physiology

VU medisch centrum

European Society of Cardiology
The European Heart House
2035 Route des Colles - Les Templiers
06903 Sophia Antipolis
FRANCE

ESC First Contact Initiative Grant report

Amsterdam, 16th March 2015

First of al, I would like to extend my gratitude towards the European Society of Cardiology council for providing me with the opportunity to visit and perform experiments at the National Institute of Health (NIH) in Bethesda, Maryland. The First Contact Initiative Grant allowed me to spend one month at the lab of Dr Robert Balaban.

The aim of my visit was to perform experiments and establish collaboration between our respective institutes. Specifically, my goals were 1) Exchange of expertise and discussing ongoing projects at each institute; 2) test compatibility of my Amsterdam setup with the NIH spectroscopy setup and if so, 3) perform experiments on isolated cardiac trabeculae. Thanks to your support, I managed to realize all these goals.

My main research interest is the adaptation of cardiac mitochondrial function upon rapid changes in workload in health and cardiac failure. I developed a novel imaging technique, where I assess changes in NADH and FAD autofluorescence upon rapid changes in workload in intact rat cardiac trabeculae. In heart failure I observed a mismatch between energy utilization and mitochondrial ATP production upon rapid changes in cardiac workload, mainly caused by mitochondrial complex I dysfunction and changes in mitochondrial calcium kinetics.

At NIH, the group of Dr Balaban is world-leader on the regulation of mitochondrial function upon changes in workload and has published numerous articles in high-impact factor journals, including Nature and Science. Their state-of-the-art spectrometry setup is able to detect very small changes in redox state and internal conductance of the mitochondrial respiratory chain. Up to now, it has only been possible to assess these variables in isolated mitochondria, such that it remains unknown how the redox status changes with workload in an intact preparation. With this ESC grant, I wanted to investigate whether meaningful spectra from contracting strips of cardiac tissue could be collected. This would provide additional information on mitochondrial function *in vivo*, as well as open a whole new

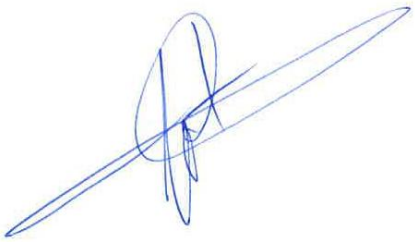
avenue for future research into the regulation of mitochondrial function in health and disease.

During my visit at NIH, I have been very lucky to receive the best possible technical assistance from support and scientific staff, including software engineers, technicians, people from the animal facility, staff members, post-docs and PhD students. After a week of optimization, we were all thrilled to see that both experimental setups were compatible In fact, the signal-to-noise ratio of the spectra from my trabeculae setup was so good that we could start collecting data for a publication. In the subsequent weeks I collected as much data as possible, despite the many snow days in Washington. Both a PhD student from National Institute of Health and myself are currently analyzing the data. The aim is to use the collected data for a collaborative publication, combining the strengths from both research groups.

Besides performing experiments in the lab, I was also able to discuss our respective projects intensively and develop interesting new ideas for future (collaborative) studies. I want to thank Dr Robert Balaban and his team for their great support during my stay. Without this, I would not have succeeded in realizing the goals of this visit.

Altogether, the visit was extremely useful and I established the beginning of a successful collaboration between the National Institute of Health in Bethesda and the VU University Medical Center Amsterdam. Your support is greatly appreciated.

Yours sincerely,



Dr Rob C.I. Wüst

Department of Physiology
Institute for Cardiovascular Research
VU University Medical Center, Amsterdam
The Netherlands