**Exploring the role of human cytoglobin in cancer therapy resistance – 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**

A series of new haemoglobins have been discovered over the past 20 years including a ubiquitously expressed vertebrate protein, cytoglobin. Although with a similar structure to the well characterised blood haemoglobin, this globin does not function as a classical oxygen carrier. Thus the physiological functions of this protein remain largely unknown. However, there has been a realisation of the importance of cytoglobin in the mechanism of cancer development and cancer therapy resistance. For example, cytoglobin-deficient mice have been found to have increased risk of cancer development in the lungs and liver when exposed to carcinogens[1]. Additionally, increased expression of cytoglobin correlates with a tumour's agressiveness[2] and could potentially be a new biomarker for cancer. Therefore, we wish to study the mechanism of how cytoglobin protects tumours and in doing so identify potential new targets against cancer therapy resistance.

We have previously investigated the various potential physiological and pathological roles of human cytoglobin through *in vitro* biochemical techniques[3,4]. We are now in a position to utilize our understanding of the biochemistry of cytoglobin to assess its role in cytoprotection under various stress conditions such as hypoxia, oxidative stress and nitrative stress and to investigate its role in cell signalling.

The aims of this studentship are to explore the characteristics of human cytoglobin and how these may relate to protection of cells against stress mechanisms within the cell and hence give valuable new insights into the role of cytoglobin in cancer therapy resistance. The project involves generation and study of cytoglobin and specific mutations in cancer cell lines through CRISPR/Cas9 gene editing, transient expression, stably transfected cell lines, and gene silencing. In this way known key functional amino acids of cytoglobin will be targeted and changes in the reactivity of the protein will be mapped to changes in cell stress response. In addition, *in situ* techniques will be used to correlate changes in the cell redox environment to changes in protein redox state.

References:


1. Thuy *et al*. *"*Cytoglobin deficiency promotes liver cancer development from hepatosteatosis through activation of the oxidative stress pathway" *Am. J. Pathol.*(2015) 185, 1045-60
2. Shaw *et al*. "Cytoglobin is upregulated by tumour hypoxia and silenced by promoter hypermethylation in head and neck cancer" *Br. J. Cancer* (2009), 101, 139-144
3. Beckerson *et al.* "Cytoglobin ligand binding regulated by changing haem-co-ordination in response to intramolecular disulfide bond formation and lipid interaction" *Biochem. J.* 465, 127-137
4. Reeder and Ukeri, "Strong modulation of nitrite reductase activity of cytoglobin by disulfide bond oxidation: Implications for nitric oxide homeostasis" *Nitric Oxide* (2018), 72, 16-23.

**Entry requirements and application procedures**
Highly motivated applicants with, or expecting, a good degree in the broad area of Life Sciences are encouraged to apply.
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: reedb@essex.ac.uk and gbrooke@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/.

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