



Call for applications: EASTBIO DTP PhD studentship:

"Targeting transient protein states for the design of chemical probes of Cyclophilins function"

Supervisors: Dr Julien Michel, Prof Alison Hulme, School of Chemistry, and Prof Malcolm Walkinshaw, School of Biological Sciences, University of Edinburgh.

We are looking for outstanding students with a passion for research at the interface of chemistry and biology for a **fully funded 4-year EASTBIO PhD studentship** (fees and stipend at the standard rate). The project is available **from September 2018** for candidates that satisfy **BBSRC studentship eligibility requirements** (see <http://www.eastscotbioldtp.ac.uk/> if you are unsure).

The main objective of this PhD project is to contribute to the development of novel chemical probes of Cyclophilins function using a range of state-of the art methodologies from chemical, structural and computational biology. Inhibition of diverse Cyclophilin isoforms could pave the way for novel therapeutic treatments in immunosuppression, neuroprotection/degeneration or viral diseases. Yet drug development efforts have been limited historically due to the challenge of selectively inhibiting a given Cyclophilin isoform.

Our laboratories have a long-standing interest in the use of biophysical, chemical, and computational methods to discover novel Cyclophilin ligands. In this PhD project you will build on our previous and current body of work and pursue Cyclophilin inhibition by exploiting protein dynamics to reveal 'transient protein states' that are not apparent in structures readily solved by X-ray crystallography experiments. We have developed a methodology to detect such transient protein states via an integrative structural biology approach that combines X-ray crystallography and protein NMR measurements with molecular dynamics simulations to deliver dynamical models of Cyclophilins. Models analysis informs the rational design of small molecules to selectively bind and stabilize such transient states. Such small molecules are selected from existing libraries, or synthesized and assayed for binding and functional behaviour using NMR and isothermal titration calorimetry experiments. Through targeting a transient protein state that is unique to a given Cyclophilin isoform, you will identify small molecules with high sub-type selectivity.

The ideal applicant will have a strong academic record, a BSc or MChem/MSc degree in Chemistry, Biochemistry or related fields, and previous research experience in structural, chemical or computational biology. The ideal candidate will also demonstrate keen interest in molecular recognition, enthusiasm for multidisciplinary research, and a passion for improving human health with small-molecules.

To apply, please send initially a cover letter and CV to julien.michel@ed.ac.uk. Informal enquiries are encouraged **as soon as possible**. Shortlisted candidates will be invited to apply formally to the EASTBIO DTP. Candidates should make initial contact by May 3rd 2018 **at the latest**. Late applications may not be considered.

For further information please visit:

<http://www.julienmichel.net/>

<http://www.wcb.ed.ac.uk/research/walkinshaw>

<https://hulmegroup.wordpress.com/>