Center for
Heart Failure Research

GUEST LECTURE:
CHFR in collaboration with Centre for Integrative Genetics, UMB

Wednesday September 3 at hrs 15:15

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"Prediction of cardiac transcription networks based on molecular data and complex clinical phenotypes"

Møterommet
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ABSTRACT

Complex regulatory networks involving epigenetic marks and transcription factors control cardiac development and function. We use integrative approach combining sophisticated techniques to construct cardiac gene regulatory networks based on correlated gene expression, transcription factor binding sites, epigenetic marks and loss-of-function studies.
We analyzed transcript levels in 190 cardiac biopsies of patients representing a broad panel of cardiac malformations. To precisely describe the cardiac phenotypes, we delineate a detailed phenotype ontology that allows description of observed clinical characteristics as well as the definition of informative meta-phenotypes. Based on the expression data phenotype-associated genes and genes with highly correlated expression patterns were depicted.
Using contracting murine cardiomyocytes we investigated the localization of key cardiac transcription factors binding sites (e.g. Gata4, Mef2a, Nkx2.5, Srf) as well as their co-occurrence with the histone acetyl transferase p300 and with sites of histone acetylation and methylation. RNA poly II occupancy, gene expression profiles and RNA interference experiments indicated the function of the analyzed transcription factors and their dependencies.
By integration of the different data sets and prediction of binding sites on optimized promoter settings, we could reveal regulatory dependencies at a global scale and identify disease associations.