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Subject: Report to European Society of Cardiology – First Contact Initiative Grant

With this letter, I would like to first express my gratitude to the European Society of Cardiology for have given me the opportunity to visit a foreign institute where I could experience doing research for one month. In this report, I will describe what I have been doing in the host institute and what the outcome is of my stay abroad from 16 September till 18 October 2010.

I visited the Research Institute of Internal Medicine at the University Hospital of Oslo – Rikshospitalet – which is directed by Prof. Dr. Pal Aukrust and Prof. Dr. Bente Halvorsen. Both focus on the role of the immune system in several cardiovascular events, including atherosclerosis. The research profile of this institute is to combine clinical medicine and molecular biology to establish a bridge between bench and bedside.

In a previous study we observed that deletion of CXCR4 in leukocyte subsets aggravated plaque development and plaques of mice with impaired CXCR4 function were characterized by a significant increase in neutrophil infiltration. In follow-up studies we provide evidence that neutrophil function is perturbed after CXCR4 deletion. More in particular that CXCR4 is critical for neutrophil senescence after activation at sites of inflammation (such as the atherosclerotic plaque) – CXCR4 ablation was seen to prevent senescent neutrophils to migrate back to bone marrow to undergo apoptosis, leading to amplified neutrophil responses at the level of the plaque. Indeed, circulating neutrophils from CXCR4 deficient mice showed increased content of intracellular ROS and higher expression of other activation markers. The goal of my visit to the University Hospital of Oslo was to investigate whether patients with acute coronary syndrome (ACS) express higher levels of neutrophils in

circulation compared to healthy subjects and to investigate whether neutrophils from ACS patients show a higher activation status compared to neutrophils from healthy subjects. The great advantage of the lab of Pal Aukrust is that they have easy access to human material. I was able to collect blood and plasma samples from 63 patients in total, of which patients with both stable and unstable angina pectoris and patients who suffer from atherosclerosis in the carotid artery. In addition, I also collected samples from healthy people. I analyzed the blood samples using flow cytometry. In that way I was able to analyze the neutrophils for several activation and oxidative stress markers as well as CXCR4 expression. (Due to the fact that these results of this study have not been published yet, these data will not be described in this report.) In addition, I also analyzed the plasma samples using ELISA to make a profile of the cytokines present in circulation. In addition to the analysis for the CXCR4 study, I was also able to isolate dendritic cells and B cells from these patients which we will use to perform micro-array analysis on. In that way, we can determine the gene expression profile on these cells which will give us more information about the genes involved in the function of these cells in atherosclerosis. All together, these results will deliver more insight into the mechanisms of atherosclerosis.

My visit to the University Hospital of Oslo in Norway has given me the great opportunity to generate a large amount of human samples on which we could do a lot of analyses and which will provide us an enormous amount of data we will be working on in the coming months. I learned new techniques which I can use now also in my resident lab. In addition, I met many new people of which many I will keep contact with to further collaborate on other projects in the near future. In addition to my work in the lab, I got the opportunity to give a presentation which was attended by several people from different institutes. I received many reactions which I can use to generate new ideas for the projects I presented. And I also met new people which I could contact for help and collaboration. I got the proposal for a postdoc position at the lab of Pal Aukrust, which is an interesting offer that I certainly will consider once finished with my PhD in the Netherlands. The research topics they are working on fit completely in my personal interests. And now at least I know the lab and how everything functions over there, which is something you cannot find out beforehand if you didn't have the chance to stay there for a few weeks. So, therefore this experience was very important to me and will certainly help me making a decision for the next institute I would like to work after my PhD is finished.

Altogether, my stay in Oslo was very educative and productive. I could generate a lot of new data which will hopefully help us to better understand the disease mechanisms of atherosclerosis. In

addition, it was a great opportunity for me to experience doing research in another institute and meeting many new people with the perspective of creating a network with people for further collaborations.

Yours sincerely,

Isabelle Daissormont