Short report – JSPS Summer Programme 2017

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Host: Prof. Hiroshi Takeshima, Kyoto University

During the JSPS Summer Programme 2017 I was able to spend 2 months in the laboratory of Professor Takeshima, at Kyoto University Graduate School of Pharmaceutical Sciences. My current research explores molecular mechanisms that underlie disrupted intracellular calcium dynamics observed in heart failure.

Damaging changes to Ca^{2+}-homeostasis occur as a result of increased spontaneous Ca^{2+}-spark frequency and dysregulated Ca^{2+}-handling within cardiomyocytes. This leads to decreased systolic contraction, unwanted irregular contractile activity and cardiomyocyte death. Accumulation of intracellular Ca^{2+} is a characteristic feature of ischaemia/reperfusion thought to result from spontaneous Ca^{2+} release from the sarcoplasmic reticulum (SR).

Mitsugumin 23 (MG23) is a newly identified SR ion-channel that displays Ca^{2+}-handling properties, challenging the idea that the cardiac ryanodine receptor is the only ion-channel responsible for SR Ca^{2+}-release. My current research suggests that MG23 plays a key role in diastolic Ca^{2+}-leak resulting in dysregulated Ca^{2+}-homeostasis (Reilly-O'Donnell et. Al 2017).

The major hypothesis underlying the proposed research was that MG23 plays a limited role in normal SR Ca^{2+}-release but during an ischaemic event, the function of MG23 is altered resulting in aberrant Ca^{2+}-dynamics, impaired contractility and cardiomyocyte death. To understand the role of MG23 in regulating cardiac function, the aim of the summer project was to establish the role of MG23 in shaping cellular Ca^{2+}-dynamics and cardiac contractility.

My preliminary data obtained during the programme suggest that both Ca^{2+} and Zn^{2+}-handling differ between WT and MG23-KO cardiomyocytes exposed to ischaemia. Therefore, MG23 may play an important role in sarcoplasmic reticulum Ca^{2+}-leak and cardiomyocyte cell death under ischaemic conditions. Future collaboration with Prof. Takeshima's Lab will aim to further understand the role of MG23 in these processes and may highlight MG23 as a potential therapeutic target in the treatment of ischaemic heart disease.

The JSPS summer programme provided me with the wonderful opportunity to experience life in Japan. To work in the laboratory of Prof. Takeshima was extremely valuable and inspiring, and I hope to continue this fruitful collaboration. I was able to visit many of the beautiful temples and sights around Kyoto, which further added to my very enjoyable time in Japan.

Reference: Reilly-O'Donnell et Al. (2017) JBC: 292, 13361-73.

Picture 1: Professor Hiroshi Takeshima overlooking my lab work

Picture 2: Gion Matsuri Festival, Kyoto