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>
> Professor James Naismith

Driving technological leaps for healthcare

As Phase 1 of The Rosalind Franklin Institute comes to a close, the Director Professor James Naismith reflects on what has been achieved in the years since its formation and offers a glimpse into plans for the next phase.

‘Since 2018, we’ve built the building, staffed it, installed beyond state-of-the-art instrumentation — which we are helping to develop — and published some of the world’s most cited papers,’ Professor Naismith says.

During Phase 1, the Institute secured over £40 million in funding from industry and peer-reviewed grant funding bodies, and delivered ground-breaking science, including neutralising nanobodies, light-driven protein editing in cells and diagnostic technologies, despite the disruption caused by the Covid-19 pandemic.

Research carried out during the pandemic has made huge contributions to the fight against Covid-19. In July 2020, the discovery that a unique type of antibody produced by llamas could provide an effective treatment against the virus made headlines around the world. Since then, researchers at the Institute have shown that a cocktail of llama-based, SARS-CoV-2 specific nanobodies that can be delivered intranasally has potent prophylactic and therapeutic efficacy in animals. Furthermore, they have developed an ambient mass spectrometry assay that can detect the presence of the virus in seconds, without the need for expensive primers or reagents.

‘In Phase 2 we really want to push forward our molecular pathology goals by driving factor-of-ten breakthroughs and in doing so, accelerate the development of novel diagnostic and therapeutic products,’ Professor Naismith explains.

Rather than pursue incremental research, The Rosalind Franklin Institute was set up harness disruptive technologies that can transform our understanding of disease. In Phase 2, Professor Naismith expects the Institute’s five scientific themes: artificial intelligence and informatics; biological mass spectrometry; correlated imaging; next generation chemistry; and structural biology to bear on a range of urgent healthcare problems such as neurodegenerative disease to antimicrobial resistance.

Turning the clock back on disease

Most complex diseases are treated when signs and symptoms manifest, which for many is quite late. Better diagnostics and new cures will require spotting the earliest stages of disease and its molecular drivers. Researchers at The Rosalind Franklin Institute are advancing and integrating technologies to shift the dial on a major challenge: infection and inflammation.

The growing threat of viruses with pandemic potential, spread of parasitic tropical diseases due to global warming and emergence of drug-resistant microorganisms underscore the need for rapidly deployable and effective technologies to detect and eliminate them. In addition, further understanding the human body’s inflammatory response will not only aid the treatment of infectious diseases but also of many chronic diseases, cancer and ageing-associated conditions that involve inflammation.

‘Genomics gives us a starting point, but it is how proteins interact with one another that is really going to provide useful insights; and by useful, I mean that will influence patient outcomes,’ Professor Naismith says.

Importantly, because the technologies that are being developed are broadly applicable, there is no limit to the scope of biology that can be probed.

Pushing frontiers in life science research technologies

During Phase 2, researchers at The Rosalind Franklin Institute will be working with partners MRC Laboratory of Molecular Biology (MRC LMB) and Diamond Light Source, to deliver the Wellcome-funded project ‘Electrifying life science’. They will develop hardware and software for three new electron imaging technologies that will revolutionise cell biology by allowing a more diverse range of researchers to watch proteins working inside cells at atomic resolution.

Leveraging the Institute’s leadership on in vivo chemical editing of proteins, the Institute plans to build the UK’s first research cyclotron facility for exploring new methods for labelling protein complexes in animal and human tissues that can be used for clinical imaging.

In addition, by developing methods to grow previously unculturable bacteria, researchers at the Institute will be able to tap into what until now was inaccessible microbial ‘dark matter’ to discover new natural products with drug-like properties.

Further plans to extend the Institute’s mass spectrometry capabilities will enable us to resolve the molecular structure of a greater range of molecular species, with greater sensitivity and 30-50 times faster.

The Franklin will also be expanding its research into nanobodies, by developing workflows to rapidly enhance their specificity and potency, with the aim of producing first line therapeutics that neutralise a novel respiratory virus within 12 weeks. To achieve this goal and improve the UK’s future pandemic preparedness, high level containment facilities will be required.

Opportunities for automation and using artificial intelligence and machine learning methods will be seized across the Institute’s entire research portfolio to efficiently speed up data gathering and analyses.

‘Phase 2 will pull everything we are doing to overcome key technological roadblocks together to unpick the biological mechanisms underlying disease and tackle the most pressing health research challenges,’ says Professor Naismith.

A national focal point for transformative change

Staff and colleagues at collaborating organisations in academia and industry are key to the Institute’s success. ‘We attract people who want to push beyond what is currently possible, who are prepared to tackle the most challenging and high-risk research,’ Professor Naismith says.

The Institute currently employs 75 researchers and collaborates with over 46 universities and 20 companies. It also offers placements for industry, training on advanced techniques, and studentships in collaboration with university partners. The Rosalind Franklin PhD student training programme that started in 2021 is enhancing the UK skills base, fostering a generation of interdisciplinary researchers skilled to work at the forefront of physical science applied to biomedicine.

‘As a high-risk technologically-focussed institute for biomedical sciences, the Rosalind Franklin Institute has a unique role in the UK’s research ecosystem,’ says Naismith. ‘Our Phase 2 plans will enable the UK to become a global leader in imaging life at molecular detail,’ he adds.