

## International PhD studentship in cardiac physiology



**Duration:** 3 years, beginning 1 January 2008

**Place of work:** University of Copenhagen, Denmark, and University of Lausanne, Switzerland

**Contract:** Fixed terms

**Deadline:** 15 November 2007

**Profile:** Master degree in molecular medicine, biology, biochemistry, or similar. Know-how within the fields of cardiac physiology, membrane protein regulation, or ion channel biology is an advantage. As the PhD study will be conducted in two different laboratories and as the project includes several different techniques it is expected that the applicant can work independently and structured. Fluency in English is a prerequisite.

**Project description:** In cardiac myocytes, the potassium channel KCNQ1 subunit assembles with the KCNE1  $\beta$ -subunit and forms a channel complex constituting the delayed rectifier current  $I_{Ks}$ , which is partly responsible for terminating the cardiac action potential. Mutations in *KCNQ1* can lead to dysfunction of the channel and cause the cardiac congenital long QT syndrome 1, which in turn may lead to serious arrhythmias such as ventricular fibrillation, and cardiac arrest. The project aims towards elucidating one of the mechanisms involved in regulating the density of the  $I_{Ks}$  channel complex at the cellular membrane – namely the regulation by its ubiquitylation. Ubiquitylation (i.e. protein labeling with ubiquitin polypeptide) of ion channels has during the past five years been shown to be an important mechanism in controlling internalization and/or degradation of membrane proteins. Recently, the two laboratories involved in this PhD project have found that  $I_{Ks}$  regulation by ubiquitylation appears to be important in the heart. This project will focus on the dynamics of  $I_{Ks}$  (turn-over time etc.) as well as on the opposite effect of ubiquitylation, which is de-ubiquitylation.

**Methods:** The regulatory mechanism of  $I_{Ks}$  channels will be addressed molecularly, biochemically, and electrophysiologically both *in vitro* (heterologous expression systems) and *in vivo*.

**Environment:** The project is a continuation of an already established collaboration between the groups of Prof. Søren-Peter Olesen, University of Copenhagen and Prof. Hugues Abriel, University of Lausanne. The laboratory of Prof. Olesen, Department of Biomedical Sciences, Uni. of Copenhagen (<http://www.mfi.ku.dk/spolab/>), harbouring 15 researchers, has specialized on the study of the molecular, cellular and *in vivo* function of voltage-gated potassium channels in the heart and in the nervous system. The core techniques in the laboratory are electrophysiological measurements of cells, molecular and cell biology and various imaging techniques. In addition, the laboratory is currently implementing new *in vivo* techniques in order to mimic arrhythmogenic conditions.

The main focus of Prof. Abriel's group, Department of Pharmacology and Toxicology, Univ. of Lausanne ([www.unil.ch/fbm/page24343.html](http://www.unil.ch/fbm/page24343.html)) is to elucidate novel molecular and cellular mechanisms underlying cardiac arrhythmias causing sudden death. The laboratory has a profound knowledge concerning cardiac ion channels and regulation of these channels by ubiquitylation.

The Ph.D. study is planned to be performed with approximately 1½ year at each university. This will give the PhD student the possibility of combining the competences of the two groups and in the same time experience two different highly dedicated scientific environments.

**Funding:** The project is funded by Danish Cardiovascular Research Academy and The Danish Agency for Science and Innovation.

**Further information:** contact prof. Søren-Peter Olesen ([spo@mfi.ku.dk](mailto:spo@mfi.ku.dk)) +45 3532 7400 or associate professor Thomas Jespersen ([tjespersen@mfi.ku.dk](mailto:tjespersen@mfi.ku.dk)) +45 3532 7557

The application in *four hard copies* including curriculum vitae, publication list and up to 3 letters of reference must be received no later than 15 November 2007 at noon by:

Prof. Sten Christensen, Director of DaCRA  
Department of Biomedical Sciences  
University of Copenhagen  
Blegdamsvej 3  
DK-2200 Copenhagen N



In addition, the application should be sent by e-mail as *one pdf-document* to: [sten.christensen@farmakol.ku.dk](mailto:sten.christensen@farmakol.ku.dk)