



To: the ESC Council on Basic Cardiovascular Science
European Heart House
2035, Route des Colles
Les Templiers – BP 179
06903 Sophia-Antipolis Cedex
France

Date: June 15th, 2013
Subject: ESC First Contact Initiative Grant

Dear Council Members,

Thank you very much for awarding me the First Contact Initiative Grant to support my visit to Prof. Martin Young's laboratory at the University of Alabama, USA. I have now been to Alabama and would like to share my experience with you.

The aim of my visit was to establish collaboration between our respective institutes. Specifically, my goals were 1. The exchange of materials/mice; 2. Exchange of expertise; intellectual input in each other's projects; 3. Possibility for myself and other lab members of the respective labs to perform a fellowship or exchange project in the other institute. Thanks to your support, I managed to realize all these goals.

My current main research project is about the influence of day-night rhythms on cardiovascular regeneration. Diurnal (i.e., relating to a 24-hour day-night cycle) rhythms influence cardiovascular physiology and pathophysiology, and disruption of normal sleep-wake cycling has been linked to cardiovascular disease. Strikingly, 10-13% of genes in the intact heart show significant time-of-day dependent oscillation. Peripheral tissues display cell-autonomous circadian oscillations, and a clockwork mechanism has now been identified within all cardiovascular cell types including cardiomyocytes. Professor Young at UAB has developed cardiomyocyte-specific clock mutant (CCM) mice, which has revealed specific roles for the cardiomyocyte circadian clock in myocardial α -adrenergic signaling, metabolism, cardiac output, and ischemia tolerance.

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The circadian clock may represent a new mediator or target for cardioprotective strategies if the mechanisms underlying the variations are further elucidated. This potentially also holds true for stem cell-based cardiac regeneration, my area of expertise.

During my visit at UAB, we were able to discuss our respective projects intensively and developed interesting new ideas. Professor Young has a vast amount of experience with circadian rhythm research in adult cardiomyocytes, which greatly benefits my stem cell project. Vice versa, he was interested in our experience with stem cells and developmental biology to answer some of his research questions that concern the development of circadian rhythms in his mice. I had a lot of interaction with all his group members and also met with several other principal investigators at the institute. I was able to derive fibroblasts from Prof. Young's CCM mice, which we later reprogrammed into induced pluripotent stem cells. Moreover, the mice are now being transported to our institute for additional collaborative projects.

Finally, we set up an exchange of students: one of my PhD students will spend 4 months in Prof. Young's lab to learn techniques and work on a collaborative project. Next year, a current PhD student from Alabama will join our group at the University Medical Center Utrecht for her postdoctoral fellowship.

Altogether, the visit was extremely useful and realized the beginning of a successful collaboration between the University of Alabama and the University Medical Center Utrecht. I trust that the collaboration will benefit basic research within the European Society of Cardiology. Your support is greatly appreciated.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'L.W. Van Laake', with a long horizontal flourish extending to the right.

Dr. L.W. Van Laake, MD PhD
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