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To

ESC Council on Basic Cardiovascular Science

Düsseldorf, January 31, 2022

First Contact Initiative Grant: Report

To the Council on Basic Cardiovascular Science,

I want to sincerely thank the ESC Council on Basic Cardiovascular Science for providing me with the First Contact Initiative Grant in 2021. It gave me an opportunity to reach out to Dr. Jose A. Gomez-Sanchez, a researcher formerly trained at the University College London and now located in the lab of Dr. Hugo Cabedo at the Instituto de Neurociencias de Alicante (CSIC - Universidad Miguel Hernández, Spain) with extensive knowledge in repair glial cells. Together, we were able to study glial biology in the heart and its link to autonomic innervation. Since my stay, Dr. Gomez-Sanchez and I do have an ongoing and fruitful collaboration.

Research Background

Sudden cardiac arrest, mostly induced by ventricular arrhythmias (VA), accounts for ~50% of all cardiovascular deaths.(1) Therapeutic approaches for VA are limited with low success rates and novel targets are needed.(2) The cardiac autonomic nervous system (CANS) is a complex network of neurons and glial cells that modulates cardiac rhythm.(3) Its disruption by denervation and re-innervation is a mechanism for generation and maintenance of VA in animals and patients.(4,5) While the CANS is explored as a target for treatment of VA, little is known about a cell type indispensable for neurons: Glial cells are an essential contributor to neuronal function and survival, assisting in development, electric activity and nerve regeneration. My previous studies have shown glial cells distributed throughout the heart and the CANS in mice and men – releasing neurotrophic

factors and modulating cardiac neurons upon damage.(6) Dr. Gomez-Sanchez has studied the molecular processes in repair glial cells after nerve injury (7–9) and has several mouse models at his disposal expressing reporters under specific glial promoters (P0-cre, PLP-creERT2, Sox10-cre) or allow the deletion of glial cells (Rosa26 eGF-DTA under PLPCreERT2, inducible by tamoxifen).

Use of the grant

From September 4th to October 7th 2021, I visited the lab of Dr. Hugo Cabedo at the Instituto de Neurociencias de Alicante, where more than 300 researchers pursue neuroscience (www. http://in.umh-csic.es/). Having spent a large part of my career in the field of autonomic innervation of the heart with a focus on cardiology, this provided me with an excellent opportunity for interdisciplinary exchange.

Dr. Gomez-Sanchez provided me with the hearts of his transgenic mouse models for analysis. I was able to use the state-of-the-art equipment and microscopes for immunohistological analyses of these hearts. Together we were able to establish that glia cells – as identified by the fluorescent tdTomato reporter – were abundantly present in the heart of all transgenic lines, having expressed P0, PLP and SOX10 at some point during development. These cells were accompanying cardiac innervation from large nerve fibers up to the smallest unit – the neuro-cardiac junction. We used another transgenic line to disrupt glia cells by tamoxifen (made possible by glial-specific tamoxifen-inducible expression of diphtheria-toxin A. As we sacrificed mice 16 days after the first injection, I took most of the hearts home to Germany, where I am studying the consequences of glia disruption in the heart.

I would like to sincerely thank Dr. A. Jose Gomez-Sanchez and Dr. Hugo Cabedo (Instituto de Investigación Sanitaria y Biomédica de Alicante, Spain) and well as his research group for their welcoming and friendly atmosphere and an amazing experience.

This experience was an important step for my personal career development, as it allowed me to build up a scientific network and work on my scientific independence. Since coming back from Alicante, I have written a grant proposal to the German Research Foundation based on the data generated in this grant, with Dr. Gomez-Sanchez as a cooperation partner. In summary, my stay at the Instituto de Neurociencias de Alicante, made possible by the First Contact Initiative Grant, was very successful and I want to express my sincere gratitude to the ESC for selecting me.

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