To:
European Society of Cardiology
The European Heart House
Councils Relation – Specialty Centre
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ESC First Contact Initiative Grant report

First of all, I would to express my gratitude to the ESC and the ESC council on Basic Cardiovascular Science for giving me the opportunity to learn at two institutes abroad, the Clinical Pharmacology Unit (CPU) and Mitochondria Biological Unit (MBU) at the University of Cambridge, UK; and the Department of Cardiovascular Medicine, at the University of Oxford, UK. Therefore, I will split this report into two parts.

University of Cambridge, Cambridge, UK

I visited the CPU and MBU of the University of Cambridge, which is supervised by Dr. Thomas Krieg and Dr. Michael P Murphy, respectively. The research profile of this lab focuses on the cardioprotection effects of different agents in ischemic heart diseases and the exact role of mitochondria in this case. MBU unit invented not only several probe to detect mitochondria specific hydrogen peroxide, namely mitoB, mitoP, but also mitoQ, mitochondria-targeted antioxidant, which is already available in the market and showed a successful implementation of molecular biology into clinical medicine.

In our previous study, we observed that the modulation of endothelial nitric oxide synthase (eNOS) with folic acid (FA) in several etiology of heart failure has a positive outcome. However, we still have a big question on the exact role of the mitochondria, as the major source of reactive oxygen species (ROS), or the effect of FA to mitochondria in this mechanism. Moreover, due to the very short half-life of ROS, it is very difficult to measure direct ROS *in vivo*. The MBU discovered a method for assessing changes in hydrogen peroxide specifically within the mitochondrial matrix of living animals using the mitochondria-targeted

ratiometric mass spectrometry probe, mitoB and mitoP. I performed the extraction for mitoB/mitoP measurement in myocardial infarction experiment, and with further collaborations, I am able to implement it in my home institution.

University of Oxford, Oxford, UK

My visit to the Wellcome Trust Centre for Human Genetics and John Radcliffe Hospital, Department of Cardiovascular Medicine in the UK under the supervision of Dr. Charalambos Antoniades has given me a great opportunity to gather knowledge in many different aspects and build up a network. Another research question in our project is the exact mechanism of FA in NOS modulation. FA has a similar moiety with tetrahydrobiopterin (BH4), the NOS co-factor, and to unravel the mechanism of FA, it is necessary to investigate the status of BH4. I got acquainted with several molecular techniques, such as BH4/BH2 measurement, GTP cyclohydrolase- and NOS activity, dyhdroethidium-derived oxidation, which all are necessary for completing the scheme and have never been done in our lab. With this experience, I will be able to measure these techniques at my current institution, not only for my project, but also for others in our group, and I believe it will give me a lot of new insight in the interaction between FA, NOS and heart failure.

This ESC FCIG enabled future collaboration and projects between labs, creating a cross-sectional, even interdisciplinary network within Europe. This grant has allowed me to conduct extensive and fruitful discussions about cardiovascular oxidative stress with Dr. Thomas Krieg, Dr. Charalambos Antoniades and their team members. My stay in Cambridge and Oxford has been very educative and provided me with plenty of insight for our experiments. I can generate a lot of new data and collect 'the missing pieces' for our projects. In addition, it has been an extremely valuable opportunity to be able to do research in a state-of-the-art lab. This visit allowed me to discuss the next step of my career personally, which would not have happened if I didn't receive this grant. I also received the opportunity to give a presentation which was attended by people from many

different fields. The results and extensive discussions presented me with a lot of feedback and generated a number of ideas for my current project

Furthermore, I would like to thank Dr. Thomas Krieg, Dr. Michael P Murphy, Dr. Carmen Menther and Dr. Edward T Chouchani, from the University of Cambridge; Dr. Charalambos Antoniades, Prof. Dr. Keith M Channon, Dr. Alexios S Antonopoulos, Dr. Mark J Crabtree, Ashley B Hale, Dr. Raja Jayaram, Dr. Xing Liu and Dr. Svetlana Reilly from the Department Cardiovascular Medicine Oxford, for their warm hospitality and for tutoring me during my visit.

This award was used for visa expenses, transportation and accommodation in Cambridge and Oxford. In summary, the concept of ESC FCIG turned out to be highly successful and this grant is very beneficial not only for my scientific development, but also for the next step in my career in basic science and cardiology.

Yours Sincerely,

Yanti Octavia, MD, MSc