JSPS Core-to-Core Programme

Project title: Novel ion channels in the sarcoplasmic reticulum

Project Duration: April 2012 to Mar 2017
Japanese Lead Scientist: Prof Hiroshi Takeshima, School of Pharmaceutical Sciences and Medicine, Kyoto University, Japan
UK Counterpart: Prof Rebecca Sitsapesan, Department of Pharmacology, University of Oxford, UK.

Description of Project
All mammalian cells contain a store of intracellular Ca^{2+} within the endoplasmic or sarcoplasmic reticulum (ER/SR). Ca^{2+} is released through specialised Ca^{2+}-release channels and provides the signals that initiate and regulate many different types of process within each cell. These processes include muscle contraction, neuron firing, fertilisation and hormone release. This collaboration arose as a result of mutual interest in this field. The Takeshima group have identified two types of novel ion channel on ER/SR membranes that support the process of intracellular Ca^{2+} release; specifically Mitsugumin 23 (MG23) and Trimeric Intracellular Cation (TRIC) channels. The Sitsapesan group collaborate to characterise the biophysical properties of these proteins and together we aim to identify their physiological roles and understand their involvement in the cardiovascular disease, osteogenesis imperfecta and cancer.

Departments and Institutions involved
School of Pharmaceutical Sciences and Medicine, Kyoto University, Japan
April 2012 – August 2013: Department of Physiology & Pharmacology, University of Bristol, UK.
September 2013 onwards: Department of Pharmacology, University of Oxford, UK.

Funding
The Kyoto-Bristol/Oxford collaboration funded travel/accommodation (3 trips) for Prof Takeshima and PhD student, Tsunaki Iida, to visit the Sitsapesan lab. This enabled discussions between the two groups, the initiation of experiments and longer term research planning. Prof Takeshima brought many biological tools including new cell lines, purified wild type and mutant proteins and selective antibodies. On three separate occasions, Tsunaki Iida worked for several weeks in the UK, teaching the Bristol/Oxford lab the required molecular/cellular techniques and learning new electrophysiological/biophysical techniques himself.

How the matching funds were sourced and used.
Grants from the British Heart Foundation (BHF) to the Sitsapesan lab and set-up funding from the Department of Pharmacology, Oxford funded all biophysical experiments. In addition, Dr Elisa Venturi (Oxford lab) obtained a JSPS Postdoctoral Fellowship to allow her to work for 3 months (October 2015-January 2016) in the Takeshima lab to learn new molecular biological and single-cell Ca2+ imaging techniques to advance progress in both Oxford and Japan.

Benefits and collaborative outcomes
Funding has provided a unique opportunity to combine the very different research skills and expertise of the Japan and UK labs that was necessary to identify the functional properties and roles of MG23 and TRIC channels. Many high impact publications have resulted. New ideas for further experimentation and grant applications have been developed. The collaboration spawned the topics for 4 PhD theses (already graduated: Tsunaki Iida, Elisa Venturi, Fiona O'Brien; to be submitted: David Eberhardt). The work led to a symposium at the international Physiology 2014 Meeting in London

sponsored by the Journal of Physiology 'A new look at structures and mechanisms regulating endoplasmic/sarcoplasmic reticulum Ca^{2+}-release in health and disease' and to several invitations to Profs Takeshima and Sitsapesan to speak at Gordon Conference Meetings.

Further applications

To develop our collaborative Oxford/Kyoto studies, our group members continue making grant applications to the BHF, JSPS and other agencies.