



Development of novel cancer treatments: structural studies of Nectin 4 in complex with bespoke anti-cancer peptides – to start October 2019

Christine Desty Scholarship, fully-funded (Home/EU fees £4630 plus stipend of £15,009) for an MSc by Dissertation (MSD) in the School of Biological Sciences, University of Essex

Scientific background

This project targets the current gap in therapeutic approaches targeting Triple Negative Breast Cancer (TNBC) that, unlike other breast cancer subtypes, lacks recommended chemotherapy treatment. Recent studies suggest that Nectin-4 is a promising target for the treatment of TNBC. Nectin-4 is expressed during foetal development, with expression declining in adult life, and it is re-expressed as a tumour-associated antigen with pro-oncogenic properties in TNBC and other cancers, including Bladder Cancer and Lung Cancer. Thus, Nectin-4 is both a promising new prognostic biomarker and specific therapeutic target for the treatment of TNBC [1].

Studies on patient samples show that Nectin-4 is highly expressed in cancer tissues, but is not detectable in healthy ones. The hypothesis is that targeting Nectin-4 with a peptide conjugated with toxin could provide a novel treatment for TNBC. Novel compounds designed at our collaborators – Bicycle Therapeutics - are targeting Nectin-4 specifically at nanomolar range and can potentially be used as homing devices, having shown success in in vitro cell assays. However their mechanism of action and exact domain tropism is unknown.

Research methodology

In collaboration with Bicycle Therapeutics, we aim to solve the crystal structure of the extracellular domain of Nectin-4 bound to these proprietary cyclic peptides, which will guide further optimisation of the peptide before preclinical and clinical studies.

Training

The student will express and purify recombinant proteins using bacterial expression system. The student will produce protein crystals suitable for investigation using X-Ray crystallography with the aim of solving the structure of the Nectin-4 extracellular domain bound to different bicycle peptides provided by Bicycle Therapeutics.

In addition to hands-on practical research skills at University of Essex, the student will attend the Diamond Light Source BAG training courses and participate in data collection and processing. This project is highly interdisciplinary and involves a high-profile industrial collaboration, plus the student will benefit from an international environment in close contact with two PhD students and two PDRA engaged in related drug discovery projects. Furthermore, if successful, this highly translational research has the potential to lead to a 3-year PhD scholarship.

Entry requirements and application procedures

Candidates should have a background in biochemistry and an interest in structural biology

Applications should be submitted electronically by **24th April 2019** see here for details

<https://www.essex.ac.uk/pgapply/enter.aspx>

You are encouraged to contact the supervisor before application: fprischi@essex.ac.uk and yb16181@essex.ac.uk If you have any queries with the online application process, please contact ecrix@essex.ac.uk

For general information about the School of Biological Sciences at the University please visit our webpages <http://www.essex.ac.uk/bs/>.

The University of Essex

The University of Essex is University of the Year - Times Higher Education (THE) Awards 2018. In the recent Research Excellence Framework 77% of research at the University of Essex research is 'world leading' or 'internationally excellent' (REF 2014). We offer world-class supervision and training opportunities and our research students work at the heart of an internationally-acknowledged and well-connected research community. In the 2013 Postgraduate Research Experience Survey, 84% of respondents said that they were satisfied with the quality of their research degree. At Essex we win awards for our pioneering student support schemes. We are the most recent winners of the prestigious *Times Higher Education* award for Outstanding Support for Students. Essex is a genuine global community. With more than 130 countries represented within our student body, and 40% of our students from overseas, we are one of the most internationally-diverse universities in the UK.