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Leiden University Medical Center

Dear ESC Counsil on Basic Cardiovascular Science,

I would like to sincerely thank the ESC Counsil on Basic Cardiovascular Science for awarding me the 2019 First Contact Initiative Grant. As a result of this grant, I was able to initiate a collaboration project between the laboratory of Experimental Cardiology at the Leiden University Medical Center (Dr. D.A. Pijnappels) and the Laboratory of Molecular and Translational Cardiac Electrophysiology at the Medical University Hospital Heidelberg (Dr. D. Thomas).

The focus of my PhD training is exploring novel therapeutic strategies for pain-free termination of cardiac arrhythmias. Such novel treatment is very much desired given that a lot of arrhythmias can only be effectively treated by painful high-voltage electric shocks that negatively affect prognosis and quality of life of patients. To study this concept of pain-free heart rhythm restoration therapy, our laboratory has developed gene therapy that allows the heart itself to generate bioelectricity that can be used for arrhythmia termination, thereby potentially making the use of painful electroshocks obsolete. Our laboratory used light-gated ion channels to control cardiac excitation in a highly specific, reversible and non-traumatizing manner, as with light one can exactly regulate the moment, duration, location, and strength of the electrophysiological manipulation. This approach may therefore allow properly controlled generation of cardiac bioelectricity for biological, shock-free arrhythmia termination. Using this approach in rat models, we were able to show that the heart can be enabled to biologically terminate ventricular tachyarrhythmias (Nyns, *Eur Heart J* 2017) and atrial fibrillation (Nyns, *Sci Trans Med* 2019).

While results of these studies hold translational potential for the development of novel therapeutic strategies for the pain-free treatment of cardiac arrhythmias, we needed to perform much-needed experiments in a large animal model before clinical translation of this promising approach can be truly considered.

With the support of the First Contact Initiative Grant, we initiated a collaboration project with the Laboratory of Molecular and Translational Cardiac

Electrophysiology at the Medical University Hospital Heidelberg. This laboratory is a renowned and dedicated electrophysiological institution with substantial experience in gene therapeutic studies for cardiac arrhythmias in large animal models, thereby making it an ideal collaboration partner for large animal experiments.

Together with my colleagues, including a basic science electrophysiologist, a micro-electronic engineer and a thoracic surgeon, I have visited the host institution in Heidelberg in order to to establish first contact with the team of Dr. Dierks, to learn various experimental techniques and to perform the first pilot experiments of this project. We have gained extensive experience in different aspects of large animal experiments, including surgical techniques, various gene delivery approaches and in vivo and ex vivo electrophysiological read outs, analysis and also immunohistology.

Because of the First Contact Initiative Grant, our laboratory has gained essential new insights in the possibilities of optogenetic cardiac gene delivery and subsequent in vivo cardiac illumination in the large animal model. With these new insights and experiences in hand, together with the results of the first pilot experiments, we hope to further progress our research as it is our ambition to pave the way for the development of autogenous pain-free anti-arrhythmic therapies.

Once again I would like to express my sincere gratitude to the ESC Council on Basic Cardiovascular Science for this opportunity. This collaboration project has greatly strengthened my research experience and also the clinical translatability of my PhD thesis.

Yours sincerely,

Emile C.A. Nyns