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ESC council

22th March 2017

ESC First Initiative Contact Grant Report

Dear Council Members,

I would like to express my great thanks to the European Society of Cardiology and the Council on Basic Cardiovascular Science for their generous award of the ESC First Contact Initiative Grant. This gave me the opportunity to visit the Laboratory of Professor Godfrey Smith at the Institute of Cardiovascular and Medical Sciences of the University of Glasgow from 18th to 30th January 2016.

Godfrey Smith's Lab is a well-known laboratory for cardiac arrhythmia research and in particular the lab is experienced in Voltage- and Calcium imaging of the intact heart of mice, guinea pigs and rabbits, a technique which I had no experience in prior to my visit. Excitingly, one of the teams in Glasgow including Dr. Allen Kelly has recently established 2-photon-voltage imaging of the intact heart enabling voltage-recordings from discrete layers up to 500 µm deep within the myocardial wall (Kelly et al., Circ. Arrhythm. Electrophysiol. 2013, Ghouri et al., J. of Biophotonics 2015) and are thus one of the few groups worldwide to be able to make such measurements.

My interest in cardiac electrophysiology was triggered in 2008 when I started my MD thesis in the lab of Jun.-Prof. Philipp Sasse at the Institute of Physiology I of the University of Bonn establishing optogenetic stimulation of cardiomyocytes and intact hearts of transgenic mice expressing the light-gated cation channel Channelrhodopsin2 (ChR2, Bruegmann et al., Nat. Methods 2010). Ever since then, I have focused my research on this specific field. There is increasing interest in the new possibilities optogenetic stimulation permits for the investigation of cardiac arrhythmias.

In contrast to electrical stimulation, optogenetic stimulation allows selective de- and hyper-polarization, which can be prolonged without temporal limitation. For example, we show that continuous illumination induces sustained depolarization which can be used to impair the excitability of cardiomyocyte monolayers and defibrillate ventricular tachycardia and fibrillation in the intact heart (Bruegmann et al., J. Clin. Invest. 2016). The aim of my visit to Glasgow was to explore how optogenetic stimulation could be

performed simultaneously with optical imaging of the voltage and calcium signals in the intact heart to allow better understanding of the technique and cardiac electrophysiology.

Towards this aim, transgenic mice expressing ChR2 in fusion to EYFP in the cardiomyocytes were shipped to Glasgow and blue LEDs (470 nm) integrated into the voltage imaging set up for the experiments. The first experiments were performed to investigate the extend that the illumination for ChR2stimulation interferes with the signal of the imaging dyes due to enhanced autofluorescence and the signal of EYFP and we are currently optimizing the set up to minimize this problem. So far, we developed already prototype hardware and a first software tool to allow analyzing the traces cleaned from this additional noise.

During my stay, I worked directly with Dr. Allen Kelly and I would like to take the opportunity to express my gratitude for all the effort he made for this project during my stay and afterwards. It was a great experience to work with him and all other team members of the laboratory who were all extremely friendly and helpful during the whole stay. I learned a lot from all scientific discussions besides and within the group meetings and enjoyed the whole stay a lot.

Importantly, this visit laid out the basis for a new collaboration between our Labs in Glasgow and Bonn to use this new approach to gain new insights into cardiac electrophysiology and arrhythmias and I am looking forward to the first results when the technique will be completely established.

Yours sincerely,

Dr. med. Tobias Brügmann

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