



The Circadian Clock as Target for Modulating Cardiac Remodeling

Background

Clocks are cell autonomous molecular mechanisms, which confer the advantage of anticipation, allowing cells to respond to stimuli in a temporally appropriate manner. Functional circadian clocks have been confirmed in all mammalian cells investigated to date, including cardiomyocytes. Analysis of gene expression in hearts collected from mice suggests that expression of 8-13% of all myocardial genes show circadian regulation in the absence of temporal patterns of environmental stimuli (e.g., light or food). The significance of the circadian clock for optimal cardiovascular health is well-established by clinical and experimental studies, exemplified by the observation that sudden cardiac death is most frequent in the early hours of the morning.

Hypothesis and experimental plan

It is the aim to understand how the cardiac circadian clock affects diseases of the heart and how we can use the cardiac clock to modulate cardiac function. The hypothesis is that:

Deranged cell autonomous circadian clocks can trigger sudden cardiac death in the vulnerable heart

We will surgically induce heart failure in mice and record 5-day electrocardiograms (ECG) from conscious, freely moving animals. We will use control mice and mice with a cardiac-specific deletion of *Bmal1*, a key transcription factor in the cellular circadian clock. We will determine the by-the-hour frequency of spontaneous ventricular ectopic activity and other specific biomarkers for cardiac arrhythmia. We will evaluate the time-of-day-dependent component of the induction of heart failure to answer the question if it matters if you get a 'heart attack' in the morning or in the evening.

Qualifications

I am looking for a brilliant student with an interest in integrated cardiac electrophysiology. You are flexible, ambitious and can work independently. You are prepared to actively participate in the shaping for your own project. You have a license and/or the motivation to work with animals.

Contact

The project is available at the Department of Biomedical Sciences, Faculty of Health and Medical Sciences, The Panum Institute. For further information and application, please contact:

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<http://bmi.ku.dk/english/research/cardiac-electrophysiology/>