



Institute of Technology

Ciência sem Fronteiras / Science Without Borders

Postgraduate Project Template

Institution:	Dundalk Institute of Technology
Title of Postgraduate Opportunity: (include level of study)	PhD Project entitled: Identifying the molecular determinant of the pacemaker current in urethral interstitial cells of Cajal.
PI Name & Contact Details:	Dr Gerard P. Sergeant Principal Investigator Smooth Muscle Research Centre Dundalk, Co. Louth gerard.sergeant@dkit.ie
Department/School:	Nursing and Science
Research Centre /Group:	Smooth Muscle Research Centre
Research Centre/Group website:	www.smoothmusclegroup.org www.icbc.ie
Brief Summary of PI research / research group /centre activity <p>The multidisciplinary Smooth Muscle Research Centre is a centre of excellence in pure & applied research capable of exploiting opportunities in life sciences. The commercialisation arm of our Centre (the Ion Channel Biotechnology Centre) uses a combination of physiology, pharmacology, molecular biology, electrophysiology and synthetic organic chemistry to focus on commercializing the results of our academic research in the Smooth Muscle Research Centre into a number of disease states including urinary incontinence, erectile dysfunction, lymphoedema, and asthma. The research involves the use of a large number of techniques which are commonly used in R&D departments of the pharmaceutical industry and include single cell and single channel patch clamping, in vitro intracellular recording from whole tissue with sharp microelectrodes, ultra high speed live cell confocal Ca²⁺ imaging, molecular biology, synthetic chemistry, ion channel cloning and mutagenesis, tissue culture and tension recording. Our state of the art laboratories are equipped with dedicated facilities to permit the study of biological processes from the molecular level through to the whole tissue. The SMRC staff were recruited from the Physiology Department, Queens University of Belfast and comprise 4 PIs (Prof Noel McHale, Dr Keith Thornbury, Dr Gerard Sergeant and Dr Mark Hollywood), 5 postdoctoral fellows and 6 PhD students. The PI's bring considerable expertise as evidenced by their publications (100 peer-reviewed papers 1998-2008) and grant income (€7.5 million 2005-2012) from NIH, Wellcome Trust, Science Foundation Ireland, Health Research Board and Enterprise Ireland. We are the only Centre in Ireland to have received NIH funding independently of US investigator involvement. The team also consists of 5 postdoctoral fellows and 6 PhD students.</p>	
Brief Description of PhD Project <p>Urinary incontinence (UI) is a distressing condition that seriously influences the physical, psychological and social wellbeing of affected individuals and has considerable resource implications for national</p>	

health services. In healthy individuals this condition is prevented by the ability of the urethra (the bladder outlet tube) to generate sustained contractions which prevent unwanted leakage of urine from the bladder. These contractions are known to be stimulated by activation of Ca^{2+} -activated chloride channels (CACCs) in specialized pacemaker cells in the urethra termed interstitial cells of Cajal (ICC). Recent studies of CACCs in other tissues suggest that they are encoded by a protein called ANO1. However, preliminary data suggests that urethral CACCs are not mediated by ANO1, but rather a novel channel, which has yet to be determined at the molecular level. This is an exciting finding as it offers the prospect for unique and tissue specific drug treatments for UI. This is an important development as pharmacological therapies for UI are currently lacking, meaning that the condition is often managed through use of absorbent pads and catheters rather than treating the underlying cause. In this study we will undertake a detailed molecular, biophysical and pharmacological characterization of CACCs in the urethra to ascertain their molecular identity.

Objective 1 (WP1): To perform detailed molecular analyses of the expression of the ANO family in urethral smooth muscle (rabbit and mice).

Objective 2 (WP2): To determine the cellular expression of ANO1 proteins in urethral smooth

Objective 3 (WP3). To perform a full pharmacological characterisation of IClCa in native urethral ICC (rabbit) and in a heterologous cell line, such as HEK-293 cells, stably expressing ANO1 which has been cloned from the rabbit urethra.

Objective 4 (WP4). To utilize transgenic mice from Professor Wards lab in which ANO1 has been 'knocked out'.

Key Attributes of Project for Brazilian Postgraduate Students

This project will allow the student to work in a dynamic, multidisciplinary environment with a world class team of scientists. Students will be exposed to a range of techniques and receive full training in ion channels, electrophysiology and Ca^{2+} imaging. The successful applicant will also enrol in our 4 Year Structured PhD programme run in collaboration in RCSI, DCU, NUIM & DkIT (BioAnalysis and Therapeutics Programme funded by PRTL V). This work should appeal to students who wish to gain a thorough understanding of ion channel function in health and how they can be targeted in disease. The student will focus on elucidating the molecular identity of the Cl^- current in novel pacemaking cells. In addition, the student will have the opportunity to spend time in the laboratory of Professor Sean Ward (University of Nevada) to study urethral function in genetically modified mice which lack ANO1 channels. Since this work will be carried out in collaboration with the commercialisation arm of the Smooth Muscle Research Centre, the Ion Channel Biotechnology Centre at DkIT, the student will be exposed to our many interactions with industry. In summary, this project will provide a valuable training opportunity in electrophysiology, ion channel cloning and mutagenesis and Ca^{2+} imaging for a new PhD student, whose skills are likely to be in high demand in the pharmaceutical industry and academia.

Name and contact details for project queries, if different from PI named above:

Please indicate graduate disciplines which are eligible for application:

B.Sc (Hons, 2:1 or higher) in Physiology, Biochemistry, Biomedical Science, BioPhysics or related disciplines.

Alignment with Science Without Borders Priority Areas:

Please indicate the specific programme priority area under which the proposed postgraduate project fits – choose only one (tick box)

Engineering and other technological areas	
Pure and Natural Sciences (e.g. mathematics, physics, chemistry)	
Health and Biomedical Sciences	X
Information and Communication Technologies (ICTs)	
Aerospace	

Pharmaceuticals	
Oil, Gas and Coal	
Renewable Energy	
Minerals	
Biotechnology	
Nanotechnology and New Materials	
Technology of prevention and remediation of natural disasters	
Biodiversity and Bioprospection	
Marine Sciences	
Creative Industry	
New technologies in constructive engineering	