Structural dynamics of Augmin in the creation of microtubule branches

Supervisory team:
Main supervisor: Prof James Wakefield (University of Exeter)
Second supervisor: Dr Jonathan Phillips (University of Exeter)

Collaborators: Dr Lindsay Cole (Applied Photophysics Limited), Dr May Yong (Alan Turing Institute)

Host institution: University of Exeter (Streatham/St Luke's)

Project description:

Cell division is a fundamental cellular process, requiring the precise nucleation and organisation of protein fibres, microtubules, into a mitotic spindle capable of chromosome segregation. The recent discovery of the conserved protein complex 'Augmin' poses major new questions of how the mitotic microtubule nucleation is controlled in cells in space and time. Augmin is an eight subunit complex responsible for recruiting the major microtubule nucleator, gamma-tubulin, to pre-existing microtubules. The Wakefield lab have recently reconstituted the complex in vitro (1) and made significant advances relating to the structure and topology of Augmin (4) but we are far from understanding how Augmin functions at the molecular level. The Phillips lab, have developed cutting-edge hydrogen/deuterium-exchange mass spectrometry (HDX-MS) approaches, together with new instrumentation and software, precisely to analyse protein structural dynamics. Recently, they have used this to visualise protein-protein interactions in large antibody complexes and to measure protein structure:function changes with millisecond time resolution. (2, 3). Together, the combined expertise of these two labs provide an unparalleled opportunity to construct structural and mathematical models describing the Augmin complex and how its dynamic behaviour relates to its crucial function underpinning cell division.

This PhD project is an opportunity for an ambitious and interdisciplinary scientist to join our team of researchers. The project will fit at the core of the group research activity of both the Phillips and Wakefield groups. The student will be supported and assisted by other members of these groups, including cell biologists, protein engineers and structural mass spectrometry experts. The student will learn hydrogen/deuterium-exchange mass spectrometry, Drosophila husbandry, cell culture, biochemistry, protein chemistry, plus familiarization with several programming languages, mathematical modelling and statistical skills.

The Living Systems Institute is an interdisciplinary home for agile researchers across traditional disciplines. It brings together mathematicians, physicists, cell and molecular biologists, biomedical scientists and engineers. We develop and use a variety of complementary analytical methods and platforms including hydrogen/deuterium-exchange mass spectrometry, cryo-electron microscopy, X-ray crystallography, nanophotonics, super-resolution microscopy and microfluidics, to describe living systems at the nanoscale. The student will be equipped with a rare and highly transferrable set of skills in both structural mass spectrometry of proteins and in vivo cell biology.

1. Tariq et al.,(2020) eLife 9. pii: e49769. 2. Kish et al., (2019) bioRxiv, 1101 3. Dobson et al., (2016) Sci Rep. 6, 38644 4. Chen et al., (2017) Biol Open. 6, 654–663