DECEMBER 2021

SUPPORTING WORLD-CLASS RESEARCH AT THE FRANCIS CRICK INSTITUTE

UPDATE PREPARED FOR THE NINEVEH CHARITABLE TRUST

CANCER RESEARCH UK

THE FRANCIS CRICK INSTITUTE

The Francis Crick Institute

Five years on from opening its doors, the Francis Crick Institute has established itself as one of the leading biomedical research institutes in the world.

Since 2016, its scientists have been shaping our fundamental understanding of human health and disease, publishing more than 2,000 scientific papers and providing significant new insights across the spectrum of biomedicine. Crick science has generated 10 spin-out companies that will take promising discoveries from the lab bench into the clinic where they can benefit patients. The institute has become a global destination of choice for emerging research talent, recruiting 32 new early-career group leaders from 14 countries, over 300 PhD students and over 600 postdoctoral researchers from around the world. And many of the Crick's faculty have been recognised through major scientific prizes, including the 2019 Nobel Prize in Physiology or Medicine.

The next chapter of the institute's journey will see us continue to embrace new opportunities to connect and collaborate, allowing us to further accelerate the pace of discovery and consolidate the Crick's status as a world-class biomedical research institute. It will be an honour and a pleasure to celebrate this anniversary of the foundation of the Crick with you all at the Nineveh Charitable Trust, as friends who have stepped in at a critical time to make a vital contribution to our crucial research. Our success would not have been possible without the shared vision and belief of supporters like you. We are delighted to present you with some of the highlights and advances that the Crick's researchers have made since your first gift in Spring 2020.

RECENT HIGHLIGHTS FROM THE CRICK

SUMMER 2021

HIGHLIGHT

Professor Mike Blackman and his group design a molecule that effectively blocks a critical step in the malaria parasite life cycle. They are now working to develop this compound into a potential first-of-its-kind malaria treatment.

HIGHLIGHT

A collaboration between Dr Samra Turajlic, Professor Charlie Swanton and Dr Paul Bates finds that cells at the centre of tumours have a less stable genome and a higher potential to spread to other parts of the body than cells at the edges of the tumour. The findings highlight the need to develop treatments that target the unique conditions found at the tumour core to eliminate the most aggressive tumour cells.

HIGHLIGHT

A collaboration between Professor Jim Smith and Professor James Briscoe's teams examines the earliest point at which the heart forms during embryo development. They reveal, for the first time, that each of the four chambers of the heart has a unique origin. Their research has implications for understanding congenital heart diseases, which affect around 1 in 180 babies worldwide.

HIGHLIGHT

Professor Caetano Reis e Sousa and his team identify a protein that helps tumours evade the immune system and, in certain types of cancers, is linked to a poorer chance of survival. The protein could become a target for an innovative new class of cancer immunotherapies.

HIGHLIGHT

Dr Naomi Moris publishes results showing how 3D models made from embryonic stem cells could be used as part of the testing process to assess whether treatments are safe for developing embryos. These models could help establish whether new drugs can be taken during pregnancy and improve the selection of compounds to move forward into further trials.

SPRING 2021

HIGHLIGHT

Professor Rickie Patani and his team identify the trigger of a key cellular change in motor neurone disease. They reveal how a 'helper' cell in the brain, known as an astrocyte, changes its behaviour and can cause harm to neurons. The findings could aid the development of new treatments for this condition, as well as many other neurological diseases with the same change, including Parkinson's disease and Alzheimer's disease.

HIGHLIGHT

Professor Stephen West and his team find that blocking a specific protein could increase tumour sensitivity to PARP-inhibitor therapy, which is used to treat a subset of ovarian, breast and other cancers. In many cases, cancer eventually develops resistance to this treatment, enabling the tumour to start to regrow. Stephen's work suggests how PARP inhibitors might be combined with other treatments to kill cancer cells before this resistance develops, or re-sensitise the cells to treatment, which could offer people with cancer an improved chance of survival.

AUTUMN 2021

HIGHLIGHT

GammaDelta Therapeutics, a biotechnology company co-founded by Crick group leader Professor Adrian Hayday initiates its first Phase I clinical trial. This marks the first in-human tests of a novel cell therapy for the treatment of acute myeloid leukaemia. This cell therapy builds upon Adrian's pioneering work into the role of a type of immune cell known as gamma-delta T cells in tackling cancer.

TACKLING THE GLOBAL COVID-19 CRISIS

The core mission of the Crick is to harness the power of multidisciplinary collaboration to address the biggest global health challenges of our time. As such, the decision to pivot our scientific expertise, facilities and resources to tackle the urgent challenge posed by COVID-19 came naturally.

In March 2020, the Crick rapidly repurposed some of its laboratory space into a virus testing facility to help address the lack of testing available to frontline healthcare staff, who faced a high risk of infection. For over a year, we tested NHS staff and patients from 10 London hospitals, the London ambulance Service and 150 care homes across the capital, processing more than half a million samples. We also made our standard operating procedures publicly available, empowering other institutions to set up their own testing programmes.

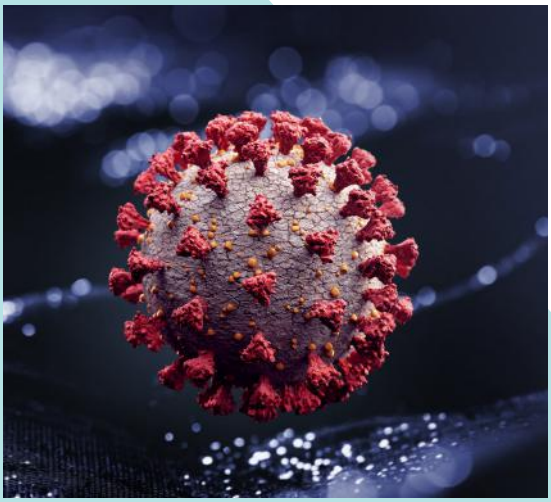
In parallel, we established a new COVID-19-related research effort. Crick researchers working across disciplines united under the common goals of increasing our understanding of COVID-19 and uncovering ways to combat the pandemic. Their work has yielded valuable results, including novel tools for antibody detection, improvements in our understanding of the virus' structure and biology, the identification of markers that predict patients' COVID-19 disease severity and the development of potential new treatments.

In January 2021, the Crick launched an NHS vaccination centre in the Manby Gallery, supported by a team of Crick staff volunteers, with the aim of vaccinating up to 1,000 people a day, seven days a week. By the time the centre closed in August 2021, it had vaccinated over 80,000 people.

Our COVID-19 research efforts continue, adding to the scientific community's pool of knowledge about the virus.

SPOTLIGHT ON THE LEGACY STUDY

HARNESSING 700,000 SAMPLES TO BETTER UNDERSTAND THE VIRUS



The Legacy study is a collaboration bringing together leading researchers across the Crick, University College London (UCL) and UCL Hospitals to better understand COVID-19. Together, these researchers are using the unique bank of over 700,000 biological samples at the Crick, gathered as part of the institute's testing, to understand more about how and why people are vulnerable to infection with SARS-CoV-2, the virus that causes COVID-19. The team seeks to understand the virus and how it behaves in individuals – how the virus is transmitted between people, how later stages of the disease develop and how the body's immune system attempts to control it.

Initial results from the study revealed that vaccinated people have lower levels of antibodies that can recognise and fight the new SARS-CoV-2 Delta variant than previously circulating variants in the UK. As the study continues, the team is now examining the effects of booster vaccines, the consequences of SARS-CoV-2 infection after vaccination, and the persistence of long-term immunity against COVID-19. Ultimately the study seeks to arm researchers, clinicians and policymakers with an up-to-date understanding of the transmission and evolution of the virus (including the emergence of new variants such as Omicron), the effectiveness of measures such as vaccines and treatments to control it, and the impact of the disease on individuals.

COVID-19 RESEARCH HIGHLIGHTS

Understanding the spread of the virus

A study led by Professor Charlie Swanton reveals high levels of asymptomatic spread of SARS-CoV-2 in hospitals during the pandemic's first peak in the UK. The study emphasises the importance of regular, accurate and rapid testing, particularly for frontline healthcare workers.

Identifying patients who need more intensive treatment

Professor Adrian Hayday and his team identify three immune signalling molecules in the blood of people with COVID-19 that could be used to predict how severely ill they will become, aiding patient management.

Revealing how the virus' spike protein functions to infect cells

Dr Steve Gamblin and his team show that the spike protein on the surface of SARS-CoV-2 can adopt at least 10 distinct structural states when it comes in contact with the human virus receptor ACE2. This new insight could inform studies into improved vaccines and treatments.

Uncovering existing immunity to coronaviruses

Findings by Professor George Kassiotis and his group indicate that pre-existing antibodies to coronaviruses, developed in response to the common cold, are frequently present in children and might explain why they are less likely to become severely ill with COVID-19.

Exposing a reduced immune response to the virus in people with cancer

Work by Professor Adrian Hayday in collaboration with Cancer Research UK scientists at King's College London reveals that people with blood cancers struggle to mount an immune response and face a much longer COVID-19 recovery than people with solid tumour cancers or no cancer.

Investigating the threat of new variants

Researchers led by Crick group leaders Dr Kate Bishop, Dr Rupert Beale and Dr David Bauer begin to study the threat of new SARS-CoV-2 variants, as part of a new national consortium.

Identifying potential new drugs for COVID-19

In a collaboration spanning multiple Crick labs, researchers screen thousands of drug and chemical molecules. In doing so, they identify a range of potential antivirals that could be developed into new treatments for COVID-19, or in preparation for future coronavirus outbreaks. The results were published as a series of seven back-to-back papers.

Tackling the symptoms of long COVID

In partnership with over 30 organisations across the UK, researchers at the Crick help to run the largest clinical study of long COVID to date, where thousands of patients trial existing drugs to see if their symptoms improve. Long COVID causes long-lasting debilitating symptoms in an increasing number of people and presents a huge challenge to healthcare and community services.

Professor Adrian Hayday

FROM CANCER IMMUNOLOGY TO COVID-19

Professor Adrian Hayday is a respected leader in cancer immunology, a member of The Royal Society and an assistant research director at the Crick. In addition to being group leader of the Crick's Immunosurveillance Laboratory, he is head of the Department of Immunobiology at King's College London, a position that gives him strong connections to clinical colleagues at Guy's and St Thomas' Hospitals, enabling him to bridge the worlds of discovery research and clinical application.

Adrian and his team at the Crick are investigating how cancer cells interact with, manipulate and evade the immune system so they can identify new possibilities for cancer treatment. They are particularly interested in studying a novel type of white blood cell called gamma-delta T cells, which Adrian and his colleagues were among the first to report in the 1980s.

Adrian's work on gamma-delta T cells has challenged conventional views in the immunology field, and has revealed special abilities of these cells that could make them a promising tool for treating cancer. Gamma-delta T cells can detect abnormal cells that threaten to develop into cancer at a very early stage and can mount a rapid and targeted attack to destroy them – all without needing authorisation or direction from other parts of the immune system.

In 2016, Adrian co-founded the spin-out company GammaDelta Therapeutics, which aims to harness the unique properties of gamma-delta T cells to develop powerful new immunotherapies for a range of cancers. Importantly, unlike other types of T cells, a donor's gamma-delta T cells can work in other individuals, which means they could present a viable off-the-shelf treatment option.

In September 2021, GammaDelta Therapeutics initiated its first Phase I clinical trial of their novel cell therapy named GDX012. These first-in-human tests will evaluate the safety and side-effects of GDX012 in people with the blood cancer acute myeloid leukaemia who still have residual disease after standard treatment. Ultimately, the hope is that this new type of immunotherapy could help more people with a wider range of cancer types to survive their disease.

Addressing the urgent challenge of COVID-19

Beginning in March 2020, Adrian and his team have also applied their extensive expertise in immunology to address pressing challenges presented by the COVID-19 pandemic. In the COVID-IP study, the team identified three immune signalling molecules in the blood of people with COVID-19 that could be used to predict how severely ill they will become. This finding provided doctors with an additional tool to identify who should be prioritised for more intensive treatment.

The lab also collaborated with Dr Sheeba Irshad and Dr Piers Patten's teams at King's College London to investigate how cancer and cancer treatments impair patients' immune response to the virus. They found that people with solid tumours could mount as strong an immune response to the virus as healthy people. However, this response was more varied in people with blood cancers, with some struggling to clear the infection for many weeks, suggesting this group needs extra protection and care.

In a further study, the team discovered that a single dose of the Pfizer COVID-19 vaccine offered little protection to most people with cancer after three weeks – in contrast to the strong protection in healthy people. A three-week booster dose drastically increased the immune response in people with solid tumours – almost to the level seen in healthy people. However, 57% of double-vaccinated people with blood cancer still did not have an antibody response to the virus. The results reinforced the need to protect these vulnerable individuals, and to prioritise booster vaccines in groups such as these with compromised immune systems.

THANK YOU

We hope you have enjoyed reading about some of the institute's successes and that this update has given you a feel for the impact your support has made at the Crick. This is only a snapshot of the incredible research that takes place every day here and we would be delighted to host you for a visit and a tour in the future so that we can bring this research to life further for you. The work of the Crick is so crucial and relevant today and this has only been made possible with your support.

On behalf of the Crick and Cancer Research UK, we would like to thank you for your exceptional support and belief in our vision since March 2020. Your gifts since the start of the pandemic have been immensely important in allowing us to divert resources into understanding and tackling COVID-19, and to continue with our vital research.

Your generosity is enabling the Crick's researchers to tackle some of society's most pressing biomedical challenges, and to drive significant progress in their fields.

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The Francis Crick Institute works in partnership with Cancer Research UK, one of our founding partners, to attract and secure philanthropic support to help us discover the biology underlying human disease and accelerate the development of new treatments. Donations are received by CRUK before being used to support the Crick's purposes. You can support the Crick by donating to CRUK.

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