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Magnetic nanoparticles: Assisted local lentiviral transduction of fibroblasts *in vitro*

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Besides heart failure, Ventricular Tachycardia (VT) is one of the most prevalent causes of death following myocardial infarction. Since cardiomyocytes are terminally differentiated cells, they are replaced predominantly by fibroblasts, which maximally proliferate on day 3 to 4 post infarction. Despite cardiac fibroblasts expressing the gap junction protein Connexin 43 (Cx43) on a basal level, propagation of the electrical conduction is reduced massively within the infarction area and VT can originate from re-entry mechanisms. Our goal is to enhance the conduction velocity within the scar by increasing the Cx43 expression in resident fibroblasts through direct intramyocardial lentiviral (LV) gene delivery or by intramyocardial transplantation of Cx43 overexpressing cardiac fibroblasts. Both the LV transduction efficiency and the engraftment of transplanted cells can be enhanced by the application of Magnetic Nanoparticles (MNP) and magnetic fields. Besides the higher transduction efficiency, the application of MNP/magnet system enables a localized lentiviral transduction *in vitro* and *in vivo*. Our cooperation partners of the Research Network Europe Japan provided a PMAO coated magnetic particle labeled with TAMRA fluorochrome. This particle is characterized *in vitro* by a low toxicity (cell loss of 20% at 25 pg/cell after 24 hours MNP treatment analyzed in MTT Assay) and high magnetic cell retention (80% of cells after 24 hours incubation and 100 pg Fe/cell). In addition the used lentiviral constructs (rrl-CMV-Cx43-IRES-eGFP and rrlCMV-IRES-eGFP) complexed well with this MNP, since gene expression in fibroblasts was similar after overnight incubation without magnet application and following 30 minutes incubation under magnetic attraction. In conclusion, we could show that our target MNP is incorporated into fibroblasts resulting in low toxic effects but high magnetic cell retention. Additionally we were able to demonstrate a successfully complexation of MNP and LV, which allows faster and localized lentiviral cell transduction.

Biography

Miriam Schiffer is especially interested in gene and cell therapy after myocardial infarction. She has completed her Apprenticeship as Biological Technician in the Grünenthal Group (2012). Focused on molecular cell biology, she graduated as Master of Science (RWTH Aachen University) in 2016. Since then, she works as Research Assistant and PhD student in the Department of Cardiac Surgery at the University Hospital Bonn.

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