On Thursday the 4th of February 2021 the DCVA iPSC-CM Journal Club hosted Prof. Dr. Thomas Eschenhagen from UKE Hamburg-Eppendorf, Germany for a special seminar on iPSC-CMs entitled 'Human iPS cells for heart research: Chances and challenges'.

Induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) have the potential to become a powerful tool for *in vitro* drug screening and disease modelling. However, iPSC-CMs present several limitations such as immaturity, functional readout, robustness of *in vitro* phenotypes and variability which prevent iPSC-CMs from reaching the clinic. Various approaches have been developed to improve the maturity of iPSC-CMs regarding structure, electrophysiology, contraction and metabolism although there is no one-size-fits all approach that addresses all these properties. For example, maturation approaches might improve iPSC-CM structure and electrophysiology, but beta-adrenergic response might still be blunted.

Several inherited and acquired diseases haves successfully been modeled in iPSC-CMs. However, there is a large scatter in data between diseased and healthy with diseased lines not always showing a clinically relevant phenotype. Stress tests such as drugs, metabolic modulators or mechanics might be necessary to evoke a phenotype and the development of these tests will prove beneficial in disease modelling. Additional insight into the disease might be offered by deep phenotyping studies where specific genetic signatures of disease can be obtained.

Multiple bottlenecks currently prevent iPSC-CMs from reaching their full potential. A major issue is the robustness of cardiac differentiation protocols, since many labs employ their own protocol with different success rates and variability in performance of the cells in e.g. safety pharmacology assays. Standardization and automatization will become necessary to reduce variability between and within labs, with a large role for robotics. Big data and bioinformatics will help us cope with large amounts of data, although the proper infrastructure is still lacking.

The quality of iPSC-CM studies can be improved by the use of cell banks, a variety in control lines and standardization of culture medium. When working with several donors, ensure creating more clones of one donor as well as more batches of one clone. Higher cell numbers are now also required for publication in certain scientific journals. Quality control can also be improved by mentioning karyotyping (abnormalities) of iPSC-CMs and other basic descriptors before submitting a study. Currently there is no best functional readout for quality control, although a list of 'training' drugs can be developed to test the iPSC-CMs for their sensitivity and specificity.

iPSC-CMs may have their shortcomings, but so does every other model used in biomedical research. The field is rapidly developing and will play a bigger role in the future, exemplified by the pharmaceutical industry implementing more iPSC-CMs in their experimental pipeline. As concluded by Prof. Eschenhagen on working in the field of iPSC-CMs: ''You should combine optimism with a grain of skepticism''. A big thank you Prof. Eschenhagen!