THE FRANCIS CRICK INSTITUTE

STRATEGY 2021
DISCOVERY WITHOUT BOUNDARIES

The Francis Crick Institute is a partnership between:

UKRI Medical Research Council

UCL

Imperial College London

King's College London

Wellcome

Cancer Research UK

THE FRANCIS
CRICK INSTITUTE

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FOREWORD

It is eight years since we published 'Discovery Without Boundaries' (DWB), our first strategy which guided the establishment of the Francis Crick Institute and its research activities. That document articulated an ambitious vision: to create a world-class biomedical research institute that would be a magnet for scientific talent from across the world, generating discoveries to transform our understanding of health and disease.

Delivering that vision required the formation of a new partnership, bringing together the UK's three major funders of biomedical research: Cancer Research UK, the Medical Research Council and Wellcome, and three of its leading research universities: UCL, Imperial College London and King's College London.

The Crick formally came into existence in 2015, through a merger of Cancer Research UK's London Research Institute (LRI) and the MRC's National Institute of Medical Research (NIMR). By early 2017 we had completed the £650 million construction phase, followed by the complex process to move people, animals and scientific equipment into the new building. The institute can now celebrate four years of operation under a single roof, with a single integrated leadership.

We are proud of what has been achieved so far. We have recruited 32 new early career group leaders from 15 countries, and integrated more than 50 collaborating groups from the partner universities. Our faculty has been recognised through major scientific prizes including a Nobel Prize in Physiology or Medicine, an Albert Lasker Award for Basic Medical Research, a Canada Gairdner International Award, two consecutive Louis-Jeantet prizes and an EMBO Gold Medal.

Our focus for the coming years will be on consolidating the Crick's status as a world-class biomedical research institute.

PAUL NURSE, DIRECTOR

We have recruited more than 300 students and more than 600 postdoctoral training fellows, established an effective operational team and launched CrickConnect, our new alumni programme. We have developed productive pre-competitive partnerships with pharmaceutical companies including GlaxoSmithKline (GSK) and AstraZeneca, and leveraged substantial external funding to support translational science projects. Our education programme has engaged more than 20,000 students from local schools.

The Crick's work has also influenced developments in the wider world. The UK has left the European Union, with significant consequences for scientific collaboration and funding, and the Crick was a vocal participant in the national debate. The COVID-19 pandemic has reinforced the critical importance of biomedical research and brought the Crick's vision of close cooperation between discovery and clinical scientists into sharper focus. The scientific community has given greater consideration to its culture and ways of working, reflected in the Crick's new strategy for equality, diversity and inclusion and an enhanced focus on mentoring and wellbeing for all our staff and students.

This document is built on the original vision in 'Discovery Without Boundaries' and should be seen as a refresh and a reaffirmation, informed by our experience as an operational institute and the new challenges we face. The first part acts as a summary, explaining what the Crick is, our vision and core principles. The second part provides a more detailed exposition of our objectives, including the broad scientific areas within which Crick scientists devise and undertake their specific research programmes. Our focus for the coming years will be on consolidating the Crick's status as a world-class biomedical research institute, strengthening the multidisciplinary scientific approach together with our three university partners, expanding our support for the wider UK biomedical research endeavour and working with the Crick's founders to ensure a sustainable future for the institute.

The Queen and the Duke of Edinburgh opened the Crick building with Paul Nurse and then Crick chairman David Cooksey in November 2016.

I am excited about the next chapter in the Crick story, and I hope this document will give you a sense of what we are trying to achieve.

Paul Nurse FRS
Director

WHAT IS THE CRICK?

The Francis Crick Institute is an independent charity, established as a UK flagship for discovery research in biomedicine.

The Crick came about through the vision of six partner organisations, who together provided the capital costs of the institute's establishment: the Medical Research Council (MRC), Cancer Research UK (CRUK), Wellcome, UCL (University College London), Imperial College and King's College London. The institute is named after the UK scientist Francis Crick, in recognition of his contributions to understanding the genetic code, the key to understanding how living things work.

The Crick began operating in April 2015, when the MRC's National Institute for Medical Research (NIMR) and CRUK's London Research Institute (LRI) merged to form the new institute. In 2016 we completed construction of our new building at St Pancras, London, and commenced operations on the new site in early 2017. Today, the St Pancras site houses more than 2,000 people employed by the Crick and its partners, with more than 100 research groups. Research groups transferring from NIMR and LRI have been joined by groups seconded from each of the three partner universities, as well as a significant number of new group leader recruits.

The institute is governed by a board of trustees, comprised of independent members and representatives from each of our founding partners. We are funded through significant core funding from the MRC and CRUK, which was inherited from our parent institutes NIMR and LRI, and further supplementary core funding from Wellcome, as well as external research grants.

OUR VISION

THE CRICK'S VISION IS DISCOVERY WITHOUT BOUNDARIES

Our mission is **world-class discovery research to understand how living things work and to drive benefits for human health**.

The Crick will explore biological mechanisms at all scales from molecules through cells to organisms. Our discoveries will enhance understanding of the fundamental processes of life, with the potential to transform the prevention, diagnosis and treatment of human disease.

To deliver our mission, the Crick will bring together people and expertise from different scientific disciplines. We will work with different types of organisations across the academic, clinical and industrial spheres. In this way, we will create a space for discovery without boundaries, and support the translation of discoveries into health benefits.

The Crick is a young institute, only commencing full operations in 2017. In the first four years, our focus was on establishing the institute and optimising our ways of working. We now aspire to consolidate our position as one of the leading biomedical research institutions in the world.

We will know we have achieved our ambition when:

- Our science and our scientists are recognised as world-leading, ambitious and creative, making discoveries that have major impacts on their fields.
- We are a favoured destination for the best scientists in the world at all career stages
- We are considered among the top employers in our field, widely recognised for our supportive and inclusive culture and high levels of staff engagement.
- We are recognised for the quality of our training at all career levels and for all types of roles, with Crick alumni in leadership positions in the UK, Europe and around the world.
- We are known for our innovative approach to translating our science, with resulting impacts on human health.
- We exemplify a healthy research culture, fostering openness, transparency and research integrity combined with high quality science.
- The UK and international public see us as a positive and accessible face of biomedical research, and science more generally.

HOW WE WORK

We are **BOLD**

We make space for creative, dynamic and imaginative ideas and approaches and are not afraid to do things differently.

We are **OPEN**

We are highly collaborative and interactive and make our activities visible to the outside world.

We are **COLLEGIAL**

We show respect for one another, work cooperatively and support the wider community.

OUR CORE PRINCIPLES

The Francis Crick Institute is an independent, standalone research institution. We share features with other successful research institutions from around the world, but combine them in a way that is unique and distinctive. Four enduring principles guide our approach:

We conduct research of the highest quality

The 55 senior and emeritus group leaders in the institute include four Nobel laureates in Physiology or Medicine and Chemistry, eight Louis-Jeantet prize winners, six EMBO Gold medallists, 26 Fellows of the Royal Society and 35 Fellows of the Academy of Medical Sciences. Our research portfolio is regularly renewed through new appointments, with an emphasis on work at the forefront of biomedical research. Our core funding enables us to provide stable, long-term support for ambitious science and promotes agile ways of working. We share resources across laboratories, with an open laboratory environment and an extensive range of science technology platforms (STPs) that provide access to state-of-the-art technology of a range and quality that would be difficult for individual research groups to replicate. This centralised approach is cost-effective and allows researchers to be bolder in their ambitions, while at the same time ensuring research groups remain small, manageable and productive.

We maintain a broad scientific portfolio, embracing interdisciplinarity and translation

The Crick operates under a single roof, with research as its core purpose. Our open and interactive culture brings together different people with a wide range of research interests and expertise, including clinicians and physical scientists from our three partner universities, and applied scientists from our partners in the pharmaceutical industry. We have no divisions or departments and our research groups have the freedom to devise and set specific research programmes within broad areas, which reflect the thematic interests of our major funders. We take a wide and inclusive view of biomedicine, integrating insights from the biological, medical, physical and information sciences, and pursuing translation opportunities whenever they arise. Our size, scientific breadth and research-active leadership enables the institute to respond rapidly to new research opportunities and priorities.

We act as an incubator of early career talent

Early career researchers, at a highly creative stage in their career, will form the majority of group leaders at the Crick. We recruit mostly through open searches, allowing us to fish in a large pool of candidates, with the ambition to create new fields driven by original and inventive scientists, rather than follow trends. We employ our early career group leaders for an unusual 12-year ('six plus six') career term, designed to enable them to rapidly build an innovative independent research programme. During their time at the Crick they benefit from focused support, advice and mentoring, with access to core-funded laboratory posts and excellent technical research facilities. When their term finishes they will be well prepared to take on leadership roles at other institutions. In this way, the Crick acts as a conduit for exceptional researchers from around the world, invigorating the biomedical research endeavour across the UK. Over time our researchers will form an influential network of UK and international alumni.

We are permeable and outward-looking

The Crick has a collaborative ethos, reflecting its origins as a partnership of six organisations seeking to pool knowledge, ideas and resources. We engage with a range of other research institutions across the world. Our scientific seminars, interest groups and conferences bring together researchers from across the Crick partnership, and in many cases from further afield. Our training programmes for early career researchers are designed to offer a broad perspective of biomedical research, including exposure to careers outside science. The Crick pursues a dynamic public engagement programme focused on our unique selling points: the presence of active research scientists, the institute's close connections to local communities, and the provision of science teaching support for local schools, including an in-house teaching laboratory for primary school children. We engage with national and international policymakers on scientific issues and use digital and media communications to interact with national and international public audiences.

These principles will guide us as we pursue our agenda and science programme for the coming years. We will focus on five priority objectives:

1. **Accelerate discovery through a culture of scientific excellence**
2. **Support the biomedical research endeavour across the UK and beyond**
3. **Drive benefits for human health**
4. **Engage and inspire with discovery science**
5. **Build capability for outstanding science support.**

OUR OBJECTIVES

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Accelerate discovery through a culture of scientific excellence 1

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Drive benefits for human health 3

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Engage and inspire with discovery science 4

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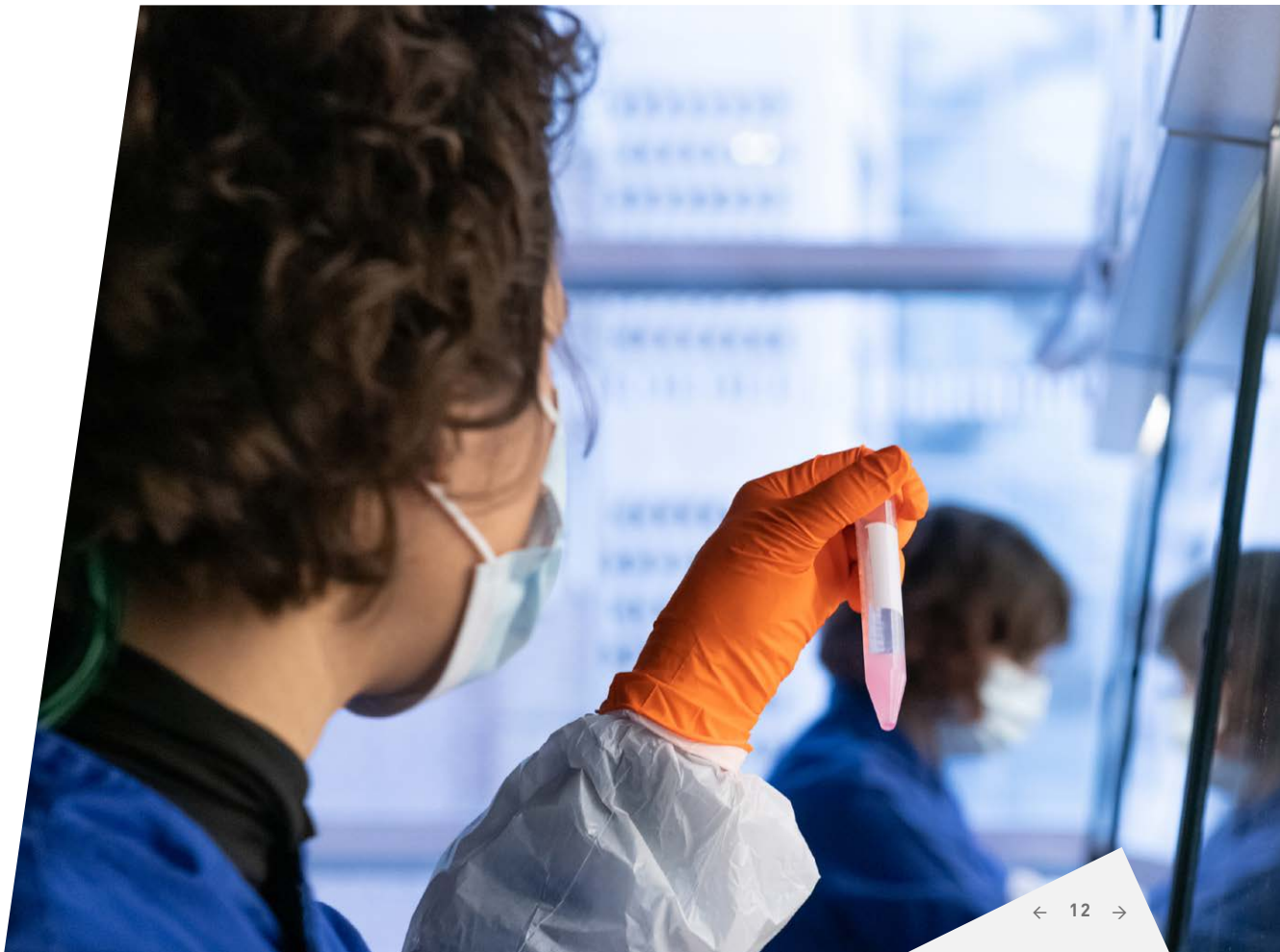
Build capability for outstanding science support 5

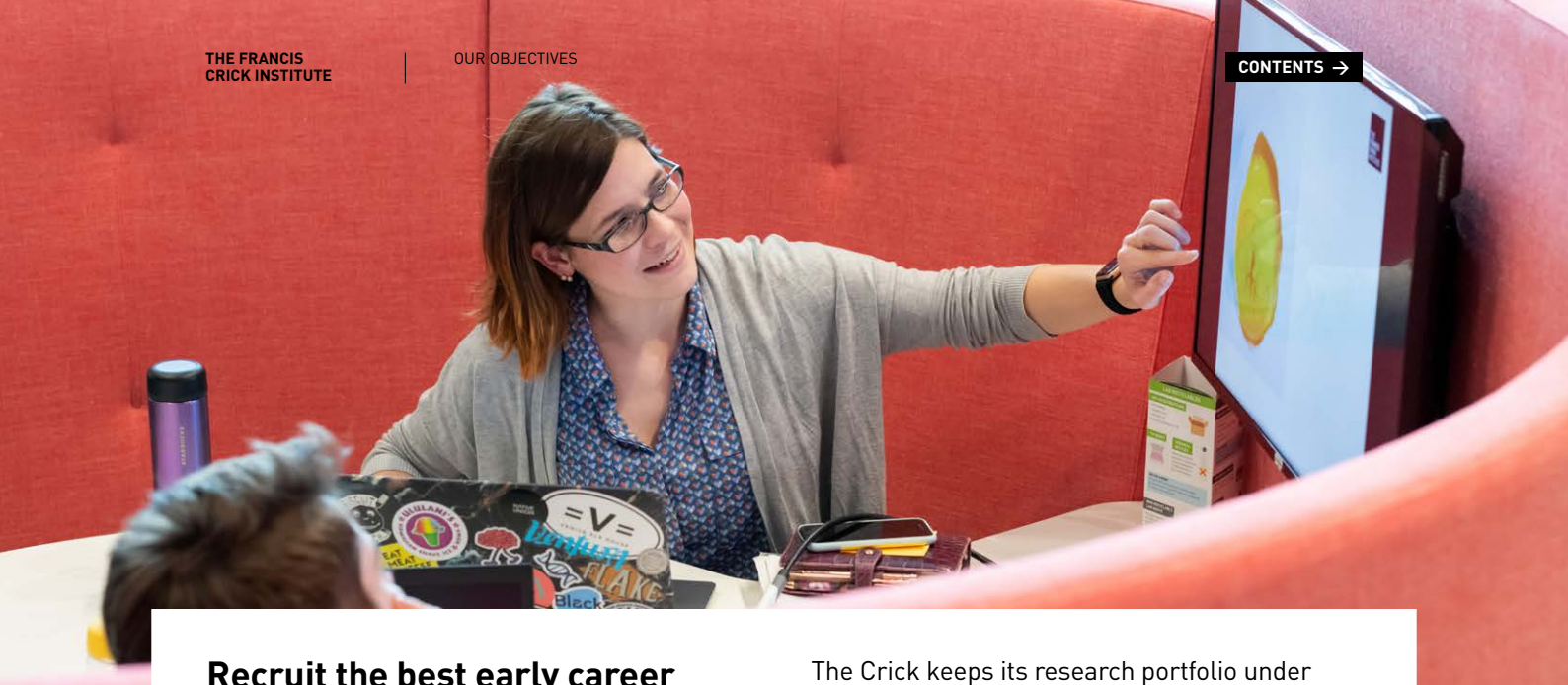
PILLAR 1:
ACCELERATE DISCOVERY THROUGH A CULTURE OF SCIENTIFIC EXCELLENCE

1

Research is a creative endeavour, driven by the vision and insight of exceptional individuals, and relying on an inclusive culture where diverse talent can thrive. The Crick will recruit outstanding researchers at all levels, supported by excellent technical staff. We will emphasise novel and interdisciplinary approaches, set high research standards and maintain them through rigorous review.

We will provide high-quality training and mentoring to assist our researchers to develop their careers and capabilities as future research leaders. We will encourage wide scientific interactions, building an open and permeable culture that brings together different disciplines and perspectives and fosters the free exchange of ideas. These principles underpin the Crick's approach to scientific discovery.





Recruit the best early career researchers from across the world, working in areas relevant to biomedicine

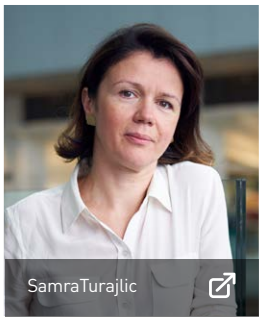
The Crick acts as a beacon for exceptional research talent from around the world. Our faculty recruitment has an emphasis on early career researchers, most of whom will be taking up their first independent post. They will develop their programmes for up to 12 years and will then receive assistance to find a position elsewhere. The high-quality resources, facilities and support available within the Crick will enable these early career recruits to take on bold and creative research questions. We consider applications from excellent candidates working in any area relevant to biomedicine – including the breadth of biology, chemistry, physics, engineering and information science, as well as the core biomedical disciplines. This open search process enables the Crick to identify the best people from a large candidate pool, working across the full spectrum of research fields. Because the Crick has no academic divisions and our faculty search is open to a wide range of scientific disciplines, we have the flexibility to hire individuals with unusual backgrounds or who are taking novel or unorthodox approaches to biological problems. In making the choice between equally excellent candidates, we will consider added value in terms of new and unexpected research fields or technical approaches, strategic synergy with existing Crick programmes, and the potential for links with existing or potential new Crick collaborators.

The Crick keeps its research portfolio under regular review. Through discussions involving the scientific leadership, faculty and the Crick's Scientific Advisory Board, we assess to what extent the portfolio addresses the research themes and focus areas outlined in the science programme, taking account of their overlapping nature. If significant gaps appear, we will complement our open search process with more focused searches. This will support our multi-disciplinary ambitions and respond to areas which are important to our founders. To date, focused searches have involved the physical and clinical sciences, with the Crick conducting joint searches with our three partner universities UCL (University College London), Imperial College and King's College London. These are much larger institutions than the Crick, with a depth of expertise across a wider range of disciplines, and which act as conduits to major London research hospitals.

The Crick aims for research groups led by early career faculty to make up around two-thirds of the total research groups within the institute, with groups led by established senior faculty accounting for the remainder. Currently, around half of Crick groups are early career, an increase from less than one third at the time the institute was established. As we approach our planned ratio for early career to senior group leaders – likely to be around 2025 – we will additionally open recruitment for senior faculty, using open, international competition. We will be seeking candidates who are exceptional scientists, and will also consider their management capability and leadership potential beyond their research programme.


Anne Schreiber


Radoslav Enchev


SamraTurajlic


Petr Znamenskiy

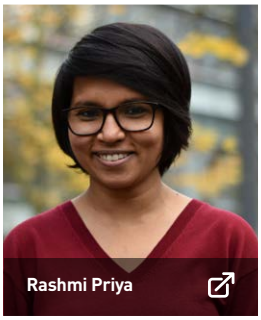

Lucia Prieto-Godino


Alberto Elosegui Artola


Louise Walport


Charlie McTernan


David Bauer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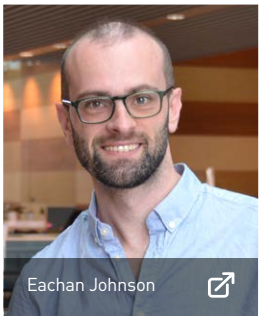
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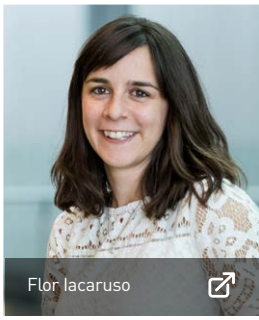
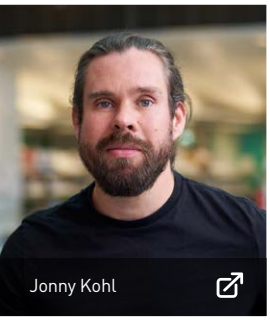

Flor Iacaruso

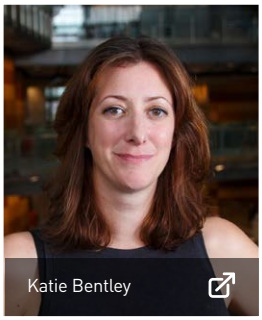

Greg Findlay

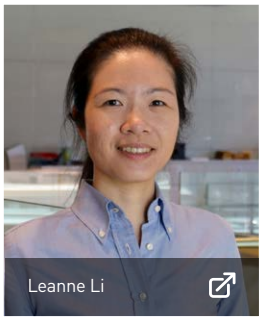
EARLY CAREER GROUP LEADERS

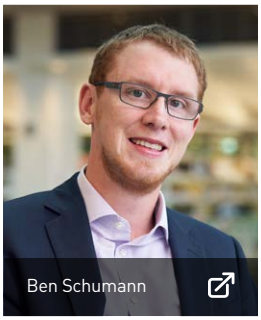
Every year since 2017, we have held open recruitment calls for new faculty members, where we look for innovative early career scientists to establish research groups at the Crick. We have now recruited 32 group leaders, clinical group leaders and physical science group leaders to the Crick and look forward to welcoming more.


Jeannine Hess


Jonny Kohl

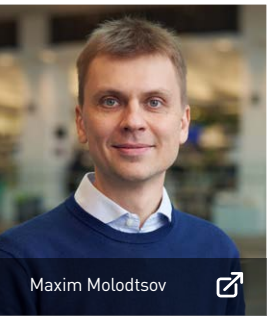

Katie Bentley


Leanne Li

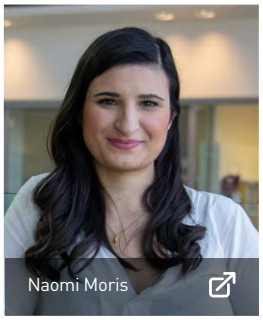

Ben Schumann


Adam Sateriale

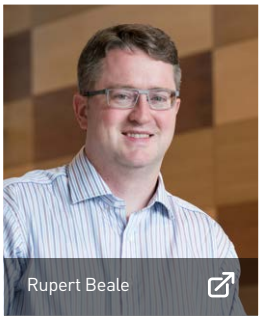

Margarida Cardoso-Moreira

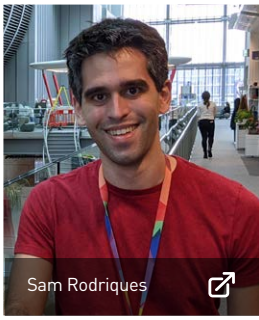

Maxim Molodtsov


Mike Devine


Naomi Moris


Pontus Skoglund


Rupert Beale


Sam Rodriques


David Balchin


Silvia Santos


Katharina Schmack


Zena Hadjivasiliou


James Lee


Philippa Matthews

Maintain high-quality science through rigorous review processes

The Crick will support research programmes that are bold, ambitious and innovative, with an ambition to be on par with the best science from around the world. Our core funding and the ready access to a range of science technology platforms (STPs) means that Crick research groups have the freedom and resources to pursue genuinely ambitious and creative research questions over the long term.

All the Crick's scientific activities will be regularly reviewed, including discovery and translational research and the STPs. The approaches employed will be tailored to the area being reviewed.

To uphold scientific excellence, our research programmes undergo rigorous, independent external review, designed to assess their scientific quality, productivity and impact. Somewhat different processes will be used to review senior and early career group leaders.

Research programmes led by senior group leaders will be reviewed every five years and will be expected to demonstrate an exceptional international standard. The reviews will inform decisions made by the Crick scientific leadership on the continuation and future level of resource for each programme. Programmes led by early career group leaders on 12-year appointments will receive a 'renewal review' in the sixth year of the appointment. The main emphasis of this review will be to support the development of the group leader and their research programme. A decision to discontinue the programme will only be made if performance is clearly unsatisfactory.

Should a review result in a decision to discontinue a research programme, the Crick will work with the group leader to ensure a smooth transition to another institution. We will provide appropriate guidance and resources to support group leaders and their teams during that transition.

Foster creative and interdisciplinary approaches

To tackle complex biological questions, novel and creative approaches are required. The Crick will foster a culture of energetic inter-disciplinary interaction and engagement, knowing that important research advances often occur at the boundaries between disciplines. We will draw on the physical sciences, engineering and information sciences as well as biological disciplines on the fringe of biomedicine, bringing in new perspectives that complement our core biomedical expertise. This will be further enhanced by the presence of scientists from industrial backgrounds. We will conduct regular horizon scans, supported by our Scientific Advisory Board and other advisors, to identify emerging areas and techniques of particular interest.

The alliance with the three Crick partner universities is central to the development of the Crick's interdisciplinary agenda. A growing number of Crick faculty are drawn from the clinical and physical sciences, either via a secondment from one of the university partners or joint recruitment. Additional university-based researchers operate satellite laboratories at the Crick. These researchers maintain a close connection with their home university and core discipline or clinical speciality, supporting their ongoing career development while also acting as conduits to support the growth of research networks between the Crick and the partner universities. Some of our university faculty bring new technological expertise from the physical sciences, stimulating the development of new technology platforms and resources through longer-term programmatic satellite groups, working with Crick science technology platforms. Further links are promoted through the Crick PhD programme, which is operated together with the university partners. Students have thesis committees comprised of Crick and university faculty, and a proportion are jointly supervised. This can lead to new opportunities for collaborative and interdisciplinary science between Crick and university research groups.

Cultivate diverse opportunities for scientific interaction

Maximising opportunities for interaction is fundamental to the Crick way of working. It is reflected in the physical design of the building, the day-to-day operation of laboratories and in Crick organisational structures.

We will promote robust scientific discussion and exchange through a variety of mechanisms, ranging from seminars, regular scientific interest groups, workshops and symposia, to informal discussion groups. The Crick has the advantage of being small enough to be able to hold meetings and events that are open to the whole institute, as well as to interested colleagues from our founding partners. At the same time, the Crick is also large enough for these events to be able to draw in participants with a breadth of scientific expertise and a range of experience, promoting engagement across disciplinary boundaries.

The Crick uses a system of bottom-up scientific interest groups to bring together researchers from across the institute to discuss current findings and ideas, strengthen connections between disparate fields of study and promote new collaborations. Interest group participation includes the university partners via a system of associate membership, engaging university researchers from disciplines that are less well represented at the Crick. This is further supported through informal 'forums', which bridge interest groups and link researchers around common technical or conceptual interests. They provide an agile platform for the exchange of ideas and interdisciplinary collaboration.

Provide excellent training, mentoring and leadership development across all levels and roles

The Crick will nurture talent, both in research and in the range of other roles needed to support that research effectively. We will ensure that high-quality, comprehensive training, together with appropriate support for career progression and development, is available to all staff across all career stages. This includes research staff following an academic career path, staff working in technical and specialist support roles in laboratories and science technology platforms, and those in operational support functions.

The majority of Crick research staff will spend a limited period at the institute – a maximum of 12 years in the case of early career group leaders, four to six years for postdoctoral training fellows and four years for PhD students – and we will ensure people make the most of this time, as well as the opportunities available at the Crick. We will inspire young scientists by celebrating the process of discovery science, drawing on the historic context and our own experience of how ideas are conceived and obstacles overcome.

Early career group leaders participate in a science leader development programme, which equips them with management and leadership skills to complement their technical skills and scientific achievements. The Crick surrounds each early career group leader with a mentoring team, led by a dedicated mentor chosen from amongst the senior group leaders, to support the development of their science programme, and their laboratory and people management skills. Additional management and leadership training is also available to senior group leaders, and the establishment of new assistant research director positions within the institute's management structure will provide opportunities to develop senior management experience.

The Crick provides an exceptional training environment for graduate students and postdoctoral training fellows (PTFs), who benefit from its stimulating multidisciplinary environment and links to multiple partners and collaborators across academia and industry. We work with our university partners, who award the degrees and provide additional student supervision and further training opportunities. Importantly, the institute is small enough for trainees to feel part of a cohort and community but is also large enough to provide diverse research training and development opportunities.

We take a broad interpretation of 'future science leaders', recognising that not all will wish to pursue an academic research career. We will draw on Crick alumni and others in our networks to assist those interested in different career paths to build experience relevant to their future chosen career. Our online community 'CrickConnect', will bring together current staff and alumni to support networking, mentoring, collaboration and career development. This ensures that individuals will continue to benefit from the Crick endeavour after they have left the institute, while the institute will also benefit from a wider pool of expertise and experience. Over time, we expect this to become a powerful tool to support mentoring and career development, particularly for junior researchers.

We will develop appropriate career paths for research and technical specialists, reflecting the increasing importance of sophisticated instrumentation for biomedical research. A key focus will be the laboratory research scientists, a diverse group with many academically trained to postdoctoral level, who play an important role in training and developing research staff. They have access to an active staff network and we will work with them to develop and extend training opportunities, including supporting professional registration as part of the Technician Commitment.

> **The science leader development programme represents an opportunity to help build a stronger community and culture at the Crick.**
>
> SILVIA SANTOS, PROGRAMME PARTICIPANT 2020

Develop an inclusive culture that nurtures diverse talent

Crick staff are drawn from diverse backgrounds and over 60 different nationalities, bringing their own personal characteristics, life experiences and perspectives to enhance the daily life of the institute and deliver our mission. We aspire to become a leader in equality, diversity and inclusion, and use our influence to support wider progress in the research community.

Our efforts to promote gender equality have been recognised through an Athena SWAN Award, and the gender balance of our early career faculty is improving. More than 40% of early group leader appointments to date are female, compared to fewer than 20% of group leaders who transferred to the Crick at its establishment. The Crick is committed to supporting the development of UK bioscience, which requires action to increase the number of women in the most senior roles. To assist with this, we will identify staff who have the potential to progress to leadership positions (whether in the Crick or elsewhere) and provide access to appropriate training, support and mentoring to further develop their leadership capability.

We will apply what we have learnt from our work on gender equality to enhance diversity more generally, taking positive action to attract, retain, develop and support a diverse staff and student population. Our active staff networks, including PRISM (the Crick's race equity network), PROUD Crick (for LGBTQ+ staff) and Enable (for staff with disabilities), will be partners in these activities.

Our priorities are to increase the understanding of the importance of diversity and awareness of diversity issues, to collect, analyse and understand diversity demographics and trends in the institute, and to improve equal opportunity in recruitment, development and engagement in order to increase diversity and foster inclusion. We will use awards and charter marks to promote action on these objectives and accelerate success by working with our Board, partners, neighbours and the wider scientific community. We will nurture and promote career development for staff from priority groups through initiatives such as the StellarHE programme to promote diverse leadership in higher education.

We are committed to widening participation and increasing diversity within our training programmes. Black researchers are under-represented in many research institutions, including the Crick, which is linked to numbers in the undergraduate student pipeline. We will explore ways to address this, although we do not operate formal undergraduate teaching programmes. We will consider how we can use our connections with schools to support school students who participate in education programmes and work experience at the Crick and who then go on to do science at university, support existing undergraduate mentoring schemes for minority ethnic students at London universities, and use our summer and sandwich placement schemes as vehicles to provide research experience opportunities to other under-represented groups.

PILLAR 2: SUPPORT THE BIOMEDICAL RESEARCH ENDEAVOUR ACROSS THE UK AND BEYOND

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The Crick aims to act as a national flagship for biomedical research, supporting the government's ambition to build a thriving science and technology ecosystem within the UK, and forging scientific links across the world. Our vision of discovery without boundaries is reflected in our support for the biomedical research endeavour across the UK, with an aspiration to develop future leaders for academia, industry and other walks of life.

We expect our staff to act as good scientific citizens, contributing to a strong biomedical community across the UK, the rest of Europe and the world. We will assist successful graduates of Crick training schemes to continue their careers at other leading institutions, contributing to the growth of a highly skilled UK science workforce across all levels and roles. We will build external interactions and collaborations with a growing number of UK and international research institutions, expanding the reach of the Crick's researcher development mission and bringing together complementary scientific capabilities for reciprocal benefit.

Help grow the UK science skills base through continuous renewal of the Crick's research portfolio

The majority of the Crick's research appointments are time limited. Our aim is to act as an incubator of science talent and support innovative research programmes and ideas that can extend and be further developed beyond the institute. The majority of Crick research staff will transition to new institutions after completing a career stage with us. The Crick is a magnet for top international talent and supporting their subsequent transition elsewhere will ensure the benefits of our recruitment approach are shared more widely, assisting other research institutions to develop their research portfolios.

New early career faculty will spend a maximum of 12 years at the Crick. This approach has been chosen to benefit the researcher, the institute and the wider scientific community. It gives young research leaders the time and resources to focus on developing a high-quality research programme and the range of skills they need to run a laboratory, without the pressure of tenure review.

It benefits the institute by creating space for new recruitment and enabling a dynamic research environment in which new ideas and capabilities are continuously introduced. And it benefits the UK scientific community, because the Crick aims to recruit exceptional people and develop them so that they are at the top of their scientific game when they move to new positions. This will strengthen the pipeline of international talent into research organisations across the UK. The Crick will support these departing group leaders by providing transitional resources, support and advice to assist them to set up a laboratory elsewhere.

Well-trained Crick PhD students and postdoctoral training fellows (PTFs) will also leave the institute once their training is complete. In line with the continuous renewal philosophy, we have a policy not to appoint graduating students to postdoctoral roles or PTFs into group leader roles. We believe that the international and diverse character of biomedical research means that researchers' training needs will be better served if they develop experience of different research environments.

Catalyse the development of scientific networks beyond the Crick

A key objective of the Crick is to be highly permeable to the outside world. The institute is strategically positioned in central London and has excellent transport connections with the rest of the UK as well as internationally. We aspire to create new opportunities by bringing together people and ideas – both in a virtual and a physical context.

At a local level the institute aims to strengthen links across the Crick partnership by identifying scientists within the three partner universities who have research synergies with the Crick and who are interested in closer interaction.

The Crick and the universities co-fund networking activities initiated by researchers in a bottom-up manner, capitalising on the critical mass of research activity that exists across London. We will further develop this approach, establishing strong local biomedical research networks with the partner universities and other nearby institutions with complementary interests.

At the national level, the Crick's excellent conference and seminar facilities make it a natural hub for scientists to interact, engage and collaborate with each other. We will expand our scientific discourse activities and promote the development of scientific networks by acting as a convener and 'go-to' destination for conferences, meetings and seminars.

Pursue added value through collaborative research activity

The Crick will continue to promote the development of close collaborative links with our three London university partners, which are critical to our interdisciplinary research agenda. Key mechanisms to establish these links are now in place and will continue to be strongly supported. These include the joint recruitment programmes in engineering, physical and clinical sciences, the joint PhD programme, and the annual university attachments scheme which has seen more than 300 researchers from the partner universities seconded to the Crick. Funding permitting, we will develop a pump-priming scheme to support new cross-discipline satellite laboratories led by engineers and physical scientists from partner universities, working with Crick biomedical researchers. We will continue to recruit early career group leaders in research areas that either complement the institute's existing capabilities, advance the interdisciplinary agenda, or contribute new facilities and technologies. We wish to recruit group leaders at the interface with engineering and will consider focused recruitment in that area. To sustain these interactions in the longer term, we will encourage secondee group leaders and joint recruits to establish satellite groups in the Crick after their return to the university.

We will increase our focus on strategic partnership opportunities and major funding consortia, working with the partner universities and other institutions with complementary capabilities, including industrial partners. Current examples include the creation of the City of London Cancer Centre – an interactive hub for cancer biotherapeutics – funded by Cancer Research UK, a partnership with the Alan Turing Institute to facilitate growth in data-centric biomedical science research collaborations, and the 4ward North Clinical PhD Academy with the universities of Leeds, Manchester, Newcastle and Sheffield, which aims to strengthen clinical academic research training in the North of England. In the coming years we will further develop our relationship with the Sanger Institute, capitalising on our scientific approaches that are complementary, and the synergies around the Sanger's main themes of cancer and ageing, human genetics, parasites and microbes. Opportunities also exist to work with the EMBL European Bioinformatics Institute on the Wellcome Genome Campus in Hinxton to strengthen our data-centric research activities. We will explore possible links with the artificial intelligence and data science communities, including Google DeepMind, Innovate UK's London Medical Imaging and AI centre, and clinical and population geneticists within the partner universities and the Academic Health Science Centres and Biomedical Research Centres.

Building on the experience of the Crick-London university partnership, we will explore the establishment of a new funding mechanism to support new collaborative projects between Crick group leaders and researchers across the UK. This will support initiatives such as satellite laboratories and joint fellowships targeted at early career clinician scientists, and group leaders working at the interface with engineering and the physical sciences. It will bring external expertise to the Crick and broaden opportunities for scientists from institutions across the UK to interact with us, helping to promote the development of research and economic opportunities beyond London and the surrounding regions.

Where practical and appropriate, the Crick will host specific initiatives and infrastructure to assist the UK biomedical research endeavour. Current examples include the UK Dementia Research Institute and the MRC Biomedical Nuclear Magnetic Resonance (NMR) Centre.

A 950 MHz nuclear magnetic resonance spectrometer. The spectrometer, part of the MRC Biomedical NMR centre, is one of only a few such instruments in the UK and provides facilities to researchers across the country.

Crick African Network fellows at the first annual meeting.

Build strong international scientific connections

The Crick has a strongly international and outward-looking focus, enabled by our diverse research workforce with many existing global connections and networks. We will continue to forge strong connections with partners elsewhere in Europe and across the world. Our approach will be science-led, prioritising bottom-up interactions driven by Crick research groups and leveraging these existing scientific links to develop higher-level relationships as opportunities arise. We will take a flexible approach tailored to the specific country context, but in many cases we will prioritise relationships with national collective groupings rather than partnerships with individual research institutions. For example, the Crick's current memorandum of understanding with the European Molecular Biology Laboratory (EMBL) aims to strengthen pan-European scientific cooperation, with an emphasis on stimulating collaborative interactions between early career scientists. A new internal international engagement forum will strengthen prioritisation and coordination of potential international partnership opportunities.

We will expand research and training opportunities for international graduate students and postdoctoral fellows, consistent with the Crick's strategic emphasis on training and future science leaders. The successful Crick African Network is a recent example of this approach. We will further progress it through the development of links with national academies, leading research institutions or groups of institutions, as appropriate to the partner country. For example, we are exploring connections and collaborations with five Indian research institutions identified by the Indian government's Chief Scientific Advisor, and with the large network of institutions that make up the Chinese Academy of Sciences, working with the President of the Academy.

We will establish international links that promote best practice in the operation and management of research institutions, as well as research links. The Crick is a founding partner of the BRIDGE (Basic Research Institutions Delivering Graduate Education) Network, established in 2018, a coalition between five international scientific institutions that share a common mission to conduct world-leading curiosity-driven research and provide graduate education. The other partners are the Rockefeller University (USA), the Weizmann Institute (Israel), the Okinawa Institute of Science and Technology (Japan) and the Institute of Science and Technology (Austria).

Building on the model provided by the Crick African Network, we will develop further networks of collaborators in low and middle-income countries. These networks will support Crick research programmes, for example in infectious diseases, while promoting the development of research capacity and infrastructure in the relevant countries.

Support Crick scientists to contribute to the scientific community beyond the Crick

Scientists working at the Crick are expected to play an active role in the wider scientific community, capitalising on their individual strengths and interests. This includes participation in external academic activities such as funding panels, review boards, learned societies, advisory boards, scientific journal editorship, or convening symposia and conferences that bring together researchers from across the UK. It may also include activities that extend beyond academic research, such as providing expert advice as part of the policy-making process, or engaging with the public, media or politicians on scientific topics.

The Crick values these contributions and will give them appropriate visibility. We will encourage participation in activities with both UK and international reach, and those that support the Crick's major funders. These wider contributions are particularly important for our senior group leaders.

Contribute to the development and dissemination of good practice in core technology provision

The Crick makes a broad and sophisticated range of core technologies available to its researchers. Centralising expertise within high-quality technology platforms is an efficient and effective way to support research, particularly in institutions with relatively small research groups, such as the Crick.

We encourage all of our science technology platforms (STPs) to develop external interactions that identify and advance best practice in their fields. The scope and scale of this will vary across platforms – ranging from participating in informal London or UK-wide interest groups, to collaborating on major UK and European infrastructure projects, hosting symposia and developing training opportunities with scientists and technologists from other institutions and industry. The Crick can play a convening role in these initiatives, seeking to learn from others as well as sharing our own experiences.

Our STPs are set up to support research at the Crick and work at close to maximum capacity. They are encouraged to work with partner facilities, where either party has specialist equipment or expertise not shared by the other that can help meet demand. We will create a single STP request portal, which will harmonise access to services for both Crick scientists and those at partner institutions. This portal, in conjunction with an ongoing digital transformation of the administrative underpinnings of the STPs, will drive ongoing improvements in service quality and a reduction in administrative activity.

We envisage our STPs to be major contributors to the Crick's national role by delivering specialist training. The concept of the Crick providing 'training for trainers' has been well received from both academic and commercial laboratories. We see this type of training as the key opportunity for the Crick to deliver a significant national impact on technology provision. We have accelerated development of our experience and capacity in e-learning for training and plan to expand this offering. Delivery of this programme will involve close collaboration with the technology facilities of our university partners.

The STPs will also develop partnerships with instrument suppliers and manufacturers to develop and test state-of-the-art equipment and explore opportunities for larger-scale industrial collaborations to develop new technological capabilities.

Promote diversity in approaches to supporting research in the UK

The UK is rightly known for the strength of its research, particularly its universities which account for the majority of research activity across the country. The Crick represents a different type of organisation – an independent, primarily core-funded institute, large enough to cover a breadth of science. The focus on research and postgraduate training, the emphasis on early career researchers leading relatively small groups (compared to university research groups operating at a similar scientific level), and the lack of divisions and departments are further distinctive features of the model.

Especially critical is the freedom given to group leaders to devise bold and original research activities and approaches, thus shaping the Crick's research direction.

We believe the UK can benefit from a more diverse research ecosystem that accommodates a greater range of approaches to the scientific enterprise. As part of the further evolution of the UK research funding system, there may be opportunities to further expand the Crick model or aspects of the model. The Crick will engage with funders and government to assist with further thinking in this area, as appropriate.

PILLAR 3: DRIVE BENEFITS FOR HUMAN HEALTH

3

The Crick aspires to use insights from discovery research to develop tangible benefits for human health and wellbeing. Success requires a culture that fosters interaction between laboratory scientists, clinicians and those engaged in translational research – a melting pot in which expertise from the academic, clinical and industrial worlds converges.

The Crick aims to accelerate the translation of scientific advances into patient benefits by systematically supporting researchers to access the expertise, capabilities and connections they need to develop their ideas. We emphasise early-stage translational research and accelerating the adoption of technology by industry. We work with a wide range of partners and focus on maximising the exploitation of knowledge for societal benefit and the wider UK economy, rather than short-term financial gain for the Crick.

Our GSK LinkLabs programme sees Crick and GSK scientists swapping working locations to work on collaborative projects.

Attract excellent clinician scientists to the Crick

To drive outstanding research in human disease, the Crick will enable high-quality clinician scientists to combine their experience of working with patients with a thorough grounding in laboratory science. Working with our university partners and the National Institute for Health Research (NIHR), we will build an outstanding cohort of clinician scientists at every stage of the clinical career pathway, by offering pre-doctoral bursaries, clinical PhD schemes and postdoctoral clinical fellowships and by recruiting independent group leaders. These clinicians will benefit from the broad and deep interdisciplinary research environment available at the Crick. By interacting with other researchers they will foster increased medical awareness and engagement across the institute, inspiring new research directions.

The Crick's approach emphasises early career researchers, consistent with the institute's overall philosophy. We recruit clinical group leaders through a range of mechanisms: early career group leader open searches, focused clinician scientist searches, and attachment schemes involving our partner universities. We will expand opportunities for clinicians at the postdoctoral career stage, a point at which many clinicians are lost to the medical research community, through a flexible scheme that allows postdoctoral clinicians to consolidate their research experience and initiate independent lines of investigation. We will grow the scale and diversity of our clinical fellowship programme to embrace a broad range of clinical disciplines. The Crick encourages all research groups to consider hosting clinical trainees, not just those groups whose research has an obvious connection with the practice of medicine.

A distinctive feature of the Crick's clinical training programmes is the access fellows have to an extensive and exciting range of scientific discourse and networking opportunities, complementing their more focused scientific training. We will continue to look for innovative ways to foster interactions between researchers from medical and non-medical backgrounds. The 'Medicine at the Crick' events, open to biomedical and clinician scientists across the UK, will continue to showcase major advances in biomedical science and to consider how they might affect the treatment of patients. These events stimulate new ideas and collaborations by bringing together laboratory-based scientists with clinicians from the Crick and beyond, as well as other groups such as science journalists, entrepreneurs and industrial scientists.

Pursue research opportunities in human biology, human disease biology and human pathogen biology

The growing cohort of clinical and applied researchers at the institute is influencing the development of the Crick's scientific portfolio. These researchers will introduce new research questions that can benefit from existing Crick expertise, or bring new perspectives and technological approaches, informed by their understanding of disease and therapeutic need. This will enable the Crick to better pursue appropriate research opportunities in human biology, human disease and human pathogens, and encourage groups of researchers to coalesce around key medical initiatives with translational potential. We will nurture bidirectional translational science, taking hypotheses from clinical observations or progressing biological hypotheses to clinical studies, capitalising on clinical infrastructures linked to our partner universities.

The Crick will emphasise the importance of using the most appropriate experimental system to explore human-orientated research. Such systems may include humanised models, human tissue and organ samples, and studies in humans. We will develop new facilities, potentially including new science technology platforms, to enable discovery science related to human biology and provide appropriate access to the broader scientific community. This will include the application of stem cell models, organoids, tissue-based approaches and humanised mouse models to the study of human biology in health and disease. We will leverage our clinical links to enable information from these simplified systems to be interfaced with 'real world' human data derived from large-scale cohort studies and clinical trials. We will work with a range of partners including the UK's NIHR, Health Data Research UK and international agencies, as appropriate to the clinical question. We will support emerging clinical opportunities and foci of interest in our science community, as well as developing broad and ambitious clinical translation opportunities focused on emerging research themes that span multiple research groups, for instance in infectious disease, neurodegeneration and oncology.

Expand clinical interactions beyond the Crick

The Crick's response to the COVID-19 pandemic provided a powerful illustration of what experimental scientists and active clinicians can achieve when they work closely together towards a common goal. The development of NHS-accredited SARS-CoV-2 testing and vaccination facilities catalysed a whole set of new interactions with clinical medicine, which are augmenting our mission in unexpected ways.

We will build on the appetite of Crick researchers for experimental medicine and research with a clinical context, and on the increased interest in collaboration from clinical colleagues – including those who previously have had only limited research engagement. By linking Crick scientists with active clinicians, industry partners and the NHS, we will support the discovery, development and implementation of new diagnostics and biomarkers. We will focus our efforts on the definition of molecular targets for prevention and treatment of disease. The CrickMed programme will allow Crick group leaders to spend time in hospital settings, gaining wider experience of clinical practice and the disease relevance of the systems they are studying.

We will explore opportunities to work with our university partners and Biomedical Research Centre (BRC)/Academic Health Science Centre (AHSC) groupings on immediate healthcare problems. Where appropriate, we will seek to embed Crick scientists leading translational projects in the BRCs, to validate and develop concepts in the right clinical environment. We will further develop and support the 'reverse satellite' programme that allows Crick group leaders to establish a satellite laboratory embedded within a university or clinical partner, increasing our capability to enable translational projects.

Create a world-class environment for research translation

The Crick focuses on maximising uptake and exploitation of ideas for societal benefit, without emphasis on early revenue generation for the Crick. We want to create an environment and culture that readily facilitates the translation of scientific discoveries with the potential to improve human health, building partnerships with industry and clinicians to accelerate the development of new technologies and therapies. We will build on our early successes to ensure that translational science and entrepreneurial activity are visible within the institute and scientists can readily find the support they need to move their ideas forward.

We will continue to integrate applied biomedical research into the institute's daily life, retaining the 'open science' ethos that has driven our industry collaborations to date. Exposing our scientists to a wide range of perspectives from industry and clinical practice will spark new ideas for discovery science projects, as well as more translational work, and provide them with hands-on experience of the industrial research and development process. We will embed translational scientists within the Crick and pursue close collaborations with the pharmaceutical and biotechnology industries, as well as the CRUK commercial partnership and LifeArc, translational organisations that have their origins with two of the Crick founders, CRUK and MRC. We will maintain our innovative pre-competitive partnerships with GlaxoSmithKline (GSK), AstraZeneca and MSD, while also seeking to diversify our interactions with the biotechnology and pharmaceutical industries, including both large and small companies. We will leverage the support available through external initiatives such as the Nucleic Acid Therapy Accelerator and London Advanced Therapies.

'HealthQuake' is a regular event series in which industry experts, investors and founders discuss the opportunities and challenges facing data-driven health start-ups.

The Crick will continue to evolve its internal translation support structures so that ideas and discoveries with potential for translation can be readily identified and effectively progressed. We will help our scientists gain access to appropriate support for translational activity, including 'pump-priming' so that projects developed at the Crick can attract further external funding.

To enable discoveries made at the Crick to quickly progress to clinical studies, we will improve access to human biological samples and facilitate experimental medicine studies, drawing on our links with the BRCs and Academic Health Science Networks, as well as national and international biobanks and consortia.

We will improve the visibility of our translation activities and successes, both within the Crick and beyond, and will continue to share and disseminate training opportunities.

We have developed a range of initiatives in entrepreneurship and company start up that include the award of seed funding, as well as high-quality mentoring by leaders in the biotechnology sector, and we will build on these initiatives. For example, working alongside organisations including the Alan Turing Institute, Health Data Research UK and Genomics England, as well as investors, our start-up accelerator KQ Labs aims to establish London's Knowledge Quarter as a leader in digital health-related technology.

We will develop a wide range of additional opportunities for translation training and discussion within the institute, including the creation and growth of spin-out companies. We will improve the level of exposure for staff at all levels, responding to the diversity of needs, and promoting a culture where Crick opinion leaders and alumni can share their experience and inspire others. As our translation portfolio develops and external applications are realised by entering partnerships with new and existing companies and licensing innovations to industry, the culture of translational science at the Crick will be further strengthened.

Deliver impact from our innovation and optimise the infrastructure to progress translation projects

We want Crick researchers to be instrumental in advancing translational science and creating health innovations with practical impact. This means applications based on Crick science being developed for human trials, as well as technologies and methods being developed to address patients' unmet needs and to advance biomedical research. Crick technology transfer will be efficient and agile, focusing on long-term impacts and progression of a strong portfolio of translation projects towards adoption by industry or the market.

Our dedicated in-house translation team provides ready access to advice and is able to nurture translational opportunities. Translational pathways are often complex and the team works with industry scientists and clinicians to provide effective support to the different phases in the development process. The Crick is aided by a translational advisory group that provides extensive experience and contacts across relevant industry sectors. We will continue to draw on this expertise to guide our translation activities and to develop new partnerships that enable early technology development and access to new technologies, working closely with the Crick's science technology platforms and research groups with applied interests.

We will look to consolidate areas of translation expertise to facilitate partnerships and attract funding at a scale appropriate to translate Crick scientific opportunities. We will help bridge the gap to external investment in translational projects by raising appropriate resources for proof-of-concept studies. We will support licensing opportunities and the creation of spin-out companies based on Crick research, building collaborations and partnerships with a range of potential funders, and developing access to local incubator space. Our approach will reflect a long-term partnership perspective with a focus on maximising impact, removing the pressure of upfront payment, early milestones and aggressive IP negotiations, which can hinder innovation.

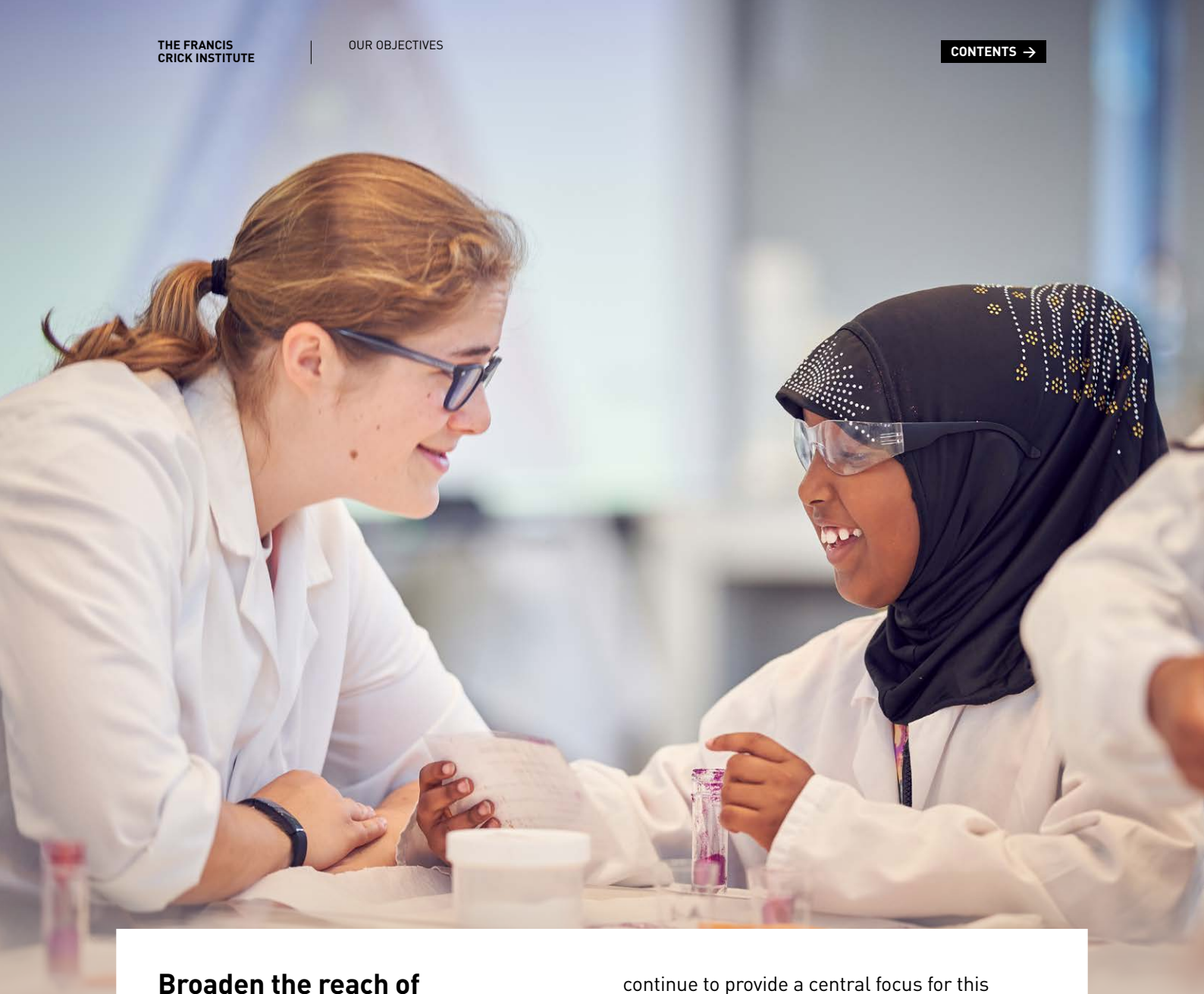
PILLAR 4: ENGAGE AND INSPIRE WITH DISCOVERY SCIENCE

4

The pursuit of scientific knowledge takes place within a wider societal context and research needs to build support from society in order to flourish. High-quality public engagement is needed to strengthen the relevance and accountability of research, improve scientific literacy, enable effective use of scientific knowledge in decision-making and build trust between the public, policymakers and scientists. We will develop our public engagement programme around our particular strengths as a research institute with access to a large number of active scientists working across the full spectrum of biomedicine.

The Crick complements the role of other organisations that have a primary mission of public engagement with science, which operate at a different scale and level of resource, but are not as close to research activity. Our activities will have local, national and international dimensions, and we will use a multi-pronged approach to engage with our target audiences.

Public engagement is highly valued by our staff and we will continue to grow the level of engagement in such activities across the Crick. We will work with our researchers to promote high-quality communication between scientists, as well as meaningful exchange of knowledge between scientists and society.



Broaden the reach of our education programmes, inspiring young people to engage with science

We have developed a local education outreach programme that offers the opportunity for the Crick to engage every school pupil in the local London Borough of Camden, every year of their school lives. With this programme the Crick interacts with more than 20,000 pupils each year. We will maintain and build on our relationships with local schools, improving our offer to inspire young people to engage with science and science careers. The Weston Discovery Laboratory located in the Crick will continue to provide a central focus for this programme, offering laboratory experience to 7–11-year olds from primary schools, who often lack access to such facilities. We will develop our careers-related learning activities and provide more opportunities for local young people and their families to access and engage with science outside the school setting.

To complement our local education outreach, we will develop interactive online resources that enable more families, adults and young people to engage with Crick science and scientists, working more broadly across the UK and internationally. We will further develop education resources linked to the institute's research and exhibitions.

Diversify our public engagement activities and embed a culture of engagement

The Crick opens up its research to the public through a programme of regular events and annual exhibitions, which currently reaches more than 25,000 visitors each year. We will support our staff to deliver activities that facilitate dialogue with public audiences, innovating and exploring new formats that inform and build public trust in biomedical science, and empower more people to engage with developments in science and technology. Careful evaluation will be used to assess, modify and evolve our programmes so we can maximise their impact. We will share our learning and approaches, seeking opportunities for synergies and the development of new approaches with our partners. We will bring diverse voices and new perspectives into our public programmes by collaborating with a range of audiences, such as patients, young people and community groups.

The Crick will work to further embed a culture of public engagement across the institute, increasing the number of staff that participate and providing high-quality training and support. We will seek to increase the visibility of public engagement activity and to communicate its benefits and successes.

Strengthen our position as an active and trusted member of the local community

The Crick will demonstrate how effective local community engagement can contribute to a better environment for both local people and Crick staff. The Crick-backed St Pancras and Somers Town Living Centre, attached to the institute, has been set up to support the local community, helping local people to deliver projects that tackle their own health, wellbeing, economic and social issues. Alongside this, we have established a programme for local employment and have built effective working relationships with local organisations, opening the door to more informal science outreach.

We will continue to build trust and raise awareness so that local people are aware of the opportunities and support available through the Living Centre and feel welcome at the Crick. We will develop new initiatives jointly with the community, experimenting with deliberative democratic approaches to explore ethical and other social issues that arise as a consequence of scientific research. Such approaches can promote an inclusive, two-way public dialogue about scientific issues, with potential for the outputs to inform the development of policy.

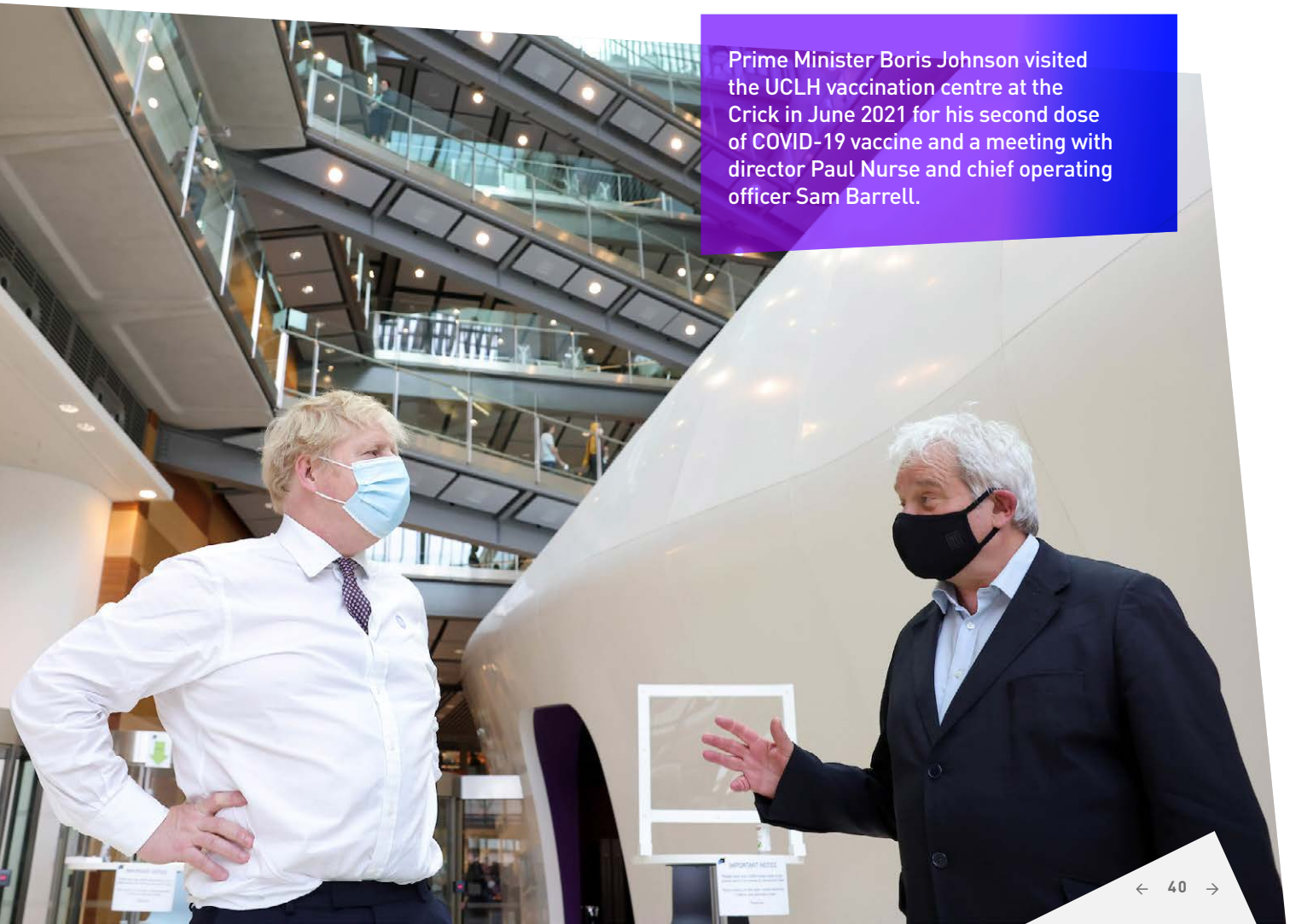
“Effective community engagement is a long-term process, built on trust and good relationships.”

HANNAH CAMM, COMMUNITY ENGAGEMENT MANAGER

Make an effective contribution to public discourse and the development of relevant policy

Regular and effective engagement between scientists and policymakers is needed to promote high-quality decision-making on issues pertaining to science. The Crick's approach to policy engagement will focus on issues where we have expertise and the opportunity to have an impact on public discourse and policy development. When it is appropriate, Crick scientists will comment on how proper understanding of relevant science is necessary to inform the development of public policy, and on policy initiatives needed to improve the quality of the science base. We will develop evidence-based policy messaging and Crick case studies to support policy engagement work on areas such as public investment in science and topical research issues. We will work with policy experts within our founder and partner organisations to broaden our joint engagement with government and related sectors. Our increasing public profile, as well as our proximity to Westminster, will help us build on our relationships with politicians, decision-makers and other stakeholders. We will also continue to encourage our scientists, who hold many different nationalities, to participate in public, policy and media engagement activities outside the UK.

We will expand the voices speaking on behalf of the Crick – and by extension the wider scientific community – ensuring that different experiences and routes into science are captured and shared. We will welcome members of the government, parliamentarians and other key policymakers and influencers to the Crick so they can see for themselves the nature and value of our work. The central location of the Crick makes it an ideal venue for overseas VIP visits organised by the Foreign and Commonwealth Office, and we will continue to facilitate such events, supporting the UK's global reputation for science and research.



Prime Minister Boris Johnson visited the UCLH vaccination centre at the Crick in June 2021 for his second dose of COVID-19 vaccine and a meeting with director Paul Nurse and chief operating officer Sam Barrell.

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Demonstrate excellence in the communication of science to scientific and non-scientific audiences

The Crick aims to set a high standard for the communication of science. We will draw on the wide range of scientific expertise found in our faculty to ensure accurate, dependable and engaging communications that support two-way dialogue with public audiences. We will be thoughtful about when and how we engage in public communication about science, speaking out when we have relevant opinions and information to contribute.

The Crick will strive to increase the reach and scope of our communication activities, attracting a wider UK and international audience, and building our profile and reputation for accurate and balanced commentary. This will require additional emphasis on digital communication channels, growing our audiences and their levels of engagement. We will develop a comprehensive programme of media relations work, increasing the volume and frequency of coverage, and will further develop our programme to establish a wider UK and international audience. An additional focus will be to work with our researchers to develop their capability to communicate with public audiences, so that we widen the range of Crick voices and reflect the diverse nature of the organisation.

As part of the Crick's programme of scientific discourse, we will work with our scientists to develop best practice in communication about research and science. We will promote high-quality communication between scientists and increase our scientists' exposure to the wider world beyond research. Our approach will focus on the need to make research accessible to a wider scientific audience, which is particularly important in the multidisciplinary research environment at the Crick. We will ask speakers at all levels to emphasise ideas and understanding, and avoid overwhelming their audience with indigestible data. We will actively expose our scientists to wider perspectives – for example through our regular programme of lectures given by leaders in fields outside laboratory science.

PILLAR 5: BUILD CAPABILITY FOR OUTSTANDING SCIENCE SUPPORT

5

World-class research needs an excellent supporting infrastructure to enable its success. The Crick's founders recognised this when they joined forces to create a new state-of-the-art research institute, and we will continue to work closely with them to realise the shared vision.

Our research performance crucially relies on the quality and range of our science technology platforms (STPs), which provide the research groups with access to cutting-edge technology, support and expertise. It also relies on a positive and supportive culture across the research labs and the in-house operations teams, which provide exceptional services to support the science and keep the Crick's highly sophisticated building and infrastructure running smoothly.

Develop a vibrant and inclusive organisational culture that prioritises staff wellbeing

A leading research institute can only operate effectively when high-quality science is underpinned by a great working culture. The delivery of our mission relies on respectful working relationships between all our staff. We will continue to build an environment where everyone feels welcome, individually valued and able to contribute to the best of their ability. We will promote respect, inclusivity and equal treatment, and reflect these principles in all strategies, policies and practices across the institute.

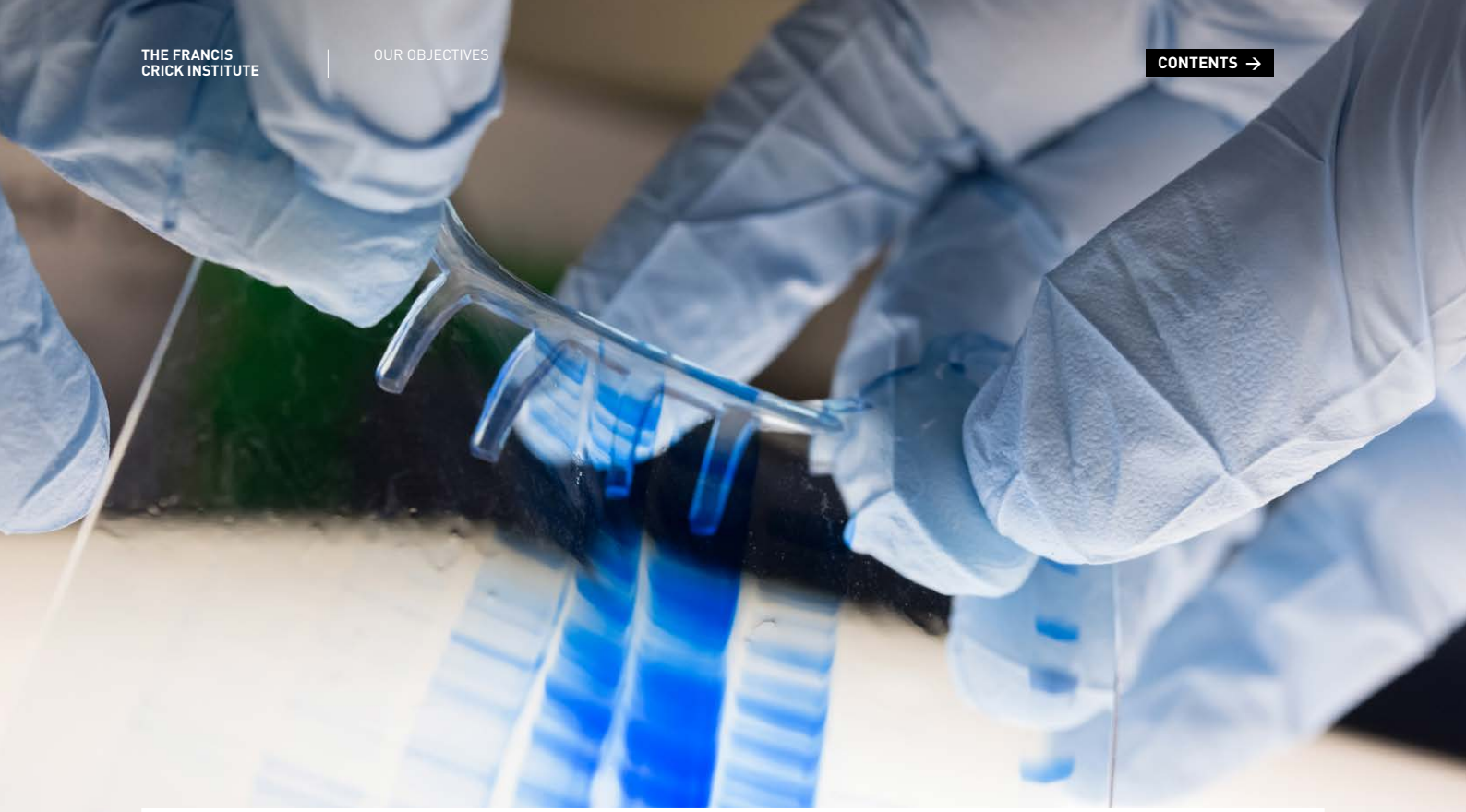
We will work together to ensure the safety, health and wellbeing of ourselves and our colleagues, including mental wellbeing. There are pressures associated with working in a high-performing research environment, and individuals need support to respond to these pressures. We will provide high-quality training in respectful communication and management and develop appropriate channels for staff to seek support and raise concerns. We will support broader initiatives to improve the academic research culture, working with our funders and partner organisations and learning from examples of good practice elsewhere.

Prioritise safety, integrity and openness in the conduct of our research

The innovative and cutting-edge science conducted at the Crick operates within a well-regulated environment. We expect our staff to respect and work within this regulatory framework. We will work carefully to ensure we achieve the right balance that allows science to prosper while meeting our regulatory duties and obligations.

We expect our staff to support the Crick's commitment to open science and conducting research with integrity, using the best laboratory and clinical practices and observing the highest ethical and professional standards. The Crick will build on the successful track record of our parent institutes and partners, maintaining standards and continuing to embed research integrity as a collective cultural responsibility. We will provide support and training and encourage staff at all levels to openly discuss and raise issues. We will capitalise on the Crick's interactive culture, in which experimental approaches and findings are regularly exposed to peer scrutiny within the institute and elsewhere, ensuring high-quality, reproducible experimental data.

We will integrate sustainability and good environmental practice into decision-making, supporting the Crick's progress towards net zero carbon. We will ensure that staff and service partners understand our sustainability principles and are empowered to deliver them. We will continually look for opportunities to reduce the environmental impact of our operations, promote responsible investment and investigate further renewables opportunities.



Further enhance STP provision to deliver an appropriate range of high-quality, cost-effective technologies

The Crick's science technology platforms (STPs) support our science by providing shared access to cutting-edge technologies. These STPs operate as a major conduit to bring capital equipment into the institute, and also provide high-quality training to staff and students. They are a key element in the Crick's approach to scientific discovery because they enable state-of-the-art equipment and technical knowledge to be effectively consolidated and shared across research groups. This avoids the need to duplicate resources within individual laboratories, which are relatively small in size. It is also a cost-effective way of providing and managing the complex technical facilities required for modern biomedical research.

In the Crick's parent institutes, STP services were delivered free at the point of use. The Crick will optimise the substantial resources located within the STPs by developing increased cost awareness amongst the user community, recharging processes for significant users, and emphasising external grant funding.

These mechanisms will be used to manage issues of excessive demand. We will explore the opportunities and benefits of outsourcing services where appropriate – a recent successful example being mouse genotyping. Each STP will regularly carry out a cost/benefit analysis of all its services to determine which would be better outsourced. For bulk service provision we will look at university partner provision as well as commercial offerings.

We will encourage STPs to work towards implementing recognised management systems to ensure continued high-quality science support. STPs will be encouraged to focus more on exploiting cutting-edge technology and developing novel protocols and methods. We will work with our funders to drive forward capital investment in the latest equipment, and with companies to develop the Crick as a beta testing site for new technologies.

We will keep our STPs under regular review to ensure they work well, are cost-effective, responsive to the needs of new research groups joining the institute and can capitalise on new advances in technology. As research needs change, specific STPs may be scaled down or closed and new STPs opened.

Develop adaptable and responsive on-site operational teams, well integrated with each other and with Crick science

Crick Operations ensures the smooth running of the institute on a day-to-day basis and its component teams seek to epitomise best practice in supporting scientific research.

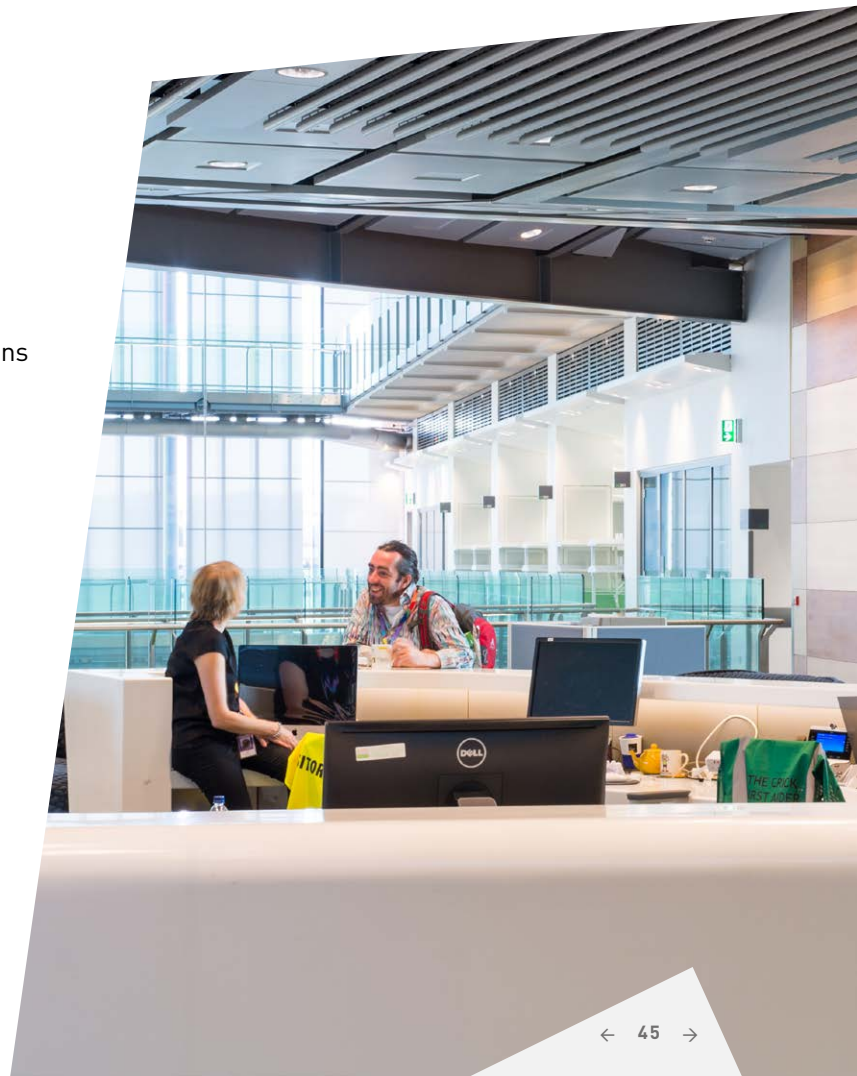
The operational teams take a proactive approach, developing full understanding of the needs of Crick science and responding quickly to emerging issues and needs. Staff with a variety of roles are physically co-located in 'hubs', which provide an initial point of contact for the research groups and encourage staff from different teams to work together to solve problems. In the coming years we will build on this approach, implementing new tools and quality-based systems to increase efficiency and enable connected ways of working across operational functions. We will continue to promote a culture of open, supportive and respectful communication across science and operations, through initiatives such as laboratory tours and scientific talks for operations staff.

We will drive continuous improvement in all our operations by engaging our staff in regular reviews of performance indicators, targets, action plans, and implementation of improvement projects that deliver a world-leading workplace environment for scientific research, and ensure Crick operations offers value-for-money services. To deliver these improvements we will gather good quality data from consistent and well-defined monitoring processes which will provide new insights within and across operational areas.

Develop a robust and reliable resource to measure Crick activities and outputs

The Crick will implement a research and management data platform for the capture, measurement and analysis of a broad range of different data covering the Crick's activities, both scientific and organisational. This reflects the volume and complexity of data needed to accurately describe what the Crick does, and will allow accurate, consistent and timely reporting.

The platform will acquire data from internal Crick systems, such as the research outputs database, HR and finance systems, together with external sources such as Scopus and PubMed. All data feeds are refreshed periodically to ensure that data are available in near real time, truly reflecting the current state of the Crick. The system will allow the Crick to track its performance over time, and to compare its performance with other organisations.



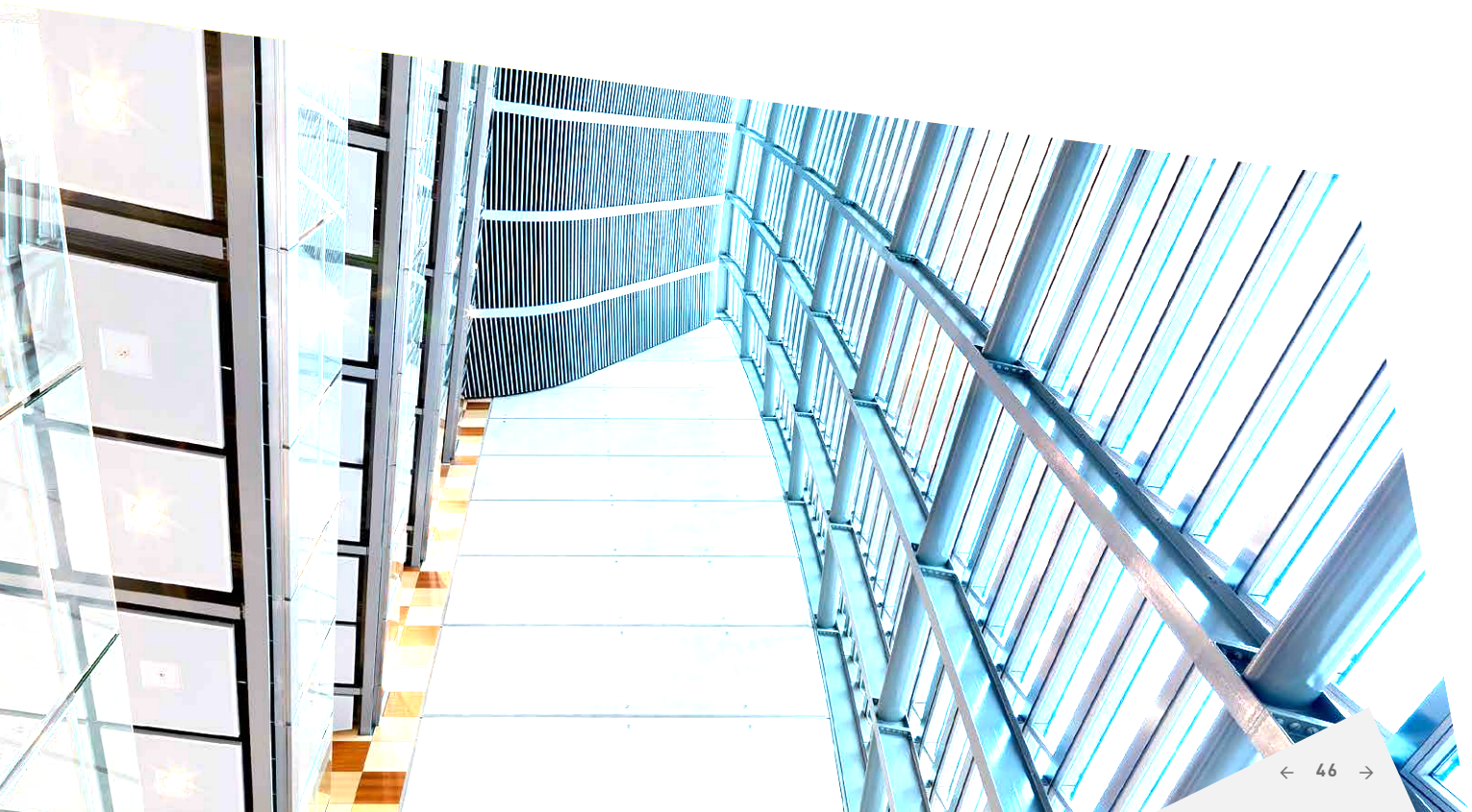
Work with our partners to achieve long-term financial sustainability

The Crick was established by six founders who shared a vision to build a world-class biomedical research institute in central London, supporting the wider research endeavour across the UK. Realising this ambitious vision has required significant investment, which will need to be sustained in the future to ensure the capital expenditure is put to best use, and that the institute is genuinely world-leading. The use of resources will be regularly evaluated to maintain a cost-effective as well as efficient operation. Charting a sustainable operational and financial path for the institute will be a key priority over the period covered by this strategy.

The Crick is fortunate to receive core funding from the MRC, Cancer Research UK and Wellcome. This core funding is critical to our strategy. It enables our focus on early career investigators, giving them the resources they need to 'hit the ground running', and supports our more established groups to pursue ambitious long-term research questions. We will continue to work with our partners to ensure that core funding underpins our research activity and is applied in a way that supports their priorities.

At the same time, there are opportunities for the Crick to diversify its income streams. We have grown our income from response mode grants, and as opportunities arise we will pursue larger, more thematic grants. We will further develop philanthropy, capitalising on the increasing profile of the Crick. A long-term objective will be to build a significant endowment, increasing the resilience of the institute. There will be additional opportunities for commercial income, particularly beyond 2026 when the Crick will be free of value added tax (VAT) constraints applied to new charitable buildings.

In addition to growing our income, the Crick will optimise operations and ensure that resources are used efficiently and effectively. We will further embed our new approach to allocating resources to laboratory groups. The model introduces a balanced core resource allocation between groups, sets limits on Crick core support for laboratory personnel and running costs, and requires that grant applications include realistic costings. As we move to a more mixed economy of core and response mode funding, this approach will facilitate our strategic emphasis on recruitment of exceptional early career group leaders, rewarding excellent performance and ensuring that shared resources are used efficiently and fairly.



Evolve the governance model, supporting our status as an independent organisation with strong founder links

The Crick is an independent institute, with the freedom to set and follow its own goals, reflecting the overall strategic objectives of the Crick founders. Our Board has a key oversight role, guiding the strategic direction for the organisation and maintaining an effective relationship between the Crick and its six founders.

In the coming years, the Crick will further strengthen its governance. The Board, working with the Executive Team, will ensure that vacancies on the Board and the Executive are filled by high-calibre people with the skills we need to guide the implementation of the Crick strategy. Both the Board and Executive, will benefit from regular strategic and operational advice provided by the Scientific Advisory Board, which is made up of outstanding scientists from around the world, many with long experience of running complex scientific institutions.

We will continue efforts to streamline our committees and standing bodies and promote innovative ways of working. We will maintain close and mutually supportive relationships with our six founder organisations, avoiding unnecessary duplication of reviewing and reporting, and ensuring open, productive and efficient ways of working.

THE CRICK SCIENCE PROGRAMME

THE CRICK SCIENCE PROGRAMME

The Crick's mission is **world-class discovery research to understand how living things work and to drive benefits for human health**. Biological knowledge lies at the heart of biomedicine, driving major improvements in the prevention, diagnosis and treatment of human disease.

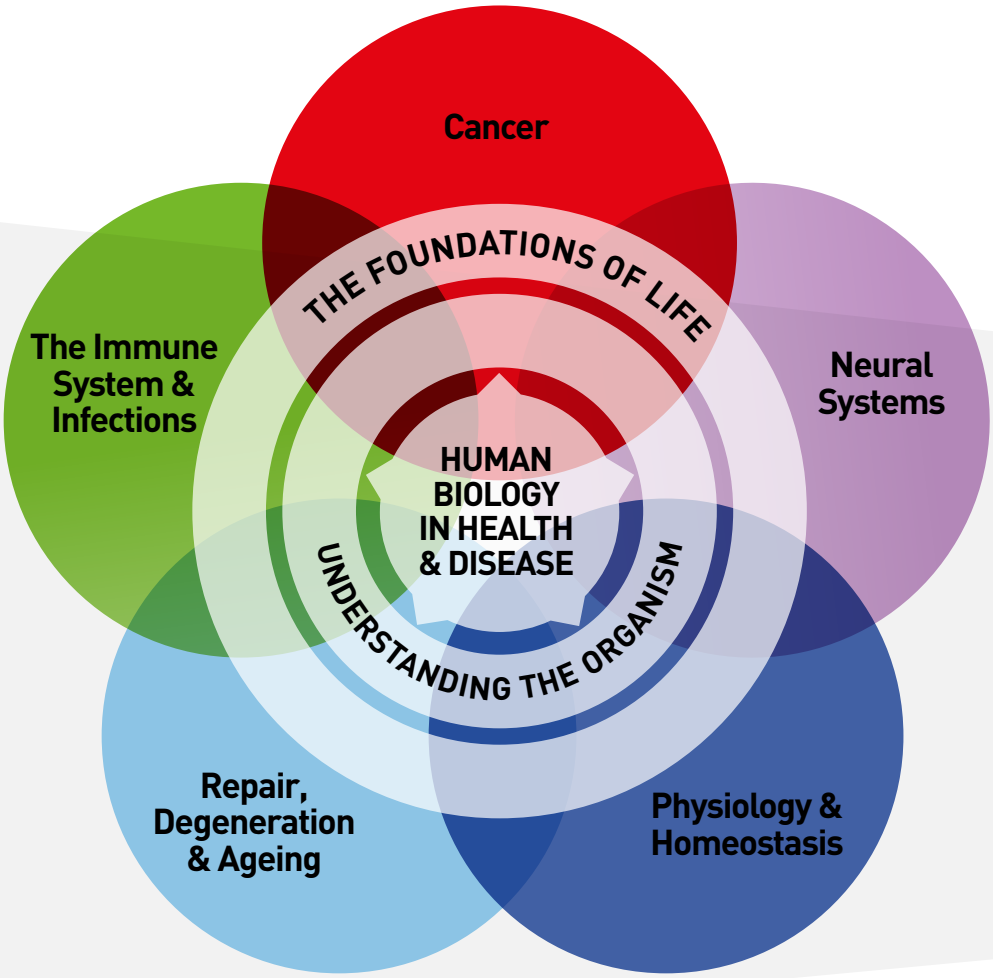
Over the years, discovery research has led to better understanding of many diseases, as well as the recognition that knowledge about one disease can inform others, sometimes in unanticipated ways. The scientific approaches needed for further advances in understanding have become more multidisciplinary, incorporating biological disciplines previously considered to be remote from biomedicine, such as evolutionary biology and ecology, as well as relevant aspects of the physical, engineering and information sciences.

Reflecting its strategic imperative to bring researchers of different stripes together under one roof, the Crick's science programme is broad and inclusive, with the flexibility to support promising and emerging fields of enquiry. Our group leaders have the freedom to devise and undertake their own specific research programmes, which are set within broad and overlapping scientific areas defined by the Crick. These areas are:

- Two overarching themes that aim to understand how living things work, spanning the scale from genes to organisms: **The Foundations of Life** and **Understanding the Organism.**
- Five more thematic areas that cover aspects of health and disease: **Cancer**; **The Immune System and Infections**; **Neural Systems**; **Repair**, **Degeneration and Ageing**; and **Physiology and Homeostasis**. The first three areas are well established, the latter two are being developed.
- **Human Biology in Health and Disease**: integration of work in the above areas with direct studies on human systems, to understand the specific ways that the human organism functions and malfunctions.

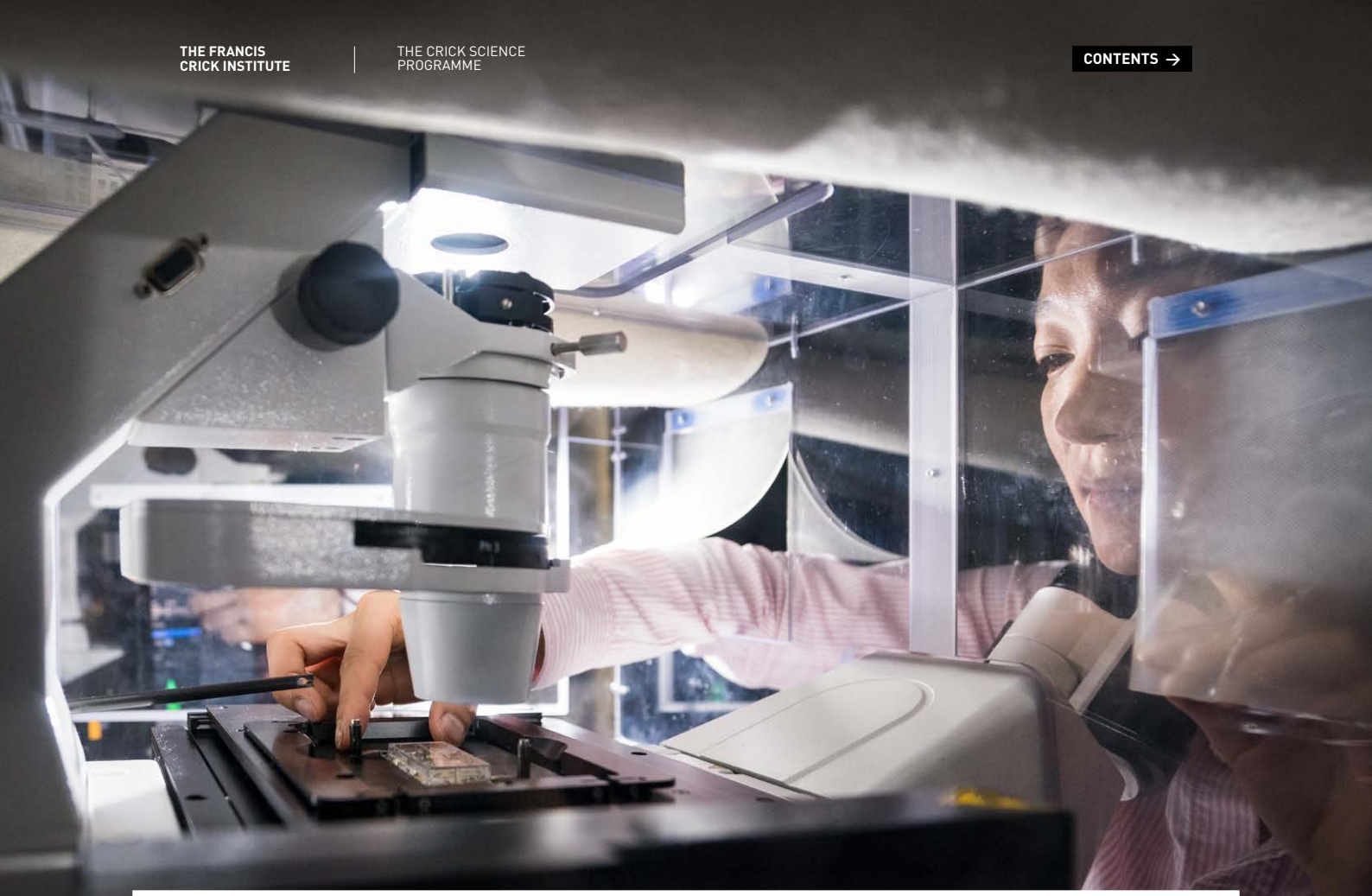
Individual Crick research groups might work within a single area or have interests in several. The broad scope of the areas allows new research directions to be readily embraced. Combined with our emphasis on continuous early career recruitment, this breadth enables the Crick to be agile, evolving our research portfolio in response to new research opportunities and funder priorities.

CRICK SCIENCE PROGRAMME



A special aspect of the Crick is the way our research laboratories are grouped and interact in the open-plan environment, alongside comprehensive STP support. This allows smaller groups to work effectively, lowering critical mass for innovative research. Research questions, approaches and methodologies developed in one area are frequently relevant to another. To promote such cross-fertilisation and synergy, rather than physically group its researchers into distinct departments, the Crick uses a 'salt and pepper' strategy that mixes researchers from different fields together. Complementing this, research interest groups, open to all, support an active programme of scientific seminars, 'chalk talks' and symposia, maximising interaction between scientists from different areas.

In the few years since the institute's establishment, our approach has led to the evolution of new clusters of research groups with distinct but complementary aims and



approaches, which have built on the expertise of existing faculty inherited from the Crick's parent institutes NIMR and LRI to shape our future research programme. An example is in the physical sciences. At its establishment the Crick had limited strengths in physics and chemistry. New recruitment (Crick early career faculty as well as targeted joint recruitments with the universities) and university secondments have strengthened this in several domains, including synthetic chemistry and single-molecule biophysics. In addition, several new or seconded groups are closely linked to STPs and are bringing new technologies which are benefiting other groups in the institute, from time-resolved cryo-electron microscopy through to advanced imaging technologies and expertise in tissue dynamics.

Collaborative interactions with the Crick's three partner universities will be of particular importance in developing our multidisciplinary science programme. These interactions range from the informal through to more formal mechanisms such as joint appointments and the university attachment programme. The universities and their associated clinical research infrastructure will be critical for clinical research and human biology, given their significant strengths in areas such as human physiology, pharmacology, human imaging and human genetics. The universities also have a depth of expertise in the physical and engineering sciences which is relevant across the thematic areas and is further complemented by the Crick's relationships with industry partners. An example is chemistry, where the Crick is already benefiting from expertise drawn from partners, leading to new interests in chemical biology as well as the development of chemical tools and techniques to study human biology.

The eight scientific areas, and the types of research questions that Crick scientists could explore within them, are described in the following section.

The Foundations of Life

— molecules, cells and information

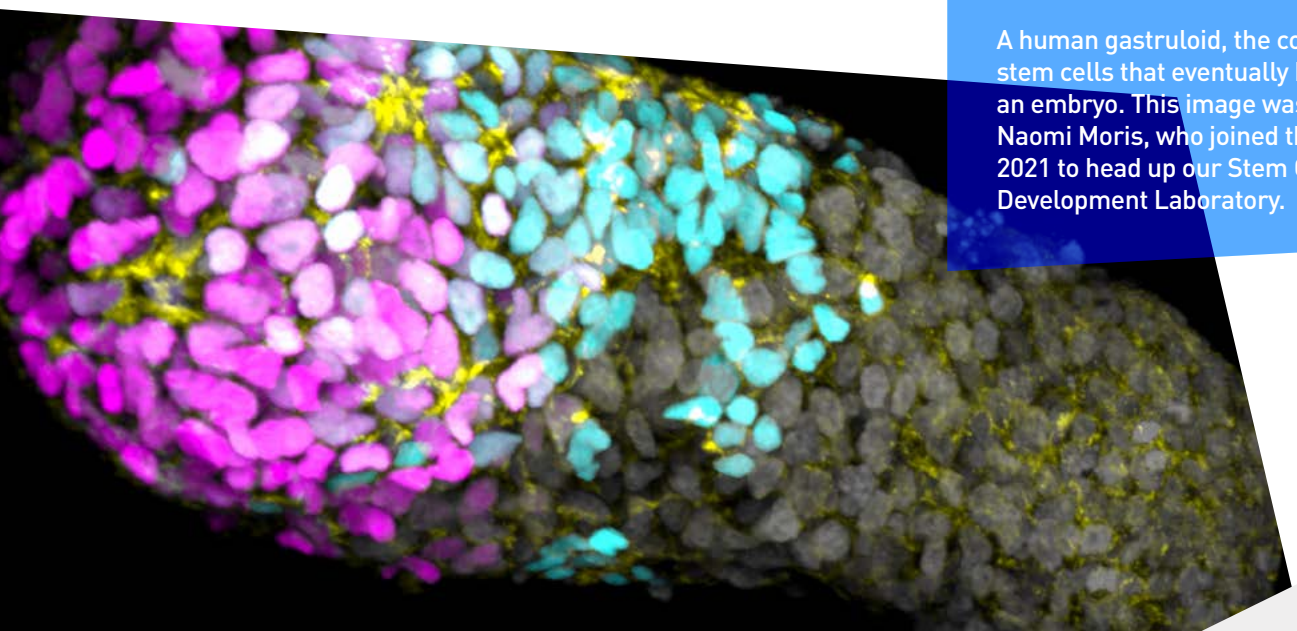
The cell is the simplest entity that can be unambiguously considered to be alive; its existence supported by a complex interacting system of molecules and molecular machines. A cell's behaviour is determined by the organisation and interaction of its constituent molecules. Macromolecular polymers such as proteins, nucleic acids, lipids and carbohydrates contribute to cellular structures, while cellular metabolism ensures that the levels of different molecules are appropriate to the cell's functional state.

The Crick will seek to understand the ways in which molecules and the assemblies and machines they generate are produced, operated, regulated and disassembled, and how these processes specify cell structures, organisation and behaviours. By understanding the basic cellular processes that form the foundations of life, we can help establish how their mis-regulation leads to disease. Often the relevant activities and interactions will be explained in terms of chemistry, but sometimes they will be more readily understood through physics.

The study of molecular components, their mechanisms of action, their organisation and interactions will promote understanding of higher-level biological processes and phenomena. These include answers to questions such as:

- How do cells generate and maintain their organisation?
- How do cells grow, reproduce and ensure homeostasis?
- How do cells age and die?
- How are diverse types of cells with similar genomes produced?
- How does cell behaviour change in response to signals and to genetic alterations in regulators?

Biology is fundamentally an information science. Moving beyond description to proper biological understanding will often require a systems approach, with a focus on how the chemical and molecular processes in question are driving the acquisition, management and use of information. Our ability to rapidly sequence genomes at high throughput is complemented by global analysis of proteins and small molecules with increasing temporal and spatial resolution. Research at the Crick will incorporate informational systems analysis, including feedback controls, patterns and dynamics. This will enable us to understand the behaviour of cell populations in response to natural and imposed selective pressures, ensure that molecular mechanisms make biological sense, and develop quantitative and predictive models of cell regulatory phenomena.



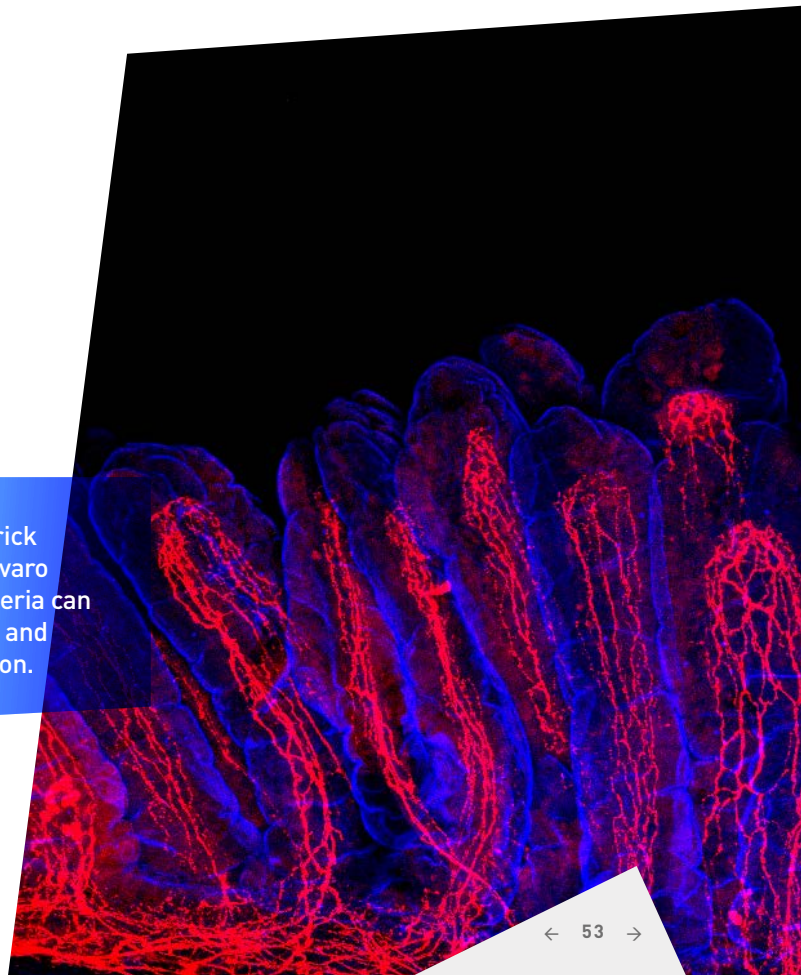
A human gastruloid, the collection of stem cells that eventually becomes an embryo. This image was taken by Naomi Moris, who joined the Crick in 2021 to head up our Stem Cell & Human Development Laboratory.

Understanding the Organism

— living things as self-regulating cell assemblies

A living organism is an interacting society of cells that self-organises during development to produce an elaborate form that continuously repairs itself, or is even able to regenerate. In the context of the organism, cell behaviour serves to promote the reproductive fitness of the organism as a whole, and constrains the physiological and behavioural mechanisms operating at the tissue, organ and whole-body level. These mechanisms, which include the nervous, endocrine and immune systems, ensure appropriate development, enable organismal homeostasis and govern the response to environmental or infectious challenge. Cells act in the context of the whole organism to generate mechanisms defining and controlling cell differentiation, regulating cell–cell and cell–substrate interactions, responding to signals and differentiating self from non-self. A multitude of specialist mechanisms exist at the organismal level to sense and respond to the environment, all underpinned by specific cell- and tissue-level structures and functions.

The Crick will identify and characterise the supracellular processes that underpin organismal behaviours, making use of advances in molecular genetics, cell biology, tissue and organoid cultures, animal models, human tissue samples and imaging technologies. These methodologies will be used to investigate organismal development and homeostasis and understand how pathologies arise due to environmental insult or genetic changes. These phenomena can be understood at least partially in terms of the chemistry and physics of molecular interactions, but sometimes mechanistic explanations at higher levels of organisation are also required. Examples include wiring networks in nervous systems, cell interactions in the immune system, mechanical stress in the vascular system, ecological models for microbiome dynamics and tissue niches, and evolutionary analyses in the context of genetic changes during the development and response to therapy of pathologies such as cancer. The Crick will therefore use a breadth of approaches to study these problems, including systems analyses from the perspective of how information is managed.



Gut villi with neuronal fibres. Crick researchers Yuuki Obata and Álvaro Castaño found that our gut bacteria can activate the healthy contraction and relaxation of muscles in our colon.

Cancer

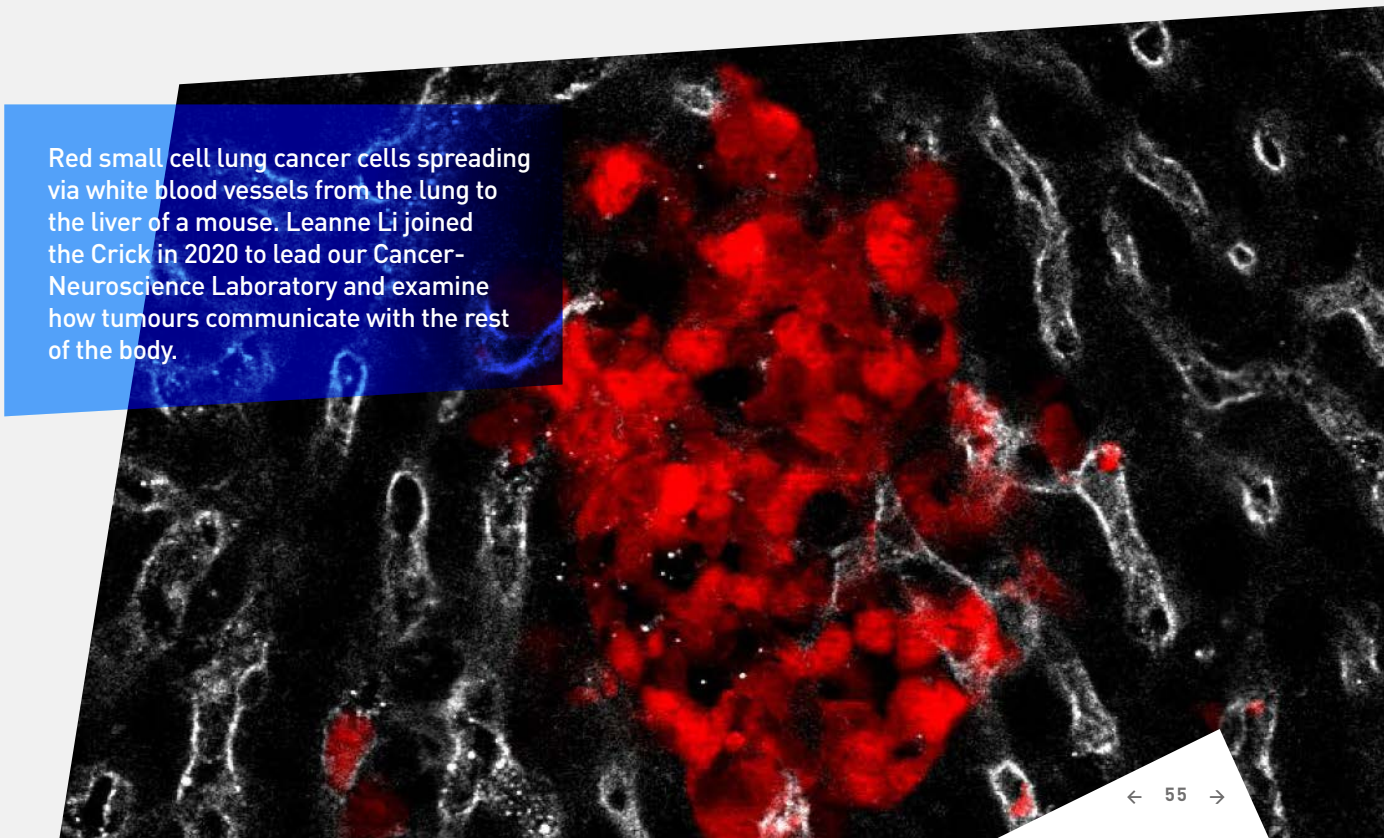
Cancers are not isolated units but interact with and impinge on all our body's processes. For this reason, cancer cross-cuts much of the research going on at the Crick and interfaces with many of the other research themes.

To fully appreciate how cancers develop and progress, we need to be aware of the processes responsible for normal cell and organism growth and development, as well as tissue regeneration. The dysregulation of these normal processes underpins almost every aspect of cancer. There is an increasing awareness that multidisciplinary approaches are required to understand and to develop new treatments for cancer, and this maps well onto the way that research is organised and pursued at the institute. Strong cross-disciplinary links have already been established and new recruitment has expanded the institute's expertise in tumour suppression, cancer evolution, cancer metabolism, and the interface between development and paediatric cancers. The Crick's collaborative and convening ethos means that the institute is also increasingly assuming a central role in London- and UK-wide cancer research initiatives, such as the CRUK City of London Cancer Centre and the RadNet radiation research hub.

The past decades have seen an explosion in our understanding of how genetic changes can drive cancer development. These studies have revealed the diverse ways in which the mutational landscape results in cancers evolving to become more malignant and resistant to therapy. The Crick is now in a position to build on this knowledge and integrate it with our growing understanding of the reciprocal interactions between the tumour and the body. Cancer therapies that harness our immune system have become effective realities for some patients, and future collaborations between immunologists and cancer researchers will identify new ways to prevent cancers concealing themselves against immune attack. The Crick can combine strengths in cancer genomics with single-cell biology, advanced imaging technology and organoid-based and genetically-engineered mouse cancer models. This will enable a detailed understanding of the molecular and cellular interactions occurring both during tumour development and the body's response, with major implications for understanding the transition to malignancy, immunotherapy and drug resistance mechanisms. The Crick's increasing focus on physiology, homeostasis and ageing will help to reveal how changes during an individual's lifetime influence cancer incidence and trajectories, beyond the simple accumulation of mutations. Understanding the metabolic demands of cancers will explain aspects of cancer behaviour, ranging from why obesity promotes cancer development through to the catastrophic muscle loss that characterises the final stages of life for many cancer patients. Moreover, this knowledge will present opportunities for dietary and other interventions to reduce cancer incidence and improve treatments.

The way in which the Crick has been set up and operates puts it in a powerful position to tackle major problems of cancer that were more difficult to pursue at its predecessor, the CRUK London Research Institute. The Crick is interdisciplinary and has strong links with both clinical and industrial translation, making the institute well placed to mobilise its extensive laboratory expertise and biomedical knowledge to rapidly advance new approaches to pathology, diagnostics and therapeutics. Technological advances are allowing major progress on a range of fronts, including the development of simple blood tests to detect and monitor cancers and the exploration of novel image analysis methods for cancer prognosis. Computational modelling and machine learning will transform our ability to diagnose cancers and model how cancers arise, how they will respond to therapy, and which treatments will be most effective for each cancer patient. The experience that the Crick has had in improving diagnostics during the COVID-19 pandemic will be useful in developing these approaches. The Crick's clinical fellow programme and new clinical postdoctoral fellowship initiative, supported by core funding, are benefiting both discovery research and strengthening the Crick's ability to study human biology, with increasing opportunities to shape and analyse clinical trials.

Cancer at the Crick will continue to develop over the coming years, building on existing strengths in cell signalling, tumour biology, immunology, cancer genomics and genome stability. Exciting opportunities exist to leverage the institute's strength in diverse areas ranging from pathogen and hominid evolution to neuroscience and the role of innervation in tissue physiology. This will be supported by interdisciplinary recruitment and emergent grassroots initiatives, such as the 'Evolution Forum' run by PhD students, which brings together researchers in population genetics, ecology and cancer. Together, these factors will ensure the Crick is well placed to drive discoveries at the cutting edge of cancer research and can readily facilitate their translation into patient benefit.



Red small cell lung cancer cells spreading via white blood vessels from the lung to the liver of a mouse. Leanne Li joined the Crick in 2020 to lead our Cancer-Neuroscience Laboratory and examine how tumours communicate with the rest of the body.

The Immune System and Infections

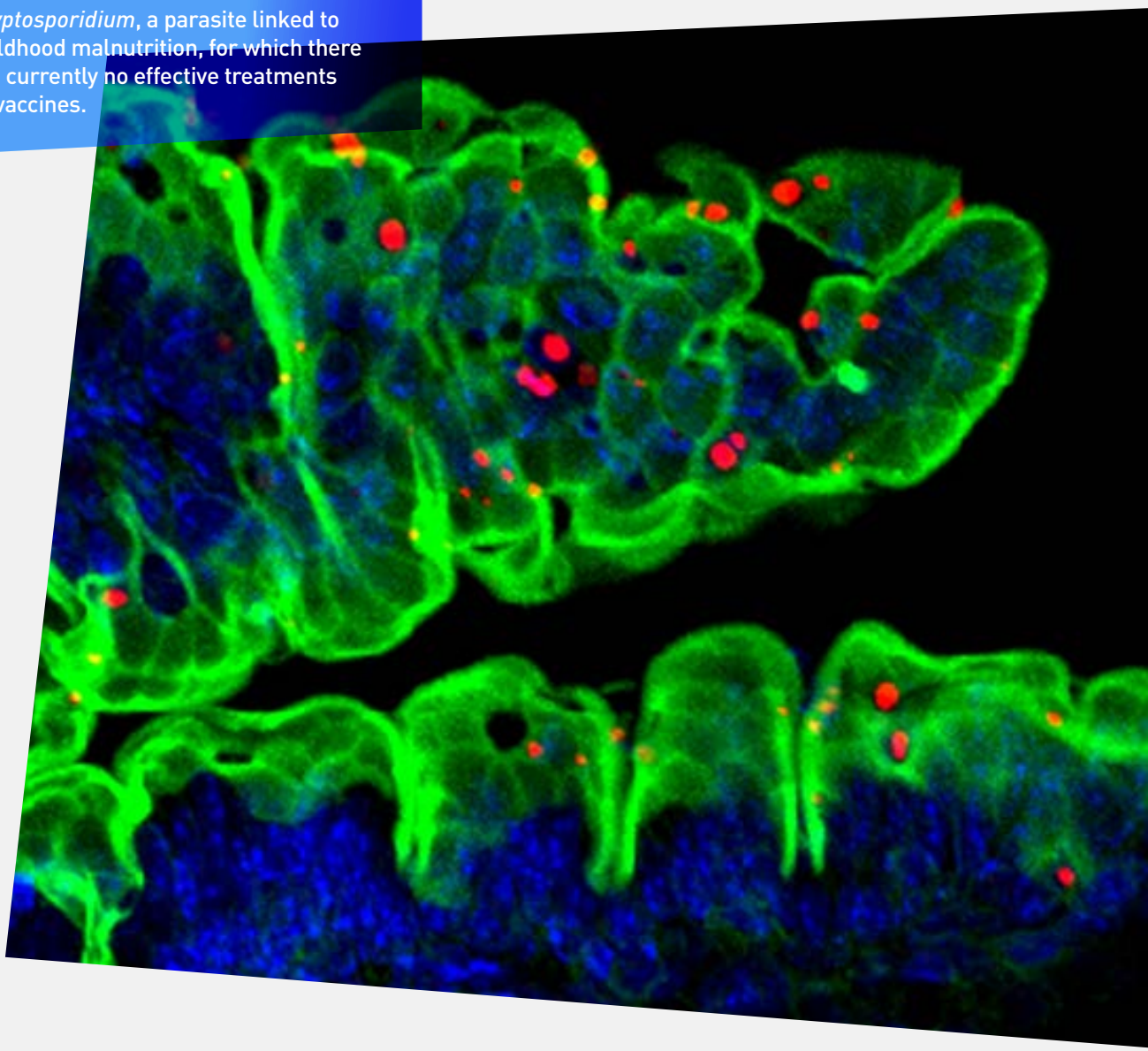
Viruses, bacteria and parasites infecting humans represent some of the most important causes of morbidity and mortality worldwide. As human societies become more interconnected and encroach into biodiverse areas of the natural environment, the earth's climate and ecology changes, and antibiotic resistance spreads, the opportunities for pathogenic microorganisms to infect humans can be expected to increase.

Crick research will enhance understanding of the fundamental biology of viruses, bacteria and parasites, which is essential to explain their ability to cause disease, evade the immune system and resist antimicrobial agents. The ongoing COVID-19 pandemic illustrates how much we still have to learn with regard to pathogen biology. By dissecting how these organisms operate, we will better understand their ability to persist in human or animal populations, how they are spread from animal reservoirs to humans (a feature of many emerging pathogens), and how they can be controlled by vaccines or antimicrobial agents. This work will lead to the development of novel diagnostics, vaccines and drugs. At its establishment Crick had strengths in influenza, malaria and tuberculosis, which has been enhanced and extended to additional pathogens including *cryptosporidium, toxoplasma* and *coronavirus*.

The cross-cutting impact of the immune system makes it an important area of interest for the Crick. Malfunctions of the immune system underlie not only susceptibility to infections, but also a wide range of autoimmune and inflammatory disorders that influence physiological functions throughout the body. For example, chronic inflammation is a major component of diseases that are linked to ageing and aspects of our lifestyles, such as atherosclerosis, metabolic disorders, neurodegeneration and cancer.

The immune, nervous and endocrine systems share mechanisms of gene regulation and cell communication and influence one another. The brain has hard-wired connections to lymphoid tissues and they also communicate through cytokines, neurotransmitters and endocrine hormones. The concept of 'memory', although mechanistically different, applies to both the immune and nervous system and immune status likely has a direct effect on learning and recall processes in the brain. Immune and nervous system interactions underlie normal brain function and are critical in injury repair and infection. Overarching studies can unravel the mechanistic basis for the link between neurodegenerative disorders and chronic inflammation, and the association of immune cell types with neurological features such as autism or depression, leading to new treatment opportunities. The integration of immunology and cancer research will allow us to investigate molecular mechanisms that determine whether a tumour is eradicated or promoted by immune and inflammatory responses. The role of immune cell types in shaping the tumour environment and promoting or suppressing metastasis is central to this process. The development of improved preclinical mouse models that better reflect the organ and tissue specific aspects of tumour growth in humans is an important goal that may help understanding of the immunological influence of particular anatomical sites in which tumours develop.

These studies of pathogen biology, immune responses and inflammation span multiple disciplines, and are particularly amenable for study at the Crick given our disciplinary breadth and collaborative ethos. Opportunities are further enhanced by the presence of embedded clinician scientists and established local and international collaborations that can foster translation from model systems to humans.



Section of a small intestine infected with red *Cryptosporidium* parasites. Adam Sateriale's lab at the Crick studies *Cryptosporidium*, a parasite linked to childhood malnutrition, for which there are currently no effective treatments or vaccines.

Neural Systems

Our brains construct and contain our sense of self, which is central to the human experience. How such experience is generated by networks of approximately 100 billion neurons remains enigmatic. Neural disorders have uniquely devastating effects, but many of these disorders are poorly understood. Understanding brain function in health and disease is therefore a critical frontier in the years to come.

The brain does not work in isolation. Its function profoundly depends on and in turn influences processes in the rest of the body. For this reason, understanding brain function is tightly linked to unpacking its interactions with the immune system and the endocrine system, amongst others. Progress in understanding the brain will also help design better algorithms for artificial intelligence, just as past advances in neuroscience underpin the ongoing revolution in artificial intelligence.

We are at a technological inflection point for neuroscience. Molecular and genome sequencing and editing techniques have in recent years allowed the life sciences to thrive and develop. For neuroscience, however, key readouts are the connectivity in neural circuits (the connectome), and the activity of neurons. Both of these fields are now close to having truly scalable, high-throughput technologies. In the coming years, this promises to make brain regions, or in the case of small invertebrates, entire brains, fully accessible by comprehensively mapping neural connections and the activity of a large fraction of neurons. Combining this information with molecular and genetic tools will enable major advances in our understanding of how neural circuits are assembled and function to generate behaviour. This includes addressing questions such as how transcriptomic diversity relates to neural function and connectivity. It will give answers to the question of how a small number of genes can construct and shape a complex network with trillions of connections, and how evolution has shaped behaviour and brain function by sculpting neural circuitry.

In the coming years, clinical neuroscience will start to see a revolution in the treatment of psychiatric and neurological diseases, driven by the combination of next generation brain–machine interfaces and deeper understanding of neural circuitry. Cellular neurophysiology in humans will in turn improve our mechanistic understanding of human brain function.

The Crick's inherited strengths in developmental neurobiology have been complemented by new recruitment and university secondments, to generate two additional areas of strength within the broad umbrella of neurobiology. The first is 'circuit neuroscience', in which neural networks are explored and mapped to explain complex phenomena like sensory pathways and decision making. The second area is neuropathology, which focuses on relationships between neurobiology and human diseases, especially neurodegenerative diseases. The Crick will integrate work at the level of molecules, cells, circuits, systems and behaviour, and foster collaborations between biologists, physicists, engineers, mathematicians and clinicians. Collaborations with the partner universities will be important, reflecting their strong and wide-ranging research and clinical interests in neuroscience, as well as interactions with other external partners such as the Alan Turing Institute and Google DeepMind.

Fluorescent image of a neuron from the cerebral cortex. Ede Rancz's group studies the circuits created by nerve cells in order to learn more about how our brains function and malfunction.

Repair, Degeneration and Ageing

Living things, from cells to organisms, become damaged and degenerate over time, and have developed mechanisms to repair damage and enable regeneration. The Crick is already strong in the area of DNA damage and repair, which we will extend to consider damage and degeneration at the level of other molecules, cells, tissues, organs and organisms.

Increased life expectancy underlies the major health threat from degenerative diseases. For example, degenerative diseases of the nervous system such as dementia currently affect around 50 million people worldwide. The risk of developing a degenerative disease significantly increases with advancing age.

Understanding the processes that lead to the degeneration of cells within different organ systems within the body, as well as their inherent capacities for repair, can drive significant benefits to human health. Unfortunately, there is no cure for the majority of degenerative diseases, so it is critical to gain an understanding of how different cell types within different organ systems respond to both ageing and disease. Understanding the capacity for, and mechanisms underlying, repair and regeneration will inform our approach to impactful therapeutic strategies.

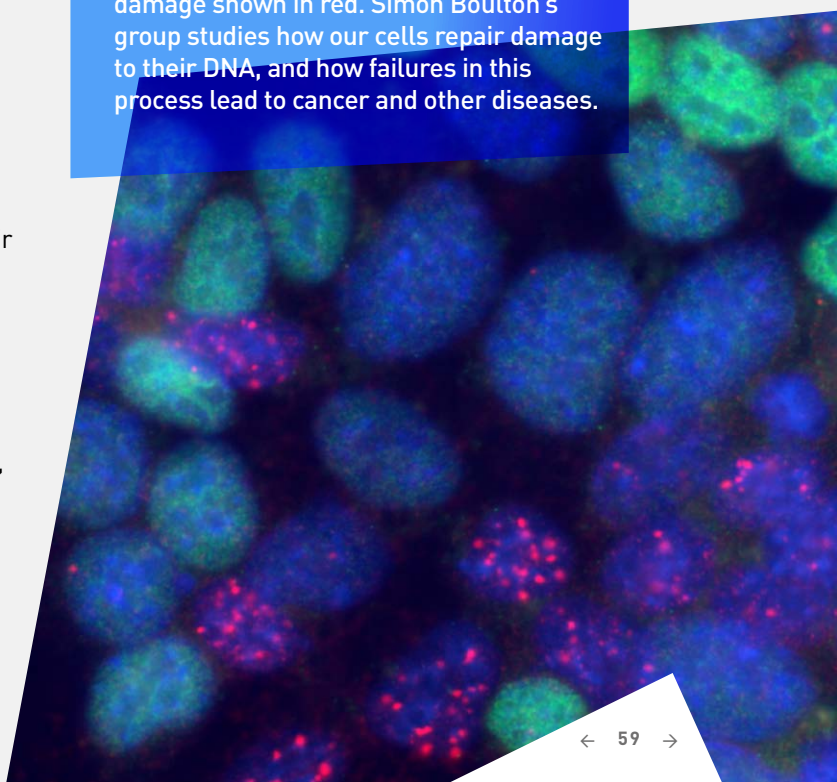
Research on the genetic component of degenerative diseases has galvanised transformational therapeutic advances including the use of antisense oligonucleotides, revolutionising the treatment of otherwise devastating conditions such as spinal muscular atrophy.

There are fundamental questions to address, for which emerging technologies now exist or are being developed:

- What are the relationships between genetic and environmental effects, cellular degeneration and altered homeostasis?
- How do different molecular processes, cell types, regions within a single organ system and distinct organ systems conspire to cause degeneration or facilitate repair?
- How does ageing contribute to degeneration and capacity for repair?
- What is the nature of the interaction between these processes and can any aspect be therapeutically targeted?
- Can biomarkers be identified for early detection and progression of degeneration across a range of clinical disorders?

The Crick will develop this area in the coming years, taking a multi-pronged approach that integrates discovery science research labs with those led by clinician scientists. Many of the biological pathways relevant to cellular degeneration and mechanisms of repair are of fundamental relevance to the other major focus areas including cancer, the immune system, and infections and neural systems.

Mouse embryonic stem cells with DNA damage shown in red. Simon Boulton's group studies how our cells repair damage to their DNA, and how failures in this process lead to cancer and other diseases.

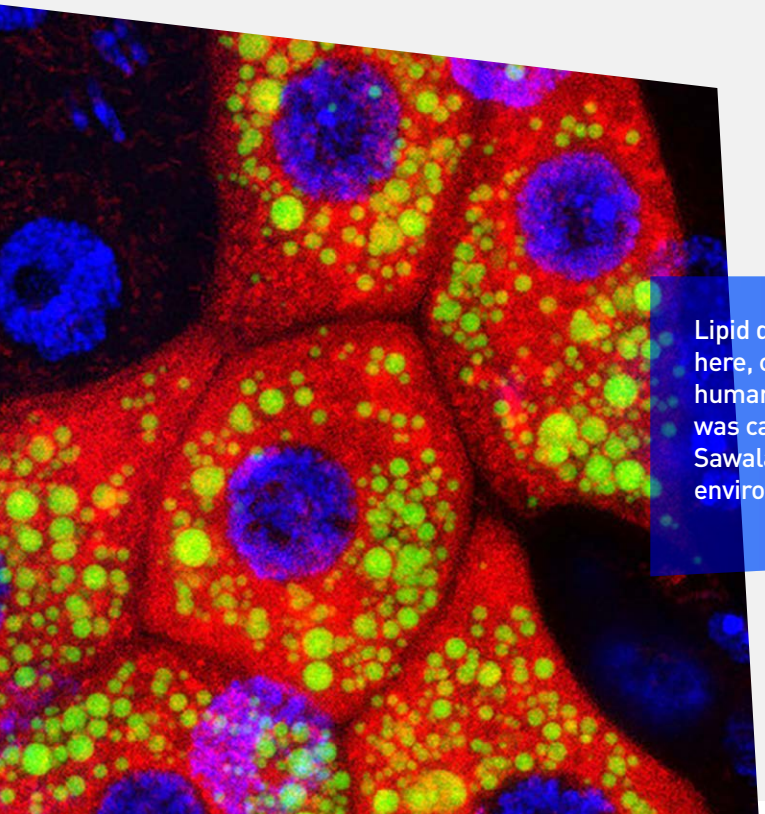


Physiology and Homeostasis

Homeostasis refers to the ability of an organism to maintain the internal environment of the body within limits that allow it to survive. Homeostasis is central to our understanding of many aspects of biology. It is fundamental to the maintenance of cells and organisms, and implicated in many aspects of human health and disease. A wide variety of physiological signals, including those from the nervous, endocrine and immune systems, are used to coordinate the behaviours of cells and tissues within the whole organism, ensuring proper functioning under different conditions. Physiological signals allow organisms to adjust their internal state in response to damage, and external stimuli and stresses such as food, temperature, time of day and social interactions. The immune system also contributes by playing a critical role in the detection and response to genetic or physical damage to cells and tissues in the absence of infection.

Misregulated or malfunctioning physiological signals lie at the heart of many diseases. For example, insulin signalling is disrupted in diabetes, while cytokine signalling is altered in cancer and cachexia. Biochemical circadian rhythms not only affect the incidence of medical conditions, but also the response to therapies. Physiological signals also regulate metabolism, which behaves abnormally in diseases such as diabetes, obesity and cancer, as well as during ageing. It is increasingly recognised that the immune response in cells and tissue plays an important role in wound healing and cancer. An important challenge is to discover how the diverse signalling processes controlling homeostasis are integrated at the molecular level in space and time during the development of human disease and the response to therapy.

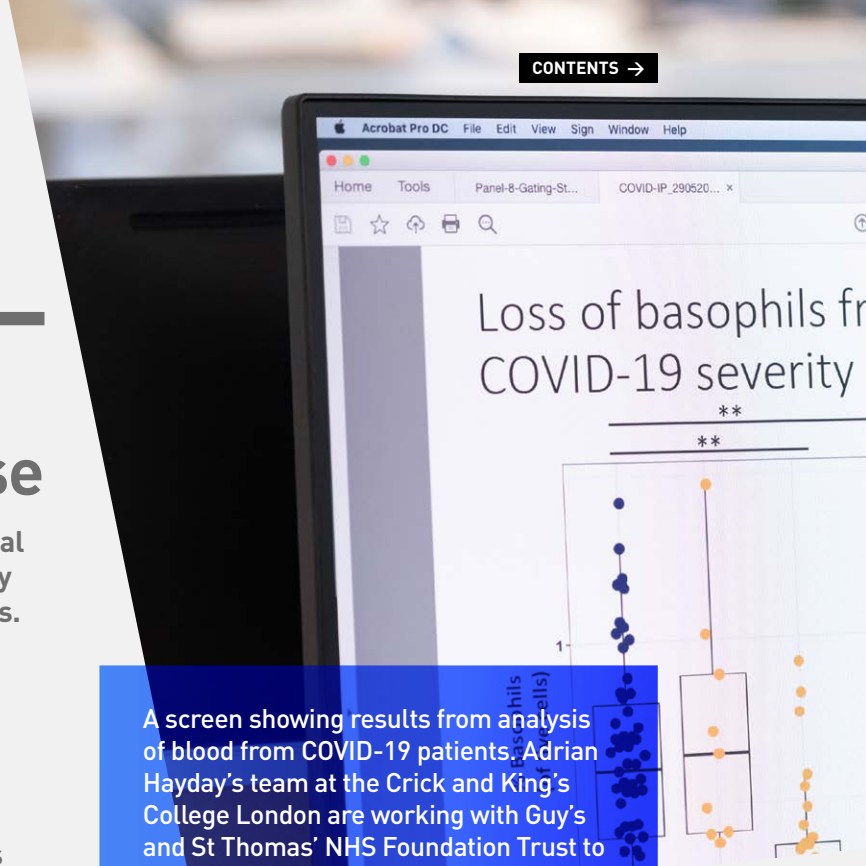
The Crick will develop this area in the coming years, particularly at its interface with disease. The institute is well placed to do so, with substantial expertise in genetics, developmental biology, cancer, immunity and neuroscience, areas where the theoretical concepts and approaches overlap with those of physiology. New gene editing methods now provide efficient tools for manipulating physiological signals and metabolic pathways in one organ and assessing their remote consequences in others. The Crick can also use its sophisticated technology platforms to detect physiological changes at the molecular, sub-cellular, cellular and tissue level with high precision. The field is ripe for new technical developments, as evidenced by recent collaborations between Crick scientists and physicists to develop mass spectrometry imaging methods, allowing visualisation of metabolism within cells and tissues at high chemical and spatial resolution.



Lipid droplets, like the ones show in green here, can build up in cells in malnourished humans and other animals. The image was captured at the Crick by Annick Sawala and Alex Gould, who study how our environment can affect our metabolism.

Human Biology in Health and Disease

Discovery research to generate biological knowledge can be rapidly and effectively pursued using a range of model systems. Applying that knowledge to humans requires elucidation of the specific ways that the human organism works, how it malfunctions and its response to external factors. The Crick will investigate the biological mechanisms underlying perturbation of homeostasis and their links with human disease. These investigations have the potential to affect human health in multiple ways: through better classification of disease, more effective diagnosis, identification of new disease-relevant biomarkers and the development of potential new therapeutic strategies and preventive measures.



A screen showing results from analysis of blood from COVID-19 patients. Adrian Hayday's team at the Crick and King's College London are working with Guy's and St Thomas' NHS Foundation Trust to analyse data from COVID-19 patients and look for indicators that could predict disease severity.

A variety of research activities considering specific aspects of human biology and disease will be pursued at the Crick. We will construct new models of human biology and disease, drawing on chemical biology, differentiation of stem cells, human organoids and engineered artificial tissue systems and humanised mouse models. New gene editing technologies will be harnessed to define and validate antimicrobial targets in human pathogens. We will leverage enhanced understanding of physiology and homeostasis at the molecular, cellular, tissue and whole-body levels. This will inform human pathophysiology and enhance understanding of the effects of external challenges such as environmental stresses, pathogens and therapeutic drugs, and internal challenges such as perturbed metabolism, immune system changes and ageing.

We are aware that mechanistic insights into human disease often have their origin in large-scale epidemiology and human genetics, and we will continue to develop appropriate links through our university and institutional partnerships. Use of this 'big data', together with novel biomarker measurements, will facilitate better diagnosis, resolve disease mechanisms and help predict patient outcomes.

The recent major expansion in knowledge of human genetics and genomics provides particular opportunities. Human biology is the outcome of evolution, and late hominid evolution has been subject to significant changes in human lifestyle. Dramatic shifts due to agriculture, urbanisation and civilisation have led to equally dramatic changes, for example in diet and pathogen exposure. These changes can be studied genetically through sequencing of ancient DNA. The availability of in-depth data on human genetic variation can be used to stratify patients, identify disease susceptibility, assist in building models of disease and aid understanding of variation in treatment responses.

SCIENCE TECHNOLOGY PLATFORMS

SCIENCE TECHNOLOGY PLATFORMS

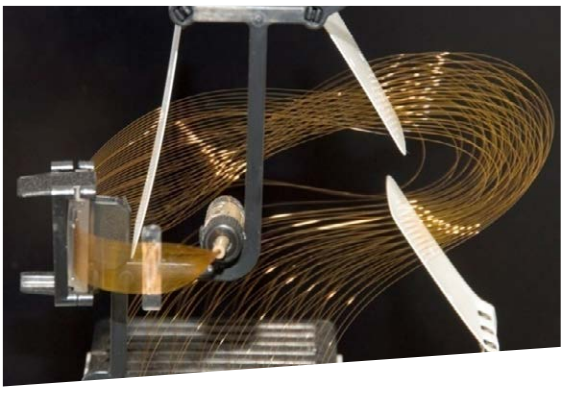
The history of science since the seventeenth century has demonstrated that scientific discovery is often driven by developments in technology. Iconic examples are the invention of the microscope, which led to the discovery of cells, and the invention of the telescope showing that moons circled Jupiter. Modern biomedical research, and the Crick science programme in particular, depends on ready access to multiple sophisticated technologies, whose effective operation requires specialist technical and academic expertise.

At the Crick, these technologies are provided through an extensive portfolio of science technology platforms (STPs) serving a wide spectrum of basic biological research, alongside a start-of-the-art vivarium and associated technologies. The current platforms comprise:

- Advanced Light Microscopy
- Advanced Sequencing
- Bioinformatics and Biostatistics
- Biological Research Facility (BRF)
- Cell Services
- Electron Microscopy
- Experimental Histopathology
- Flow Cytometry
- High-throughput Screening
- Human Embryo and Stem Cell Unit
- Making Lab
- Metabolomics
- Peptide Chemistry
- Proteomics
- Scientific Computing
- Structural Biology.

The Crick also hosts two major centres that provide national and international support. The MRC Biomedical NMR Centre supplies access to a range of NMR instruments to both Crick researchers and extramural life sciences researchers from the UK academic community. The Worldwide Influenza Centre is one of six centres in the world responsible for analysing flu viruses circulating in the human population.

In addition, the institute provides effective centralised support of routine scientific services such as media and buffer preparation, wash up, sterilisation and fermentation, ensuring economies of scale.

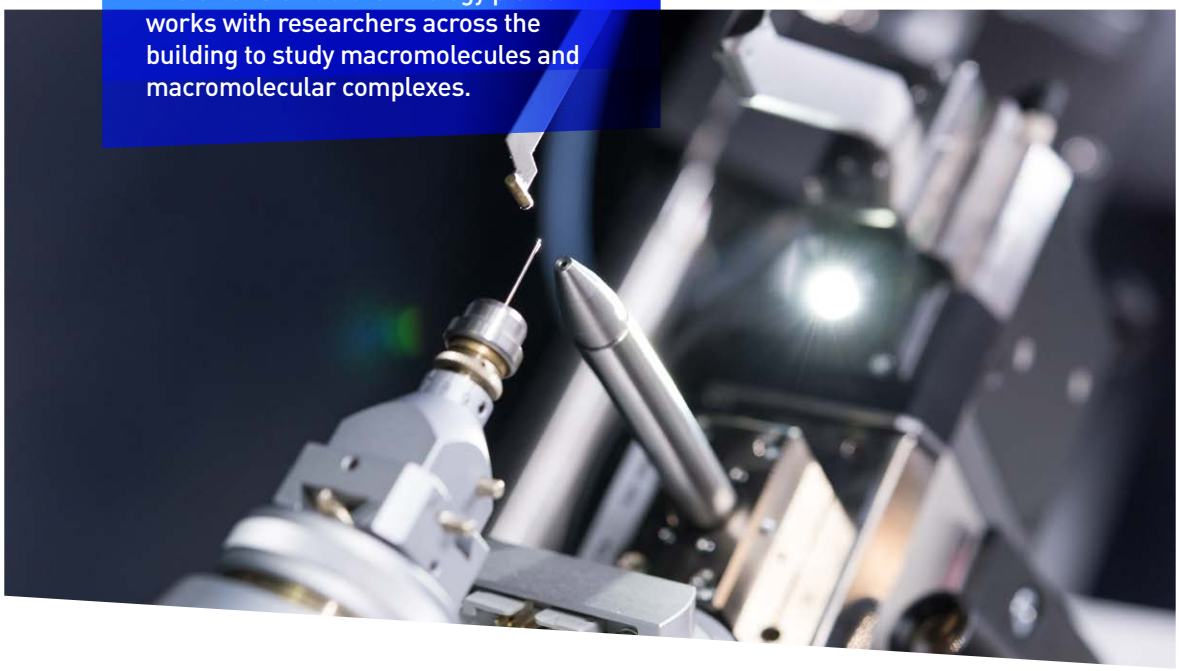


Our Fly Facility manages and maintains more than 8,000 different genetic strains of *Drosophila* and provides a range of technical services, including microinjection and performing genetic crosses.

Expert scientists working in the STPs guide and advise researchers on the most effective ways that the platforms can contribute to research projects, with a focus on collaboration and joint experimental design. Crick researchers are free to access any platform but work within a defined core resource budget for platform access, or must obtain external funding. The institute's size justifies the cost-effective establishment of many technologies in-house, and where this is not the case we work with our university and industry partners, as well as external commercial operations, to allow Crick researchers to access external facilities and resources, and vice versa.

Adoption of new technologies is important in defining new routes to scientific discovery, and the Crick will conduct regular horizon scanning exercises involving STP leads and user groups. We will also use a bottom-up approach, harnessing STP development to the needs and aspirations of group leaders, who are encouraged to work in partnership with the Crick STPs to develop access to the new technologies they require. Our broad scientific portfolio will also create an attractive environment for end-stage development and testing of new technologies across a spectrum of applications. Alongside innovation, the operational model of the platforms will ensure that there are no barriers to the import and development of new technologies.

Scientists from the Crick's senior leadership oversee the operation of the STP portfolio, working with each platform's operational management. To ensure that the portfolio is kept at the cutting-edge level we will conduct regular reviews of each platform or service by experts in the technology concerned. Reviews will assess the strategic vision and future plans, technical repertoire, development work, service provision and training activities, and their findings will inform any subsequent restructuring and investment.



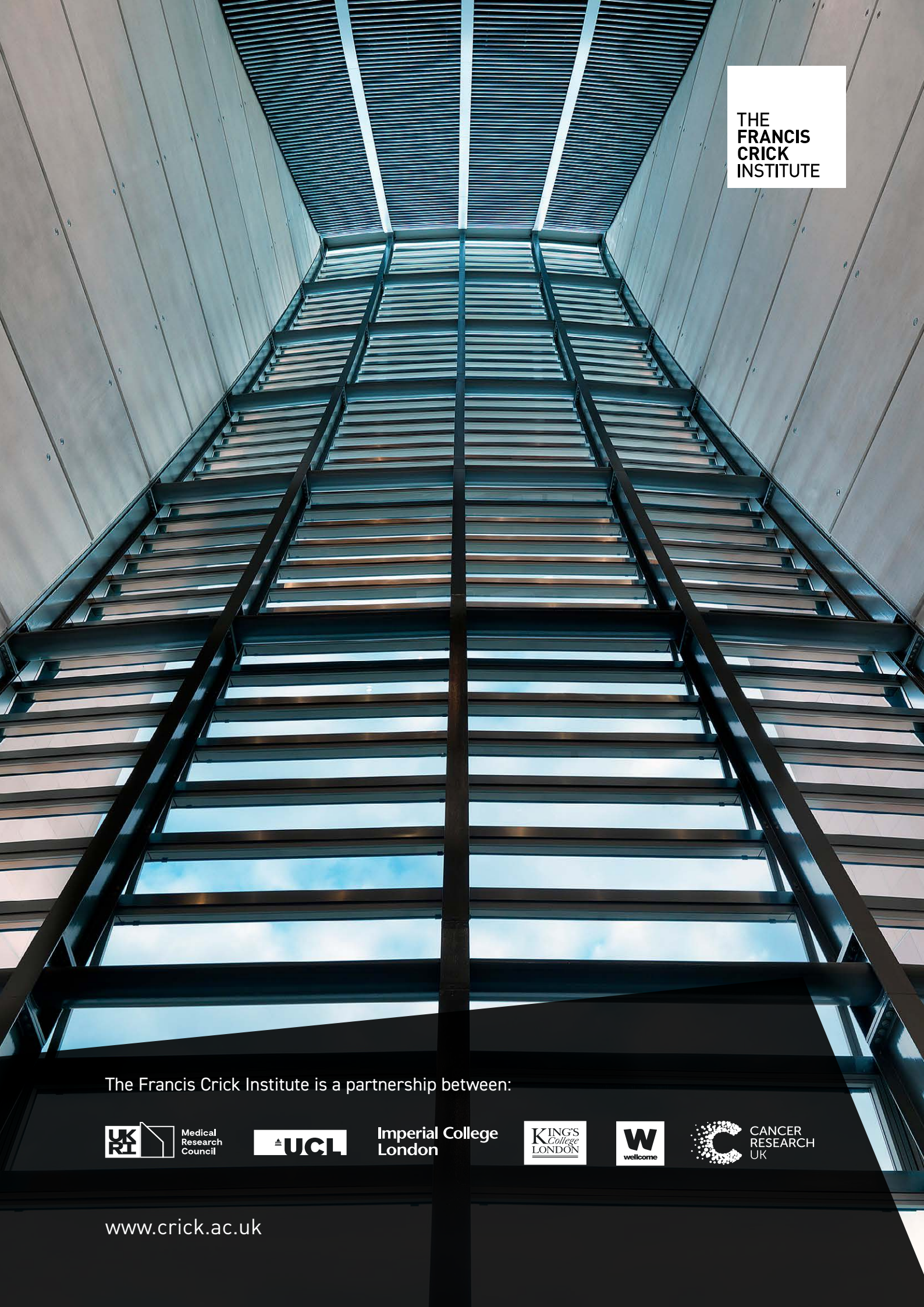
The Crick's Structural Biology platform works with researchers across the building to study macromolecules and macromolecular complexes.

There will be a range of possible routes to the development of new technology platforms, with some platforms growing organically from the pooling of resources by multiple research groups or groups with new technical expertise joining the institute. An example of the latter is the Making Lab, which was the result of a collaborative interaction with a group from one of the Crick's partner universities. A formal decision to establish a new platform will be supported by assessment of the scientific case in consultation with the Crick's Scientific Advisory Board, external advisors, and potential users. Platforms whose operation is no longer needed, or which are not scientifically or economically competitive with outside provision, will be discontinued. User committees drawn from across the Crick will ensure that user requirements drive platform development, providing strategic input to the facility head, informal feedback on day-to-day operation and advice on platform access.

Examples of technological opportunities the Crick will consider in the coming years include:

- Data science – provision of software tools and platforms to make software engineering, data science and analysis methods (including machine learning) straightforward and available to all researchers.
- Human biology – platform technologies to support the application of stem cell models, organoids, and tissue-based approaches to the study of human biology in health and disease.
- Single-cell technologies – quantifying biological molecules such as proteins, nucleic acids and metabolites at single-cell resolution.

Training will play an important role in maximising effective use of Crick STPs. It will facilitate service provision, increase platform usefulness by empowering users, and aid the development and implementation of new technologies. The Crick will share technology platform operational and scientific best practice with facilities worldwide, hosting visitors from other institutions. At the institute level, the STPs will contribute to academic training by co-hosting trainees with Crick research groups.



THE
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The Francis Crick Institute is a partnership between:

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