Electrospun collagen scaffolds for the cardiac graft of cardiomyocytes derived from human pluripotent stem cells

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Collagen, the most abundant component of extracellular matrix, is a molecule of choice for the development of cellular biomaterials, because it can interact with most cell types and can facilitate their adhesion and growth. In this study, electrospun nanofibrous collagen patches were used to provide a biocompatible physical support for the graft of human pluripotent stem cells derived cardiomyocytes (hPCS-CM) for the treatment of the failing heart. Different types of clinically approved collagen were studied for their ability to form high quality uniform fibers by electrospinning using a benign solvent system based on ethanol, water and salts. Atelectocollagen – that contains 95% of type I and 5% of type III – exhibited the best performance. After appropriate crosslinking using cyto compatible agents based on citric acid (concentrated to 5% or 10%), the collagen was placed to special holders for cell culture.

The electrospun collagen patches were used for culture of newborn rats cardiomyocytes, showing regular beating after 3 days of culture. They already have been successfully used for the culture of hPCS-CM. Finally, the electrospun collagen patches have been implanted in mice with dilated cardiomyopathy and have exhibited excellent biocompatibility. Cardiac function measured by echocardiography before and after the graft, histological, and molecular studies showed no detrimental effects of the collagen scaffold. Our next target is the implantation of hPCS-CM-seeded scaffold in mice with dilated cardiomyopathy.

Adult cardiomyocytes proliferation blockage by nuclear ephrin-B1:

Adult cardiomyocytes (CMs) proliferation in the natural blockage of adult CMs proliferation. Recently, we have explored the specific role of the P3K pathway in the proliferation of adult CMs. 

The possibility to reboot the proliferation of adult resident cardiomyocytes (CMs) has emerged as a promising avenue in cardiac regenerative medicine. For that purpose, there is an urgent need for identifying the molecular mechanisms involved in the natural blockage of adult CMs proliferation. Recently, we have recently demonstrated that ephrin-B1 expression in the CMs nuclei acts as a specific inhibitor of the adult CMs proliferation. Here, we have explored the specific role of the P3K pathway in the proliferation of adult CMs. 

Fluorescent immuno staining showed a specific loss of nuclear ephrin-B1 in p110-pathway KO but not in KI mice, suggesting a specific role of the PKA-anchoring function of the p110-pathway. 

These results demonstrated for the first time the specific role of the cAMP/PKA pathway in ephrin-B1 nuclearization. The possibility to reboot the proliferation of adult resident cardiomyocytes (CM) has recently emerged as a new promising avenue in cardiac regenerative medicine. For that purpose, there is an urgent need for identifying the molecular mechanisms involved in the natural blockage of adult CM proliferation. We recently identified ephrin-B1 as specific inhibitor of the CM rod-shape allowing the cardiac tissue cohesion. Interestingly, we found that ephrin-B1 knock-out mice (KO) compensate aging stress through a surprising CM hyperplasia, suggesting an atypical proliferation of adult CM. Cell cycle genes profiling performed by qRT-PCR showed that old KO CM significantly up-regulated genes involved in all cell cycle phases. Progression of CM throughout the cell cycle was confirmed by flow cytometry and revealed the presence of the replicative S-phase only in old KO CM. Proliferation was next...