CHAIN-FLOREY SCHEME 2019

10TH YEAR

MRC | London Institute of Medical Sciences

Group portrait including Howard Florey and Ernst Chain. (Date unknown)

Back row left to right: S. Waksman, H. Florey, J. Trefonel, E. Chain, A. Gratia

Front row left to right: P. Fredericq, M. Welsch

Taken by unknown photographer in Oxford. Credit: Wellcome Collection

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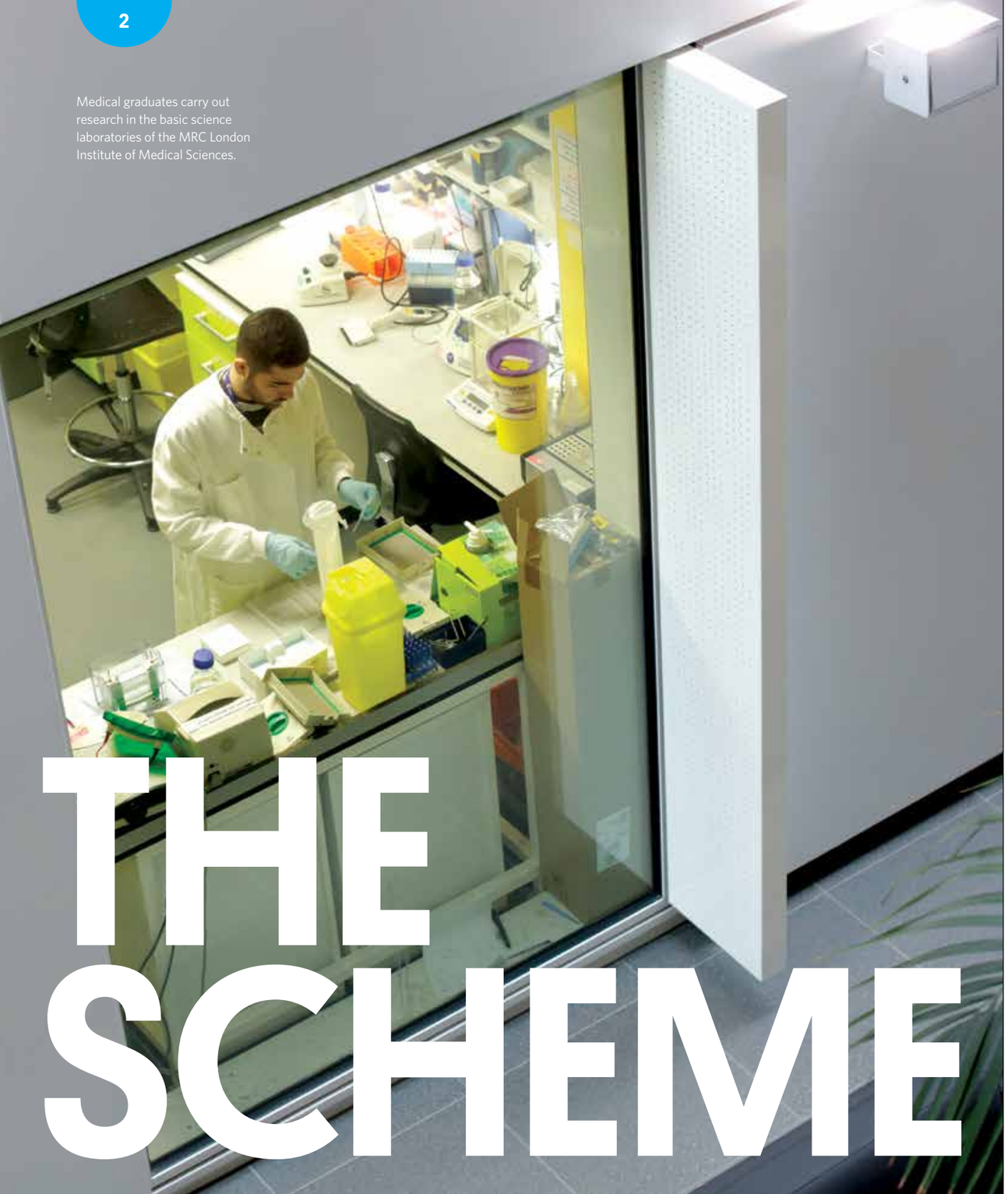


Medical graduates carry out research in the basic science laboratories of the MRC London Institute of Medical Sciences.

THE SCHEME

INTRODUCTION

The translation of scientific discoveries into new therapies is an enduring challenge for medical sciences. The MRC London Institute of Medical Sciences (LMS) aims to be at the forefront of innovative biomedical research and to promote the translation of its research for maximal benefit. Based at Imperial College London's Hammersmith Hospital campus in West London, the Institute is ideally placed to facilitate translational pull-through of its research.

The Institute set up the Chain-Florey Clinical Research scheme in 2009 to offer world-class training to medical graduates at key stages of their careers. The scheme brings medical graduates into the Institute's basic science laboratories. Awardees are allowed the time and space to develop the skills they need to bridge the boundary between the clinic and the lab, and to drive medical science forward.

This translational training scheme is jointly funded by the UK's Medical Research Council (MRC, which is part of UK Research and Innovation) and the National Institute for Health Research (NIHR) through the Imperial Biomedical Research Centre (BRC). Clinical and scientific mentoring ensures that Chain-Florey researchers keep in touch with their medical roots, quickly settle into their research environment and successfully grow their own research portfolio.

The scheme began in 2009 as a Clinical Research Fellowship scheme, which offered clinicians the opportunity to carry out a PhD. Since then, the scheme has nurtured a growing cohort of clinical academics: 22 Fellowships have been awarded and 17 graduates have emerged ready to tackle clinical research questions with scientific precision. The scheme expanded in 2014 to fund Clinical Research Lectureships. These positions offer the opportunity to combine postdoctoral research with progression to independent clinical academic status over a two-year period. The first Lectureship was awarded in 2014 and 4 Lecturers are now in place. In 2015, the scheme recognised the need to support doctors during their early clinical training and provided four months research placements to Foundation Year 2 (FY2) Trainees. The placements attract exceptional young doctors who would otherwise be unable to move into a basic science group until much later in their training. Due to the current demand for junior doctors the FY2 programme is currently paused.

The latest extension of the Chain-Florey portfolio is a small cohort of more senior clinical groups. "We are proud of the vibrant community of Chain-Florey's which we have built over the years. It's now important that we continue to grow our opportunities for clinical researchers," Amanda Fisher, director of the LMS, explains. "The Senior Clinical Lectureship positions recognise this need. The development of clinical academics at this more senior level will be an exciting new addition to the Chain-Florey scheme."

"The interface between science and medicine should remain porous. The Chain-Florey scheme reignites a longstanding collaboration to provide medical graduates with an opportunity to undertake cutting-edge fundamental research. It is important that we continue to grow such opportunities within the MRC London Institute of Medical Sciences. Our new Senior Clinical Lectureship positions recognise this need and are an exciting addition to the Chain-Florey scheme."

Amanda Fisher, Director of MRC London Institute of Medical Sciences

WHY IS THE SCHEME CALLED CHAIN-FLOREY?

In 1940, Howard Florey, Professor of Pathology at the University of Oxford, elevated penicillin from scientific curiosity to medical revolution. The collaboration between Florey and the biochemist Ernst Chain, supported by the practical knowledge of Norman Heatley, resulted in the isolation and first medical application of an antibiotic. Against the backdrop of World War II, Chain and Florey worked in a makeshift lab on a shoestring budget to unravel the secrets of penicillin.

Alexander Fleming had stumbled upon the antibiotic potential of penicillin a decade earlier, with no inkling that his serendipitous discovery would lay the foundation for one of the most important medical advances of the 20th Century. Its power was harnessed long after Fleming had abandoned the project. At a time when hundreds of lives were being lost every day, and a simple scratch could open the door to fatal infection, the combined expertise of a clinically trained pathologist and a biochemist changed the medical world. From the first miraculous demonstrations of the life-saving potential of penicillin in mice in May 1940, Ernst Chain and Howard Florey worked tirelessly to optimise its production, saving millions of human lives. Their achievements were recognised in 1945, when they shared the Nobel Prize in Physiology or Medicine with Alexander Fleming.

ERNST BORIS CHAIN

(1906–1979)

A German-born British biochemist and 1945 co-recipient of the Nobel Prize for Physiology and Medicine for his work on penicillin.

Credit: Benjamin Chain

HOWARD WALTER FLOREY

(1898–1968)

An Australian pharmacologist and pathologist who shared the 1945 Nobel Prize for Physiology and Medicine with Ernst Chain and Alexander Fleming for his role in developing penicillin.

Credit: Australian National University

It is in celebration of this unique collaboration that the Chain-Florey scheme is named. Antibiotics – perhaps the most important 20th Century drug discovery – stand as a tribute to the importance of the culmination of scientific endeavour and medical purpose. In previous decades, the relationship between science and medicine was arguably more transparent. This scheme reignites that longstanding collaborative tradition and provides medical graduates with the opportunity to undertake cutting edge fundamental research.

"Opportunity to undertake cutting edge fundamental research."

MENTORING IS A VITAL PART OF THE SCHEME'S SUCCESS

The Chain-Florey scheme was founded to spur the development of the next generation of world-class academic clinicians in the UK. Mentoring is key to its success: Fellows have two academic and one clinical mentor; Lecturers have one external and one internal mentor.

"Working away in a basic science environment, it could be easy for the Fellows and Lecturers to lose track of their clinical training and future careers," says Professor Dominic Withers, Head of Clinical Research, LMS-Group Head and Clinical Chair in Diabetes & Endocrinology. "What's fantastic about the Chain-Florey scheme is that Fellows and Lecturers are embedded in a lab but can also speak to an experienced clinician who understands the clinical academic career path."

"Clinical mentoring is vital for all clinical academics and especially for the Chain-Florey scheme where the trainee will be undertaking research in a basic science laboratory. Talking with a mentor can be particularly helpful for Fellows as they start their programme and need to adapt to the steep learning curve of academic training. Later, mentors also help with making decisions about their career trajectory and provide independent support and advice", says Professor Waljit Dhillo, Professor of Endocrinology at Imperial College London.

"The Fellows have to learn a totally different way of thinking," adds Professor Irene Roberts, Weatherall Institute of Molecular Medicine. "They have to employ tremendously different skills to those that make you a successful clinician. The best part of being a mentor is seeing that change in them over time."

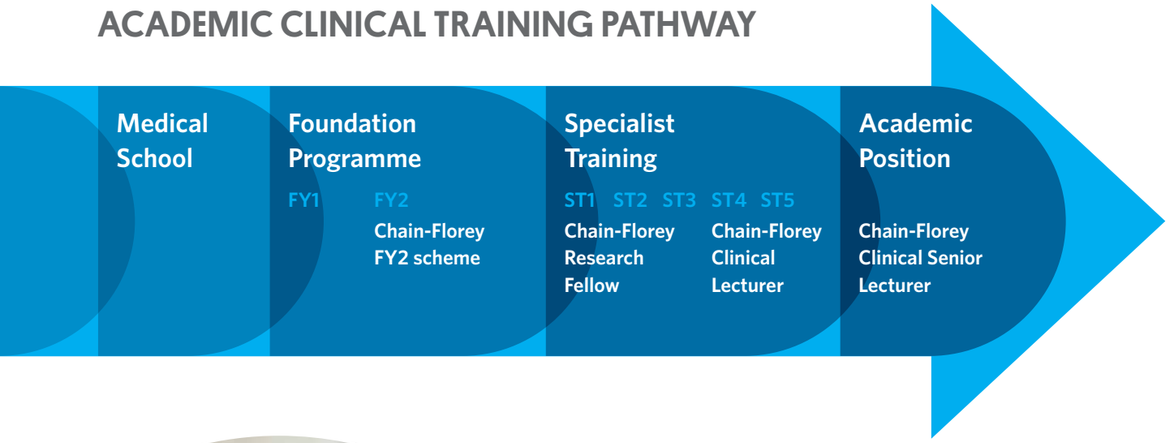
10 YEARS OF DRIVING MEDICAL SCIENCE FORWARD

2019 marks the tenth year of the Chain-Florey Clinical Research Scheme. In the pages that follow you will hear more from those who support and advocate the Chain-Florey scheme, find information on eligibility for the clinicians who are interested in applying and hear from the alumni, including one of the first cohort who has now received a Clinical Professorship.

ABOUT THE SCHEME

The Chain-Florey scheme includes Clinical Research Fellowships, Foundation Year 2 (FY2) Placements, Clinical Lectureships and Clinical Senior Lectureships. Fellowships offer clinicians the opportunity to carry out a PhD, the second are aimed at clinicians who have a PhD but are still near the start of their clinical training, the third offers the opportunity to combine postdoctoral research and moving towards independence with completion of clinical training and the fourth the next step in establishing their research independence.

ACADEMIC CLINICAL TRAINING PATHWAY



APPLYING TO THE SCHEME: ELIGIBILITY CRITERIA

CHAIN-FLOREY CLINICAL RESEARCH FELLOWSHIPS

The Fellowships are for medical graduates who aim to pursue a career as an academic clinician during their specialist training. Fellows carry out three years of PhD research in one of the basic science groups at the MRC London Institute for Medical Sciences (LMS). Chain-Florey projects must involve human tissues or samples or be otherwise related to human disease of relevance to the Academic Health Science Centre strategy. Having completed their PhD, Fellows will return to their postgraduate clinical training. Funding is provided for the Fellow's salary and consumables.

Eligibility criteria

→ NHS Doctor in training in the UK

CHAIN-FLOREY FOUNDATION YEAR 2 (FY2) PLACEMENTS

The Chain-Florey Foundation Year 2 (FY2) programme is a collaboration with the North West Thames Foundation School and attracts exceptional clinicians during their second academic foundation year. The scheme allows clinical trainees who have completed their PhD and have a strong publication record to undertake four months of research in an LMS laboratory. The LMS provides salary funding and consumables during their research stay.

The stay is designed to support a future application for Academic Clinical Fellowships.

Eligibility criteria

→ Clinical trainee in academic foundation year 2

→ Completed PhD

→ Strong publication record

CHAIN-FLOREY CLINICAL LECTURESHIPS AND SENIOR LECTURESHIPS

Chain-Florey Clinical Lectureships and Senior Lectureships provide support for clinician scientists who have already successfully completed a PhD or post-doctoral fellowship in basic science. Since 2014, the two-year Lectureships have been awarded in renal medicine, cardiovascular sciences, endocrinology and metabolism, haematology. As with Fellowships and Placements, funding is provided for salary and consumables. Additionally, Lecturers are provided with a technician. The Clinical Senior Lectureships are for 4 years and will have high quality experimental medicine experience. We anticipate the Clinical Senior Lecturers will attract significant external funding in establishing their research independence.

Eligibility criteria

→ Clinician scientist, up to completion of clinical training (CCT)

→ Hold a PhD or post-doctoral fellowship in basic science

→ Clinical Senior Lecturers will be expected to have significant post-doctoral research experience and hold appropriate specialist qualification (CCT)

Open positions are advertised throughout the year on the LMS and Imperial website.

For more information, visit:
https://lms.mrc.ac.uk/about-us/chain-florey-clinical-research-scheme-2/

If you are interested in the Chain-Florey programmes and would like to discuss which option is best for you please contact Sharon Citrone:
s.citrone@lms.mrc.ac.uk

In the pages that follow you will hear from those who support and advocate the Chain-Florey scheme.

They contribute to developing a generation of clinical academic leaders equipped to address translational questions in the most rigorous way.

ADVOCATES

"We are developing clinical academic leaders for the future."

PROFESSOR SIR JOHN SAVILL

Former Chief Executive, Medical Research Council

"The Chain-Florey scheme provides a fantastic opportunity for clinical Fellows and Lecturers to work with outstanding basic biomedical scientists at the MRC London Institute of Medical Sciences. A key focus for the MRC is to ensure that we are developing clinical academic leaders for the future who are grounded in excellent science, which they can link to their own clinical expertise. Such clinicians will play a critical role in developing knowledge and in ensuring translation of research findings into clinical situations.

The MRC London Institute of Medical Sciences is a unique discovery science laboratory embedded in Imperial at the Hammersmith Hospital campus. This site has a long tradition of excellence in training clinicians in research and fostering cross-disciplinary collaborations. I and many of my colleagues have benefited enormously from the opportunities offered here. This scheme does a fine job of providing support for clinicians to gain robust scientific training while retaining relationships with their clinical mentors. There are many challenges in ensuring that both sides of this equation are delivered effectively and I am delighted with the success of this scheme in this regard.

The Chain-Florey scheme is a tribute to Professor Fisher, her team and of course to the Fellows, Lecturers and Trainees, who have embarked on this challenging but exciting course – it is a real pleasure to read their profiles, which reflect their commitment and enthusiasm. I wish them and all their successors well."

"We're now using the Chain-Florey model as a template for many other schemes."

PROFESSOR JONATHAN WEBER

Dean of the Faculty of Medicine, Imperial College London

"I am a tremendous enthusiast of the Chain-Florey scheme. Clinician scientists are in short supply, and are a very difficult group to train. With these posts, we agreed from the very beginning that they'd have to be held in a non-clinical lab, but that there would be a clinical mentor to bridge the divide. The Fellows would need strong mentoring, but with the right support it would be an extremely productive programme. The MRC London Institute of Medical Sciences is the jewel in the crown for Imperial College London in terms of fundamental discovery biology, and we're delighted to have this landmark scheme there. We're now using the Chain-Florey model as a template for many other schemes.

The advantage of the scheme is that clinicians and scientists learn to communicate. That communication is bilateral and durable. It can last a whole career, and is the key to this sharp end of translational medicine. This experience will give Fellows not only the skills, but also the tools to ask fundamental questions about clinical issues in the most rigorous way.

The next step for the Chain-Florey Fellows is for us to be able to support the most successful in their post-doctoral careers, where the restrictions of clinical training challenge time for research. I am therefore delighted by the creation of the Chain-Florey Lectureships which will guarantee the research career progression of our most able Fellows and I look forward to our first Chain-Florey Clinical Senior Lecturer appointment."

"This scheme is a shining example of the sort of career-shaping programme we are in need of."

PROFESSOR DAME SALLY DAVIES

Chief Medical Officer for England

"Advances in medical practice are powered by cell and molecular biological research. Innovative medicines are reliant on fluent communication between scientists and doctors, and I am in full support of any scheme that fosters such collaboration. The training that the Chain-Florey scheme provides in the basic science laboratories of the LMS will give them the perfect foundation to build careers that bridge the medical and scientific worlds.

Keeping a firm grip on their clinical work while adapting to the novel challenges of academic life is challenging. I am strongly in support of mentorship schemes for young medical professionals, and this one is paving the way for great futures. The LMS is ideally located at the Hammersmith Hospital, and the clinical mentorship ensures that while Trainees, Fellows and Lecturers grow as scientists, their clinical skills do not wane.

Translational research in this country is an absolute priority, so fostering the links between the academics and practitioners of public health is vital. The Chain-Florey Fellows and Lecturers are developing strong relationships with world-class biomedical researchers, and those bonds will last throughout their careers. Training our brightest clinicians in the art of fundamental science will be productive for practical medicine and biomedical science. This scheme is a shining example of the sort of career-shaping programme we need."

"Chain-Florey's will become role models, and they should themselves champion this sort of approach to help to create look-alike schemes."

PROFESSOR SIR ROBERT LECHLER

Professor of Immunology,
Vice-Principal (Health), King's College London
Executive Director of King's Health Partners Academic Health Sciences Centre
President, The Academy of Medical Sciences

"One of the key characteristics of a successful Chain-Florey applicant is a serious commitment to research and discovery, as opposed to just a desire to advance your career and thinking a PhD will help. Then there needs to be a willingness to take a risk. Being a Chain-Florey, is a character-building experience: As a junior doctor you're actually quite a responsible person, people listen to you and follow your instructions. You go into a laboratory when you know next to nothing and you feel a bit of an idiot. But all of this is hugely valuable, because it helps to inculcate modesty and to dispel certainty, which is a dangerous thing.

The Chain-Florey scheme is a really good exemplar. I don't think that its alumni are going to change the world on their own, but they will become role models, and they should themselves champion this sort of approach to help to create look-alike schemes. I'm very committed to fostering the careers of clinician scientists to help to create an ecosystem that has a mixture of non-clinical basic scientists and clinician scientists working together in an academic medical centre where you've got the opportunity for clinical pull as well as discovery push."

"High hopes for Chain-Florey alumni: ultimately it's this cadre of people who become the leaders of the profession."

PROFESSOR SIR KEITH PETERS

Emeritus Regius Professor of Physic, University of Cambridge

"Clinician scientists are a rare, but necessary, cadre of people: for teaching, to enable science in healthcare, and for the biotech and pharmaceutical industry - where they are valued because they understand scientific methodology as well as medicine. The people who are going to make the in-roads are the ones who can pick the problems that are tractable. Physician scientists can do that because they understand that disease is not homogeneous, and they also understand what you can and cannot do with clinical research. An awful lot can be done in mice, flies and worms, but ultimately the research has got to be done on humans. I have high hopes for Chain-Florey alumni: Ultimately, it's this cadre of people who become the leaders of the profession. They need to have experience, in a very high-quality environment, of being surrounded by those whose business all day and every day is to do research."

"This is a very exciting scheme, and incredibly important."

PROFESSOR DAME KAY DAVIES

Director, MRC Functional Genomics Unit, Dr Lee's Professor of Anatomy, University of Oxford

"A gap develops when basic scientists work on a problem in isolation, with no feeling for patients' needs. You need a full understanding of the clinical phenotype before you can design a research strategy. A clinically trained person adds a tremendous amount. They bring with them a breadth of knowledge about the whole body that simply doesn't exist without them. Of course, many of them have no idea of the basic science, so it really is an exciting two-way process. Some of them take to it like a duck to water, but not all. But they're consistently very bright and highly motivated, so they more than make up for it. If you're trying to practise and do research, you need a clinic within running distance, as it is at the Hammersmith. The Chain-Florey scheme is ideally placed to promote and support these Fellows. Now more than ever, it's a challenge for a clinician to take time off during their career. But being in a lab broadens their outlook tremendously. This is a very exciting scheme, and incredibly important."

"The raw brain power of many of the young doctors attracted to research training is pretty formidable."

PROFESSOR SIR STEPHEN O'RAHILLY

Director, Metabolic Research Laboratories and MRC Metabolic Diseases Unit, University of Cambridge

"I have benefited enormously from working in an environment where basic and clinical scientists rub shoulders with each other on a day-to-day basis. It really helps to foster cross-disciplinary thinking. It can bring to basic scientist's clinical perspectives they may not have. The rigour and technologically innovative aspects of contemporary science can enlighten the clinician, who may not have previously appreciated what was possible.

The Hammersmith Campus has been a Mecca for clinical science for many decades. What it's done very well over the past 10 or 20 years is to strengthen fundamental science, ensuring it doesn't lose links with the hospital. The raw brain power of many of the young doctors that are attracted to undertake a period of research training is pretty formidable. When you combine that with some of the best scientists in Britain, then that's a recipe for new ventures and points of light. This is the kind of environment that the MRC London Institute of Medical Sciences and the broader Imperial campus can provide."

"The Chain-Florey scheme is excellent because it sets out to train young clinical researchers within the ambience of world-class molecular biology."

PROFESSOR ROBERT SOUHAMI

Emeritus Professor of Medicine, University College London

"I fully support the inspiration that comes from the original scientists at the heart of the Chain-Florey scheme. Chain and Florey saw what Fleming had shown, and knew that this was something killing bacteria. Something in the petri dish had extraordinary importance biologically and potentially therapeutically. These days an equally important finding might arise from within a randomised trial. In a therapeutic trial in cardiovascular disease, it was found that in patients given aspirin, the likelihood of colorectal cancer was considerably diminished. Equally interesting was that in those taking aspirin who developed the cancer, it was less likely to have spread. What is the molecular basis of this? It's essential that clinicians interested in research think about, and understand, basic biology and that molecular biologists are aware of new clinical findings. The Chain-Florey scheme is excellent because it sets out to train young clinical researchers within the ambience of world-class molecular biology. They are in a critical environment, where they share setbacks and advances with the scientists and understand what new techniques might offer within clinical research. At the LMS, scientists are selected from among the very best nationally and internationally, which means that a young clinical scientist can think broadly and seize opportunities."

"If you're really going to advance translational medicine, these are the people who will be the leaders."

PROFESSOR SIR ANDREW MCMICHAEL

Professor of Molecular Medicine, University of Oxford

"When I first went into a non-clinical institution, it was fairly accidental. It was good to be able to concentrate entirely on learning how to do research without having to worry about going to clinics and ward rounds. Now clinical training has become much more formalised, and it can be hard to meet all the requirements to keep your clinical career on track and carry on your work as a scientist. This kind of scheme makes it possible. Getting people started on this career path gives them choices. If you're really going to advance translational medicine, these are the people who will be the leaders. They are mature, highly motivated, and learn very quickly. They have skills that are very useful for practising as a scientist, but have respect for the full-time clinicians dealing with patients. My father was a Professor of Medicine at Hammersmith Hospital, so I grew up there. I've seen it develop, and with this top-class research centre – the MRC London Institute of Medical Sciences – in the grounds it is a fantastic place to work."

"My father would have been very supportive of this scheme."

PROFESSOR BENJAMIN CHAIN

Professor of Immunology, University College London

"I once met the doctor who administered the first injections of penicillin, when he was a very old man. He said it was the most exciting moment of his life. He had a patient who he knew for sure would be dead by the next morning. He gave him this stuff, and the next day the patient was sitting up in bed, chatting.

At that time, the link between scientists and doctors was so close. The barrier has only emerged relatively recently. The Chain-Florey scheme is breaking down a wall that was never there before.

My father felt very strongly that, in principle, it was very important to have close links between the clinic and lab. He thought that a lot of scientific discoveries of medical importance had come from medical observations. He would have been very supportive of this scheme.

My father and Florey were an early example of a very successful multidisciplinary approach. The medical profession is very resistant to change, while scientists constantly want to change things. These Fellowships bridge that divide between the conservative and progressive attitude, and get somewhere in between."

THE SUPERVISORS

PROFESSOR DAME AMANDA FISHER

Director, MRC London Institute of Medical Sciences
Head of Lymphocyte Development

PROFESSOR LUIS ARAGON

Head of Cell Cycle

DR ANDRE BROWN

Head of Behavioural Genomics

PROFESSOR DAVID CARLING

Head of Cellular Stress

PROFESSOR STUART COOK

Head of Cardiovascular Disease Mechanisms

PROFESSOR NIALL DILLON

Head of Gene Regulation and Chromatin

PROFESSOR JESUS GIL

Head of Cell Proliferation

PROFESSOR PETRA HAJKOVA

Head of Reprogramming and Chromatin
Section Chair Epigenetics

PROFESSOR OLIVER HOWES

Head of Psychiatric Imaging

PROFESSOR BORIS LENHARD

Head of Computational Regulatory Genomics

DR ENRIQUE "FADRI" MARTINEZ-PEREZ

Head of Meiosis

PROFESSOR IRENE MIGUEL-ALIAGA

Head of Gut Signalling and Metabolism
Section Chair Genes and Metabolism

DR DECLAN O'REGAN

Head of MR Facility
Consultant Radiologist

DR PETER SARKIES

Head of Epigenetic Inheritance and Evolution

PROFESSOR DOMINIC WITHERS

Head of Metabolic Signalling
Head of Clinical Research, Institute of Clinical Sciences

At the heart of the Chain-Florey scheme are the Fellows, Lecturers and FY2 Trainees who step away from the hospital bed to undertake research at the laboratory bench. On the following pages you will hear from those who are currently working in the basic science labs of the MRC London Institute of Medical Sciences (LMS). Our growing cohort of alumni will tell you what they have done next and how their time as a Chain-Florey has shaped their careers.

Their stories can be your inspiration.

THE COHORT

DR HANNAH BECKWITH
2017

Fellow, Gut Signalling and Metabolism Group

Imperial's Hammersmith Hospital has a reputation for its clinical research. Since the early 20th century, landmark studies have been conducted at the West London site, notably into conditions of the heart and kidney. Internationally renowned renal consultants and academic clinicians work in what has now become one of the largest Renal and Transplant Centres in Europe.

It is no surprise that the LMS has recruited many promising renal and heart specialists to the Chain-Florey scheme from its hospital neighbour. Hannah Beckwith is the latest addition to this illustrious group. As a renal registrar (ST6 level) and Academic Clinical Fellow with Matthew Pickering and Terence Cook at Hammersmith, she heard about the scheme from colleagues, successfully applied and joined three weeks ago. "The Chain-Florey scheme has an excellent reputation amongst my renal colleagues. Many have been Fellows themselves. They have set very high standards", Hannah says. "I'm extremely pleased and excited to be now joining the scheme for my own work."

Hannah's first exposure to research was as an Erasmus student in the Netherlands. As part of a BSc in Pharmacology, she undertook a 12-week research project with Rob Hoeben at Leiden University. She then returned to the UK and completed her medical training at the University of Edinburgh. Yet her research time in Leiden had given her an appetite for more.

As a Chain-Florey, Hannah will be working in the Gut Signalling and Metabolism group led by Irene Miguel-Aliaga. The group uses flies to explore how brain and gut communicate, and pioneered the genetics of neurons in the guts of flies. So for the next three years, Hannah's focus will shift from the kidneys to the gut: she will be looking at plasticity of the intestinal epithelium during reproduction, with a particular focus on epithelial transporters.

The epithelium is a layer of cells in the lining of the intestine; epithelial cells play a key role in various body processes: they absorb food, act as a barrier against harmful substances, play a role in immune defence, and have neuroendocrine functions. "I'm excited to understand better how epithelial transporters change, adapt and react to internal changes during reproduction", Hannah says. "It is great to be working with a lab which has pioneered much of the work in this area."

Unlike most in her group, Hannah will be using organoids and mouse models to explore these questions. "Organoids are fascinating" Hannah says. "They are really exciting new tools in basic and translational research. Essentially, an organoid is like a mini and simplified version of an organ that grows in a dish. It's derived from a cell or tissue culture, exhibits realistic organ structures, and can mimic physiological processes and organ functions. The technique for growing organoids was developed about 7 years ago and has rapidly improved since then. They now allow us to model human development or disease in vitro. I am thrilled to have the opportunity to work with them. I think organoids will revolutionise the way we undertake medical research in the future."

And in the long-term? "Epithelial transporters are hugely important in renal processes", Hannah explains, "so whilst working in the gut as a Chain-Florey, my long-term hope is that I will translate my findings back to kidney transporters." "Additionally," Hannah explains, "epithelial transporters are commonly used drug targets for metabolic processes such as Diabetes Mellitus, a leading cause of end stage renal disease worldwide. Who knows, maybe one day I will be able to combine all of my interests – pharmacological and renal; clinical and academic. I feel sure the Chain-Florey scheme will equip me well for my future."

"I'm excited to understand better how epithelial transporters change, adapt and react to internal changes during reproduction. It is great to be working with a lab which has pioneered much of the work in this area."

FELLOW

DR CERIS OWEN
2016

Fellow, Lymphocyte Development Group

The childhood cancer, Wilm's tumour, mostly affects those younger than five. It grows in the kidneys and was the focus of Ceris Owen's early investigations as a research graduate. In the Cancer Epigenetics Laboratory based in Bristol, Ceris and colleagues identified a cell surface receptor expressed in developing kidney cells. They found that the genes which are used to produce these receptors are epigenetically silenced early in Wilm's tumour growth. According to Ceris, it's now known that the same silencing can occur in cancers that affect adults, such as colorectal cancer.

In the ten years since his initial research, Ceris has stepped away from the laboratory and qualified as a physician, training to the level of medical registrar. This year he has returned to his research roots, joining the LMS as a Chain-Florey Fellow to explore cancer at the cellular level.

He has joined the Lymphocyte Development group, supervised by LMS director Amanda Fisher. Ceris says he's interested in exploring the how external signals are interpreted by cells, and how these signals are communicated to the nucleus resulting in epigenetic changes to chromatin during development. By understanding how this happens in healthy cells, he aims to better understand how it can go wrong contributing to the development of cancer.

"It's very interesting to try to unpick what the changes are that lead from normal cell function, to cancer cells. If you can understand these changes, then that potentially leads to interventions to block some of them" says Ceris.

Ceris says it's important for clinicians to have an understanding of how medicines can develop from an initial breakthrough, through basic research, into clinical trials and on to become a treatment used to help patients. "In fact, ultimately, I'd like work in that place between very hard scientific research, and looking to develop novel therapies, particularly for cancer," says Ceris.

Traditional chemotherapy drugs target all fast growing cells, but can kill healthy cells too, and often cause distressing side effects such as ulcers, immunosuppression and hair loss. "The aim now is to look at each cancer individually and say, well, what is the cellular context of this cancer, what are the mechanisms by which this particular cancer is reliant, and how can we target specific treatments for this specific cancer," says Ceris. "The aim is to individualise treatments and minimise side effects."

"I'd like to work in the place between very hard scientific research and looking to develop novel therapies, particularly for cancer."

FELLOW

DR JOCELYN WALBRIDGE 2016

Fellow, Meiosis Group

"Joining the LMS as a Chain-Florey Fellow has been the best move I've ever made!" A bit over a year ago, Jocelyn Walbridge was working shifts as a registrar in obstetrics and gynaecology at speciality training level 5. In the morning, she might rush into emergency surgery to help an expectant mother and her baby, before seeing women with suspected gynaecological cancer in the afternoon. But despite this drama, Jocelyn was looking forward to a new challenge – and found it in basic science research.

"I really enjoy my clinical job, but I was delighted to be given the opportunity and time to explore an area in depth at the basic science level," says Jocelyn. She joined the Meiosis group in October 2016 and began her academic work under the supervision of Enrique (Fadri) Martinez-Perez.

Jocelyn is exploring the root causes of a rare type of ovarian cancer, called ovarian germ cell tumours. These tumours originate in a woman's egg cells, though scientists don't understand exactly how or why this happens. It's difficult to study in people, so Jocelyn uses the nematode worm Caenorhabditis elegans as a model system.

Initially, she studied a mutant strain of worms that had previously appeared to grow tumours from their developing eggs. These worms carry a genetic mutation in a protein important for cell division, and it seemed some of the egg cells had problems progressing through meiosis – the cell division that leads to male or female gametes – instead growing uncontrollably and becoming cancerous. Jocelyn thought that a ring-shaped complex of proteins, called cohesin, may play a role. This is because cohesin's activity is affected by the genetic mutation that makes the worms develop tumours. Cohesin normally regulates the separation of sister chromatids during meiosis and mitosis, the two types of cell division. More recently, cohesin has also been shown to help to control the way that cells express the information in our genes, and it is faults in this area that Jocelyn thought may be causing the tumours.

Jocelyn spent the first few months into her Fellowship trying to reproduce the observation – but it proved surprisingly difficult. The tumours were present, but were not consistently reproducible. This has led her to focus on the other aspect of her investigation, looking more broadly at the role of a particular group of cohesin proteins in meiosis and gene expression. Much current cohesin research focuses on mitosis – the cell division that produces two new cells identical to each other and to the parent cell. Yet Jocelyn is excited by the many potential applications of her work in meiosis: "This type of cell division directly affects the gametes – our sperm or egg cells – and therefore defects may result in subfertility, miscarriage and developmental abnormalities as well as cancer. It's great to do a project that is broad and has so many potential applications in my specialty." At the moment, her work requires a steady hand – and love for precision. Using latest CRISPR technology, Jocelyn is creating worm mutants under the microscope. She injects proteins into the germline of worms that are 1mm long at the most. She finds this manual aspect of her work very satisfying. "I think my experience with keyhole surgery comes in handy" she adds with a smile.

What will come next? Jocelyn's ultimate goal of her research is to develop better treatments for her patients. "As a gynaecologist who's interested in oncology, I'm lucky to have found a project looking at some really fundamental science which could eventually have implications for my clinical practice," says Jocelyn. She is the first obstetrics and gynaecology clinician to join the LMS on the Chain-Florey scheme. "It's slightly out on a limb, and I rather like that."

"As a gynaecologist who's interested in oncology, I'm lucky to have found a project looking at some really fundamental science which could eventually have implications for my clinical practice."

DR WILL SCOTT 2018

Obesity is a generation defining health problem because of its role in diabetes, heart disease and cancers. Will is interested in understanding why some of us are more susceptible to obesity and the serious complications of obesity than others. He believes that epigenetics mechanisms which regulate the genetic blueprint may provide us with some answers.

Will is a specialist registrar in Diabetes and Endocrinology on the North Central London rotation. He graduated in Medicine from the University of Birmingham in 2005, then undertook an MRC funded PhD at Imperial College London working with Professors Jaspal Kooner and John Chambers in 2012. During his PhD he used DNA sequencing-based approaches to identify genetic and epigenetic changes to the DNA sequence in people with obesity. Will joined the MRC LMS as a Chain Florey Lecturer in 2018 to explore the biology behind some of the most compelling findings from this work.

Epigenetic switches which reside on the DNA are responsible for activating genes in distinct parts of the body. They are the reason a fat cell is different from a muscle or a brain cell even though these cells each contain the same DNA encoded genes. This property means epigenetic switches have huge potential to cause diseases like obesity by changing activity of important genes. Will is using genome editing tools to study what effects epigenetic switches have on nearby genes, and exactly what these genes do in human fat cells.

The next step is to understand how these epigenetic switches are turned on or off by good or bad lifestyles. "If we can find this out we may be able to identify people at risk of obesity, then actively change the switches in these people to stop them from developing these problems. Another similar approach would be to change these switches in people who are already affected to treat this condition".

Will also plans to continue to use DNA sequencing-based approaches to identify new epigenetic switches that might explain why some obese people get diabetes, heart disease and cancer while others do not. This is an area which is not currently well understood.

"To look at ways we might be able to visualise how these epigenetic switches change over the lifespan, and what happens to them in response to our daily lifestyle choices. Ultimately, the reason we all do this work is to try to develop treatments which can improve the lives of our patients", Will explains his long-term aims and motivations for his research.

LECTURERS

DR HARRY LEITCH 2017

FY2 Trainee 2015

The germline has long fascinated researchers, as it forms the perpetual link between the generations. Harry Leitch is establishing himself as one of the new generation of investigators studying this enigmatic cell lineage, with the goal of answering longstanding questions and contributing new innovations.

Harry came to the LMS after completing his first foundation year of clinical medicine in Cambridge. Previously, he had combined his medical training with a PhD and postdoctoral research in the labs of Azim Surani and Austin Smith. He worked alongside Petra Hajkova's group as a foundation year 2 academic trainee in 2015. Using this experience as a springboard, he successfully moved into an Academic Clinical Fellowship position in paediatrics at Imperial College London – only to be awarded a prestigious BBSRC New Investigator grant a few months later. This award has allowed him to set up his own Germline and Pluripotency group at the LMS.

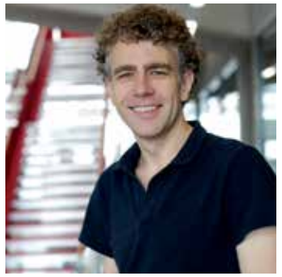
Life begins from a single cell - the fertilised egg. This single cell undergoes multiple rounds of division forming a multicellular embryo. After a couple of days, a small group of cells are established, which will be able to give rise to every cell type of the body – a property called pluripotency. As the embryo progresses through development, pluripotency disappears and cells become more specialised. However, during early development it is essential to set aside some cells that have the capacity to form the next generation. These cells are called germ cells and are the precursors of sperm or eggs. While the sperm and egg appear very specialised, upon fertilisation they fuse to form a new embryo, which gives rise to more pluripotent cells and the cycle begins afresh. Herein lies the paradox of germ cells - although overtly specialised, they are the only differentiated cell type that can directly produce pluripotent cells in the next generation. We do not understand how these conflicting demands are controlled and regulated. In fact, the range of differentiation options available to a given cell, has not yet been empirically verified in germ cells.

This is where Harry's work starts. "I'm trying to understand the properties and potential of the germ cell lineage as a model to understand cell identity and how cells make decisions during development. This knowledge will not only influence our understanding of embryonic development but will inform how we can direct stem cells to make useful cell types", he says. "My primary motivation is to answer these fundamental questions, but I hope we will be able to apply this knowledge to impact human fertility research and regenerative medicine approaches."

Recent advances have enabled early germ cells to be induced from mouse embryonic stem cells. These in vitro derived cells are capable of making sperm and eggs, which in turn can make live mice. If applied to human cells, this research has the potential to revolutionise fertility treatment. Harry will test the properties of these cells in both mouse and humans, laying the foundations from which it may be possible to safely translate this technology to the clinic.

In addition to working with mouse and human germ cells in culture, Harry also utilises chimaeric animals by injecting cells of interest into 'host' embryos. When the donor cells integrate and contribute to the developing embryo, the resulting organism is a mixture of host and donor cells. "Chimaeras have been an important tool in biomedical research for many years. However, with recent advances chimaeras can be formed that contain a contribution from two different species, and it may soon become possible to grow whole human tissues or organs in an animal host. This is hugely exciting for regenerative medicine and has re-invigorated the field. One important question is how easily chimaeric cells might access the germline. We are developing tools to examine this more closely, as well as assessing whether we can manipulate cells to make them contribute in unexpected ways".

"There are a whole range of ethical considerations that this field of research raises. Whether it is the idea of making gametes in a dish, human-animal chimaeras or human germline editing, this requires an ongoing dialogue between basic scientists, clinicians and society", Harry acknowledges. "I'm lucky to be able to try to advance knowledge through my work, and can't emphasise enough how the Chain-Florey scheme has helped me to get closer to my research goals. But the LMS also has a great tradition in connecting with the public in innovative ways – which is a different challenge and an exciting opportunity."



DR JAMES WARE 2016

Picture a heart that is 'baggy' and stretched on one side. Its thin muscle is too weak to pump blood around the body. This disease, called dilated cardiomyopathy, affects 1 in 250 people and can lead to sudden death. Earlier diagnosis may help to save lives.

Cardiologist James Ware seeks to understand the genetics of the disease. James is sponsored by the Wellcome Trust and has joined the LMS as a Chain-Florey Lecturer equivalent and leads the Cardiovascular Genomics and Precision Medicine group. He is also a group head at the National Heart and Lung Institute at Imperial and consultant cardiologist at Royal Brompton Hospital. He works closely with Professor Stuart Cook, who leads the LMS Cardiovascular Disease Mechanisms research group.

The pair first worked together in 2008, when James completed his PhD at the LMS. He went on to post-doctoral research at the LMS, Imperial College, Harvard Medical School, and the Broad Institute. James is exploring computational methods for genome interpretation, with a particular focus on inherited cardiac conditions, and gene discovery in patients with unexplained cardiomyopathies. "We are also studying a large cohort of healthy volunteers who have had cardiac MRI and gene sequencing at the LMS, looking for genetic determinants of heart structure and function," James says.

Dilated cardiomyopathy can be caused by mutations in a gene that produces a protein called titin. It is the largest protein in the human body, and acts like a spring within muscle tissue, including the heart.

Many patients with dilated cardiomyopathy have DNA mutations in the Titin gene, that disrupt formation of the Titin protein. But about 1 in 100 people have similar mutations and remain healthy. "That really threw a spanner in the works," says James. By examining the differences between the two groups, he's been able to work out why some mutations cause disease, and others don't.

"We can use this information to screen patients' relatives to identify those at risk of developing the disease, and help them to manage their condition early," explains James.

Together with Stuart Cook and Declan O'Regan, he is now finding out more about the role of titin in the healthy heart by creating 3D images using the cutting-edge magnetic resonance imaging (MRI) facilities in Hammersmith Hospital.

"We are continuing to carry on with our gene discovery projects, particularly early onset childhood dilated cardiomyopathy. We apply genomic approaches to study the molecular pathways underlying disease in human heart muscle, engineered heart tissue, and other cellular models." says James. "If scientists can find out more about titin, they may one day be able to develop new ways to treat dilated cardiomyopathy.

"We can use this information to screen patients' relatives to identify those at risk of developing the disease, and help them to manage their condition early."

DR ANTONIO DE MARVAO 2015

Fellow 2012-2015

Antonio de Marvao is a cardiologist. He's trying to understand the factors in our genetic make-up and in our environment that influence the shape of our hearts and how our hearts function, both when we're healthy and when things go wrong.

"During my PhD, as a Chain-Florey Fellow, I focussed on finding a better way to phenotype the heart. We developed a new Magnetic Resonance Imaging (MRI) technique that allows us to image the heart in 3D, thereby acquiring unprecedented amounts of information about the heart's function and structure, in one go."

Antonio then worked with colleagues to develop a machine-learning computer programme that automatically analyses these high-resolution images in 3D. They recruited some 2,000 healthy volunteers, scanned their hearts and gathered data on their genetic sequences, blood pressure, levels of physical activity, smoking and past medical history. Through collaborations with doctors and scientists across the world they have also analysed thousands of scans from patients with diseases of the heart muscle.

This novel method was then applied in several studies including one looking into a heart muscle condition called dilated cardiomyopathy, which causes heart failure. It is a disease where the heart muscle becomes stretched and thin, and is unable to pump blood around the body efficiently. Combining the genetic data from 1400 healthy adults with the 3D MRI scans, Antonio created extremely detailed 3D "virtual hearts". From looking at the 3D heart models he found that healthy people with the titin mutations have a slightly enlarged heart, compared with those without the mutations. This supports the findings in mice which suggest titin mutations, even in the absence of dilated cardiomyopathy, are having an impact on the way heart cells' source energy at a molecular level. Initially, the heart is able to compensate for this problem but loses its capacity to cope when there are additional stressors. "Our next step is to find out which are the specific genetic factors or environmental triggers, such as alcohol or viral infection, that may put certain people with titin mutations at risk of heart failure."

Antonio views the clinical lectureships as unique because there are so few opportunities that provide dedicated time for research. "Normally the period after the PhD is the hardest, because you don't yet have enough research under your belt to set up your own lab and you have to finish your clinical training. The Chain-Florey scheme is so special because it allows you to just keep going – with research and clinical training in tandem."

He finds combining clinical and academic training extremely demanding, but thinks tensions between the two lines of work may prove beneficial for his later career: clinical academics need excellent time management. "On the clinical side you have to acquire all the skills and knowledge expected from a full-time trainee. Then your academic development is assessed using criteria such as publications in high impact journals, securing your own funding and demonstrating research excellence in your field, despite the ever-increasing pressure to provide clinical services."

"Having a research project closely aligned with your clinical interest helps to improve your productivity. Securing a clinical Lectureship at an institution such as Imperial College, where I'm in daily contact with so many successful and inspirational senior clinical academics, is a fantastic training opportunity."

And in the long term? "I aim to continue as a clinical academic, to look after patients and to be inspired to lead my own bedside-to-bench-to-bedside programme in translational research." Though his overarching scientific goal is to define the genes and biological pathways that lead to heart disease, he has other goals too. "Once I have developed credible foundations in clinical practice and science I hope to influence health and medical science policy making and drive improvement in patient care."

"The Chain-Florey scheme is so special because it allows you to just keep going – with research and clinical training in tandem."

"Once I have developed credible foundations in clinical practice and science I hope to influence health and medical science policy making and drive improvement in patient care."

ALUMNI

DR TOMOKI ARICHI 2009–2012

Fellow

When Tomoki Arichi joined the Neonatal Medicine and Cognitive Neuroimaging Groups with a Chain-Florey Fellowship his keen interest in paediatric neurology had already taken him to Birmingham Children's Hospital, Great Ormond Street Hospital and The Johns Hopkins Institute in Baltimore. For his PhD project, he worked on developing and optimising functional MRI (fMRI) techniques for premature and newborn babies. Babies born prematurely have a lifetime high risk of difficulties with all the different capacities of the brain, such as movement and learning. "What's very exciting about imaging is that we can use it to understand what's going on in the developing brain in a completely non-invasive way," explains Tomoki. "Were they born 30 years ago, these babies wouldn't have survived." But getting accurate fMRI data from babies is problematic and some of Tomoki's research has focussed on designing and testing tools that might help, including a device that moves the baby's hand, and a technique for presenting different odours.

Now as an MRC Clinician Scientist and Clinical Senior Lecturer in the Centre for the Developing Brain at King's College London and an Honorary Consultant in Paediatric Neurodisability at the Evelina London Children's Hospital, Dr Arichi continues to build on the research started in his Chain-Florey Fellowship. "At the moment, my work is particularly focussed on three projects looking at different aspects of functional brain activity in early human life," he explains. The first is to use foetal fMRI to understand brain activity in the womb as this will be vital to improve monitoring in the early stages of brain development. The second is to collect fMRI data simultaneously with EEG to correlate the indirect information about brain activity obtained from MRI with the more 'direct' information about the electrical neural activity derived from EEG. And lastly, he'll collect fMRI data to study infants as they learn, which in the long run will be applied to intervention and therapy programmes for infants with brain injury.

Collaboration with the Human Robotics Group at Imperial College London, where Dr Arichi has held a visiting position for some years, remains central to his work. "I'm supervising a PhD student developing the robotics and experimental paradigm for the learning project – testing if babies can learn an association between sound and a passive motor stimulus." This allows babies to be given very precise (and safe) patterns of stimulation inside the MRI scanner, and can also provide quantitative information about the infant's behaviour, such as how they move.

When he started his Chain-Florey Fellowship Tomoki's were among only a few studies of fMRI in babies. "Today they're much more commonplace," he says, "They've become central to some large cohort studies, such as the human connectome project. We can now link fMRI findings with other imaging modalities, clinical information, and even genetics."

Getting the right balance between clinical and research commitments hasn't been a problem for Dr Arichi. "Senior colleagues are very supportive of both areas of my work, allowing me to focus the right amount of time on each." What's more a significant proportion of his research applies directly to the patients he's seeing in the clinic. "Some of the imaging acquisition and processing methods we've developed over the years were done specifically to get better images for our clinical practice, so it's very rewarding to see those being used every day in our department. Other methods will take a long time to translate to clinical practice but are already informing us about pathogenesis."

"Embrace and enjoy the experience," is Tomoki's advice to new Chain-Florey Fellows. "Particularly the opportunity to completely immerse yourself in the research world."

"It's practically impossible nowadays to get stuck into research fully during clinical training," says Dr Arichi. "Schemes like the Chain-Florey Fellowships are so important to allow clinicians to totally focus on stepping outside their comfort zone."

Tomoki is an MRC Clinician Scientist and Senior Lecturer at King's College London with clinical work caring for children with cerebral palsy as an Honorary Consultant in Paediatric Neurodisability at the Evelina London Children's Hospital. He also holds a visiting position in the Bioengineering Department at Imperial College London where new robotic tools for assessing infant motor function are developed.

DR JONATHAN BOND 2009–2012

Fellow

The very first Chain-Florey Fellow, haematologist Jonathan Bond, last year added another 'first' to his name when he was appointed to the newly-created University College Dublin Brendan McGonnell Chair of Paediatric Molecular Haemato-oncology. We caught up with Professor Bond ten years on from the launch of the Chain-Florey Scheme.

At the outset of his Fellowship project in 2009, looking at transcriptional regulation in normal and leukaemic B cells in Niall Dillon's Gene Regulation and Chromatin Group, Jonathan hadn't originally planned to do basic science. "I was interested in doing research but saw myself doing something a bit more translational." But having immersed himself in the project, his finding that the transcription factors FOXP1 and IKAROS interact with the G2A gene to affect response of leukaemia patients to treatment, could have been the game changer. "This discovery was a very exciting moment for me," Jonathan recalls. Having initially thought, "when I finish I'll be going back to clinical work," Jonathan realised that he wanted to stay with research.

A post-doc position in Elizabeth Macintyre's team at L'Hôpital Necker-Enfants Malades, in Paris allowed Jonathan to continue in a similar area but this time focussing on non-B cell leukaemias, a project that he realised was "exactly what I wanted to do." During his five and a half years there, out of necessity becoming fluent in French, Jonathan went on to direct three main strands of his own research: exploring the connection between disrupted epigenetic regulation and fusion oncoproteins in acute myeloid leukaemia; using high-throughput sequencing analysis to hunt for genetic abnormalities in T-cell leukaemias that could be used to better predict prognosis and therefore direct the most appropriate treatment; and participating in a France-wide project looking at polycomb gene abnormalities in paediatric myeloid leukaemia.

Having trained at Trinity College Dublin, returning to Ireland's capital to take up a professorship sounds like the realisation of a long-held ambition, but Jonathan modestly admits he had no grand plan. "It was more the case that opportunities arose, and I took them".

Now based at Our Lady's Children's Hospital and Systems Biology Ireland at University College Dublin, Professor Bond is currently setting up his lab. While there are already teams working on other childhood malignancies, Jonathan's will be the first at the institute dedicated to leukaemia research. He'll be taking advantage of the core facility on site that's already well-equipped to provide the sequencing, genomics and proteomics technologies his projects require. Professor Bond's studies of childhood and adolescent leukaemias will focus on the mechanisms of oncogenesis and why, for some patients, treatment fails. With genetic and epigenetic information, the aim is to develop better treatments for poor risk cases. Continuing a research strand established during his Chain-Florey Fellowship, Jonathan will also be investigating how genes and transcription are disrupted in leukaemia.

Professor Bond 's responsibilities are now largely for full-time research, with some teaching. "However, I don't do experiments myself anymore", he says. "Now I get the thrill of my team getting results." And he is glad that he can maintain a clinical interest in the hospital and in the establishment of a biobank of haematological malignancy samples.

Asked what advice he'd pass on to new Chain-Florey Fellows, Jonathan is sure "You've got to follow the research you're interested in, because if you're not interested no-one else will be."

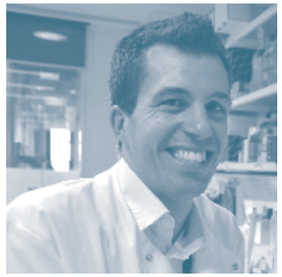
Jonathan is Brendan McGonnell Chair of Paediatric Molecular Haemato-oncology at University College Dublin, Ireland.

DR AMIT PATEL
2010–2013

Fellow

Amit Patel started his Chain-Florey Fellowship in 2010 in Luis Aragón's Cell Cycle Group. Completed in 2013, his project used gene-editing techniques to construct a cellular model system of DNA damage and repair. His novel discovery that a DNA double strand break during telophase is repaired in a way that makes it inherently mutagenic has implications in understanding cancer formation and relapse after treatment. "The Chain-Florey scheme paves the way for you to be as comfortable in the research lab as you are in the hospital", says Amit. He completed his post-doctoral research at the Institute of Cancer Research, London, and is currently Programme Director of the Stem Cell Transplantation and Cellular Therapy Unit at Clatterbridge Cancer Centre NHS Foundation Trust, and a Principal Investigator at the University of Liverpool. Amit is UK Chief Investigator for 10 clinical trials, and is investigating cellular and other immunotherapies for patients with haematological malignancies, graft-versus-host disease and sepsis. Recent examples include completion of the first human trial using induced pluripotent stem cell-derived cell therapy.

Amit is a Consultant and Honorary Senior Lecturer in Stem Cell Transplantation/Cellular Therapy and Intensive Care Medicine. He is also Director of Research and Scholarship within the University of Liverpool School of Medicine, and NIHR North West Coast Clinical Trials Network Lead for Haemato-Oncology.



DR THOMAS OATES
2010–2013

Fellow

Thomas Oates has no doubt that the three years spent in research have added to his clinical practice. "I feel more able to take an analytical approach to clinical questions based on my scientific training." During his PhD, Thomas looked at single base resolution analysis of DNA methylation in crescentic glomerulonephritis using bioinformatic methods. "This now means I can tackle clinical projects with much greater ease than previously. Genomic technologies and analysis are seen as a key part of the future of medicine, and my first-hand insight into this fast-expanding topic will be extremely useful in appraising the introduction of these techniques into the NHS."

After completing his training as a renal specialist registrar at Imperial College Healthcare NHS Trust. Thomas then became a National Institute of Research Clinical Lecturer at University College London, He is currently a Consultant Physician and Nephrologist at the Royal London Hospital.

DR JAMES TOMLINSON
2010–2014 Fellow
2015–2017 Lecturer

Renal specialist James Tomlinson was awarded a Chain-Florey Clinical Lectureship in 2015, having completed a Chain-Florey Fellowship the previous year. During his PhD project in James Leiper's Nitric Oxide Signalling Group, James investigated the mechanism of renal fibrosis, which can be triggered by almost any kidney injury – from acute illness to inflammatory disease. Using cells in culture and mouse models, he looked at the role proteins in the nitric oxide (NO) pathway play in the scarring process. He discovered that enzymes acting to increase NO biosynthesis, the dimethylarginine dimethylaminohydrolases (DDAHs), have a significant impact on fibrotic kidney disease. The clinical lectureship enabled James to develop this work further while completing his clinical training at Hammersmith Hospital. Studying patients with chronic kidney disease who receive kidney transplants, James explored how the donor and the patient's genes affect the long-term health of the transplanted kidney. The gene encoding the enzyme DDAH1 was of particular interest. "A background level of DDAH1 activity may not be a good thing in people who suffer kidney injury," says James. To help resolve the debate an ultimate goal would be to develop a drug to inhibit DDAH1. Of course, the lectureship was not without its challenges. "Switching between the lab and the clinic – can be difficult," admits James. "One moment you're pipetting DNA into hundreds of small plastic tubes and the next you're going off to do various clinical procedures on the wards".

James is currently a Consultant Nephrologist with the Imperial College Healthcare NHS Trust.

DR JESS ZHAO
2010–2013

Fellow

The youngest to embark on a Chain-Florey Fellowship, Jess started her research straight after her two clinical foundation years. "I would definitely recommend this fellowship to doctors with an interest in basic science. It provides an excellent opportunity to carry out exciting research supported by experts in their fields." Jess Zhao completed her PhD research project in the Cellular Stress Group with Dave Carling. "The Chain-Florey Fellowship has given me the opportunity to work in a fantastic lab and has confirmed my desire to become an academic clinician. Finding the right balance of clinical and research work has been more challenging than I expected, and it's still something I'm working on." Having returned to complete her core medical training, she is particularly interested in specialising in care of the elderly.

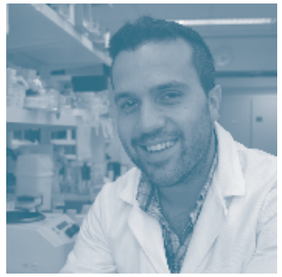
Jess is currently working as a GP.

DR ALLIFIA ABBAS NEWSHOLME
2011–2015

Fellow

"Learning the language of science has been a real eye-opener," says Allifia Abbas Newsholme. Her PhD project in Amanda Fisher and Matthias Merkenschlager's Lymphocyte Development Group involved developing a system to image gene expression changes in real time. The system will be useful for looking at how environmental factors influence changes in gene expression during pregnancy. "It's an uncomfortable thing to unfetter yourself from your clinical preoccupations," Allifia says as she reflects on her fellowship. But now she has the confidence of a clinician, able to "talk the language of science"

Allifia is currently a Renal Transplant Registrar at Guy's and St. Thomas'.



DR PHILIP WEBSTER
2011–2014

Fellow

"The Chain-Florey Fellowship is an excellent opportunity to acquire solid, basic science training for any doctor intending to have a career in academia," says Philip Webster, who completed his PhD under Anthony Uren in the Cancer Genomics group. Phil looked at the kinetics and genomics of BCL-2-driven lymphoid malignancies, focussing on B-cell death. "I wanted to gain knowledge, experience and learn new techniques within the genomics of the immune system and then apply this to my interest in autoimmune diseases." Having returned to his speciality training in renal medicine, he intends to pursue an academic career path.

Phil is currently a Consultant Nephrologist with the Imperial College Healthcare NHS Trust and an Academic Clinical Lecturer at Imperial College.

DR PARVIN BEGUM
2012–2015

Fellow

"The best thing about the Chain-Florey Fellowship is having the time to concentrate on research, not having to do research on the side of your day-to-day work," says Parvin Begum. Her interest in genetics and epigenetics brought her to the Institute's Epigenetic section, where she worked in Niall Dillon's Gene Regulation and Chromatin Group. She investigated the role of a protein, the mitotic kinase Aurora B, in lung cancer. "Cancer patients with tumours that overexpress Aurora B have a poor prognosis compared to those who don't but we know little about the mechanisms underlying this," Parvin explains.

Parvin has continued her respiratory specialist registrar training in the London Deanery South program.

DR ELIZABETH BYRNE
2012–2015

Fellow

For her fellowship project, Elizabeth Byrne looked at the changes that occur in Schwann cells after nerve injury. She developed a method for separating the Schwann cells from the rest of the nerve in order to look at the RNA expression levels. "The results showed differences in gene expression between Schwann cells from injured and uninjured nerves – a finding that may prove key in our understanding of peripheral nerve repair." Elizabeth's time in Simona Parrinelo's lab has helped her realise what she wants from a career in the future, she has learnt many translational skills which she feels will be useful in her role as a histopathologist.

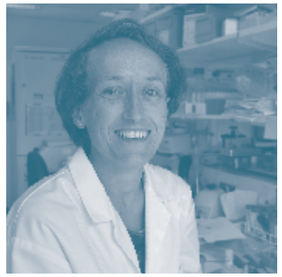
Elizabeth has been awarded an MPhil and is now enjoying her return to histopathology at Northwick Park Hospital. She plans to apply for a subspeciality training in neuropathology.

DR ANDREW INNES
2012–2015

Fellow

Andrew Innes spent his time as a Chain-Florey Fellow in Jesús Gil's Cellular Senescence Group studying the molecular mechanisms of senescence, a critical step in the biological ageing of cells as well as a formidable barrier in the prevention of cancer. "The approaches used during my PhD such as next-generation sequencing and genome editing with CRISPR technology are key tools in research, and experience with these will improve my understanding of others' research, as well as being useful techniques going forward into a postdoc project." His advice for current and future Fellows: "Learn from the others in your lab and don't be reticent to ask!"

Andrew is now an NIHR Clinical Lecturer in the Department of Haematology at Imperial College London, and is continuing some of the work he started in his PhD, as well as embarking on some new research areas in leukaemia.



DR ELEANOR SANDHU
2012–2015

Fellow

What makes salt so attractive that some patients cannot stick to a medically required low-salt diet? During her Fellowship, Eleanor Sandhu worked with Mark Ungless (Neurophysiology) and Dominic Withers (Metabolic Signalling) to investigate the networks involved in regulating salt appetite. Her work was inspired by dialysis patients on a low-salt diet with whom she had worked as a doctor. "I've been very lucky that I had the freedom to create my own project," she says. Eleanor hopes that there might be help for dialysis and heart failure patients if research can uncover a way to reduce their salt appetite through some form of manipulation.

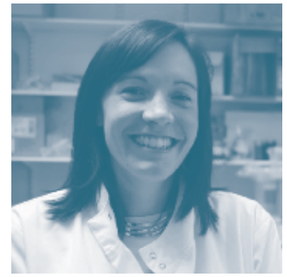
Following her PhD Eleanor re-joinined the London Deanery Renal programme to continue her specialist registrar training. In 2018 Eleanor was awarded an Imperial Post-CCT Research Fellowship in the Department of Medicine at Imperial College London. During this fellowship she plans to start investigating the potential role of a gut hormone, uroguanylin, on salt appetite satiety. To facilitate clinical investigation of salt appetite she also plans to establish fMRI as a means of objectively assessing salt appetite in haemodialysis patient.

DR HARPREET LOTA
2013–2015

Fellow

"I've always wanted to understand the underlying mechanisms of the diseases that as a doctor I have been coming across daily", explains Harpreet Lota about her motivation to join the Chain-Florey scheme. Her research on fibrotic lung disease was connected with her time as a respiratory registrar at the Royal Brompton Hospital. Her early experimental findings formed the basis of a targeted genetic study investigating the association between single nucleotide polymorphisms, longitudinal lung function decline and survival in a well-phenotyped cohort of patients with idiopathic pulmonary fibrosis. Her time as a Chain-Florey Fellow has been an invaluable foundation for future clinical research.

Harpreet is currently completing her training in respiratory medicine in the North West London Deanery.



DR JENNET WILLIAMS
2013–2017

Fellow

Jennet Williams started her Chain-Florey Fellowship in 2013 when she was well into her training as a medical oncologist. Fascinated by the Warburg effect – the observation that cancer cells metabolise glucose differently to normal cells – she was therefore thrilled to join Dave Carling's Cellular Stress Group, experts on AMP-activated protein kinase (AMPK), a key enzyme in energy homeostasis. For her PhD project Jennet investigated the effects of activating AMPK in the liver of a mouse model during the development and progression of liver cancer and explored how mutation of an AMPK subunit affects activation of the enzyme. "Cancer research is evolving rapidly and much of the progress made has been at the basic science level." says Jennet. "As a speciality, medical oncology really lends itself to a career as a clinician scientist. It's incredibly challenging but do-able."

Jennet is currently completing her training in medical oncology in the South London Deanery.

DR AMIT ADLAKHA
2014–2017

Fellow

A lung transplant can save patients' lives. But if a patient's immune system recognises the new organ as foreign it may attack and destroy it. Drugs called calcineurin inhibitors are used to suppress the immune system, but at the same time they increase susceptibility to deadly fungal infections. As a Chain-Florey Fellow with Boris Lenhard's Computational Regulatory Genomics Group, Amit Adlakha investigated how calcineurin inhibitors put patients at risk and how they affect which genes are expressed in cells, helping to clarify how the immune system is prevented from fighting fungal infection and how it could be boosted to retaliate. The fellowship, Amit commented, enabled him to learn techniques that he'd only read about in medical school, and "has been really good for teaching me to think ahead".

Amit is now a Consultant in Intensive Care and Respiratory Medicine, working at the Royal Free Hospital, London.

DR PRATHEEBAN NAMBYIAH
2014–2017

Fellow

Pratheeban Nambyiah came to do a PhD in André Brown's Behavioural Genomics group "to explore some of the actions of anaesthetics that we don't think about quite so much in day-to-day practice". An unusual Chain-Florey Fellow in that he started his academic career at a relatively late stage having recently finished specialist training in paediatric anaesthesia, Pratheeban was aware that anaesthetics might have longer term effects that persist beyond the actual episode of the anaesthetic itself. He used the nematode worm C. elegans, its short life-span making it an ideal model organism, to match quantifiable behaviours with genetics. Exposing the worms to anaesthetics and looking for subtle changes in behaviour long after the obvious effect of the anaesthetic has worn off, he investigated whether behavioural nuances were reflected as changes within the functional architecture of that worm's nervous system.

Pratheeban is now a Consultant Paediatric Anaesthetist at Great Ormand Street Hospital for Children.

DR JULIE GLANVILLE
2015–2018

Lecturer

As a Chain-Florey Lecturer haematologist Julie Glanville was able to develop ideas that came out of her PhD at the University of Oxford, where she studied T-cells and HIV, and became really interested in the emerging chimeric antigen receptor technology – engineering a patient's own T cells (CAR-T cells) to recognise and kill malignant or virally-infected cells bearing specific proteins. As a means to use T cells therapeutically to treat viral infections in the immunosuppressed patient post-transplant, Julie has been looking at signalling molecules and the epigenetic state of T cells to see how they might be used to enhance killing. With the aid of a research assistant provided by the Chain-Florey scheme, Julie's research has identified a T-cell co-receptor that may have therapeutic benefits for cellular therapy. "This is at a really basic science level which is where the LMS excels. The challenges now are to patent, publish and establish collaborations with industry to see if this will translate into therapies," says Julie.

Julie is currently completely her specialist training in Haematology in the North West London Deanery.

DR WILSON TO
2015

FY2 Trainee

Wilson To gained his PhD in Physiology before completing medical school. He then joined North Central Thames as an academic foundation trainee. Being awarded an FY2 position under the Chain-Florey scheme he worked with Amanda Fisher's Lymphocyte Development group on developing and utilising a new generation imaging system to study epigenetic change. The scheme provided him with an opportunity to explore an area of science that he believes will be influential in shaping patients' care in the future. "The experience and contacts have been invaluable", Wilson says about his time at the Institute.

Wilson is currently completing his Core Surgical Training in the North West London Deanery and working as a Urology Academic Clinical Fellow at the London Deanery.

DR JAYANT RANE
2016

FY2 Trainee

When Jayant Rane was accepted on the Chain-Florey scheme he had just re-joined his clinical training after a long time away from the bedside. While Jayant said that "taking it up after eight years of PhD and post-doctoral work at the University of York and King's College London was a bit daunting at first," the placement became an ideal bridge and provided a more seamless way back into the clinic while maintaining his links with basic science. Working in Peter Sarkies' Epigenetic Inheritance and Evolution group, Jayant investigated whether DNA methylation affects mutation rates on exposure to alkylating medications, research that contributed to a publication in Nature Genetics in 2018.

Jayant is currently a core medical trainee based in South London, with the intention of applying for the academic clinical track in medical oncology.

FY2 TRAINEES

DR ASMA SOLTANI
2016

FY2 Trainee

"The FY2 training programme has been an invaluable experience. It allowed me to strengthen my skills in imaging and to explore high-resolution imaging techniques.", says Asma Soltani, a graduate from Paris Descartes Medical School in France, where she gained both her MD and PhD in Neurosciences as part of the MD-PhD programme. At the LMS, Asma was hosted in Simona Parrinello's Cell Interactions and Cancer Group. She looked at the morphology of glial stem cells after activation in the sub-ventricular zone. Her work involved preparing samples from mouse brain tissue including immunostaining techniques and confocal imaging.

Asma has moved on to an Academic Paediatric Trainee position in Cambridge with the East of England deanery.

DR PHIL OSTROWSKI
2016

FY2 Trainee

Phil Ostrowski worked as an FY2 Trainee with Stuart Cook's Cardiovascular Disease Mechanisms group and Declan O' Regan, Head of MR Facility. He looked into myocardial structure and function in healthy volunteers and subjects with mutations of the titin gene, which encodes the largest human protein, a key component of muscles throughout the body. Phil used a variety of commercial and in-house software to interpret the imaging studies and to look for links between genetic variability and cardiac phenotype. "The most enjoyable element of my work was having a clearly defined translational aspect to my research," Phil says.

Phil is currently training as a specialist registrar in clinical genetics at St. George's Hospital, London

DR ALEXANDER O'NEILL 2017

FY2 Trainee

Having previously completed a PhD in molecular imaging from King's College London (2012) and a graduate medical degree from Oxford (2016), for his Chain-Florey FY2 Trainee position Alexander O' Neill joined Oliver Howe's Psychiatric Imaging Group. He used imaging to probe the physical consequences of use of antipsychotic drugs in patients with psychosis and healthy controls. Alexander found this work hugely rewarding because it involved both clinical elements (patient recruitment, assessment) and academic aspects (imaging data). He also developed the management skills required for running a clinical trial. "The placement is a perfect bridge in terms of my background in basic science and previous clinical work, allowing me to understand the nuances of clinical research but also giving me exposure to a fascinating discipline as well as working in an ambitious and fun team!".

Alexander is currently completely his foundation training in the North West London Deanery.

DR REEM BEDAIR 2017

FY2 Trainee

Reem Bedair had recently finished her PhD in Radiology from the University of Cambridge when she was appointed as an academic FY2 doctor at Imperial College Healthcare Trust. She undertook her academic placement with Declan O' Regan, Head of MR Facility, where she was involved in a project that combined quantitative imaging of the heart with genomic studies to understand cardiovascular biology and disease. Reem enjoyed her FY2 placement, at the time saying: "It offers the flexibility of combining acute and general clinical practice with substantial academic research."

Reem is now a Clinical Radiology Speciality Registrar and NIHR Academic Clinical Fellow at Cambridge University Hospitals NHS Foundation

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