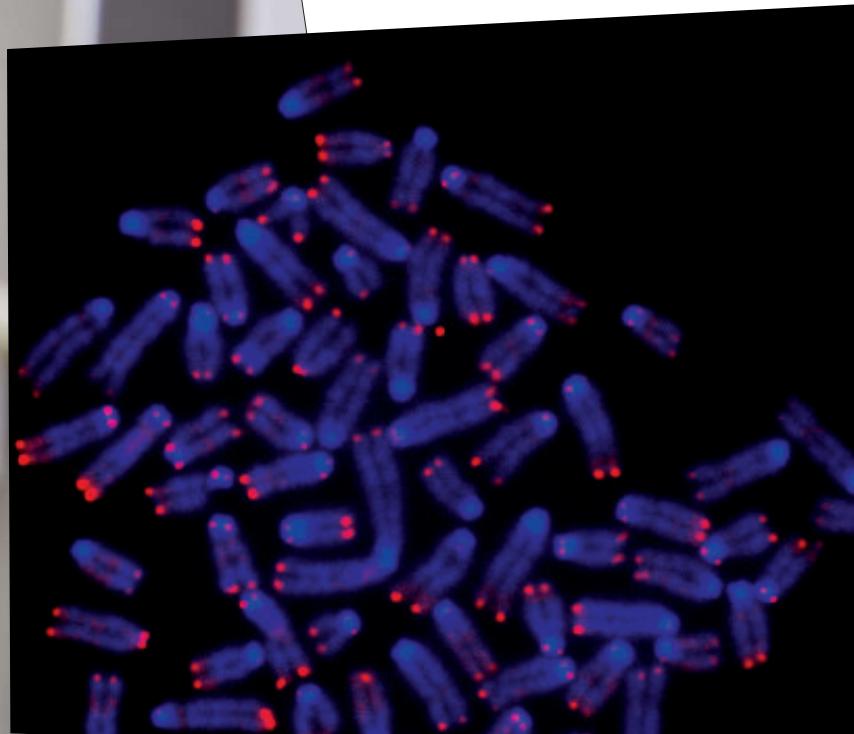
#### Cancer connection

When activated abnormally, telomerase is a driver of cancer as it allows cells to divide uncontrollably. Understanding more about telomerase and its functions is giving new insight into how some classes of anti-cancer drugs work.

"In order to translate science effectively into new treatments, you need to understand how systems work at this detailed mechanistic level," says Simon.

Cell (2018) 172, 439

*First author Pol Margalef in the lab. Mouse chromosomes with telomeres labelled in red (right).*





# A YEAR IN SCIENCE

Our people, facilities and their achievements have helped advance research at the Crick this year.

# New group leaders arrive

Three outstanding early-career scientists are setting up new research groups at the Crick.

NUMBER OF APPLICANTS

380



Three scientists arrived at the Crick in early 2018 to set up new research groups, having been hired in our first round of recruitment for early-career group leaders.

Selected from almost 400 applicants via a highly competitive process, Pontus Skoglund, Silvia Santos and Lucia Prieto-Godino have begun establishing their new teams and their research.

All three are keen to take advantage of the unique career structure we provide at the Crick, which has been specifically designed to provide opportunities for talented early-career researchers to develop themselves and their research.

Unusually, new group leaders remain with us for no more than 12 years before being supported to find scientific leadership positions elsewhere. This may be at other UK institutions or beyond, establishing links across the world.

This process is intended to develop future science leaders for biomedical science – a key aspect of our national role.

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I'm really excited to be at the Crick and I look forward to developing my lab and making the most of all the cutting-edge technology and supportive teams that are here.

**Silvia Santos**

## FUTURE SCIENCE LEADERS CONTINUED

**Lucia Prieto-Godino**



### **Lucia Prieto-Godino**

Originally from Madrid, Lucia moved to the UK to study for her PhD at the University of Cambridge before taking up a five-year postdoc position in Lausanne, Switzerland.

The goal of Lucia's lab is to understand how evolution sculpts nervous systems, giving rise to new behaviours. Studying how neural circuits change over evolutionary timescales can provide important insights into how brains work and what goes wrong in disease. Her team is studying these issues using the fly olfactory systems, the neural circuits responsible for sense of smell. By comparing fly species that exhibit different preferences for the fruit they feed and breed on, Lucia and her team can start to tease apart how neural circuits responsible for odour-guided fruit preference behaviours have evolved.

"Observing animal behavioural diversity, I cannot help but wonder: how can brains' intricate neuronal connections evolve through random mutation and selection to produce all these different behaviours?" says Lucia. "I am absolutely fascinated about this question, and we know so little about it!"

Lucia's research requires a multidisciplinary approach, combining a variety of methods across fieldwork, bioinformatics, electrophysiology, imaging, behavioural analysis – such as looking at how the flies react to their favourite fruit – and genetic manipulation.

"I love the Crick's interdisciplinarity, and I immediately thought that there would be lots of opportunities for collaborations," she says. "I feel so fortunate to be part of such an amazing and welcoming community of researchers."

### **Pontus Skoglund**

Following a PhD at Uppsala University in Sweden, Pontus undertook a postdoctoral research fellowship at Harvard Medical School, where he studied population history and historical admixture in the Americas, South Pacific, and Africa.

He now leads the Ancient Genomics Laboratory at the Crick and describes his field as currently one of the most interdisciplinary in science. Ancient genomics brings together a diverse range of research from areas including anthropology, archaeology, history, evolution, biochemistry, statistics and computational genomics, in order to understand our evolutionary past through fragments of DNA.

"You can think of ancient genomics as a kind of time-travel," he says. It involves examining the human genome through time and space, he explains, which helps us to understand the processes that have shaped our biology and that are still shaping our biology today. "For

**Pontus Skoglund**



example, through ancient DNA we are able to investigate the transition in human societies from hunting and foraging to agriculture. Furthermore, we can investigate the impact and effects of this transition on human diet and human biology. I'm particularly excited about the possibility of studying genetic variants that changed very rapidly, or at least rapidly on evolutionary timescales."

Pontus believes that the Crick's mission to understand the biology underlying human health and disease fits perfectly with his research. "Contemporary human biology is a direct product of evolution and ancient genomics is the best way to study human evolution directly," he says.



You can think of ancient genomics as a kind of time-travel. For example, through ancient DNA we are able to investigate the transition in human societies from hunting and foraging to agriculture.

**Pontus Skoglund**

**Silvia Santos**



#### **Silvia Santos**

Silvia's career path has exposed her to a variety of academic cultures. Originally from Portugal, she studied at the University of Glasgow and the European Molecular Biology Laboratory before working at Stanford University and the MRC's London Institute of Medical Sciences.

Her lab at the Crick is investigating control principles in cell decision-making by studying two important cell decisions which serve as paradigms for their research: cell division and cell differentiation (committing to a specific fate), using human embryonic stem cells as a model system.

Silvia and her team deploy a distinctive combination of theory (mathematical modelling and image analysis) and experiment (live cell imaging, quantitative molecular biology, biochemistry and chemical biology). This combination has been key to their ability to uncover regulatory principles in cell decision-making.

Silvia says that the Crick feels like her 'scientific home', because aspects of her PhD experience that shaped her as a scientist are explicit in the Crick's strategy and culture: the lack of departmental structures, the freedom to pursue curiosity-led research and the commitment to training scientists.

"I'm really excited to be at the Crick and I look forward to developing my lab and making the most of all the cutting-edge technology and supportive teams that are here," she says.

# Joined-up thinking

Researchers from UCL, Imperial and King's are adding to the breadth of research at the Crick.

Thanks to the innovative way we work with our university partners, scientists from UCL (University College London), Imperial College London and King's College London are able to carry out and extend their research on attachments at the Crick.

This continues to generate new collaborations, bring specialist knowledge to the Crick and enable research across a wide range of disciplines.

Secondments allow a group leader to transfer all or part of a research group to the Crick for an agreed period, while satellites are small groups of university researchers embedded in a Crick research group for an agreed period.

**Jernej Ule**



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This close proximity has enabled rapid exchange of new insights and ideas.

**Jernej Ule, UCL**

**Jernej Ule**

Seconded to the Crick from UCL, Jernej Ule's group is investigating how RNAs and proteins come together in our cells, and how this contributes to development or disease, with a focus on motor neurone disease (MND) – a fatal disease also referred to as amyotrophic lateral sclerosis (ALS). “Unless you know the primary cause of a disease you are only ever going to be able to ameliorate the symptoms, not reverse the process.”

“My group of nine researchers are all based at the Crick, where we have greatly benefited from work with different research facilities and initiated important new collaborations,” explains Jernej. “Our lab is next to the computational biology and MND labs, and this close proximity has enhanced our collaborations and enabled rapid exchange of new insights and ideas.”

**Ed Tate**



### **Ed Tate**

Ed Tate manages a research group split between Imperial College and the Crick, and is an example of how university attachments can bring expertise in the physical sciences to collaborations at the Crick.

"We work with chemistry but we apply it to biology," says Ed. "When we see a biomedical or biological problem we think would be interesting to try to solve, we can decide to tackle it from a new perspective – and the Crick enables us to do that very effectively."

His satellite group at the Crick comprises six team members who each work on something different: one works on TB, one on malaria, three work on cancer and one works on chemistry.

"Over the last year or two, the research focus at the Crick has enabled us to make more progress on certain specific projects than in the previous five years or more," Ed believes. "At the Crick, we can work in a biology-focused environment and collaborate with other scientists to the benefit of all. To say that unexpected science comes from people talking to each other over coffee is a bit of a cliché – but it's absolutely what happens."

### **Snezhana Oliferenko**

On a five-year secondment from King's College London, Snezhana Oliferenko's group of six researchers is studying the comparative biology of cell division – in particular the mitotic strategies of two different yeasts.

"Cell division is fundamental to all biological life on earth," says Snezhana. "If we can understand more about different strategies of cell division – as demonstrated by the two yeasts – we will gain greater knowledge of evolution, human development and disease."

She explains that being at the Crick has given her team the opportunity to collaborate with others and to use research facilities to study areas beyond their core expertise. "You can always find the skills and knowledge you need here," she says. "It's a great environment for meeting like-minded people and talking science. It's also a very good experience for my team to be exposed to interesting and diverse thinking."

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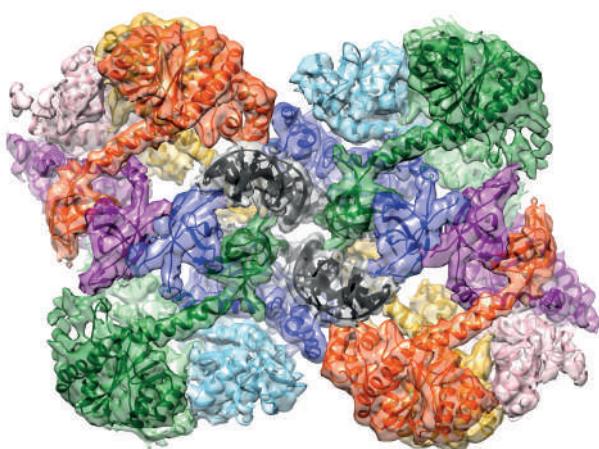
It's a very good experience for my team to be exposed to interesting and diverse thinking.

**Snezhana Oliferenko,  
King's College London**

**Snezhana Oliferenko**



# Focusing on the molecules of life



The biochemical processes of life are being revealed in atomic detail using sophisticated new microscopes which are revolutionising the field of structural biology.

#### CryoEM facility

Scientists at the Crick are using a technique called 'cryo-electron microscopy' or cryoEM, imaging complex biological processes in atomic detail.

The multi-million-pound microscopes use focused electron beams rather than light, resolving greater detail. Using electrons, they can see down to the molecular systems at work in our cells and tissues. Flash-freezing samples to around -190°C using liquid nitrogen preserves biological structure and gives the technique its name: 'cryo' means cold or frozen.

CryoEM has improved significantly in the past few years, moving from seeing proteins as fuzzy blobs to being able to resolve the full molecular structure. These advances were recognised in the award of last year's Nobel Prize for Chemistry. The Crick has a set of these microscopes available for research in its Structural Biology science technology platform, led by Phil Walker.

The Crick's cryoEM facility is located in the basement, 20m below ground. The 4m high box enclosing the microscope manages the temperature, air flow and vibrations that could disturb the images collected.

The whole microscope is set on a base mounted on compressed air that actively dampens vibrations and disturbances, while metal in the walls of the room shields the microscope from stray magnetic fields.

Automated computer control of the microscope allows data to be continuously collected overnight and to be operated remotely.

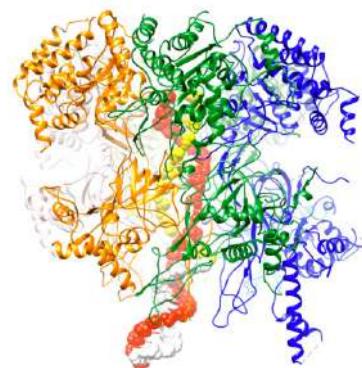
The Crick has two of these state-of-the-art Titan Krios instruments, funded by the Medical Research Council, along with several smaller instruments to support a wide range of science at the Crick.

Thanks to related Wellcome funding, a third Titan Krios microscope will also be housed at the Crick for use by a consortium of London universities and institutes: Imperial, the Institute of Cancer Research, King's and Queen Mary University of London. This collaboration should see further sharing of skills and expertise in cryoEM among the research community in London. The large investment in these microscopes by the Crick, its founders and collaborating organisations, reflects the depth of insight cryoEM can now give into biological processes.

The improvement in the microscopes has come from a range of developments. New cameras that are much more sensitive, better sample preparation and new data processing approaches have all come together to give a significantly greater level of detail with cryoEM.

*Opposite: Phil Walker, Andrea Nans and Peter Rosenthal work on a Titan Krios cryo-electron microscope. Below: Structure of the integrase molecular machinery from a virus related to HIV. Courtesy of Peter Cherepanov, Group Leader at the Crick.*

*Above: Molecular structure of a helicase as it begins to unwind DNA. Courtesy of Ferdos Abid Ali in the Alessandro Costa lab.*



# Bringing academia and industry closer together

Projects with GSK and AstraZeneca are combining expertise and delivering scientific progress.

Seeing scientific findings and discoveries develop into new treatments is a key priority for the Crick. We achieve this in many ways – such as by creating collaborative links with others who can help take ideas forward.

Our partnerships with GSK and AstraZeneca enable scientists from these companies to work alongside Crick researchers – sharing ideas, expertise and approaches while working together on promising early-stage projects. It offers the scientists a chance to learn new skills, broaden their experience and develop their careers.

### Industrial revelation

As a PhD student in Caroline Hill's lab at the Crick, Daniel Miller made a discovery that looked interesting. He'd been looking at a particular cell signalling pathway in breast cancer in mice and found a related protein that was produced in high amounts. It appeared to help drive growth of the cancer cells.

Daniel spent nine months at AstraZeneca in Cambridge on a joint project to take these findings forward. "We came up with lots of ideas we would never have thought of on our own," he says.

Thanks to the collaboration, Daniel joined a team at AstraZeneca which uses a state-of-the-art platform to produce antibodies that bind tightly to proteins of interest. Having successfully made antibodies against the protein he discovered during his PhD, Daniel is now back at the Crick seeing if they neutralise the protein in breast cancer cells in mice.

The group's next steps will be to see if the antibodies have the same effects in human cancers. "We're now collecting samples from biopsies of patients with pancreatic, breast and skin cancers," explains Daniel.

Daniel found the AstraZeneca experience immensely rewarding and is including pharma companies in his search for his next position. "During my PhD, I was drawn to the idea of working in an industry setting. I'm enthusiastic about taking the basic biology and turning it into new drugs," he says.

### New perspectives

A medicinal chemist by training and with more than a decade of experience at GSK in the US, Hilary Eidam is currently working in Barry Thompson's Epithelial Biology Laboratory at the Crick, through a partnership between the Crick and GSK.

The lab focuses on organ size control, and the pathway which tells a body when organs, such as the heart, have grown large enough during development. The hope is that the lab's work could ultimately provide insights into the possibilities of organ regeneration.

When Hilary's 18-month spell at the Crick ends and she returns to Philadelphia, she'll be taking some valuable lessons home with her. "Although my 12 years in drug discovery have given me a deep knowledge of the challenges involved in taking a drug through from molecule to patient, and great experience of working on pharmacokinetics, I've never had deep biology expertise or training," she says. While her chemistry skills are valued by the team at the Crick, she feels she's gained significant biological insight during her time at the institute. "I'm now able to bring a different perspective to my work that will make a big contribution to projects back at GSK."

"I'll also be able to draw on the different ways of working I've experienced here," Hilary adds. She points to the fact that people rarely call or email each other at the Crick – communication is always face-to-face in real time. "That's a really collaborative approach and something that we can all learn from."

"Collaborations like this between academia and industry can be highly beneficial to mankind," Hilary believes. "To borrow a thought from Sir Keith Peters: academia and industry are both vital, and their areas of expertise have very little overlap – why on earth wouldn't we work together and rise to the challenges posed by human healthcare?"

## Freedom to develop

A spin-out company can be the best way to assemble a team of dedicated scientists and experts and source the significant investment needed to develop a technology. Over the last three years, we have licensed intellectual property to three spin-out companies in partnership with our founders and external investors.

Achilles Therapeutics aims to develop a truly personalised approach to cancer therapy that harnesses the immune system to destroy cancer cells. Professor Charles Swanton, a Group Leader at the Crick, is one of four founders of the company that draws on the discovery research carried out at the Crick and UCL. Achilles was launched in May 2016 with a financing round of £13.2m led by Syncona, with the Cancer Research Technology Pioneer Fund and the UCL Technology Fund.

GammaDelta Therapeutics is exploiting the unique activities of gamma delta T cells that are found in the body's tissues where cancers and inflammatory diseases take hold. The new company draws on work by Adrian Hayday and Oliver Nussbaumer of the Crick and King's College London which could lead to new immunotherapies for a broad range of cancers and autoinflammatory diseases. GammaDelta Therapeutics was co-founded in 2016 with support from life sciences investors Abingworth and Cancer Research Technology. The spin-out company received a \$100m cash injection from drug firm Takeda Pharmaceuticals in 2017 to further develop its new class of immunotherapies.

Ervaxx is a spin-out created by investment company SV Health Investors based on the research of George Kassiotis' lab at the Crick on human endogenous retrovirus (HERV). These retroviruses normally lie dormant within our genomes, but can become active in cancer cells. Ervaxx intends to develop a pipeline of first-in-class cancer vaccines based on these findings.

Hilary Eidam & Daniel Miller



# Patterns in art and science

The latest exhibition at the Crick showcases a series of unique collaborations between scientists and artists in the field of sculpture, film and spoken word.

The Crick's exhibition, *Deconstructing patterns: art and science in conversation*, provides a fresh perspective on the patterns found within our bodies.

Presented over three 'zones', *Deconstructing patterns* explores different molecular and cellular patterns studied at the Crick, each one introduced by a unique artist commission. The artworks offer an alternative way of visualising and describing the forms and functions that so intrigue our scientists. By taking patterns apart, deconstructing them, both the artists and scientists are seeking new insights into the puzzle of how the complexity of the human body arises.

In *Infinite Instructions*, DNA research and the search for the patterns amongst huge genomic data sets provide the starting point for an immersive sound installation by the award-winning poet Sarah Howe and sound artist Chu-Li Shewring.

For the *Transforming Connections* zone, artist Helen Pynor has created a mesmerising installation that combines light, photography and sculpture to explore the movement of patterns during the metamorphosis of the fruit fly. The commission is based on the work of Iris Salecker's lab, which investigates the development of the visual part of the fruit fly's brain.

Finally, *Breaking Symmetry* challenges our understanding of patterns even further, highlighting the creativity inherent in asymmetry, which is essential to the healthy development of all organisms. Nate Goehring's research group worked closely with young people on a summer filmmaking project at Holborn Community Association. The result is a wonderfully surreal fictional narrative created by the students which offers a metaphor for the lab's research into the first appearance of asymmetry in the nematode worm.

'Deconstructing Patterns' runs until 1 Dec 2018 in the Manby Gallery at the Francis Crick Institute.

Visitors find patterns in a sound installation by Sarah Howe and Chu-Li Shewring (far right), while another finds out about the science which inspired it (right).



## Engaging and inspiring our visitors

Deconstructing patterns is the latest in a programme of exhibitions and events that aims to excite and inspire the public with science.

The Crick's size, location and profile means that we have a unique opportunity to share our work with the general public, schools, our local community and beyond.

Our programme gives people a rare opportunity to connect with our researchers, explore what goes on behind the scenes at the Crick and gain fascinating insights into our research.





## AWARDS AND APPOINTMENTS

# Rewarding research

Our work was recognised by a host of high-level awards in 2017/18.



**Jonathan Stoye**

### Royal Society Fellowship

Jonathan Stoye, Group Leader at the Crick, was elected a Fellow of the Royal Society in recognition of his work on genetic interactions between retroviruses and their hosts. Retroviruses, a family of viruses that includes HIV, are able to insert their genetic code into healthy host cells. Jonathan was one of the first virologists to look at natural mechanisms of immunity, and in 1996 cloned the first mammalian gene found to offer natural immunity to retroviruses, the Fv1 mouse gene. His work has helped to shape the field as we know it today.

### Fellows of the Academy of Medical Sciences

Group Leader Robert Wilkinson and David Roblin, previously Chief Operating Officer and now our Senior Scientific Translation Fellow, were both elected Fellows of the Academy of Medical Sciences. David has made many contributions to translational medicine, turning research discoveries into treatments that directly benefit lives and the economy. Robert has worked on tuberculosis and HIV in South Africa and London while maintaining a first-class research programme.



**Charlie Swanton**

### EMBO membership

Charlie Swanton was elected to membership of the European Molecular Biology Organisation [EMBO]. This came just a few weeks after the announcement of his winning the 2016 San Salvatore Foundation award for research that is leading to new approaches to anti-tumour therapeutics.



**Rafael di Marco Barros**

### Pontecorvo Prize

Cancer Research UK's Pontecorvo Prize for best PhD thesis was awarded to Rafael di Marco Barros, who completed his PhD in Adrian Hayday's lab. Rafael's research focused on the mechanism by which cells that line the intestinal wall may regulate the composition of immune cells in surrounding tissues, contributing to intestinal health and disease.

### New Year's Honours

Three Crick scientists were recognised in the 2018 New Year's Honours list. Sir Keith Peters was appointed Knight Grand Cross (GBE) for his impact on medicine and science, while Professor Robin Lovell-Badge became a CBE for services to genetics, stem cell biology and the public understanding of science. DeepMind co-founder Demis Hassabis, who sits on the Crick's Scientific Advisory Board, was awarded a CBE for services to science and technology.



**Sir Peter Ratcliffe**

#### **Buchanan Medal**

The Royal Society awarded our Clinical Research Director, Professor Sir Peter Ratcliffe, its prize for distinguished contributions to the biomedical sciences. Peter was awarded the Buchanan Medal for his ground-breaking research on oxygen sensing and signalling pathways which mediate the responses of cells to low oxygen levels.



**Cristina Lo Celso**

#### **Foulkes Foundation Medal**

Cristina Lo Celso, a stem cell biologist at Imperial College London with a satellite group at the Crick, won the Academy of Medical Sciences Foulkes Foundation Medal. The prize was awarded in recognition of her work in using stem cells to study how leukaemia develops and relapses. The Foulkes Medal is awarded biennially to a rising star within biomedical research.

#### **In addition, the year saw:**

- The inaugural Sir David Cooksey Prize in Translation awarded to Lucy Collinson, Martin Jones, Lizzy Brama and Chris Peddie, who have pioneered new electron microscopy imaging techniques at the Crick.
- Emeritus scientist Tomas Lindahl was elected a fellow of the American Association for the Advancement of Science for distinguished contributions to the study of DNA repair mechanisms.
- Our Chief Information Officer (CIO), Alison Davis, was named the UK's CIO of the Year at the Women in IT awards.
- Our building beat 90 finalists to win the Silver Jubilee Cup for best overall project in the Royal Town Planning Institute's (RTPI) Awards for Planning Excellence.

# Supporting new discoveries

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We're really proud to be supporting a scientist at such a dynamic, ground-breaking facility and thrilled to be part of the amazing work that the Crick carries out.

**Alix Green, Josh Carrick Foundation**



**Josh Carrick**

We are grateful to the wide range of partners, funders and donors who come together to support the Crick.

With their help, we are training leading scientists and funding researchers as they collaborate across disciplines to pursue greater understanding of our biology, and improve prevention, diagnosis and treatment of human disease.

Already, the Crick's approach is proving that research is better and moves faster when people work together, sharing their discoveries and expertise. We need to build on this momentum and ensure the Crick's community of leading researchers have the funding they need to carry out their work.

The Crick is now launching a fundraising partnership with Cancer Research UK to attract and secure philanthropic support to help further its mission of understanding human disease and accelerating the development of new treatments.

Investment from generous donors is vital for sustaining and extending our high-quality research programme.

One of these supporters is the Josh Carrick Foundation, which was set up in 2012 in memory of Josh Carrick, who died of testicular cancer at the age of 23. The foundation's trustees have developed a fundraising strategy to support research into cancer and raise awareness of testicular cancer.

The foundation's generous donations help to fund the work of Group Leader Erik Sahai, whose research focuses on how cancer spreads through the body.

"We have supported Erik since 2013 and believe the work he is doing to understand why cancer spreads and why existing therapies sometimes fail is fundamental to the fight against the disease," explains Alix Green, a trustee of the foundation. "We're really proud to be supporting a scientist at such a dynamic, ground-breaking facility and thrilled to be part of the amazing work that the Crick carries out."



**Erik Sahai**

# Looking forward

## **Discovery Without Boundaries**

We will continue to support our research groups and science facilities to pursue discoveries at the forefront of biomedicine. As new collaborations and opportunities become more established at the Crick, we expect to see many more examples of research advances, similar to those from the past year highlighted on pages 8 to 23.

Recruitment and training of outstanding early-career scientists remains a priority for the institute, with a large proportion of existing faculty engaged in the search process. Eight more new appointments will arrive in the coming year – including four researchers who will lead new groups in physics, chemistry and informatics as applied to biomedical problems, the result of a joint recruitment process with our three university partners.

As well as broadening our research in the physical sciences, we are improving our connections and collaborations with clinical research, and during the coming year we will launch our first dedicated call for clinical candidates wishing to start a research group at the Crick. We will be providing more research training for clinicians and building closer links with partner institutions on the medical implications of our research. We recently launched a new postdoctoral clinical

fellowship scheme, which complements the existing PhD level opportunities at the Crick for clinicians wishing to gain from a full training in basic science and do research at a leading institute. ‘Medicine at the Crick’ is a new series of events starting this year for scientists and clinicians from the Crick and the wider UK biomedical research community. The themed events – the first one is on gene and gene editing therapy – will stimulate new collaborations in medical research and demonstrate how advances in biomedical sciences could benefit patients in the future.

As well as broadening the interdisciplinary nature of the Crick’s research, benefiting from the sharing of ideas and expertise, we aim to ensure our leading researchers have the funding they need to carry out their work. The Crick is launching a fundraising partnership with Cancer Research UK to attract and secure philanthropic support to help further its mission in understanding human disease and accelerating the development of new treatments. Investment from generous supporters is vital for sustaining and extending our research programme.

Offering the best possible support to science is a necessary part of achieving our aim of being world class in biomedical

research. A review of the structure and effectiveness of our operations functions has been carried out, and an operational delivery plan is being developed to make us better able to deliver the Crick’s strategy ‘Discovery Without Boundaries’. This will make our operational support for science more consistent, better coordinated and responsive to people’s needs.

A great place to work strategy is also being developed in consultation with staff and students from across the institute. This aims to make sure we have everything in place to attract, train and develop staff who are engaged in the Crick’s work and vision, and who know their work is valued.

We continue to build on these strong foundations for pursuing discoveries in biological and biomedical science, making sure we attract the best people, they have the right support and our work is truly multidisciplinary – all with a commitment to excellence in our research. During 2018/19 we will have our first formal review by our funders – referred to as the Crick Establishment Review – which will assess whether the Crick’s set-up, governance and strategic direction is progressing as expected.

# Financial review

As the Institute completes its third full year of operations, the financial results continue to move towards a position of an operational institute rather than one in transition from a set-up and construction project, albeit the dynamic nature of operations means there will always be new funding streams and activities replacing others.

Total income for the year was £146.6m (2017: £160.6m), of which the large majority, £144.5m (2017: £159.9m), comes from research grants (or similar types of income) from its various funders. In the previous year this funding included £6.6m of donated assets in the form of scientific equipment (none in 2018), and donated services and facilities of £3.9m (2017: £9.0m). The drop in income is explained by the falling away in these donated assets, services and facilities, which were all related to the support provided by the Institute's founders during the

set-up phase of the organisation, and the transition to full operation.

Core funding is secured from funders for the next 2 years.

Total expenditure of £175.1m (2017: £168.2m) means that the institute shows a deficit of £28.5m (2017: £7.6m). The deficit position is driven by the depreciation charge (£22.1m, 2017: £14.0m) now made to the Statement of Financial Activities following occupation and commencement of use of the new building, and a full year of that charge now being incurred annually.

Net assets at 31 March 2018 are £605.7m (2017: £634.2m). This is primarily represented by fixed assets, and those assets primarily represented by the new laboratory building.

The statutory position includes:

- Non-recurring costs that relate to the costs of the set-up of the institute,

and the project management of construction and costs of moving to its new laboratory building;

- The costs of depreciation of the building. The building cost was funded up-front by contributions from the institute's founders, recorded as share capital. Future capital replacement of component parts of the building is funded under a lifecycle costs arrangement that is part of the overall joint venture agreement.

These costs are charged to the Statement of Financial Activities in the year, having originally been funded by share capital. This means that for the foreseeable future, the Statement of Financial Activities will show a large deficit.

The statutory position excludes capital expenditure managed against and funded by annual core grants (albeit the depreciation element of that expenditure over time is included).

The Crick's longer term financial planning includes a review of its underlying and recurring result, which on a non-statutory basis is:

	2018 £m	2017 £m
Statutory result for the year	<b>(28.5)</b>	[7.6]
Building depreciation	<b>22.1</b>	14.0
Other depreciation	<b>17.5</b>	13.4
Capital expenditure funded from annual grants and donated assets	<b>(11.1)</b>	(29.2)
Building project revenue costs	<b>1.5</b>	8.8
Premises rent paid in kind (Clare Hall)	<b>—</b>	3.3
Non-statutory underlying result for the year	<b>1.5</b>	2.7

## Reserves policy

The charity reviews its reserves policy each year, taking account of its planned activities and the financial requirements forecast for the forthcoming period.

The charity's ongoing operational mission is funded via grants from both shareholders and external grant providers.

Share capital has been invested by the founding shareholders to establish the institute, and these funds are represented by the charity's assets. Over time, depreciation on the new building, currently

representing a major part of the charity's assets, will accumulate as a deficit on the unrestricted funds.

Free reserves of a charity are often defined in relation to the level of unrestricted funds. The expected deficit on unrestricted funds means that the charity must take a slightly different approach, and the Crick defines its free reserves as equal to the value of net current assets, less:

- any restricted funds held as net current assets;

- any amounts drawn down from shareholders in relation to the building project and not yet expended;
- deficit budget plans;
- other contracted capital commitments;
- other relevant adjustments.

The trustees have regard to the information contained in Charity Commission guidance note CC19, "Charity Reserves: Building Resilience", and in particular the guidance on ensuring the maintenance of beneficiary services and the risks of unplanned closure associated with the charity's business model.

Free reserves under this definition are:

	2018 £m	2017 £m
Net current assets	<b>25.6</b>	29.6
Restricted funds held within net current assets	<b>(3.0)</b>	(2.1)
Unexpended building project funds	<b>(4.5)</b>	(6.5)
Capex budget rollover	<b>(4.4)</b>	(6.2)
	<b>13.7</b>	14.8

The trustees believe that the charity should have access to free reserves equivalent to three months' core funding income in order to maintain the viability of the institute, being approximately £30m.

A £20m standby facility (corresponding to approximately two months' expenditure) has been made available by the shareholders. If free reserves held in cash are less than three months' expenditure, should a material adverse event occur that threatens the charity's overall liquidity, the charity will be able to call on this facility to support its operations.

The remaining £10m is made up of amounts held by the institute, and the current position of £13.7m means that the charity is operating at a level slightly above the target, which the trustees consider to be satisfactory.

#### Investment policy

At this stage of the establishment of the institute, the investment policy continues to be confined to the management of short-term liquid funds. The investment principle is to achieve the secure investment of excess cash resources of a short-term nature, diversified to ensure limited concentration of investment. This principle has been achieved during 2017/18.

Assets are safeguarded by investing only with approved counterparties. Investments are risk-averse and non-speculative, and the charity places no income reliance on interest earned. Investments are selected to ensure security, liquidity and diversification. The charity's investment return objective is to ensure that investments earn a market rate of interest consistent with its income principle.

#### Going concern

The trustees consider that the charity has adequate resources available to it to continue in operational existence for the foreseeable future having made appropriate enquiries, reviewed contracts and confirmed support from the shareholders. The trustees additionally consider that the charity will continue to have adequate resources through shareholders' committed funding to cover all existing capital commitments. Shareholders have committed funding for operational spending which is sufficient to deliver a balanced budget. Accordingly, the trustees have adopted the going concern basis in preparing the financial statements.

# GOVERNANCE

The trustees present their annual directors' report and strategic report together with the consolidated financial statements for the charity and its subsidiary (together, 'the Group') for the year ended 31 March 2018, which are prepared to meet the requirements for a directors' report and financial statements for Companies Act purposes.

The financial statements comply with the Charities Act 2011, the Companies Act 2006, and the Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK (FRS102) effective 1 January 2016 (Charity SORP).

The trustees' report includes the additional content required of larger charities.

## Reference and administrative details

The Francis Crick Institute Limited ('the charity', 'the institute' or 'the Crick') is registered with the Charity Commission, charity number 1140062. The charity has operated and continues to operate under the name of the Francis Crick Institute. The Francis Crick Institute is a public benefit entity.

Charity number: 1140062

Company number: 6885462

Registered office: 1 Midland Road, London NW1 1AT

### Advisers

Auditor	Deloitte LLP	3 Victoria Square, Victoria Street, St Albans AL1 3TF
Bankers	HSBC Bank plc	60 Queen Victoria Street, London EC4N 4TR
Solicitors	CMS Cameron McKenna LLP Herbert Smith Freehills LLP	Mitre House, 160 Aldersgate Street, London EC1A 4DD Exchange House, Primrose Street, London EC2A 2EG
Internal auditor	KPMG LLP (to 31 March 2018) RSM UK (from 1 April 2018)	15 Canada Square, London E14 5GL 170 Midsummer Boulevard, Milton Keynes MK9 1BP

### Directors and trustees

The directors of the charitable company are its trustees for the purposes of charity law.

	Appointed	Resigned	Appointment
Lord Browne of Madingley [Chair]	1 August 2017		Independent
Sir David Cooksey [Chair]		1 August 2017	Independent
Kate Bingham	8 May 2017		Independent
Professor Doreen Cantrell		21 September 2018	Medical Research Council
Professor Margaret Dallman			Imperial College London
Dr Jeremy Farrar			Wellcome Trust
Ian Foulkes	21 September 2018		Cancer Research UK
Dr Lynne Gailey		8 May 2017	Independent
Brian Gilvary	10 September 2018		Independent
Professor Peter Gruss		31 January 2018	Independent
Sir Harpal Kumar		29 June 2018	Cancer Research UK
Professor Sir Robert Lechler			King's College London
Dame Ottoline Leyser	21 September 2018		Independent
Professor David Lomas			University College London
Professor Fiona Watt	21 September 2018		Medical Research Council
Lord Willetts of Havant			Independent
Philip Yea		21 September 2018	Independent

### Organisational management and responsibilities of the Board

The trustees are responsible for ensuring that the charity's aims are being met. The trustees set strategy, decide priorities, establish funding policies and allocate budgets. The trustees develop and agree the overall scientific strategy and policies related to biomedical research and innovation and monitor and review risk, progress and performance.

The Board has established sub-committees to assist with its responsibilities as follows:

#### Audit and Risk Committee

The Audit and Risk Committee reviews matters of internal control, risk, compliance with reporting requirements, and liaison with, and monitoring of, internal and external auditors.

Philip Yea (Chair)	Resigned 21 September 2018
Brian Gilvary (Chair)	Appointed 10 September 2018
Kate Bingham	Appointed 8 May 2017
Dr Lynne Gailey	Resigned 8 May 2017
Christopher Mottershead	

#### Remuneration Committee

The Remuneration Committee reviews remuneration matters, setting the overall pay policy for the institute, setting pay for the Executive Committee, and deciding on overall annual salary increases.

Lord Willetts (Chair)	Appointed 8 May 2017
Dr Lynne Gailey (Chair)	Resigned 8 May 2017
Sir David Cooksey	Resigned 1 August 2017
Dr Jeremy Farrar	
Professor David Lomas	

#### Nominations Committee

The Nominations Committee reviews and approves key non-executive appointments.

Lord Browne (Chair)	Appointed 1 August 2017
Sir David Cooksey (Chair)	Resigned 1 August 2017
Professor Margaret Dallman	
Jeremy Farrar	
Lord Willetts	

The executive team, led by the Chief Executive Officer, Sir Paul Nurse, reports directly to the trustees and is responsible for the day-to-day management of the charity's operations and activities.

#### Executive Committee

Sir Paul Nurse*	Chief Executive Officer
Dr Samantha Barrell*	Chief Operating Officer
Dan Fitz*	General Counsel / Company Secretary (from October 2018)
Jane Hughes*	Director of Communications
Dr Steven Gamblin*	Director of Science Operations
Professor Malcolm Irving	University Partner Liaison
Stéphane Maikovsky*	Chief Financial Officer
John Macey*	Director of Human Resources
Sir Richard Treisman*	Research Director

\*Key management personnel

There is a clear organisation structure, with documented lines of authority and responsibility for control. The trustees approve the annual budget and expenditure targets, and monitor actual and forecast budgets and cash flows.

#### Key appointments during the year

Lord Browne of Madingley, the former BP chief executive, became the Chairman of the Francis Crick Institute in autumn 2017.

As Chairman, Lord Browne leads the Crick's Board of Trustees in its role overseeing the institute's activities and making sure the right strategy, resources and governance are in place to realise our vision for research excellence.

Lord Browne was chief executive of BP from 1995 to 2007, is a former President of the Royal Academy of Engineering and was Chairman of the Tate galleries for ten years. He sits as a crossbench member of the House of Lords and was the government's lead non-executive director from 2010 to 2015. He is currently Executive Chairman of L1 Energy and Chairman of Huawei Technologies (UK), and is a member of the boards of a number of other private and not-for-profit organisations.

Sam Barrell is the Chief Operating Officer at the Francis Crick Institute, responsible for leading the operational management and running of the institute. She is driving efforts to ensure the Crick works as effectively as possible in supporting the science being carried out here.

# GOVERNANCE CONTINUED

Sam joined the Crick in September 2017 from a career in the NHS as a noted healthcare leader and former GP. As Chief Executive of Taunton and Somerset NHS Foundation Trust, she led a Global Digital Exemplar for the NHS rated “outstanding” for care. Previously she was the Chief Clinical Officer leading the formation of South Devon and Torbay Clinical Commissioning Group, at the time of the 2012 reforms of the National Health Service.

Sam sits on a number of advisory boards for science and healthcare networks and was awarded the CBE in 2014.

## **Structure, governance and management**

The charity is a charitable company limited by shares.

### **Governing Document**

The charity is governed by its Articles of Association originally adopted on 20 January 2011, revised on the accession of new shareholders on 14 October 2011, and again on 4 December 2015.

### **Trustees**

The Articles of Association of the charity provide for the appointment of directors, who also act as trustees. The directors of the charity are its trustees for the purposes of charity law, and throughout this report are collectively referred to as the trustees.

Each of the charity's six shareholders nominates a trustee, and there are five independent trustees including the Chair. Independent trustees are chosen from a variety of backgrounds for their skills and experience. A tailored induction programme is provided for trustees on appointment. Trustees act on a voluntary basis and are not remunerated.

### **Related parties**

The charity's shareholders are Cancer Research UK, the Medical Research Council, Wellcome Trust, University College London, Imperial College London and King's College London. The shareholders have entered into a Joint Venture Agreement which, inter alia, establishes the basis on which funding will be made available to the charity. The charity has two wholly owned subsidiaries:

— UKCMRI Construction Limited which exists to design and construct the building for the new institute, a project that is now in its final run-off stages.

— Francis Crick Trading Limited which is currently dormant but that will be used in future to carry out trading activities.

### **Pay policy for key management**

Key management are the members of the Executive Committee who are employees of the charity (as listed on page 43).

The overall remuneration packages for key management are set by the Remuneration Committee. When new members of the key management group are appointed, a benchmarking exercise is carried out by the institute's Human Resources team.

The overall policy is that the institute pay is set using the upper quartile of the Higher Education and Charity sectors and median to lower quartile of the Pharmaceuticals sector as benchmarks. The overall package is approved by the Remuneration Committee prior to a formal offer being made.

Individual pay awards for key management are then made annually by the Remuneration Committee based on a review of performance carried out by the Chief Executive Officer and Chief Operating Officer.

### **Strategic report**

#### **Objectives and activities**

#### **Charitable objects**

The charity's objects, as set out in its Articles of Association, are:

The advancement of human health and education for the benefit of the public by the promotion and carrying out, directly or indirectly, of all aspects of biomedical research and innovation, which shall include in particular the following:

1. Establishing, operating and managing a centre for medical research and innovation;
2. Engaging in, encouraging and supporting:
  - i. Research into any of the biosciences,
  - ii. The discovery, invention, improvement and development and application of preventions, treatments, cures, diagnostics and other medical agents, methods and processes that may in any way prevent or relieve illness, disease or disorders of whatever nature (including, without limitation, all forms of cancer), and
  - iii. Developing and training scientists and supporting biomedical research endeavours.

### **Public benefit**

The trustees confirm that they have paid due regard to the public benefit guidance published by the Charity Commission and have referred to the guidance in the Charity Commission's general guidance on public benefit when reviewing their aims and objectives and in planning future activities. In particular, the trustees have considered how planned activities will contribute to the aims and objectives they have set.

In addition to the public benefits anticipated from the operation of science established at the Francis Crick Institute, the charity has also set out to deliver a broad spectrum of investment in engagement with the public, as described above under 'Discovery Without Boundaries Mission 5: Engage and inspire the public'.

### **Risk management and principal risks**

The Board is responsible for setting the Crick's strategic objectives, and the associated risk appetite and risk management culture. The Board takes an active role in the management of risk, and undertakes a risk review every six months.

The Board is responsible for approving the Crick's risk management policy which identifies eight categories of risk: Science, Translation, Infrastructure, Funding, People, Reputation, Safe Working Environment and Information.

The Board delegates to the Audit and Risk Committee the responsibility of reviewing risk management arrangements for identifying and monitoring risk and the effectiveness of internal control systems. The Audit and Risk Committee sits on a quarterly basis to undertake their reviews.

The Board delegates to the Crick's Executive Committee the day-to-day management of risk. The Executive is therefore responsible for implementing the risk management policy and effective risk management and internal control systems. The Executive Committee reviews risks on a quarterly basis.

Each risk category is headed by a coordinator and together the coordinators form the Crick's Risk Management Team. The coordinators are responsible for identifying risks with risk owners (usually functional heads), developing action plans to manage the risk and monitoring progress against actions. They also maintain a risk register. Risks that are above institute appetite level are reviewed by the Risk Management Team on a quarterly basis and are reported to the Executive Committee, the Audit and Risk Committee, and the Board.

Risk management is encouraged and conducted at all levels in the organisation. The top 10 risks above the Crick's risk appetite level, and their current management are summarised in order below.

Risk Category	Risk	Management of risk
<b>Funding</b>	The funding available is not sufficient to deliver the Discovery Without Boundaries strategy or meet budget expectations.	Management is working with Founders to agree core funding and overhead recovery.
<b>Infrastructure</b>	Disruption to science arising from noise, vibrations and electromagnetic interference from CrossRail 2 construction and operation.	Undertake technical analysis to determine need for mitigation and agree actions with CrossRail 2.
<b>Funding</b>	Not receiving budgeted overhead income from Universities.	Management is working with University partners to agree their contributions to overheads.
<b>Information</b>	Cybersecurity breach.	Security awareness training programmes are being developed and investment is being made in security infrastructure.
<b>Funding</b>	A crisis affects Founders from delivering planned Core funding.	The Crick is diversifying its income stream by developing a philanthropy programme. A three-month expenditure reserve has been developed to protect against short-term liquidity pressures.
<b>Reputation</b>	Institute review is critical of performance resulting in funding cuts and loss of reputation.	Regular communication about Crick research, investment in communications and reputation management and engagement with Founders will ensure that this risk is being managed.
<b>Safe Working Environment</b>	Injury or death from experiments or unexpected emergency response.	Risk assessments and compliance with policies and procedures and training of emergency responders will reduce the likelihood of such an event occurring.
<b>Funding</b>	Inability to replace EU grant income after Brexit.	A grants strategy is being developed which will include for example plans to pursue new sources of grant funding.
<b>Science</b>	Clinical culture and emphasis on human biology does not develop.	Recruitment of clinical group leaders is underway. Opportunities for interaction with clinical groups including seminars will increase engagement of clinical research.
<b>Science</b>	Inability to develop the multidisciplinary agenda.	The establishment of joint Crick – University initiatives is underway, with some events already completed.

Other areas of risk include credit and liquidity risks. Credit risk exposure is reduced by procurement selection procedures for any significant supply contracts entered into by the charity. The liquidity risk which the charity may be exposed to is managed by the provision of funding from the shareholders and cash flow management.

### Employee policies

#### Employment of disabled persons

The Crick recognises that one in three of the UK population is either disabled or close to someone who is, and one in five of the UK workforce is likely to have a disability, with those disabilities being either visible (for example, a mobility issue or visual impairment) or invisible, such as dyslexia or depression.

The Crick also recognises that to recruit and retain the best people, it must concentrate on ability, rather than disability, to maximise talent pools and utilise key skills. By focusing on key skills and competencies, the Crick can minimise bias and employ the best person for the job.

On learning that an applicant or an employee has a disability, the Crick will consider making reasonable adjustments. Detailed guidance has been produced and is available to managers in helping them determine what adjustments might be needed and whether those adjustments are reasonable.

# GOVERNANCE CONTINUED

## Employee engagement

The Crick is committed to ensuring that its employees are engaged with and enthusiastic about working at the Crick and contributing to Discovery Without Boundaries.

This takes a number of forms:

- The front page of the Crick intranet is a key source of news about Crick events, Crick achievements and Crick in the news.
- Regular all-staff “town hall” events are held in which employees are able to talk to and raise questions with the Chief Executive Officer and Chief Operating Officer.
- A Staff Consultative Forum has been set up, and any planned changes that will affect staff are discussed with the forum at formal meetings.
- An externally conducted and benchmarked staff survey is carried out bi-annually and the results acted on at a senior level.

## Statement of trustees' responsibilities

The trustees (who are also directors of the Francis Crick Institute Limited for the purposes of company law) are responsible for preparing the Trustees' Annual Report and the financial statements in accordance with applicable law and United Kingdom Accounting Standards (United Kingdom Generally Accepted Accounting Practice) including FRS 102 “The Financial Reporting Standard applicable in the UK and Republic of Ireland”.

Company law requires the trustees to prepare financial statements for each financial year which give a true and fair view of the state of affairs of the charitable company and the group and of the incoming resources and application of resources, including the income and expenditure, of the charitable group for that period.

In preparing these financial statements, the trustees are required to:

- select suitable accounting policies and then apply them consistently;
- observe the methods and principles in the Charities SORP;
- make judgements and estimates that are reasonable and prudent;
- state whether applicable UK Accounting Standards have been followed, subject to any material departures disclosed and explained in the financial statements; and
- prepare the financial statements on the going concern basis unless it is inappropriate to presume that the charitable company will continue its activities.

The trustees are responsible for keeping adequate accounting records that disclose with reasonable accuracy at any time the financial position of the charitable company and enable them to ensure that the financial statements comply with the Companies Act 2006. They are also responsible for safeguarding the assets of the charitable company and the group and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

The trustees are responsible for the maintenance and integrity of the corporate and financial information included on the charitable company's website. Legislation in the United Kingdom governing the preparation and dissemination of financial statements may differ from legislation in other jurisdictions.

## Disclosure of information to the auditor

The trustees who held office at the date of approval of this trustees' report confirm that, so far as they are each aware:

- there is no relevant audit information of which the charity's auditor is unaware; and
- each trustee has taken all the steps that they ought to have taken as a trustee to make themselves aware of any relevant information and to establish that the charity's auditor is aware of that information.

This confirmation is given and should be interpreted in accordance with the provisions of s418 of the Companies Act 2006.

## Auditor

Deloitte LLP have held office as company auditor following appointment by resolution of the Board on 4 February 2011, and have indicated their willingness to be reappointed for another term.

## Approval

The trustees' report incorporating the Strategic Report and Directors' Report was approved by the Board of Trustees and signed on its behalf by:

### Lord Browne of Madingley

Chairman  
21 September 2018

# INDEPENDENT AUDITOR'S REPORT TO THE MEMBERS AND TRUSTEES OF THE FRANCIS CRICK INSTITUTE LIMITED

## Opinion

In our opinion the financial statements of the Francis Crick Institute (the 'charitable company') and its subsidiaries (the 'group'):

- give a true and fair view of the state of the group's and the parent charitable company's affairs as at 31 March 2018 and of the group's incoming resources and application of resources, including the group's income and expenditure, for the year then ended;
- have been properly prepared in accordance with United Kingdom Generally Accepted Accounting Practice including Financial Reporting Standard 102 "The Financial Reporting Standard applicable in the UK and Republic of Ireland"; and
- have been prepared in accordance with the requirements of the Companies Act 2006.

We have audited the financial statements which comprise:

- the consolidated statement of financial activities (incorporating the income and expenditure account);
- the group and parent charitable company balance sheets;
- the consolidated cash flow statement; and
- the related notes 1 to 25.

The financial reporting framework that has been applied in their preparation is applicable law and United Kingdom Accounting Standards, including Financial Reporting Standard 102 "The Financial Reporting Standard applicable in the UK and Republic of Ireland" (United Kingdom Generally Accepted Accounting Practice).

## Basis for opinion

We conducted our audit in accordance with International Standards on Auditing (UK) (ISAs(UK)) and applicable law. Our responsibilities under those standards are further described in the auditor's responsibilities for the audit of the financial statements section of our report.

We are independent of the group and of the parent charitable company in accordance with the ethical requirements that are relevant to our audit of the financial statements in the UK, including the Financial Reporting Council's (FRC's) Ethical Standard, and we have fulfilled our other ethical responsibilities in

accordance with these requirements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

## Conclusions relating to going concern

We are required by ISAs (UK) to report in respect of the following matters where:

- the trustees' use of the going concern basis of accounting in preparation of the financial statements is not appropriate; or
- the trustees have not disclosed in the financial statements any identified material uncertainties that may cast significant doubt about the group's and the parent charitable company's ability to continue to adopt the going concern basis of accounting for a period of at least twelve months from the date when the financial statements are authorised for issue.

We have nothing to report in respect of these matters.

## Other information

The trustees are responsible for the other information. The other information comprises the information included in the annual report, other than the financial statements and our auditor's report thereon. Our opinion on the financial statements does not cover the other information and, except to the extent otherwise explicitly stated in our report, we do not express any form of assurance conclusion thereon.

In connection with our audit of the financial statements, our responsibility is to read the other information and, in doing so, consider whether the other information is materially inconsistent with the financial statements or our knowledge obtained in the audit or otherwise appears to be materially misstated. If we identify such material inconsistencies or apparent material misstatements, we are required to determine whether there is a material misstatement in the financial statements or a material misstatement of the other information. If, based on the work we have performed, we conclude that there is a material misstatement of this other information, we are required to report that fact.

We have nothing to report in respect of these matters.

## Responsibilities of trustees

As explained more fully in the trustees' responsibilities statement, the trustees (who are also the directors of the charitable company for the purpose of company law) are responsible for the preparation of the financial statements and for being satisfied that they give a true and fair view, and for such internal control as the trustees determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, the trustees are responsible for assessing the group's and the parent charitable company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless the trustees either intend to liquidate the group or the parent charitable company or to cease operations, or have no realistic alternative but to do so.

## Auditor's responsibilities for the audit of the financial statements

Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion.

Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with ISAs (UK) will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements.

A further description of our responsibilities for the audit of the financial statements is located on the FRC's website at: [www.frc.org.uk/auditorsresponsibilities](http://www.frc.org.uk/auditorsresponsibilities). This description forms part of our auditor's report.

# INDEPENDENT AUDITOR'S REPORT TO THE MEMBERS AND TRUSTEES OF THE FRANCIS CRICK INSTITUTE LIMITED CONTINUED

## Report on other legal and regulatory requirements

Opinions on other matters prescribed by the Companies Act 2006.

In our opinion, based on the work undertaken in the course of the audit:

- the information given in the trustees' report, which includes the strategic report and the directors' report prepared for the purposes of company law for the financial year for which the financial statements are prepared is consistent with the financial statements; and
- the strategic report and the directors' report included within the trustees' report have been prepared in accordance with applicable legal requirements.

In the light of the knowledge and understanding of the company and its environment obtained in the course of the audit, we have not identified any material misstatements in the strategic report or the directors' report included within the trustees' report.

## Matters on which we are required to report by exception

Under the Companies Act 2006 we are required to report in respect of the following matters if, in our opinion:

- adequate accounting records have not been kept by the parent charitable company, or returns adequate for our audit have not been received from branches not visited by us; or

- the parent charitable company financial statements are not in agreement with the accounting records and returns; or
- certain disclosures of trustees' remuneration specified by law are not made; or
- we have not received all the information and explanations we require for our audit.

We have nothing to report in respect of these matters.

## Use of our report

This report is made solely to the charitable company's members, as a body, in accordance with Chapter 3 of Part 16 of the Companies Act 2006. Our audit work has been undertaken so that we might state to the charitable company's members those matters we are required to state to them in an auditor's report and for no other purpose. To the fullest extent permitted by law, we do not accept or assume responsibility to anyone other than the charitable company and the charitable company's members as a body, for our audit work, for this report, or for the opinions we have formed.

**Jonathan Gooding, FCA  
(Senior statutory auditor)**

For and on behalf of Deloitte LLP  
Statutory Auditor  
St Albans, United Kingdom  
21 September 2018

# CONSOLIDATED STATEMENT OF FINANCIAL ACTIVITIES (INCORPORATING THE INCOME AND EXPENDITURE ACCOUNT)

YEAR ENDED 31 MARCH 2018

	Notes	Unrestricted funds £'000	Restricted funds £'000	Total 2018 £'000	Total 2017 £'000
<b>Income from</b>					
Core and related funding	3	127,398	73	<b>127,471</b>	144,636
Research grant funding		19	17,020	<b>17,039</b>	15,294
Charitable activities	5	1,269	422	<b>1,691</b>	370
Investment income		153	—	<b>153</b>	231
Other income		273	—	<b>273</b>	78
		129,112	17,515	<b>146,627</b>	160,609
<b>Expenditure on</b>					
Charitable activities	6	158,670	16,491	<b>175,161</b>	168,169
		158,670	16,491	<b>175,161</b>	168,169
<b>Net expenditure before transfers</b>					
Transfers between funds	18	26	[26]	—	—
<b>Net expenditure</b>		[29,532]	998	<b>(28,534)</b>	[7,560]
<b>Reconciliation of funds</b>					
Share capital issued and subscribed		—	—	—	1,423
<b>Net movement in funds</b>		[29,532]	998	<b>(28,534)</b>	[6,137]
Total funds at 1 April		630,026	4,182	<b>634,208</b>	640,345
Total funds at 31 March	18	600,494	5,180	<b>605,674</b>	634,208

All results are from continuing operations.

There were no other recognised gains or losses other than those listed above.

See note 16 for comparative Consolidated Statement of Financial Activities analysed by funds.

# BALANCE SHEETS

31 MARCH 2018

	Notes	Group 2018 £000	Group 2017 £000	Charity 2018 £000	Charity 2017 £000
<b>Fixed assets</b>					
Intangible assets	11	<b>138</b>	180	<b>138</b>	180
Tangible assets	12	<b>579,985</b>	604,387	<b>580,301</b>	604,707
Investments	13	—	—	—	—
		<b>580,123</b>	604,567	<b>580,439</b>	604,887
<b>Current assets</b>					
Debtors	14	<b>13,511</b>	16,762	<b>13,504</b>	16,426
Cash and cash equivalents		<b>38,569</b>	39,740	<b>38,556</b>	39,373
		<b>52,080</b>	56,502	<b>52,060</b>	55,799
<b>Liabilities</b>					
Creditors falling due within one year	15	(26,529)	(26,861)	(26,482)	(26,140)
<b>Net current assets</b>		<b>25,551</b>	29,641	<b>25,578</b>	29,659
<b>Net assets</b>		<b>605,674</b>	634,208	<b>606,017</b>	634,546
<b>Funds</b>					
Called up share capital	17	<b>629,566</b>	629,566	<b>629,566</b>	629,566
Share premium	17	<b>12,751</b>	12,751	<b>12,751</b>	12,751
Unrestricted funds	18	(41,823)	(12,291)	(41,480)	(11,953)
Restricted funds	18	<b>5,180</b>	4,182	<b>5,180</b>	4,182
		<b>605,674</b>	634,208	<b>606,017</b>	634,546

Notes 1 to 25 form part of these financial statements.

A separate Statement of Financial Activities and Income and Expenditure Account for the charity has not been presented as the charity has taken advantage of the exemption afforded by section 408 of the Companies Act 2006. The results for the charity are disclosed in note 13.

The financial statements of the Francis Crick Institute Limited were approved and authorised for issue by the Board of Trustees on 21 September 2018 and signed on its behalf by:

## Lord Browne of Madingley

Chairman

Company registration number: 6885462

# CONSOLIDATED CASH FLOW STATEMENT

YEAR ENDED 31 MARCH 2018

	Notes	2018 £000	2017 £000
<b>Cash flows generated by operating activities</b>	22	<b>13,999</b>	15,649
<b>Cash flows from investing activities:</b>			
Interest received		153	231
Proceeds from sale of equipment		—	38
Purchase of tangible fixed assets		(15,323)	[37,992]
<b>Net cash flows used in investing activities</b>		<b>(15,170)</b>	[37,723]
<b>Cash flows from financing activities:</b>			
Cash proceeds from issuing shares		—	1,423
<b>Net cash flows from financing activities</b>		<b>—</b>	1,423
<b>Net decrease in cash and cash equivalents</b>		<b>(1,171)</b>	[20,651]
<b>Cash and cash equivalents at beginning of year</b>		<b>39,740</b>	60,391
<b>Cash and cash equivalents at the end of the year</b>		<b>38,569</b>	39,740
<b>Reconciliation to cash at bank and in hand:</b>			
Cash at bank and in hand		<b>38,569</b>	39,740
Cash equivalents		—	—
<b>Cash and cash equivalents</b>		<b>38,569</b>	39,740

# NOTES TO THE FINANCIAL STATEMENTS

YEAR ENDED 31 MARCH 2018

## 1. Accounting policies

The principal accounting policies adopted, judgements and key sources of estimation and uncertainty in the preparation of the financial statements are as follows:

### a. Basis of preparation

The financial statements have been prepared in accordance with Accounting and Reporting by Charities: Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland [FRS 102] (effective 1 January 2015) – [Charities SORP (FRS 102)] and the Companies Act 2006.

The Francis Crick Institute Limited meets the definition of a public benefit entity under FRS 102. Assets and liabilities are initially recognised at historical cost or transaction value unless otherwise stated in the relevant accounting policy notes.

As described in the Trustees' Report, the trustees consider that the Francis Crick Institute Limited has adequate resources available to it to continue in operational existence for the foreseeable future having made appropriate enquiries, reviewed contracts and confirmed support from the shareholders. Accordingly they have adopted the going concern basis in preparing the financial statements.

### b. Group financial statements

The financial statements consolidate the results of the charity and its wholly owned subsidiary UKCMRI Construction Limited on a line-by-line basis. The results of the subsidiary are disclosed in note 13.

### c. Fund accounting

Unrestricted funds are general funds that are available for use at the trustees' discretion in furtherance of the objectives of the Francis Crick Institute Limited.

Restricted funds are funds that have been donated or granted for a specific use. These funds are expended in accordance with the requirements of the donor or grantor.

### d. Incoming resources

Income is recognised in line with the SORP requirements for entitlement, probability and measurement.

The charity's core funding is in the form of multi-period but time-limited grants which are subject to annual renewal from funders based on a review of science and the agreement of annual budgets. These grants are recognised on an annual basis.

Research grants fall largely into two categories: paid on a reimbursed expenditure basis, or paid on a science milestone basis.

Income on reimbursed expenditure grants is recognised in line with the relevant expenditure, and in line with achievement of milestones on the science milestone basis. The reimbursed expenditure and science milestone requirements represent donor imposed conditions that otherwise limit the recognition of income.

Investment income represents the interest receivable on short-term cash deposits.

### e. Gifts in kind

Gifts in kind represent donated premises and associated facilities at an estimated market value. Donated services for seconded staff are estimated on the charity's salary bandings for equivalent posts.

**f. Expenditure and irrecoverable VAT**  
Expenditure is accounted for on an accruals basis. Expenditure includes any VAT which cannot be fully recovered, and is reported as part of the expenditure to which it relates.

Charitable activities expenditure comprises the costs of the primary activities of the Francis Crick Institute Limited, including establishing a centre for medical research and innovation. Other expenditure represents those items not falling into any other heading.

Termination payments are recognised when the employee(s) involved have been informed of their employment end date and the amount of their termination payment entitlement.

Lab consumables are written off once purchased and are not carried as stock.

### g. Allocation of costs

Institute departments are classed either wholly or in part as directly charitable (on a time basis), or as support to the institute.

Support costs are defined as those costs incurred in the operational teams providing support in finance, IT, HR, building services, communications and public engagement.

Executive office and legal teams are classed as part support and part direct, and that part classed as support is reported under the governance heading, along with the cost of external audit.

The allocation of support costs across the charitable expenditure headings is in proportion to the directly incurred costs under each heading as a proxy for the size of that activity and the effort involved in supporting each type of charitable work.

### h. Pension costs

The charity participates in both defined benefit and defined contribution type pension schemes.

For defined contribution pension schemes, the amount charged to the Statement of Financial Activities in respect of pension costs is the total of contributions due in the year. Differences between contributions payable in the year and contributions actually paid are shown as short term liabilities at the year end.

The defined benefit scheme that the charity participates in is a multi-employer pension scheme and is unable to allocate underlying assets and liabilities to individual employees. Contributions are accounted for on the same basis as for a defined contribution scheme.

### i. Intangible fixed assets

The Francis Crick Institute is engaged in research for the purposes of discovery and/or enhancement of existing knowledge. This is not driven by, but on occasion can result in, patentable or potentially exploitable discoveries. Any internally generated intangible assets arising in this way are not capitalised.

On the founding of the institute, following the 1 April 2015 transfers from the National Institute of Medical Research and the London Research Institute, the institute became owner of certain patents and other intellectual property. These were recognised in the financial statements at fair value (based on the present value of expected future cash flows) and are amortised on a straight line basis over the life of those assets and cashflows, for terms between two and 18 years, subject to annual reviews for impairment.

#### j. Tangible fixed assets

Tangible fixed assets are held at cost less accumulated depreciation.

Depreciation is calculated using the straight line method to allocate the cost of each asset to its residual value over its estimated useful life. Depreciation commences from the date an asset is brought into service.

The period over which assets are depreciated is as follows:

– IT equipment and software	— 3 years
– Fixtures, fittings and furniture	— 5 years
– Corporate systems	— 7 years
– Scientific equipment	— 5 years
– Vehicles	— 5 years
– Leasehold Buildings (fabric)	— Term of the lease
– Building plant and infrastructure	— 3 – 50 years

#### k. Fixed asset investments

The charity's investment in its trading subsidiaries are stated at cost, measured by reference to the nominal value only of the shares issued.

The charity invests in spin-out companies, used to further its translational science objectives. Unlisted investments in early stage spin-out companies will be valued at cost less impairment, unless a reliable fair value basis is available.

#### l. Heritage assets

Heritage assets are books, manuscripts, specimens, objects or other assets that have historic, scientific, artistic, technological, geophysical or environmental qualities and are held and maintained principally for the contribution to knowledge and culture.

The Crick holds heritage assets inherited from its predecessor institutes (National Institute for Medical Research and London Research Institute) comprising mainly of objects and artefacts of scientific and historical interest. The collection is held in storage on site at the Crick lab with the intention to place some of the collection on permanent display. These assets have not been capitalised as there is no reliable information concerning their cost and the cost of valuation would be disproportionate to the benefit of the resultant information.

#### m. Taxation

As a registered charity, the Francis Crick Institute Limited is exempt from taxation on its income and gains falling within chapter 3 of part 11 to the Corporation Taxes Act 2010 and section 256 Taxation of Chargeable Gains Act 1992, to the extent that these are applied to charitable purposes.

The trading subsidiary does not generally pay UK corporation tax because its policy is to donate distributable profits to the Charity as Gift Aid.

#### n. Operating leases

Rentals under operating leases are charged to the Statement of Financial Activities on a straight-line basis over the lease term.

#### o. Financial instruments

Financial assets and financial liabilities are recognised when the Group becomes a party to the contractual provisions of the instrument. All financial assets and liabilities are initially measured at transaction price (including transaction costs).

The charity and group only have financial assets and financial liabilities of a kind that qualify as basic financial instruments. Basic financial instruments are initially recognised at transaction value and subsequently measured at their settlement value with the exception of managed investments which are held at fair value and gains and losses recognised in the Statement of Financial Activities.

Trade and other debtors are recognised at the settlement amount due after any trade discount offered. Prepayments are valued at the amount prepaid net of any trade discounts due. Cash at bank and cash in hand includes cash and short-term highly liquid investments with a short maturity of three months or less from the date of acquisition or opening of the deposit or similar account. Creditors and provisions are recognised where the charity has a present obligation resulting from a past event that will probably result in the transfer of funds to a third party and the amount due to settle the obligation can be measured or estimated reliably. Creditors and provisions are normally recognised at their settlement amount after allowing for any trade discounts due.

## 2. Critical accounting judgements and key sources of estimation uncertainty

In the application of the Group's accounting policies, which are described in note 1, the trustees are required to make judgements, estimates and assumptions about the carrying amounts of assets and liabilities that are not readily apparent from other sources. The estimates and associated assumptions are based on historical experience and other factors that are considered to be relevant. Actual results may differ from these estimates.

The estimates and underlying assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognised in the period in which the estimate is revised if the revision affects only that period, or in the period of the revision and future periods if the revision affects both current and future periods.

The trustees consider that the most significant critical judgements or sources of estimation uncertainty relate to the valuation of donated facilities and fixed asset depreciation terms.

# NOTES TO THE FINANCIAL STATEMENTS CONTINUED

YEAR ENDED 31 MARCH 2018

## 3. Analysis of income from core and related activities

	Unrestricted funds £000	Restricted funds £000	2018 Total £000	2017 Total £000
Core funding from founding shareholders	118,763	—	<b>118,763</b>	116,918
Other grants	4,702	63	<b>4,765</b>	11,552
Prizes	—	—	—	500
Donated services and facilities	3,858	—	<b>3,858</b>	9,000
Donated assets	—	—	—	6,631
Donations	75	10	<b>85</b>	35
	127,398	73	<b>127,471</b>	144,636

## 4. Analysis of grant income by funder type

	Unrestricted funds £000	Restricted funds £000	2018 Total £000	2017 Total £000
Research Councils	50,193	1,270	<b>51,463</b>	59,748
UK-based charities	69,790	6,480	<b>76,270</b>	74,951
UK-based higher education institutions	2,508	1,316	<b>3,824</b>	2,380
UK-based government bodies	—	673	<b>673</b>	128
UK-based industry, commerce and public corporations	866	943	<b>1,809</b>	430
EU government bodies	—	5,287	<b>5,287</b>	4,917
Other overseas grants	104	1,055	<b>1,159</b>	1,144
Other grants	23	59	<b>82</b>	66
	123,484	17,083	<b>140,567</b>	143,764

## 5. Analysis of income from charitable activities

	Unrestricted funds £000	Restricted funds £000	2018 Total £000	2017 Total £000
Research conferences	352	422	<b>774</b>	46
Staff restaurant	788	—	<b>788</b>	314
Building letting	129	—	<b>129</b>	10
	1,269	422	<b>1,691</b>	370

## 6. Analysis of expenditure on charitable activities

	Direct costs £000	Support costs £000	2018 Total £000	2017 Total £000
Crick Lab set-up	2,366	1,492	<b>3,858</b>	9,375
Scientific research and translation	104,471	65,855	<b>170,326</b>	157,999
Developing and training scientists	599	378	<b>977</b>	795
	107,436	67,725	<b>175,161</b>	168,169

## 7. Analysis of support costs

	Crick Lab set-up £000	Scientific research and translation £000	Developing and training scientists £000	2018 Total £000
Governance	6	260	1	<b>267</b>
Finance	62	2,716	16	<b>2,794</b>
Information Technology & Services	287	12,683	73	<b>13,043</b>
Human Resources	66	2,925	17	<b>3,008</b>
Building Services	1,020	45,017	258	<b>46,295</b>
Communications and Public Engagement	51	2,254	13	<b>2,318</b>
	1,492	65,855	378	<b>67,725</b>

	Crick Lab set-up £000	Scientific research and translation £000	Developing and training scientists £000	2017 Total £000
Governance	15	256	1	272
Finance	138	2,322	12	2,472
Information Technology & Services	470	7,925	40	8,435
Human Resources	146	2,440	12	2,598
Building Services	1,738	29,298	147	31,183
Communications and Public Engagement	119	2,002	10	2,131
	2,626	44,243	222	47,091

## 8. Net expenditure for the year

	2018 Total £000	2017 Total £000
Net expenditure is stated after charging (crediting):		
— Depreciation of owned assets	<b>39,601</b>	27,386
— Amortisation of intangible fixed assets	<b>42</b>	58
— Operating lease rentals	<b>2,055</b>	952
— Foreign exchange losses	<b>59</b>	30
— (Profit) / Loss on disposal of fixed assets	<b>(208)</b>	14
Auditor's remuneration:		
— Fees for the audit of the charity's annual financial statements	<b>51</b>	50
— Fees for other services to the group	<b>3</b>	19
— Fees for the audit of subsidiary companies	<b>8</b>	8

## 9. Analysis of staff costs, trustee expenses and the cost of key management personnel

### a. The average monthly number of employees was:

	2018 Total No.	2017 Total No.
Charitable activities	<b>1,134</b>	1,093
Support	<b>160</b>	167
	<b>1,294</b>	1,260

### b. Their aggregate remuneration comprised:

	2018 Total £000	2017 Total £000
Wages and salaries	<b>58,257</b>	55,459
Redundancy and termination	<b>1,472</b>	980
Social security costs	<b>5,594</b>	5,205
Pension costs	<b>5,494</b>	5,430
	<b>70,817</b>	67,074

Remuneration includes stipends paid to PhD students of £4,152k (2017: £3,916k). PhD students are not employees of the institute.

# NOTES TO THE FINANCIAL STATEMENTS CONTINUED

YEAR ENDED 31 MARCH 2018

## 9. Analysis of staff costs, trustee expenses and the cost of key management personnel CONTINUED

c. The number of employees whose emoluments, excluding pension contributions and employer's national insurance but including benefits in kind, were in excess of £60,000 was:

	2018 Total No.	2017 Total No.
£60,000 - £69,999	45	58
£70,000 - £79,999	35	29
£80,000 - £89,999	12	11
£90,000 - £99,999	15	16
£100,000 - £109,999	11	7
£110,000 - £119,999	3	5
£120,000 - £129,999	4	3
£130,000 - £139,999	3	6
£140,000 - £149,999	3	3
£150,000 - £159,999	4	1
£160,000 - £169,999	1	2
£170,000 - £179,999	1	2
£180,000 - £189,999	1	2
£190,000 - £199,999	2	—
£210,000 - £219,999	1	1
£220,000 - £229,999	3	1
£260,000 - £269,999	2	1
£370,000 - £379,999	—	1
£380,000 - £389,999	1	—
	<b>147</b>	149

## d. Key management personnel

The key management personnel of the charity are listed on page 43. The total remuneration (including pension contributions and employer's national insurance) of the key management personnel for the year totalled £2,023k (2017: £1,730k).

## e. Trustees' remuneration

No Trustees received remuneration during the current or prior year. Total travel and subsistence expenses of £1,953 were paid to two trustees (2017: £1,565, two trustees). The Charity has maintained throughout the year Trustees' and Officers' liability insurance for the benefit of the Charity and its Trustees.

## 10. Tax on profit of trading subsidiary

The actual tax charge for the year differs from the standard rate for the following reasons:

	2018 Total £000	2017 Total £000
(Loss) / profit of trading subsidiary	(10)	19
(Loss) / profit multiplied by standard rate of United Kingdom corporation tax of 20%	(2)	4
Adjustment for prior year tax charge	—	1
Effect of:		
— Expenses not deductible for tax purposes	2	5
Total tax charge for the year	—	10

In 2015, the Institute of Chartered Accountants in England and Wales obtained a QC's opinion on the treatment of gift aid donations by charitable trading companies to their parent charities. The opinion stated that the payments must be considered as distributions under UK company law, and not simply donations. This means that such trading companies may now only make such payments out of distributable reserves, and to the extent that they have incurred expenditure disallowed for tax purposes, may now incur tax charges.

## 11. Intangible fixed assets

	Intellectual property £'000
<b>Group and charity</b>	
<b>Cost</b>	
At 1 April 2017 and 31 March 2018	<b>281</b>
<b>Amortisation</b>	
At 1 April 2017	101
Charge for the year	42
At 31 March 2018	<b>143</b>
<b>Net book value</b>	
At 31 March 2018	<b>138</b>
At 1 April 2017	<b>180</b>

## 12. Tangible fixed assets

Group	Fixtures, fittings, furniture £'000	IT equipment and software £'000	Scientific equipment £'000	Buildings £'000	Total £'000
<b>Cost</b>					
At 1 April 2017	7,618	15,662	47,832	568,152	<b>639,264</b>
Additions	1,247	1,768	8,668	3,752	<b>15,435</b>
Disposals	—	—	(642)	—	<b>(642)</b>
At 31 March 2018	8,865	17,430	55,858	571,904	<b>654,057</b>
<b>Depreciation</b>					
At 1 April 2017	1,396	4,796	14,661	14,024	<b>34,877</b>
Charge for the year	1,643	5,475	10,390	22,093	<b>39,601</b>
Disposals	—	—	(406)	—	<b>(406)</b>
At 31 March 2018	3,039	10,271	24,645	36,117	<b>74,072</b>
<b>Net book value</b>					
At 31 March 2018	5,826	7,159	31,213	535,787	<b>579,985</b>
At 1 April 2017	6,222	10,866	33,171	554,128	<b>604,387</b>
 <b>Charity</b>					
<b>Cost</b>					
At 1 April 2017	7,618	15,662	47,832	568,476	<b>639,588</b>
Additions	1,247	1,768	8,668	3,753	<b>15,436</b>
Disposals	—	—	(642)	—	<b>(642)</b>
At 31 March 2018	8,865	17,430	55,858	572,229	<b>654,382</b>
<b>Depreciation</b>					
At 1 April 2017	1,396	4,796	14,661	14,028	<b>34,881</b>
Charge for the year	1,643	5,475	10,390	22,098	<b>39,606</b>
Disposals	—	—	(406)	—	<b>(406)</b>
At 31 March 2018	3,039	10,271	24,645	36,126	<b>74,081</b>
<b>Net book value</b>					
At 31 March 2018	5,826	7,159	31,213	536,103	<b>580,301</b>
At 1 April 2017	6,222	10,866	33,171	554,448	<b>604,707</b>

# NOTES TO THE FINANCIAL STATEMENTS CONTINUED

YEAR ENDED 31 MARCH 2018

## 13. Fixed asset investments

The Francis Crick Institute Limited owns the entire issued share capital of UKCMRI Construction Limited and Francis Crick Trading Limited, both companies incorporated in the United Kingdom and registered in England and Wales with their registered offices at 1 Midland Road, London NW1 1AT. UKCMRI Construction Limited provides design and construction services to the Francis Crick Institute Limited. Francis Crick Trading Limited is currently dormant. The shares are held at cost, being £4 for UKCMRI Construction Limited (2017: £4) and £1 for Francis Crick Trading Limited (2017: nil).

A summary of UKCMRI Construction Limited's results is shown below:

	2018 Total £000	2017 Total £000
<b>Profit &amp; loss account</b>		
Turnover	<b>3,482</b>	9,803
Cost of sales	<b>(3,481)</b>	(9,791)
Gross profit	1	12
Operating costs	<b>(11)</b>	(12)
Operating loss	<b>(10)</b>	—
Other interest receivable and similar income	—	19
	<b>(10)</b>	19
Tax on ordinary activities	—	(10)
	<b>(10)</b>	9
Distribution payable (Gift Aid)	—	(35)
Retained loss for the year	<b>(10)</b>	(26)
Opening shareholder's (deficit)/funds	<b>(19)</b>	7
Closing shareholder's deficit	<b>(29)</b>	(19)

## Balance sheet

	2018 Total £000	2017 Total £000
Current assets	<b>389</b>	4,541
Current liabilities	<b>(418)</b>	(4,560)
Total net liabilities	<b>(29)</b>	(19)

A summary of the results of the parent charity is set out below:

	2018 Total £000	2017 Total £000
Total incoming resources	<b>146,627</b>	160,625
Total outgoing resources	<b>(175,156)</b>	(168,151)
Net movement in funds	<b>(28,529)</b>	(7,526)

Investments in unlisted companies:

	Holding £	2018 Proportion held %	2017 Proportion held %
Gammadelta Therapeutics Ltd	157	<b>2.9%</b>	6.9%
Achilles Therapeutics Ltd	2	<b>1.8%</b>	2.8%

Both of the above investments are in limited companies incorporated and registered in England and Wales.

## 14. Debtors

	Group 2018 £000	Group 2017 £000	Charity 2018 £000	Charity 2017 £000
Trade debtors	<b>990</b>	3,854	<b>990</b>	785
Prepayments and accrued income	<b>4,793</b>	6,794	<b>4,793</b>	6,794
Amounts owed by group undertakings	—	—	—	3,043
Amounts owed by related parties	<b>7,054</b>	5,215	<b>7,054</b>	5,215
Other debtors	<b>674</b>	899	<b>667</b>	589
	<b>13,511</b>	16,762	<b>13,504</b>	16,426

**15. Creditors: amounts falling due within one year**

	Group 2018 £000	Group 2017 £000	Charity 2018 £000	Charity 2017 £000
Trade creditors	<b>5,458</b>	6,940	<b>5,454</b>	6,131
Accruals and deferred income	<b>10,700</b>	11,121	<b>10,380</b>	10,805
Other creditors	<b>2,376</b>	2,586	<b>2,377</b>	2,419
Amounts owed to related parties	<b>7,995</b>	6,214	<b>7,995</b>	6,117
Amounts owed to group undertakings	—	—	<b>276</b>	668
	<b>26,529</b>	26,861	<b>26,482</b>	26,140

**16. Comparative Consolidated Statement of Financial Activities**

	Unrestricted funds £000	Restricted funds £000	Total 2017 £000
<b>Income from</b>			
Core and related funding	144,103	533	144,636
Research grant funding	—	15,294	15,294
Charitable activities	370	—	370
Investment income	231	—	231
Other income	78	—	78
<b>Total</b>	<b>144,782</b>	<b>15,827</b>	<b>160,609</b>
<b>Expenditure on</b>			
Charitable activities	154,271	13,898	168,169
<b>Total</b>	<b>154,271</b>	<b>13,898</b>	<b>168,169</b>
<b>Net (expenditure) / income before transfers</b>	(9,489)	1,929	(7,560)
Transfers between funds	762	(762)	—
<b>Net (expenditure) / income</b>	<b>(8,727)</b>	<b>1,167</b>	<b>(7,560)</b>
<b>Reconciliation of funds</b>			
Share capital issued and subscribed	1,423	—	1,423
<b>Net movement in funds</b>	<b>(7,304)</b>	<b>1,167</b>	<b>(6,137)</b>
Total funds at 1 April 2016	637,330	3,015	640,345
Total funds at 31 March 2017	630,026	4,182	634,208
<b>17. Called up share capital</b>			
	2018 Total £000	2017 Total £000	
<b>Allotted, called up and fully paid</b>			
Ordinary shares of £1 each	<b>629,566</b>	629,566	
Share premium account	<b>12,751</b>	12,751	
	<b>642,317</b>	642,317	

# NOTES TO THE FINANCIAL STATEMENTS CONTINUED

YEAR ENDED 31 MARCH 2018

## 18. Movements in funds

Group	1 April 2017 £000	Income £000	Expenditure £000	Transfers between funds £000	31 March 2018 £000
<b>Unrestricted funds</b>					
General funds	(12,291)	129,112	(158,670)	26	<b>(41,823)</b>
<b>Restricted funds</b>					
Crick Lab set-up	248	353	(70)	—	<b>531</b>
Research grants	3,892	17,162	(16,417)	(27)	<b>4,610</b>
Other	42	—	(4)	1	<b>39</b>
	4,182	17,515	(16,491)	(26)	<b>5,180</b>
Share capital – par	629,566	—	—	—	<b>629,566</b>
Share premium	12,751	—	—	—	<b>12,751</b>
	642,317	—	—	—	<b>642,317</b>
Total funds	634,208	146,627	(175,161)	—	<b>605,674</b>
 <b>Charity</b>					
Charity	1 April 2017 £000	Income £000	Expenditure £000	Transfers between funds £000	31 March 2018 £000
<b>Unrestricted funds</b>					
General funds	(11,953)	129,112	(158,665)	26	<b>(41,480)</b>
<b>Restricted funds</b>					
Crick Lab set-up	248	353	(70)	—	<b>531</b>
Research grants	3,892	17,162	(16,417)	(27)	<b>4,610</b>
Other	42	—	(4)	1	<b>39</b>
	4,182	17,515	(16,491)	(26)	<b>5,180</b>
Share capital – par	629,566	—	—	—	<b>629,566</b>
Share premium	12,751	—	—	—	<b>12,751</b>
	642,317	—	—	—	<b>642,317</b>
Total funds	634,546	146,627	(175,156)	—	<b>606,017</b>

Group	1 April 2016 £000	Share issues £000	Income £000	Expenditure £000	Transfers between funds £000	31 March 2017 £000
<b>Unrestricted funds</b>						
General funds	(3,564)	—	144,782	(154,271)	762	(12,291)
<b>Restricted funds</b>						
Crick Lab set-up	1,079	—	—	(69)	(762)	248
Research grants	1,902	—	15,817	(13,827)	—	3,892
Other	34	—	10	(2)	—	42
	3,015	—	15,827	(13,898)	(762)	4,182
Share capital – par	628,143	1,423	—	—	—	629,566
Share premium	12,751	—	—	—	—	12,751
	640,894	1,423	—	—	—	642,317
Total funds	640,345	1,423	160,609	(168,169)	—	634,208
<b>Charity</b>						
<b>Unrestricted funds</b>						
General funds	(3,260)	—	144,798	(154,253)	762	(11,953)
<b>Restricted funds</b>						
Crick Lab set-up	1,079	—	—	(69)	(762)	248
Research grants	1,902	—	15,817	(13,827)	—	3,892
Other	34	—	10	(2)	—	42
	3,015	—	15,827	(13,898)	(762)	4,182
Share capital – par	628,143	1,423	—	—	—	629,566
Share premium	12,751	—	—	—	—	12,751
	640,894	1,423	—	—	—	642,317
Total funds	640,649	1,423	160,625	(168,151)	—	634,546

Transfers between general funds and restricted funds of £26k consist of the release of excess funds received (in line with the terms and conditions of the individual funders) and the financing of a deficit on several completed grants. In 2017, transfers of £762k consisted of grant funding of the Paradigm sculpture now available for use to the Institute as an unrestricted asset.

The shareholders have provided funds to the Charity for the purpose of establishing the Institute. Restricted funds relate to scientific computing and individual scientific projects.

# NOTES TO THE FINANCIAL STATEMENTS CONTINUED

YEAR ENDED 31 MARCH 2018

## 19. Analysis of assets and liabilities between funds

	Unrestricted funds, non-charitable trading funds and share capital £000	Restricted funds £000	31 March 2018 £000
<b>Group</b>			
Intangible fixed assets	138	—	<b>138</b>
Tangible fixed assets	577,843	2,142	<b>579,985</b>
Current assets	44,301	7,779	<b>52,080</b>
Current liabilities	(21,788)	(4,741)	<b>(26,529)</b>
At 31 March 2018	600,494	5,180	<b>605,674</b>
 <b>Charity</b>			
Intangible fixed assets	138	—	<b>138</b>
Tangible fixed assets	578,159	2,142	<b>580,301</b>
Current assets	44,281	7,779	<b>52,060</b>
Current liabilities	(21,741)	(4,741)	<b>(26,482)</b>
At 31 March 2018	600,837	5,180	<b>606,017</b>
 <b>Group</b>			
Intangible fixed assets	180	—	180
Tangible fixed assets	602,286	2,101	604,387
Current assets	47,520	8,982	56,502
Current liabilities	(19,960)	(6,901)	(26,861)
At 31 March 2017	630,026	4,182	634,208
 <b>Charity</b>			
Intangible fixed assets	180	—	180
Tangible fixed assets	602,606	2,101	604,707
Current assets	46,817	8,982	55,799
Current liabilities	(19,239)	(6,901)	(26,140)
At 31 March 2017	630,364	4,182	634,546

## 20. Employee retirement benefits

The Francis Crick Institute Limited operates both defined contribution and defined benefit pension scheme arrangements.

New employees are entitled to join the defined contribution pension scheme. Employer contribution rates vary according to the contribution rates of individual employees. The amount paid in employer contributions to the defined contribution scheme was £3,887,424 (2017: £3,393,492).

The defined benefit pension scheme is the Medical Research Council Pension Scheme (MRCPS). Employees of the former National Institute for Medical Research who transferred to the Francis Crick Institute Limited on 1 April 2015 have remained members of this scheme.

MRCPS is a funded defined benefit pension scheme that prepares its own scheme statements. Benefits accrue at the rate of 1/80th of pensionable salary for each year of service. In addition a lump sum equivalent to three years' pension is payable on retirement.

Members pay contributions of between 6.0% and 6.5% of pensionable earnings to the Scheme. The Francis Crick Institute Limited pays contributions of 14.9% of pensionable earnings to the Scheme. The amount paid in employer contributions to the defined benefit scheme was £1,549,807 (2017: £1,997,192). The institute is indemnified against an employer contribution rate in excess of 14.9%, under an agreement whereby the Medical Research Council would reimburse the Institute for costs incurred at any future rate greater than 14.9%.

The required contribution rates are assessed every three years in accordance with the advice of the Government Actuary. The latest finalised actuarial assessment of the MRCPS was 31 December 2016.

	2016 valuation £m	2013 valuation £m
Market value of assets	<b>1,406</b>	1,054
Actuarial scheme liabilities	<b>(1,246)</b>	(894)
Surplus	<b>160</b>	160
 Scheme funding level	 <b>113%</b>	 118%

The current financial assumptions used to calculate scheme liabilities are:

	2018 %	2017 %
Rate of increase of salaries	<b>3.3</b>	3.3
Rate of increase of pension payments	<b>2.3</b>	2.3
Discount rate	<b>2.6</b>	2.5
Inflation rate	<b>2.3</b>	2.3
Expected return on equities	<b>2.6</b>	2.5
Expected return on bonds	<b>2.6</b>	2.5
Expected return on overall fund	<b>2.6</b>	2.5

## 21. Financial commitments

### Operating lease commitments

The total future minimum lease payments under non-cancellable operating leases for each of the following periods are:

Group and charity	2018		2017	
	Land and buildings £000	Other £000	Land and buildings £000	Other £000
Within one year	<b>203</b>	<b>429</b>	1,544	509
Between one and five years	<b>829</b>	<b>536</b>	805	964
After five years	<b>587</b>	—	780	—
	<b>1,619</b>	<b>965</b>	3,129	1,473

The Francis Crick Institute Limited had unprovided capital contractual commitments of £2,933,109 at 31 March 2018 (2017: £7,185,930).

# NOTES TO THE FINANCIAL STATEMENTS CONTINUED

YEAR ENDED 31 MARCH 2018

## 22. Reconciliation of net expenditure to cash generated by operating activities

	Group 2018 £000	Group 2017 £000
Net expenditure for the year	<b>(28,534)</b>	[7,560]
Depreciation and disposal adjustments	<b>39,446</b>	27,067
Amortisation of intangible fixed assets	<b>42</b>	58
Donated assets adjustment	—	(6,631)
Amortisation of lease	—	3,323
Interest receivable	<b>(153)</b>	(231)
<b>Operating cash flow before movement in working capital</b>	<b>10,801</b>	16,026
Decrease (increase) in debtors	<b>3,521</b>	(9,191)
(Decrease) increase in creditors	<b>(323)</b>	8,814
Cash generated by operating activities	<b>13,999</b>	15,649

## 23. Related party transactions

Advantage has been taken of exemptions under FRS102 33.1.A not to disclose balances or transactions between the parent charity and the wholly-owned subsidiary.

### a. Funding from shareholders including shares allotted

No shares were allotted during the year.

2017	New funding received £000	Shares allotted £000
Medical Research Council	—	—
Cancer Research UK	721	(721)
Wellcome Trust	542	(542)
University College London	160	(160)
Imperial College London	—	—
King's College London	—	—
	1,423	(1,423)

Loans are provided by shareholders to finance the Francis Crick Institute Limited's establishment of a medical research centre before conversion to share capital. Whilst in place, loans are unsecured, interest free and have no repayment date.

### b. Other transactions

	Year ended 31 March 2018		Year ended 31 March 2018	
	Purchases from related parties £000	Income and recharges from and to related parties £000	Amounts due from related parties £000	Amounts due to related parties £000
Medical Research Council	(467)	52,225	2,957	(303)
Cancer Research UK	(1,448)	55,254	518	(6,805)
Wellcome Trust	(88)	20,534	2,381	(1)
University College London	(437)	1,934	852	(320)
Imperial College London	(377)	951	95	(256)
King's College London	(591)	1,135	251	(310)
	(3,408)	132,033	7,054	(7,995)

	Year ended 31 March 2017		Year ended 31 March 2017	
	Purchases from related parties £000	Income and recharges from and to related parties £000	Amounts due from related parties £000	Amounts due to related parties £000
Medical Research Council	(4,706)	57,789	942	(792)
Cancer Research UK	(967)	54,087	1,116	(4,893)
Wellcome Trust	(249)	20,436	2,350	(123)
University College London	(206)	797	741	(70)
Imperial College London	(306)	744	11	(128)
King's College London	(520)	987	55	(208)
	(6,954)	134,840	5,215	(6,214)

**c. Donated services and facilities**

	2018 Total £000	2017 Total £000
Services	<b>2,333</b>	903
Premises	—	6,572
Land	<b>1,525</b>	1,525
	<b>3,858</b>	9,000

**d. Other related party transactions**

The land on which the Francis Crick Institute laboratory has been built has been made available at nil cost by the Medical Research Council, Cancer Research UK, the Wellcome Trust and University College London. A gift in kind of £1,524,545 (2017: £1,524,545) has been recognised, the estimated market value of the annual rent.

The Wellcome Trust incurred costs on behalf of the Francis Crick Institute Limited, which it has recharged, totalling £88,045 (2017: £248,714) including hospitality charges and lab consumables.

Cancer Research UK incurred costs on behalf of the Francis Crick Institute Limited, which it has recharged, of £1,448,367 (2017: £966,941) including the cost of providing seconded staff and building rent.

The Medical Research Council incurred costs on behalf of the Francis Crick Institute Limited, which it has recharged, of £467,136 (2017: £4,706,454) in providing seconded staff, lab consumables and service charges for the Mill Hill premises.

Imperial College London incurred costs on behalf of the Francis Crick Institute Limited, which it has recharged, of £376,550 (2017: £306,430) in providing seconded staff, lab consumables and course fees. Research lab staff have been seconded to the Crick at nil cost, a gift in kind of £12,187 (2017: £nil) has been recognised for these services.

University College London incurred costs on behalf of the Francis Crick Institute Limited, which it has recharged, of £436,667 (2017: £206,024) for student tuition fees, lab consumables and seconded staff. Research lab staff have been seconded to the Crick at nil cost, a gift in kind of £1,354,450 (2017: £454,399) has been recognised for these services.

King's College London incurred costs on behalf of the Francis Crick Institute Limited, which it has recharged, of £590,982 (2017: £520,090) in providing seconded staff and lab consumables. Research lab staff have been seconded to the Crick at nil cost, a gift in kind of £966,904 (2017: £448,256) has been recognised for these services.

**24. Contingent liabilities**

The Crick has entered into a guarantee with HSBC Bank PLC in favour of the Environment Agency for the value of €95,000. The guarantee was required in order to obtain a licence to dispose of radioactive sources used by an item of scientific equipment.

**25. Post balance sheet events**

There are no relevant post balance sheet events to report.



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