



Kv11.1 Potassium Channel in Murine Cardiomyocytes?

Background

Kv11.1 is a voltage-gated potassium channel that is important for cardiac repolarization. Many drugs, new and old, block Kv11.1 and hampers cardiac repolarization. Delayed repolarization increases the risk of cardiac arrhythmia and sudden death. Many drugs are stopped in development by the pharmaceutical industry based on Kv11.1 block.

It is generally accepted, although perhaps wrong, that cardiomyocytes from mice do not have functional Kv11.1 channels, and mice have not been used in the pharmaceutical industry to screen new, potential drugs for Kv11.1 block. We have preliminary evidence that Kv11.1 is indeed present in the mouse heart and that it may be functionally relevant for murine repolarization, but only at night, when the mouse is active.

Hypothesis and experimental plan

It is the aim to understand the role of Kv11.1 in cardiac electrophysiology in the mouse. The hypothesis is that:

Potassium current governed by Kv11.1 is present in the mouse heart

We will record and analyze 5-day electrocardiograms (ECG) from conscious, freely moving animals. We will administer pharmacological Kv11.1 blockers via different routes to the animal (orally, injections, implantations of pumps) to register the effect of block in a time-of-day dependent manner. We will reverse the day-night cycle in some mice to compare electrophysiological parameters at day and apparent night. We will perform advanced electrophysiological testing in anesthetized mice after cardiac catheterization, in the isolated perfused heart and potentially in disaggregated single cardiomyocytes. This project may have large implications for the pharmaceutical industry.

Qualifications

I am looking for a brilliant student with an interest in integrated cardiac electrophysiology and pharmacology. You are flexible, ambitious and can work independently. You are prepared to participate actively in 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/heart_circulatory/cardiac-electrophysiology/