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Post-infarct arrhythmia prevention via intramyocardial transplantation of Cx43 expressing fibroblasts

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After myocardial infarction, one of the major complications, besides a reduced Ejection Fraction (EF), is the occurrence of Ventricular Tachycardia (VT). The loss of cardiomyocytes in the infarction area is structurally compensated by their replacement with fibroblasts during scar formation. The massive loss of Cx43 expression within the infarct zone hampers electrical conduction and favors Ventricular Tachycardia (VT) by re-entry mechanisms. Therefore, we hypothesized that intramyocardial transplantation of Cx43 expressing embryonic Cardiac Fibroblasts (eCF) following myocardial infarction could reduce post-infarct VT incidence. eCF were harvested on E13.5 and cultured for 7 days and transduced with either a Cx43-IRES-GFP or an IRES-GFP Lentivirus (LV) constructed *in vitro*. Subsequently, they were loaded with fluorescently labeled, PMAO coated magnetic nanoparticles (MNP) overnight. Mice (female CD1, 10-12 weeks) underwent cryogenic induction of myocardial infarction and 200 cells were subsequently injected into the infarction area, either with or without application of a magnetic field. Functional analyses were performed 14 days post operation by echocardiography and electrophysiological examination. Injected eCF were retained in the infarction area as shown by GFP expression of fibroblasts in the infarction area as well as the presence of the MNP. In the Cx43 transduced eCF injected mice, an increased expression of Cx43 in fibroblasts could be observed. Functional examination revealed significantly increased anterior wall thickening (AWT) and improved arrhythmia resistance in mice injected with Cx43 expressing eCF (+Magnet, 25.0% VT incidence, n=8) compared to mice injected with GFP control virus (+Magnet, 77.7% VT incidence, n=9). However, there were no significant differences in global left ventricular function (fractional shortening) between groups. In conclusion, the transplantation of Cx43 expressing eCF protects against VT after myocardial infarction but does not improve heart function.

Biography

Esther Carls has completed her Bachelor's degree in Life Sciences in 2011 and her Master's degree in Clinical Molecular Sciences in 2012 focusing on macrophage cell therapy in atherosclerosis. Further, she has worked at the University of Edinburgh on macrophage cell therapy in renal ischemia. Presently, she is working at the University Hospital Bonn, Department of Cardiac Surgery on cell and gene therapy in myocardial infarction. Her primary research interest is in cardiovascular diseases. She is also a PhD student, working under the guidance and supervision of Professor Wilhelm Roll.

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