The Cambridge Pharmaceutical Cryo-EM Research Consortium

The Cambridge Pharmaceutical Cryo-EM Research Consortium brings together partners from academia and industry to share access to a Titan Krios™ cryo-transmission electron microscope, an advanced technology used to produce 3D images of complex structures at the near-atomic scale.

Located in the University of Cambridge's Nanoscience Centre, the microscope is used by researchers from the university, the Medical Research Council Laboratory of Molecular Biology (MRC-LMB), and five pharmaceutical companies (Astex Pharmaceuticals, AstraZeneca, GSK, Heptares Therapeutics, and UCB). As part of a three year agreement with this consortia, the company who designed and produced the microscope, FEI, part of Thermo Fisher Scientific, is providing expert guidance on the use of cryo-EM, including sample preparation and data collection services.

Designing effective treatments for disease often requires detailed knowledge of the structure of molecular complexes, such as pathogens or the potential therapeutic targets. Historically, determining these structures has relied on x-ray crystallography and NMR spectroscopy. However, the sample preparation these methods require can affect the conformation of proteins, altering their 3D structure.

"Cryo-EM 3D models allow us to see and understand the workings of protein-based molecular machines that we could not analyze before... The technique was rapidly adopted by leading academic researchers and is now finding its way into early stage discovery and development in the pharmaceutical industry."

Peter Fruhstorfer, vice president and general manager of the Life Sciences business, FEI

The advantage of cryo-EM is that samples can be visualised without the need for chemical fixation or crystallisation, ensuring the shape observed is the true structure of the protein in its native environment.

Multiple cryo-EM images can be integrated together using a software developed by MRC-LMB scientist Sjors Scheres to generate 3D models. This allows researchers to visualise, and so better understand, the structure of complex, dynamic molecular assemblies down to the scale of individual atoms. Cryo-EM has already been used to produce 3D images of viruses, ribosomes, mitochondria, and enzyme complexes, and is informing our understanding of these proteins and their actions in the body.

Through this consortium members are learning how cryo-EM can be used to advance our understanding of key molecular complexes and thus aid the discovery and development of new therapeutic agents across a range of disease areas.

Source: https://www.mrc.ac.uk/news/browse/pioneering-lmb-research-behind-new-cryo-em-consortium/