University of Essex

Biological Sciences at the University of Essex

A FULLY-FUNDED 3 YEAR PHD SCHOLARSHIP IS AVAILABLE FROM OCTOBER 2018

Structure-function relations of non-symbiotic plant hemoglobins and their role in stress response mechanisms.

Background:
Over the past couple of decades, several new classes of hemoglobin have been discovered that are appear not to bind oxygen as their main function. The physiological functions of these metalloproteins are largely unknown, unlike their well characterised oxygen-carrying cousins. Plants have three classes of the non-symbiotic hemoglobins (nsHbs). Each class of nsHb has distinct structural and biochemical properties likely relating to a diverse array of physiological roles, all related to their ability to act as redox active enzymes (1). Evidence suggests that class 1 nsHbs are related to nitric oxide regulation. Overexpressing class 2 nsHbs show enhanced survival to hypoxic stress and has been shown to promote the accumulation of polyunsaturated lipids in seeds. Combined class 1 and class 2 silencing leads to seedling death. Class 3 nsHbs (often referred to as the truncated Hbs) appear to be ubiquitous in plants, however very little is known about their cellular role. The first crystal structure of this class of protein from *Arabidopsis thaliana* was recently discovered at Essex (2).

Aims:
The aim of this interdisciplinary collaboration between the PSF and PPG groups is to gain a clearer understanding of the mechanisms and roles of these proteins in cell signalling and stress response. It is the intention that this research will identify novel targets for treatments of disease or plant productivity enhancement as a platform for future funding (e.g. BBSRC/Leverhulme) and the progression from model systems (*A. thaliana*) to agriculturally relevant crops (e.*g.* oil seed rape, wheat, and grain legumes*)*. The project will also foster the current collaboration with colleagues in Lund, Sweden working on nsHbs from sugar beet (*Beta vulgaris*).

Objectives:
1. To investigate the function of the three classes of nsHbs and their role in stress response and cell signalling. Proteins are generated recombinantly will be studied using a variety of spectroscopic and spectrokinetic techniques including rapid reaction kinetics (stopped-flow, laser flash spectroscopy), EPR and crystallographic structural studies of these proteins. Studies will focus on putative biological reactions with molecules such as nitric oxide, nitrite, H_2O_2 and lipid peroxidation.
2. To design and generate site-directed mutants to examine factors that affect the redox-reactions of the protein with substrates relating to potential physiological functions (e.g. distal histidine mutants to effect reactions with nitric oxide, nitrite, H_2O_2) or key structural residues such as the N terminal extension that constitutes the dimeric interface of class 3 proteins (2).
3. To examine the role of nsHbs in plant stress signalling we will generate knockout lines (single and double mutants in different combinations) using RNAi and/or CRISPR technology. A range of stress responses will be tested (pathogens and abiotic stress) assessing stress progression such as the production of ROS, lipid peroxidation, protein oxidation and antioxidant defences.

References:

1) Reeder, B.J. “The redox activity of hemoglobins: From physiological functions to pathologic mechanisms.” Antioxid. Redox. Sign. (2010) 13(7) 1087-1123
2) Reeder B.J., Hough M.A. “The crystal structure of class 3 non-symbiotic plant hemoglobin from Arabidopsis thaliana reveals a novel N-terminal helical extension” *Acta Cryst.* (2014) D70, 1411-1418

Entry requirements and application procedures
Informal queries may be addressed in the first instance to Dr Brandon Reeder reedb@essex.ac.uk or Dr Uli Bechtold ubech@essex.ac.uk Applications should be submitted electronically by **28th February 2018.** See https://www.essex.ac.uk/pgapply/enter.aspx for details. The intended start date for this 3-year, fully-funded PhD studentship is 4th October 2018. This scholarship will be to the value of £12,500 per annum plus UK/EU tuition fees.

Please note: International students need to have additional funding to cover the difference in tuition fees which is £11,815.00, evidence will be requested that you have these additional funds.

Applicants should write 500 words explaining why they are interested in this project and submit this with their CV.

This scholarship is generously supported by a bequest from the estate of Professor Peter Nicholls (https://www.theguardian.com/theguardian/2014/dec/30/peter-nicholls-obituary**)**

The University of Essex
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.