**O3-8**

## Mesenchymal stem cells improve functional and morphological integration of induced pluripotent stem-cell derived cardiomyocytes into ventricular tissue

*Khalil M. (1), Rubach M. (1), Hannes T. (1), Udink ten Cate F. (1), Choi Y. (2), Neef K. (2), Pillekamp F. (3), Hescheler, J. (4), Brockmeier K. (1), Adelmann R. (1)*
*(1) Department of Pediatric Cardiology, University of Cologne*
*(2) Department of Thoracic Surgery, University of Cologne*
*(3) Department of Pediatric Cardiology, University of Duesseldorf*
*(4) Institute for Neurophysiology, University of Cologne*

Introduction: Transplantation of induced pluripotent stem cell-derived cardiomyocytes (iPS-CMs) into damaged myocardium might become a therapy to improve contractile function. However, current knowledge on the mechanisms of cell integration and processes of physiological reconstitution as well as mechanical and electrical coupling after transplantation into the host tissue is still fragmentary. There is cumulating evidence reporting beneficial effects of cell transplantation strategies combining a source for CMs with other cell types. From these observations we hypothesized that non-myocytes might be necessary for an improved functional integration.
Aim: To investigate whether murine mesenchymal stem cells (MSCs) improve functional and morphological integration of iPS-CMs into cardiac tissue.
Methods: Murine ventricular slices (diameter 300 µm) were cocultured with iPS-CMs and MSCs for 4 days. Integration was evaluated by visual methods, intracellular recordings via sharp electrodes and fieldpotential recordings and propagation maps via multi-electrode array (MEA) measurements. Data are represented as mean ± standard deviation, level of significance is set to $p<0.05$
Results: IPS-CM clusters had an average beating frequency of 333± 140 (n=32). Vital slices with (n=28; 77.5 ± 54.8 bpm) or without (n=29; 77.7 ± 43.7 bpm) iPS-CM clusters served as controls and displayed similar average frequencies after 4 days of co-culture. Co-cultures of vital slices with IPS-CMs and MSCs (n=16; 237.6 ± 132.6 bpm, $p<0.001$) showed a significant increase in beating rates compared to the controls indicating an improved electrical integration of the iPS-CMs. The improved integration of rapidly beating iPS-CM cluster induce a raised frequency of the slice, meaning that the IPS-CM cluster serves as a pacemaker for the cardiac slice. Morphological observations as well as propagation spread studies indicate that the improved engraftment is mediated by MSCs.
Conclusion: We conclude that non-cardiac cells like MSCs support morphological and electrical integration of iPS-CMs. MSCs are an easy accessible cell source and could be used in future as mediator cells for a successful transplanatation of iPS-CMs.