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Study of the mechanisms of epigenetic regulation involved in gene reprogramming during heart failure

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Project

Epigenetic markers have recently emerged as key players in the development of cardiovascular disease, suggesting that chromatin modifiers may represent promising targets for the development of new therapies.

Cardiac hypertrophy, an early marker in the clinical course of heart failure, is regulated by various signalling pathways that activate a specific gene program characterized by the re-expression of certain fetal genes and repression of genes specific to mature cardiomyocytes. Although the data show a specific epigenetic signature in hypertrophic cardiomyocytes, the link between well-characterized signalling pathways and epigenetic changes is still poorly understood.
The genome-wide study of several histone markers revealed that the methylation profile of histone H3 lysine 4 (H3K4) is significantly altered in the hypertrophic heart.

We have recently identified two epigenetic enzymes that modify the methylation profiles of H3K4 in cardiomyocytes during cardiac stress. We are trying to understand the impact of these two enzymes on gene regulation and the mechanisms regulating their activity and/or recruitment to their target genes. To this end, several ChIP-seq experiments have been performed.

The candidate will participate in the analysis of ChIP-seq data and the identification of genomic targets of the identified epigenetic enzymes using cellular (primary cardiomyocytes in culture) and mouse (KO, AAV injection) models. He(she) will attempt to characterize the molecular mechanisms involved in the transcriptional regulation of some identified target genes.

Keywords : transcriptional regulation, epigenetic, chromatin remodeling, histone modifications, cardiac disease, mouse model
Techniques: Isolation, culture and transfection of primary cardiomyocytes, ChIP-qPCR, ChIP-seq data analysis, RNA extraction, RT-qPCR, vector construction, protein immunoprecipitation, Western blot

Last publications

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