

PhD Studentship

Supervisors: Dr Filippo Prischi and Dr Greg Brooke

Characterisation of RSK Isoforms in Cancer Proliferation and Metastasis.

30% of all human cancers feature upregulated MAPK signalling (including lung, breast, colorectal, pancreatic cancer and melanoma). Despite the promise of novel treatments targeting the MAPK pathway, the majority of patients ultimately develop therapy resistance. As such, there is a growing need for novel therapeutic strategies that can prevent and/or overcome therapy resistance. The p90 ribosomal S6 kinase (RSKs) protein family holds promise as a novel therapeutic target. In fact, RSKs are the very downstream effectors of the MAPK pathway and are implicated in cell proliferation, survival, migration, and invasion. Loss of RSK regulation can lead to tumorigenesis, cardiac disease, and incorrect neuronal development. RSKs are an important family of serine/threonine kinases composed of four isoforms: RSK1/2/3/4. Studies on samples from lung cancer patients have shown that RSK1 levels are reduced compared to non-tumorigenic samples, while the amount of RSK4 is increased. Although the connections between RSKs and cancer are established, there is very little information on the different roles the four members of the RSK family have in cancer.

A major limitation on previous studies has been a restricted single protein focused approach. This PhD project will be the first comprehensive and comparative study on RSK1-4, which have different roles in cancer. In order to design novel RSK isoform selective drugs, it is vital to understand differences among the RSK family members and exploit them for the development of novel therapeutic treatments. In particular the successful candidate will characterise the different activation mechanisms of the four RSK isoforms, solve their structures and validate the roles of cations on enzymatic activities. Using a range of biophysical, biochemical and cellular techniques the aim of this project is to advance our knowledge in RSK signaling pathways, in relation to cancer progression and metastasis.

This project is highly interdisciplinary and the successful candidate will develop skills in recombinant protein expression, protein purification, structural biology (SAXS, X-RAY), cellular and biochemical characterisation (cell culture, transfections, proliferations assays, cell motility assays, MST, fluorescence spectroscopy and SPR). In addition to hands-on practical research skills, generic professional skills development will be supported internally via Proficio, the innovative professional development scheme available at University of Essex, or externally via Diamond Light Source, CCP4 and BAC training courses. The PhD student will acquire a set of skills that will strengthen his/her future career and contribute to the UK's pool of highly trained researchers for academia and industry.

The studentship offers a stipend of £12,500 per annum (tax free) and covers fees at the UK/EU student rate (£4,410) for a period of three years. Applications should be submitted electronically by **28th of February**, see [here](#) for details, with shortlisted candidates invited for interview shortly after. For general information about the School of Biological Sciences at the University click [here](#).

Entry requirements and application procedures

Informal queries may be addressed in the first instance to Dr **Filippo Prischi**, email fprischi@essex.ac.uk +44 1206 873326

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.