UMR INSERM 1060 / Université Lyon 1/ INRA 1235/ INSA de Lyon

CarMeN

«**Car**diovasculaire, **M**étabolisme, Diab**é**tologie et **N**utrition »

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Aim: Report for the ESC First Contact Initiative Grant.

Dear Council Members,

First, I would like to thank you for awarding me the ESC First Contact Initiative Grant in autumn 2012 which has been essential for deeper understanding of my current research, as well as my career development. The grant gave me the opportunity to visit and collaborate with the laboratory of Pr Gyorgy Hajnoczky at Thomas Jefferson University (Philadelphia, USA) in November 2012. During my stay, I discussed the data of my current research with all the members of the team, I had the opportunity to discover their techniques and goals but also to take part in a larger meeting between labs whose research is focused on mitochondria. Furthermore, at the end of my visit, we had taken the decision that I will join his group for a postdoctoral fellowship.

In the team 5 « Cardioprotection » of CarMeN which is a biomedical research laboratory in cardiovascular diseases, metabolism, diabetology and nutrition, my research goal is to understand the mechanisms of cardiomyocyte death during ischemia-reperfusion in order to develop new cardioprotective strategies. More precisely, my last PhD work is focused on the IP3-receptor Ca^{2+} channeling complex located at the reticulum-mitochondria interface and its role during myocardial infarction and thus cardioprotection. Some partners of the complex has been recently identified, including the chaperone Grp75 and the porin VDAC. However, we postulate that other regulatory partners could be involved in this Ca^{2+} channeling complex. Pr Hajnoczky research is focused on the sarcoplasmic reticulum-mitochondria physical and functional coupling for the regulation of local and direct calcium exchanges between the two organelles, notably in the heart under both physiologic and pathologic conditions. In this context, they recently demonstrated that hypoxia-reoxygenation

inhibits mitochondrial fusion, highlighting a crucial role for mitochondrial dynamics during myocardial infarction. Thus, presenting my data to his team was of great help to improve my study at the level of Ca^{2+} signaling notably. Indeed, after discussions on my results, they proposed me new targets involved in the Ca^{2+} channeling complex but also further experiments to perform to complete my analysis. Moreover, I became acquainted with all the lab members discussing on their projects and my current knowledge on a more physiological background led to enriching discussions and opened potential collaborations between our two labs.

I was also able to observe most of their imaging techniques, notably for the study of in live mitochondrial dynamics but also calcium fluxes by fluorescence microscopy using probes specific to each compartment. It included genetically targeted fluorescent proteins of different colors, which allow simultaneous calcium measurements in multiple organelles. Furthermore, they introduced to me their powerful molecular toolkit for quantification and perturbation of the SR-mitochondrial interface using synthetic interorganellar linkers that they had recently established. This unique toolkit is recognized as one of the most powerful means to the study of local signaling. So, it gave me a great overview of the different techniques used for the study of Ca^{2+} signaling.

Finally, I was able to attend a “mitochondrial circle meeting” which regroups different labs in Philadelphia with a common research goal on mitochondria. It was of great interest since I was involved in interesting discussions on mitochondrial dynamics and interactions with reticulum in other pathologies.

Thus, my visit to Pr Hajnoczky lab was a very enriching experience since it helps me to broaden and to improve my studies but also to create a collaborative network. Moreover, the very high rank lab of Pr Hajnoczky, who is an expert in calcium signaling, will be a crucial step for me to improve my research and my knowledge in this field. Indeed, the decision made at the end of my stay to join his team as a postdoctoral fellow will contribute to develop my skills in imaging and molecular techniques and combined with my research background on the physiology of cardioprotection, we hope that it will favor the identification of new therapeutic targets for myocardial infarction.

To conclude, I would like to thank the ESC for providing me the opportunity to do this internship but also Pr Gyorgy Hajnoczky and all his lab members for their great welcoming during my stay.

Best regards,

Mélanie PAILLARD