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The use of pluripotent stem cells to study cardiac conduction system development and disease

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The majority of cardiac fatalities occur due to cardiac arrhythmias. Clinical data implicate distal parts of the specialized cardiac conduction system, the Purkinje fiber network, as main trigger of ventricular tachyarrhythmia. Owing to the rareness of this cell type, deficiencies in understanding processes governing Purkinje cell differentiation and physiology remain. The discovery of induced cell reprogramming has made generation of target cells from somatic human tissue practical. We recently published a reporter gene based embryonic stem cell model of murine Purkinje cells. Using this cell model, we could perform high throughput transcriptional profiling and compare the expression profile to previous published data obtained from adult hearts. We detected high expression of described Purkinje cell transcription factors, including Tbx3, Tbx5, Irx3, Irx5, Etv1, Hopx, and Nkx2.5. Ongoing work characterizes the top-enriched transcription factors towards their transdifferentiation potential, namely generation of Purkinje cells from pluripotent stem cells or fibroblasts. Towards translational applications, we extended our research to human induced pluripotent stem cells (hiPS). We identified cardiomyocyte subpopulations expressing Purkinje cell markers, including Etv1 and Cntn2 (2.9% Cntn2+TroponinT+ and 2.7% Cntn2+Etv1+) and detected increased Cntn2 expression over time. Additionally, we have developed a human iPS Purkinje cell reporter line by targeting the Cntn2 locus with a fluorescent reporter gene using CRISPR/Cas9 technology. Using these complementary approaches, we seek to optimize the generation of cardiac conduction system cells for downstream applications, including screening platforms for urgently needed anti-arrhythmic drugs, as clinical tools in personalized medicine approaches or for regenerative cell replacement therapies.

Biography

Karen Maass has joined NYU School of Medicine in 2008 after completing her PhD at the Rheinische Friedrich-Wilhelms-Universität in Bonn, Germany and a Post-doctoral Fellowship in Experimental Electrophysiology at Upstate Medical University in Syracuse, NY. She is Research Assistant Professor of Medicine at the NYU Leon H Harney Division of Cardiology, and specializes in mouse molecular genetics, embryonic stem cell biology and experimental models of cardiovascular development and disease, evidenced by numerous publications. She also serves as an Associate F1000 Faculty Member for Cardiovascular Pharmacology and as a Scientific Reviewer, including the American Heart Association's Regenerative Cell Biology peer review committee.

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