Unlocking the therapeutic potential of E3 ubiquitin ligases through structure-function studies and Cryo-EM

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Project description

The ubiquitin system is currently regarded as the next source of therapeutic targets. As such, preventing the degradation of essential proteins is an attractive option in age-related disorders such as cancer and neurodegeneration. E3 ubiquitin ligases play a key role in protein ubiquitination, by mediating the transfer of ubiquitin onto protein substrates. Depending on the type of ubiquitin signals added, this can trigger the recognition and degradation of protein substrates by the Ubiquitin-Proteasome System. The HECT (Homologous to E6-AP carboxyl terminus) family of E3 ubiquitin ligases is an exciting source of candidate therapeutic targets, given their Cys-based enzyme activity. However, the limited structural information and biochemical knowledge of these large enzymes has so far hindered their development as novel drug targets, despite mounting evidence for their importance in human health.

In this project, the student will undertake structure-function studies of HECT E3 ubiquitin ligases. The student will be trained in protein expression and purification, ubiquitination assays, biophysical techniques, protein crystallography and state-of-the-art Cryo-EM. An important goal will be to also establish strategies for the expression and purification of full-length HECT E3 enzymes in eukaryotic systems, for Cryo-EM studies and future drug discovery projects. The GW4 Cryo-EM facility has state-of-the- art instruments which represent a unique opportunity for the student to be trained by experts on cutting-edge techniques. This project will also benefit from ongoing international collaboration with experts in proteomics and chemical biology as well as supportive and dynamic research environments at Bath and Bristol.

Applications

Applicants must have obtained, or be about to obtain, a First or Upper Second Class UK Honours degree, or the equivalent qualifications gained outside the UK, in an appropriate area of science or technology such as Biochemistry. Further studies and laboratory experience gained for example through a Master Degree in Structural Biology/Biochemistry would be highly advantageous. We encourage interested applicants to get in touch with Dr Licchesi to discuss suitability for the project prior to submitting a formal application. More details at https://www.findaphd.com/search/ProjectDetails.aspx?PJID=101673

Applications should be submitted on the University of Bath's online application form for a PhD in Biosciences:
https://samis.bath.ac.uk/urd/sits.urd/run/siw_ipp_lgn.login?process=siw_ipp_app&code1=RDUBB-DT01&code2=0003
Please ensure that you quote the supervisor's name and project title in the 'Your research interests' section. You may apply for more than one project if you wish but you should submit a separate personal statement relevant to each one.

Funding Notes

Studentships provide funding for a stipend at the standard UKRI rate (currently £14,777 per annum, 2018/19 rate), research and training costs and UK/EU tuition fees for 4 years. UK and EU applicants who have been residing in the UK since September 2016 will be eligible for a full award; a limited number of studentships may be available to EU applicants who do not meet the residency requirement. Applicants who are classed as Overseas for tuition fee purposes are not eligible for funding.

Deadline: Monday, December 03, 2018