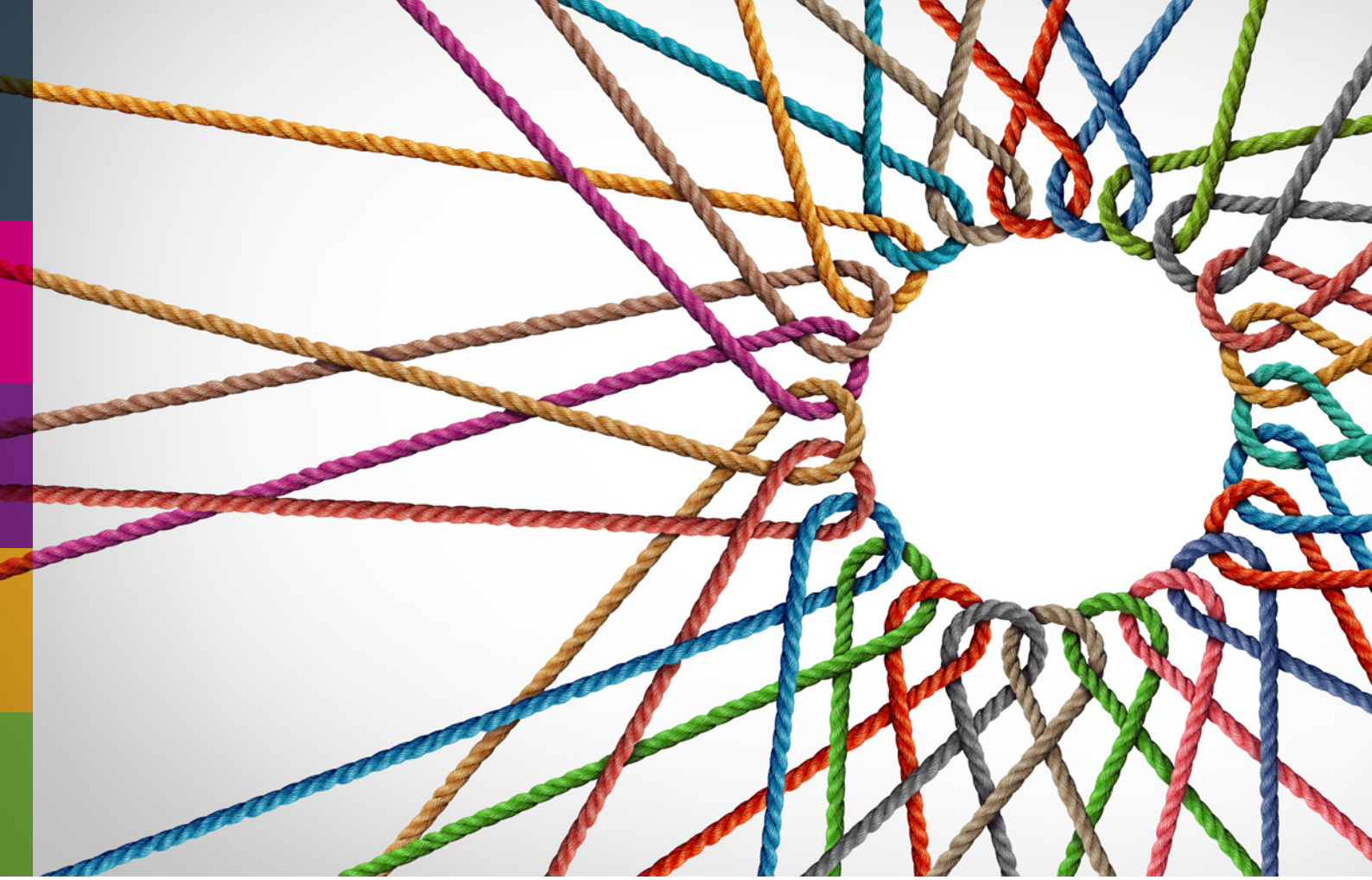


The Rosalind Franklin Institute

Changing the way we see life

Partnerships and collaborations

About The Rosalind Franklin Institute

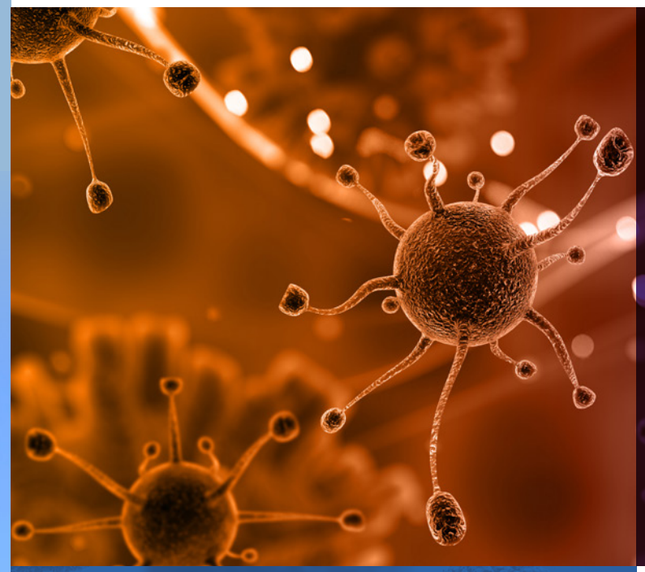
The Rosalind Franklin Institute is the UK's life science focused national interdisciplinary research Institute, based in the UK's Golden Triangle, with member organisations across the UK. Our research teams of engineers, physicists, biologists and chemists are creating new technologies which will transform our ability to visualise and probe cellular life. These technologies will be applied to the most important research challenges in life science and medicine.

Our technologies are unique, ambitious, and developed in partnership with industry and academia to ensure they will benefit the research community. Based at The Franklin hub throughout their development, our tools can give industry access to beyond state of the art technologies in advance of their maturation into the community.

The Franklin 'Factor-of-Ten' is a rule of thumb metric we apply to our technologies. We will not invest in projects which offer only incremental advances, or those which could be undertaken by a single party acting alone under grant funding. Instead, we focus our resources on 'factor of ten' shifts – on tools which create an order of magnitude change in the capability, resolution, or capacity of a technique, to change the way we see life in a leap.

Biological applications

Our technologies will be exploited across a breadth of disease areas, however, to ensure the biological relevance of our tools, we have a science focus on infection and the body's response to it. Using our technologies, we can image the shape and chemistry of life at a cellular level in both pathogens and human cells, and develop protein tools which have applications in imaging, and potential development capabilities as therapeutics and diagnostics.



AMR:

Antimicrobial resistance is widely acknowledged as one of the principal threats to human health in coming decades, already accounting for 700,000 deaths per year and rising.

The economics of antibiotic development are unfavourable, but the need is higher than ever. Using advanced technologies at The Franklin, we will better understand mechanisms of resistance, we will observe dynamic drug action in the cell, and our small molecule and protein modification tools can be applied against microbial disease.

Key techniques: Cellular tomography, In-cell chemistry, High Throughput Discovery

Understanding viral action:

Electron tomography has already shown promise in visualising viral replication and infection. Understanding the biological mechanisms of viral action offer the potential to understand both existing and emerging diseases. Our tools in cellular tomography will advance this capability even further.

The ability to respond quickly to emerging viral disease with novel reagents to image, diagnose or treat pathogens essential. Nanobodies, tiny antibodies derived from camelids, produced by The Franklin, can be used to stabilise proteins for advanced imaging, but because of their specificity and stability, also show incredible promise as therapeutics and diagnostics.

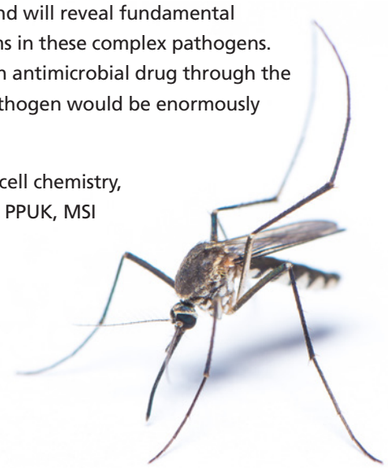
Key techniques: Protein Production UK (PPUK), Mass Spectrometry Imaging (MSI)

Intracellular pathogens:

Intracellular pathogens, as diverse as malaria and chlamydia, cause a huge burden of disease around the world, but their study is hampered by complex life cycles, and difficulties in imaging.

Imaging across multiple dimensions – in chemistry, time and space, could enable the action of novel compounds to be investigated, and will reveal fundamental biological mechanisms in these complex pathogens. The ability to track an antimicrobial drug through the human cell to the pathogen would be enormously valuable.

Key technologies: In cell chemistry, Cellular tomography, PPUK, MSI



Key technologies for exploitation

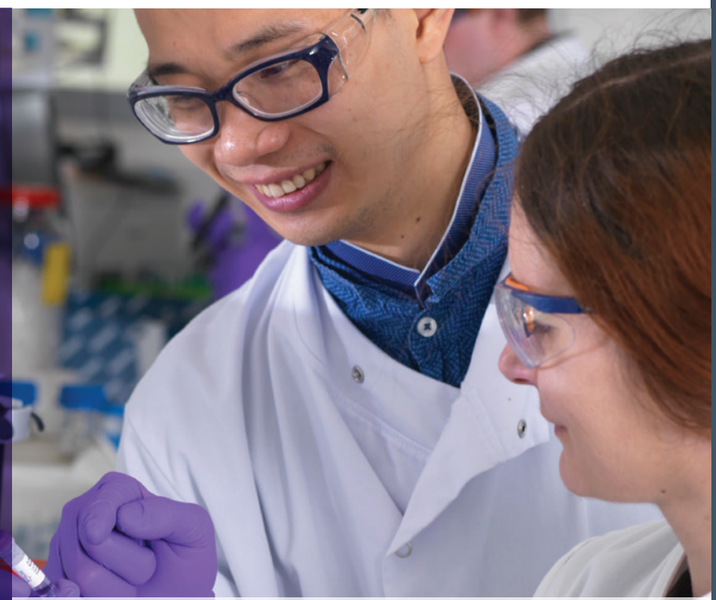
Our work at The Franklin is driven by a clear aim of making transformative leaps forward in life science. Five complementary scientific themes are together developing beyond-state-of-the-art technologies that will allow us to see the biological world in new ways – from single molecules to entire systems. These technologies, developed in partnership with industry and academia, can help answer research problems across life science. We welcome collaborations to address your research questions that would benefit from early access to these transformative technologies.

Protein Production UK:

Dedicated to creating faster, more effective sample management for imaging in a number of techniques, using X-rays or electrons. PPUK has a specialist capability in nanobody production – put to the test during the coronavirus pandemic, which saw novel nanobodies with nanomolar affinity for the SARS-CoV-2 spike protein engineered from library screens to publication in only 12 weeks. Nanobodies are already recognised for their utility in imaging, and their potential as a therapeutic and diagnostic are being investigated around the world.

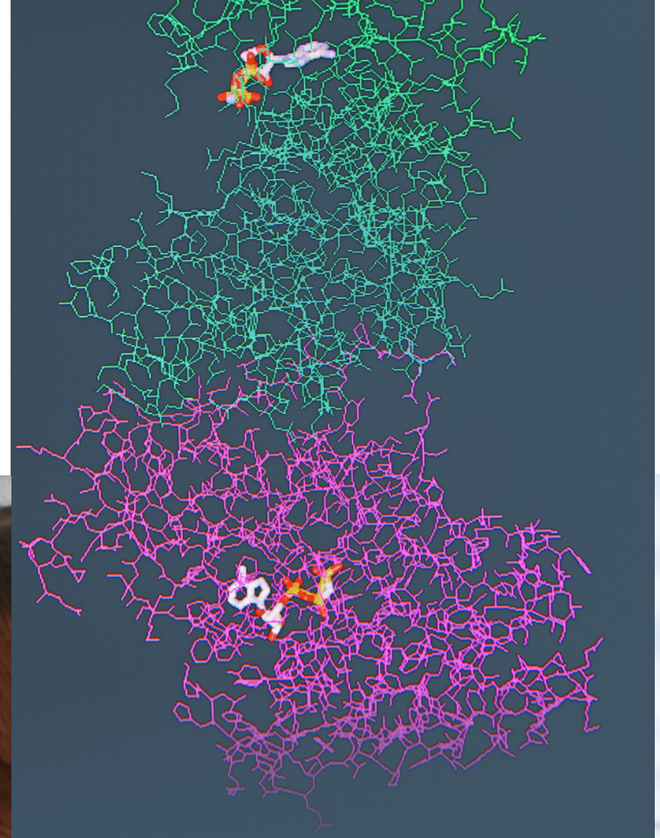
Correlative Imaging Platforms:

Our Correlated Imaging team, led by Professor Angus Kirkland, are working on a number of novel electron and optical imaging instruments. In collaboration with JEOL we are developing two new electron microscopes, both with time resolved capability. The first is optimised for cryo electron Ptychography over a wide voltage range and the second, with Chromatic correction for imaging thicker liquid and cryo samples. Together with Associate Professor Marco Fritzsche in collaboration with the Kennedy Institute for Rheumatology at the University of Oxford we are constructing the Biophotonic Correlative Optical Platform (BioCOP). This system will provide high performance optical imaging of cells in vivo and will allow the study of primary immune cell cultures in the context of human health and disease. Overall, these instrument will enable imaging over multiple length (from atoms to cells) and time scales (from microseconds to minutes).



Cellular tomography:

Supported by Wellcome, and in collaboration with Thermo Fisher Scientific, Professor James Naismith and the Structural Biology team are developing tools to enable true cellular tomography; cryo-electron imaging of large volumes. We have already seen the impact of electron imaging on structural biology, with cellular tomography we will see a further factor of ten shift in capability. Known as 'Amplus' the Franklin is leading global efforts in cellular tomography, with high energy microscopes, unique milling and sample preparation facilities in development. Complementary techniques in time resolved electron imaging and microscopy can all be applied at The Franklin, offering a unique imaging environment to explore the structure of biological systems.



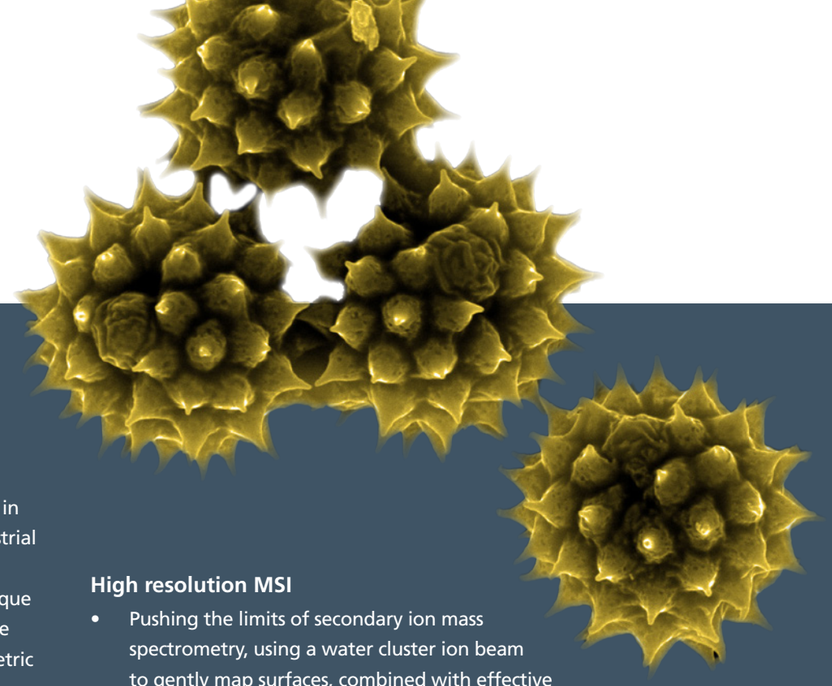
In-cell chemistry and synthetic biologics:

Protein modification carried out inside the cell is the ultimate aim of our chemistry theme. The team, led by Professor Ben Davis, imagines the potential of gentle, light driven protein modification as an alternative to gene therapy. The techniques are also applicable to imaging, in conjunction with cellular tomography and other techniques.

Control of cells through the "editing" of functional biomolecules could allow reprogramming of events as diverse as inflammatory response to tissue formation. The team are developing methods to break and form bonds in vitro and in vivo that can be applied to, for example, selective change of proteins and glycans. These include attractive targets such as proteoglycans for such chemical editing as their complexity prevents precise control by biological methods. Intracellular applications can also be explored for epigenetic programming allowing de novo cellular epigenetic control of chromosomal gene expression and transmission in living cells and organisms.

High throughput drug discovery:

A high throughput lab developed in collaboration with University of Leeds, which can develop and test workflows for small molecule synthesis. The ability to open chemical space to a wider and more adventurous range of molecules is of vital importance to the increasingly unproductive world of drug discovery. The Franklin can offer extensive cross theme partnerships, meaning in addition to the high throughput lab, you can gain access to fragment screening, AI driven synthesis, imaging and synthetic biologics.



Mass spectrometric imaging:

The Franklin team, led by Professor Josephine Bunch and Zoltan Takats, aim to increase both the resolution and breadth of analytes available in MSI by at least a factor of ten. Working with our teams in electron imaging, our university partners and industrial collaborators, combinatorial techniques and multi disciplinary investigations make best use of the unique chemical insight obtained using spectrometry. Three projects will converge to create our mass spectrometric imaging capability;

A new hybrid instrument for high resolution imaging

- Developed in collaboration with researchers at Bruker, NPL, Imperial College London, University of Birmingham and University of Oxford researchers, this machine will enable the detailed mappingdetailed mapping of biological molecules, including structural characterisation and protein confirmation studies

High resolution MSI

- Pushing the limits of secondary ion mass spectrometry, using a water cluster ion beam to gently map surfaces, combined with effective post-ionisation to boost the sensitivity and range of detection. This work is done in collaboration with NPL and University of Manchester.

Microscope mode MSI

- Ultrafast, high throughput imaging using a new microscope mode secondary ion mass spectrometry, created in collaboration with University of Oxford and Ionoptika, will enable multiple locations in a sample to be investigated at once.

AI and informatics:

AI and informatics underpin and support all of our technologies. From digital twinning in the design stages, to data management, segmentation, and the novel use of citizen science to provide training data. All Franklin technologies are highly data intensive, some capable of producing peta-bytes of data per experiment. Our AI team, led by Dr Mark Basham, are connected to a specialist network across the UK to provide solutions to our data intensive research problems.

Our expertise and collaborations with national facilities, organisations including the Alan Turing Institute and Ada Lovelace Institute, and collaboration on infrastructure such as the high performance computing 'Baskerville' facilities at University of Birmingham enables our research teams to analyse and interpret this high volume complex data.

Routes to collaboration

Using our technologies, we can help you answer research problems across life science.

Collaborate with us: Developing our technologies is best done hand in hand with the communities who will use them – we are keen to collaborate in the development stage of our technologies, to bring both test questions and technical expertise.

Research consortia: We are happy to act as a hub for multi party collaborations with academics and industries working together to develop and utilise our technologies to address pressing research problems.

Studentships, placements and training: As a skills hub, we can offer placements for industry, training on advanced techniques, or studentships in collaboration with our university partners.

Contact us:

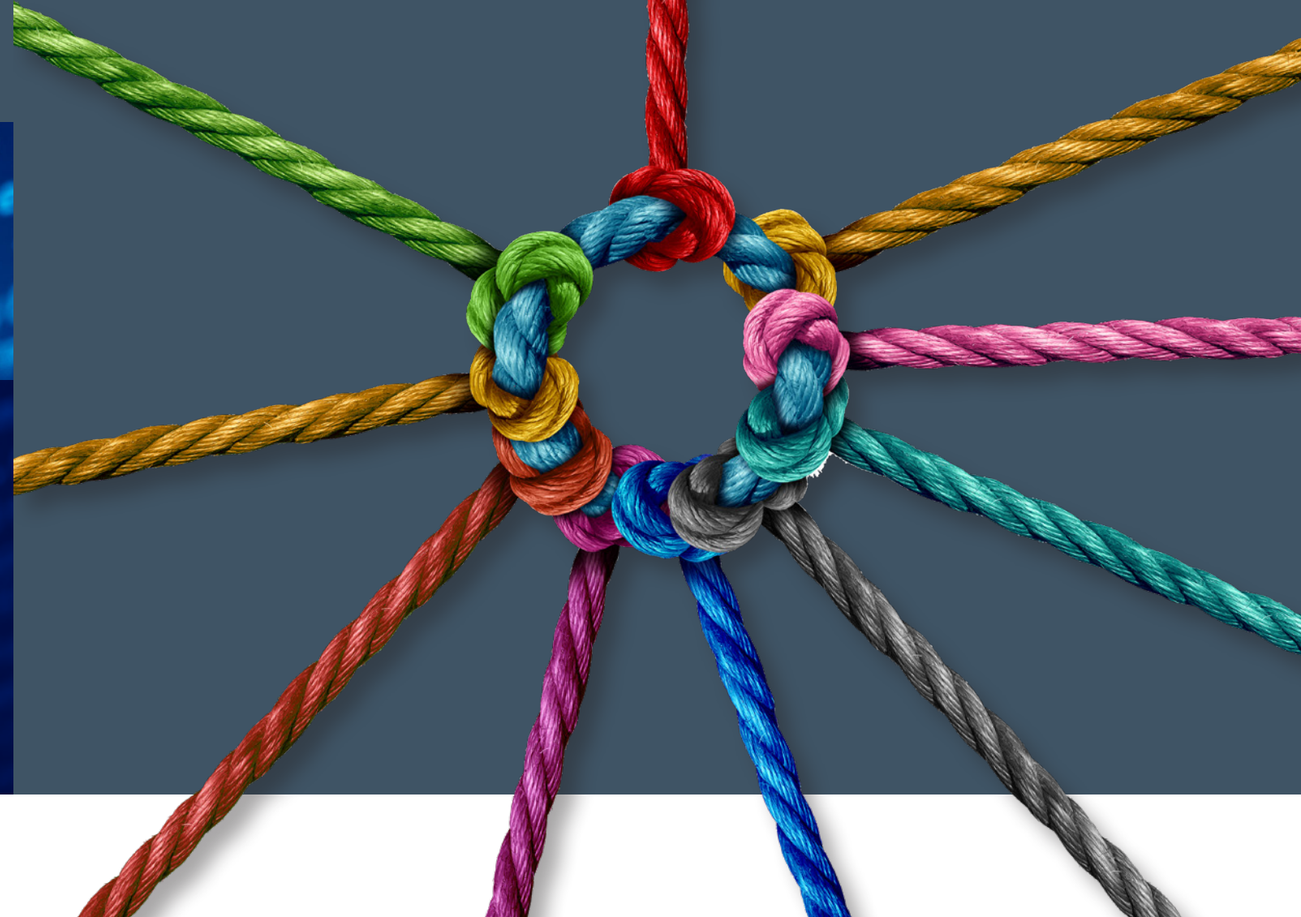
General:
Info@rfi.ac.uk

Enquiries:
Head of Business Development and Partnerships

Dr Roisin Nicamhlaoibh
Roisin.nicamhlaoibh@rfi.ac.uk

Twitter:
@RosFrankInst

www.rfi.ac.uk



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Engineering and Physical Sciences Research Council

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