Genetic forms of peripartum heart failure: an iPSC-based approach to identify underlying pathomechanisms and development of corresponding preclinical mouse models

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Peripartum cardiomyopathy (PPCM, occurring in ~1:1500 pregnancies with a mortality range of 5-30%) is a rare heart disease in previously healthy young women, which occurs towards the end of pregnancy or in the months following delivery (postpartum). Recent research has shown that impairment of the vascular system is a major factor in the development of PPCM. More recently, it has been discovered that at least 15% of PPCM patients carry gene variants associated with genetic cardiomyopathies, a feature also confirmed in our German PPCM cohort. However, it is unclear whether these gene variants, mostly heterozygous missense or frame shift mutations, are disease causing, an important information not only for the patient but also her children. Moreover, it is not known whether they change the cardiomyocyte physiology requiring specific personalized treatment. The aim of this project is therefore to generate induced pluripotent stem cells (iPSC) from mutation carrying patients and their relatives for differentiation of cardiomyocytes to evaluate the disease potential of pathogenic gene variants, to analyze the physiologic and molecular phenotype of these cells and to investigate the effect of pharmacologic treatment. The Hilfiker-Kleiner lab (MHH, Hannover, Germany) and Binah lab (Technion, Haifa, Israel) join forces to address this important topic in the present collaborative research project.

Projektbeteiligte

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