Publications

Léger L, Aliakbarshirazi S, Zahedifar P, Aalders J, Van Der Voort P, De Geyter N, Morent R, van Hengel J, Ghobeira R. Combinatorial effects of surface plasma-treating and aligning PCL/chitosan nanofibers on the behavior of stem cell-derived cardiomyocytes for cardiac tissue engineering. Applied Surface Science. **2024**

Léger L, Declercq C, Aalders J, Van Acker-Verberckt K, Braeckmans K, van Hengel J. Photoporation-mediated spatial intracellular delivery of stem cell-derived cardiomyocytes. MethodsX. **2024**

Xiong R,…, Léger L, et al., Photothermal nanofibres enable safe engineering of therapeutic cells. Nature Nanotechnology. **2021**

In preparation

Léger L, Aalders J, De Bleeckere L, Vitiello L, Rampazzo A, Calore M, van Hengel J. Generation of a human induced pluripotent stem cell line UGENTi002-A from an arrhythmogenic cardiomyopathy patient carrying a heterozygous c.817C>T DSP variant and isogenic control using CRISPR/Cas9 editing.

Léger L, Aalders J, Van Acker-Verberckt K, Vitiello L, Rampazzo A, Calore M, van Hengel J. Isogenic iPSC-derived cardiomyocyte modeling of DSP arrhythmogenic cardiomyopathy reveals electrical abnormalities.

Léger L, Ferron S, van Hengel J, Calore M. Circulating microRNA dysregulation in hypertrophic cardiomyopathy, dilated cardiomyopathy and arrhythmogenic cardiomyopathy: a systematic review.

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GHENT UNIVERSITY

FACULTY OF MEDICINE AND HEALTH SCIENCES

One cell type, infinite possibilities: utilizing human pluripotent stem cells for modeling arrhythmogenic cardiomyopathy and cardiac tissue engineering

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Background

Arrhythmogenic cardiomyopathy is a complex, heterogeneous genetic disease characterized by fibro-fatty infiltration of the heart muscle. Importantly, electrical abnormalities can precede these ultrastructural changes, with a constant risk of sudden cardiac death. Emergence of the life-threatening complications remains a mystery, however, having stem cell-derived models at our disposal, early pathophysiological events can be better understood.

Stem cells hold immense value in disease modeling, but also for developmental studies and drug discovery applications. These studies often benefit from bringing in components into the cells, to study their function. Photoporation, an emerging gene-editing delivery method, creates transient holes in the cell membrane, allowing the entry of biomolecules into the cells. This technique can be applied to stem cells, but also to differentiated cells.

Stem cell-derived cells are often relatively immature, hampering their translational value. A scaffold consisting of polycaprolactone and chitosan nanofibers was generated by electrospinning to more closely mimic the cardiac topological environment. To allow cell growth, these scaffolds need to be biofunctionalized. This can be achieved through plasma activation.

Main findings

The thesis presents a patient-specific induced pluripotent stem cell model for arrhythmogenic cardiomyopathy, which, when differentiated into heart muscle cells, exhibits a distinct phenotype compared to an isogenic control. This well-characterized model holds promise for understanding pathophysiological mechanisms occurring in ACM patients.

Efficient photoporation of pluripotent stem cells and their derived cardiomyocytes allows efficient intracellular delivery of biomolecules and has the potential to accelerate translation to clinical applications.

Additionally, stem cell-derived cardiomyocytes cultured on plasma-treated nanofibers showed structural maturation and patterned organization, offering valuable tools for future cardiovascular disease research.

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Thank you for your interest.