

European Society of Cardiology
The European Heart House
Councils Relations - Specialty Centre
2035 Route des Colles
Les Templiers - BP 179
CS 80179 BIOT
06903 Sophia-Antipolis Cedex
France

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ESC First Contact Initiative Grant final report

To begin with, I would like to express my gratitude to the European Society of Cardiology (ESC) for their support of this enriching experience, which did not only allow me new scientific insights, but also to extend my scientific network, foster important collaborations for my future career and enriched my personal life with many unforgettable moments and experiences.

My PhD work at the VU University Medical Center (VUmc, Amsterdam, The Netherlands) focuses on molecular, structural and functional abnormalities of lung endothelial cells in the pathogenesis of Pulmonary Arterial Hypertension (PAH). We recently identified a novel dysfunction in endothelial cells from lungs of patients with different PAH etiologies, which manifests as a delayed morphological adaptation to high levels of fluid flow (HSS, blood flow). I visited the laboratory of Dr Paul Yu at Brigham and Women's Hospital (BWH) part of Harvard Medical School (Boston, Massachusetts, USA) for a period of 3 months to probe specific questions on the role of bone morphogenic protein (BMP) signaling in response to fluid shear stress, as mutations in the BMP receptors and dysbalanced BMP signaling are highly associated with PAH. Dr Yu is a specialist in BMP signaling and developed several models (including small animals) to study gain- and loss-of-function mutations in the BMP signaling cascade.

The fellowship included an animal training course covering basics to work with small laboratory animals as well as the isolation and cultivation of mouse lung derived endothelial cells that I used to develop a new protocol to follow the binding, trafficking, and signal transduction of fluoro-labeled BMP9 in real-time with confocal microscopy. Due to some breeding issues with the BMP receptor knock-out animals we adapted our initial goals and used human pulmonary endothelial cells from lungs of PAH patients instead for next generation RNAseq. Here we compared the transcriptome of control vs. PAH cells before and after the application of HSS.

The results of this study were incorporated in a collaborative publication that is submitted and momentarily under review.

In summary, the BWH was an ideal place to perform research. The international student exchange is efficiently organized and a specialized contact person guided me through all organizational tasks like visa, facility access, safety training and health screening. The BWH is part of the Longwood medical campus, where I had free access to numerous scientific trainings, presentations and modern research facilities. In general, the research environment was stimulating and people were open and friendly, which made it easy to contact other departments and share expertise and equipment. Dr Yu welcomed me with open arms, was supportive, energetic, curious and very approachable. It was a joy to learn from him and all the talented scientists working with him. Besides the experimental work I was able to benefit from Dr Yu's experiences and network and we initiated future collaborative studies between BWH and VUmc that comprise enlargement of the donor pool for the RNAseq as well as inclusion of more specialized questions regarding BMP9 as a molecule to normalize the endothelial phenotype in PAH.

I would like to thank Dr Yu and his team, my supervisor Dr Harm Jan Bogaard and the Phaedra consortium (www.phaedraresearch.nl) for their great support, which made my visit an enriching experience, both scientifically and personally.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'R. Szulcek', written in a cursive style.

Robert Szulcek

Department of Physiology and Pulmonology
Institute for Cardiovascular Research
VU University Medical Center
Van der Boechorststraat 7
1081 BT Amsterdam
The Netherlands