



UNIVERSITÄTSMEDIZIN  
GÖTTINGEN : UMG



## International Graduate Research Programme in Cardiovascular Science



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The **International Graduate Research Programme in Cardiovascular Science** contains a collection of seminars, training courses, method courses and development opportunities for PhD research students. Its purpose is to provide support for PhD students in their professional, personal and career development. The modules can be booked by students, who are enrolled in the programme

### Seminars

**Cardio-Lunch:** The Cardio-Lunch is a weekly seminar, which fosters interaction between the participating science groups in the cardiovascular field. In the seminar PhD students and early stage researchers are reporting on the progress of their work and discuss under supervision new results or recent papers. Each participating PhD student is expected to give an oral presentation at least 1 time per year.

**External speaker Seminar:** Invited external researchers present overviews of relevant topics in the field of cardiovascular science in a weekly seminar. The students are encouraged to interact with the invited speakers.

## Training Courses

Topic	Organizing Department
Cardiac channelopathies	Biochemistry I
Cardiac physiology: Langendorff preparation	Cardiovascular Physiology
Stem cell-based therapy for heart regeneration	Cardiology and Pneumology
Developmental biology of the cardiovascular system	Anatomy and Embryology
Anatomy and developmental morphology of the heart	Anatomy and Embryology
Autoimmunity and cardiac diseases	Cellular and Molecular Immunology
Biosignal and Biomedical Image Processing	MPI for Dynamics and Self-Organization

### Details

#### Cardiac channelopathies

The course will provide an overview of monogenetic inherited disorders, in which genes encoding ion channels are mutated. Examples for such diseases are Long QT syndrome or Andersen Cardiodysrhythmic Periodic Paralysis. Genotype-phenotype relationships and the molecular pathogenesis of the diseases will be explored. Purpose of the course is to enhance molecular understanding of the different ion channels underlying cardiac electrophysiology.

#### Cardiac physiology

The course will provide computer simulation of experiments with isolated perfused mammalian hearts (Langendorff preparation). The simulated responses include heart rate, ventricular force and coronary blood flow. Purpose of the course is to extend the basic understanding in cardiac mechanic and physiology as well as the cardiac response after pharmacological intervention (sympathomimetics/antagonists and cardiac glycosides).

#### Stem cell-based therapy for heart regeneration

The course will introduce students to the general concepts of stem cells, intrinsic cardiac regeneration, and stem cell-based drug screening and cellular therapy for the treatment of cardiovascular diseases. The aim of the course is to provide the current information about the biology of stem cells derived from all sources (embryo, fetal tissue, and adult), and about the state of the science on stem cell-based therapies for heart regeneration.

#### Developmental biology of the cardiovascular system

The module will provide basic understanding in some clinically important topics of the developmental biology of the cardiovascular system (e.g. vasculogenesis, angiogenesis, control of myocardial differentiation).

#### Anatomy and developmental morphology of the heart

The module will provide basic understanding in clinically relevant aspects of the anatomy of the mature human heart (e.g. coronary vessels, cardiac conduction system, muscle arrangement). A further goal of the course is to extend the basic understanding in the morphogenesis of the heart.

#### Autoimmunity and cardiac diseases

The course will provide an introduction into principle mechanisms of autoimmune diseases. We will discuss how immunological self tolerance is established and which triggers can elicit autoimmunity. The students will then present diseases, such as cardiomyopathy, myocarditis, endocarditis, or Dressler syndrome, and explain how autoimmune processes

can contribute to their pathogenesis. Purpose of the course is to extend the basic understanding of immune processes that contribute to the pathophysiology of cardiac diseases.

### **Biosignal and Biomedical Image Processing**

The course provides a short introduction to the analysis of biological signals. We will discuss basic and advanced signal processing concepts including spectral analysis, digital filters, wavelet transform, multivariate analyses (PCA, ICA), image processing, segmentation and reconstruction. Theoretical concepts will be illustrated using practical examples and experimental data. The purpose of this course is to provide a basic understanding of signal processing algorithms and software.

## **Method Courses**

<b>Topic</b>	<b>Organizing Department</b>
Solubilisation of cardiac membrane proteins	Biochemistry I
Assessing promoter activity by luciferase assays	Cardiovascular Physiology
<i>In vitro</i> differentiation of human pluripotent stem cells into cardiomyocytes	Cardiology and Pneumology
Second messenger signalling in cardiomyocytes	Cardiology and Pneumology
Fluorescence imaging of cardiac cells	Pharmacology
Tissue engineered myocardium	Pharmacology
Ultrasound biomicroscopy	Pharmacology
Genotyping of genetically engineered mice	Pharmacology
Flow cytometry	Cellular and Molecular Immunology
Cell culture techniques	Cardiology and Pneumology
Cardiac echocardiography in mice	Cardiology and Pneumology
Fluorescence microscopy	Cardiology and Pneumology
Optical Measurement Techniques	MPI for Dynamics and Self-Organization

### **Details**

#### **Solubilisation of cardiac membrane proteins**

Membrane proteins are critical to the electrophysiology and signal transduction processes of the heart. Their biochemical analysis is often difficult due to low abundance or aggregation. The course will discuss optimisation strategies for the enrichment and solubilisation of membrane proteins employing different detergents. We will monitor the efficiency of the process by SDS polyacrylamide electrophoresis and quantitative Western blotting.

#### **Assessing promoter activity by luciferase assays**

Promoter activity is commonly determined by luciferase assays. The use of different luciferase species, methods of transient transfections, the pros- and cons- of the method etc. are discussed. Cells will be transfected with reporter gene constructs and an internal control. Subsequently luciferase activity will be determined by luminometry.

#### ***In vitro* differentiation of human pluripotent stem cells into cardiomyocytes**

One of the most attractive aspects of pluripotent stem cells is their differentiation potential. Human embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) will be cultured on mouse embryonic fibroblasts and expanded *in vitro*. Methods for *in vitro* differentiation of human ESCs and iPSCs into cardiomyocytes via embryoid bodies as well as characterisation of functional cardiomyocytes will be introduced in the course.

### **Second messenger signalling in cardiomyocytes**

This course will provide novel insights into how the intracellular signalling by cAMP is organized in space and time in living heart muscle cells. We will use isolated adult mouse or rat cardiomyocytes expressing a fluorescent biosensor for cAMP to perform real-time monitoring of this second messenger at resting state and upon stimulation with physiological ligands which increase (norepinephrine) and decrease (acetylcholine) the cardiac function. The students will learn how to use fluorescent microscopy and biosensors to study intracellular signalling and biochemical processes with high temporal and spatial resolution.

### **Fluorescence imaging of cardiac cells**

Isolated primary cells from heart tissue can be characterized by immunofluorescence analysis of certain marker proteins, e.g.  $\alpha$ -actinin for cardiomyocytes, vimentin for cardiac fibroblasts and smooth muscle cells and smooth muscle myosin heavy chain for smooth muscle cells. Within this course 2D cultures of cardiac cells will be prepared by enzymatic digestion of heart tissue and afterwards cell-type specific marker proteins will be detected by indirect immunofluorescence and confocal microscopy.

### **Tissue engineered myocardium**

Heart cells can be assembled into three-dimensional tissue, so called Engineered Heart Tissue (EHT). EHTs demonstrate structural and functional properties of native myocardium and may find applications in studies of heart muscle development, drug testing and development, disease modelling, and heart muscle repair. Within this course EHTs will be constructed and subjected to functional (isometric force measurements) and morphological analyses (high resolution whole mount imaging and image reconstruction).

### **Ultrasound biomicroscopy**

Rodent models are widely used in experimental cardiology to simulate common disease states (e.g. myocardial infarction, heart failure). Here, heart muscle function is generally assessed by echocardiography. Within this course morphological and functional assessment of anaesthetized and ventilated rats or mice will be performed by ultrasound biomicroscopy (UBM). Morphological assessment includes 3D UBM, functional assessment includes the calculation of ejection fraction, fractional area shortening, and tissue strain.

### **Genotyping of genetically engineered mice**

The reliable identification of genetically engineered mice in a litter is crucial to the efficient pursuit of research and in reducing the number of mice involved in a research project. Within this course the genotype of transgenic and knockout mice will be determined by PCR after DNA extraction from mouse tails.

### **Flow cytometry**

Flow cytometry is commonly used to determine the expression of proteins on the single cell level. In addition to fluorochrome-labelled antibodies, fluorescent reporters, such as the green fluorescent protein, or DNA intercalating dyes are frequently used. For many biological processes (e.g. apoptosis and proliferation) flow cytometric assays exist. Different flow cytometric methods will be presented and the pros- and cons- of these methods will be discussed. The students will perform basic flow cytometric experiments.

### **Cell culture techniques**

Cell culture techniques are essential to study cell signalling and function. Techniques for primary and secondary cultures will be applied to various cardiovascular cell types. In addition stem cell culture techniques including cell proliferation and differentiation protocols will be applied.

**Cardiac echocardiography in mice**

Echocardiography is a key method to evaluate cardiac dimensions and function under in vivo conditions. Performance of echocardiography and Doppler measurements will be discussed and practice in mice. Relevance of various parameters will be discussed.

**Fluorescence microscopy**

Fluorescence microscopy is a key method to identify specific proteins of cells as well as dynamic processes such as ion cycling and metabolism. Proteins will be stained with antibodies. Dyes will be used to study sodium and calcium cycling. Confocal microscopy will be used for analysis. The study will include FRET-techniques (Fluorescent Resonance Energy Transfer).

**Optical Measurement Techniques**

The course offers a short introduction to biomedical optical imaging techniques. We will provide a short introduction into classical optics and optical instruments. We will cover the advanced topics including confocal microscopy, spectral optical imaging, optical coherence tomography, fluorescence imaging. The purpose of this course is to provide fundamental understanding of optical techniques widely used in cardiovascular research.