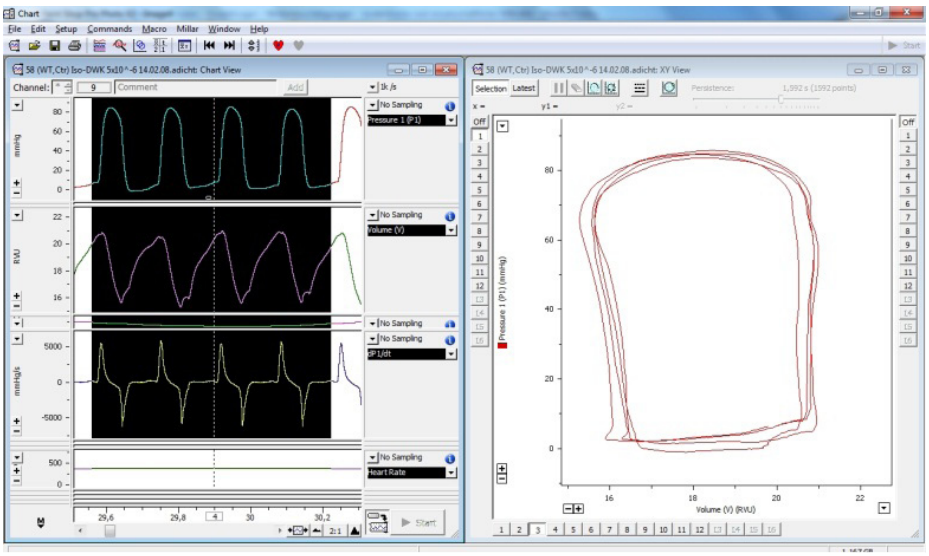
# Cardiovascular and cellular function (CarCeF)

## Introduction

Genetic or other mouse models are frequently used to define molecular mechanisms underlying cardiac diseases and associated changes of electrical and mechanical properties of the myocardium. We offer scientific expertise for the design, performance, analysis and interpretation of experiments aiming at the comprehensive cardiovascular phenotyping of mice in-vivo, in the isolated heart and in adult or neonatal primary cardiac myocytes. The techniques offered range from functional measurements in-vivo, e.g. by electrocardiography or invasive hemodynamic analysis by left ventricular catheterization, to detailed studies of cellular function, e.g. by single-cell electrophysiology or live cell imaging. The latter techniques are also applied in non-cardiomyocytes and are offered for studies in other fields of research on an individual basis.

## Cardiovascular phenotyping of mice in-vivo by surface ECG and left ventricular catheterization

Conventional surface electrocardiogram (ECG) or telemetric ECG recordings are useful, established tools to screen for altered cardiac electrical activity in mice during light sedation or in absence of anesthesia, respectively. Electrocardiogram recordings are offered under basal conditions and after catecholamine stimulation or during stress tests. The detailed characterization of left ventricular function by pressure or pressure-volume (on demand) catheters represents a good starting point to screen for altered mechanical properties and hemodynamic changes in genetically altered mice. The standard program of left ventricular hemodynamic assessment includes measurements in the absence and presence of β-adrenoceptor stimulation.




*Simultaneous recording of left-ventricular pressure and volume in a catheterized mouse*

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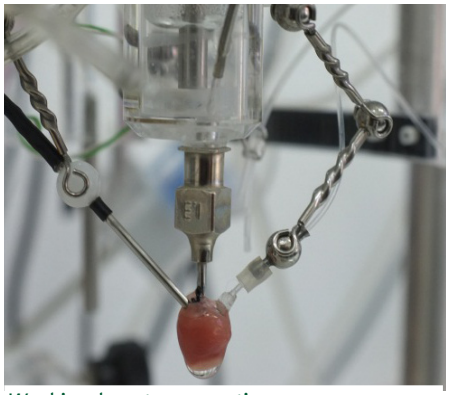
## Assessment of cardiac function on a multicellular level

Functional studies in the isolated mouse heart or in atrial preparations allow a detailed assessment of myocardial performance under various defined mechanical conditions (e.g. pre-load, after-load or pre-stretching, respectively) in absence of covariates effective in the whole animal, e.g. due to physiological reflexes or hormones. At first, isolated mouse hearts are retrogradely perfused according to Langendorff before cannulation of the left atrium and switching to an orthograde perfusion (Working heart).



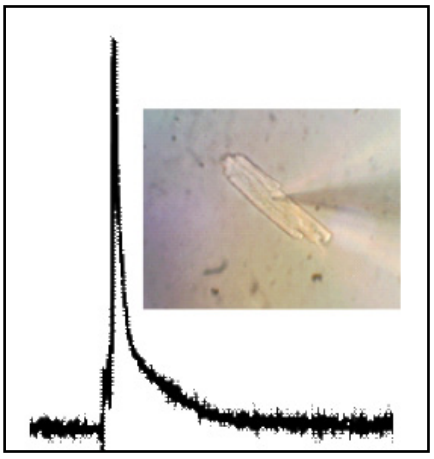
*Working heart preparation*

In both perfusion-modi hemodynamic and electrical parameters are monitored by the use of pressure transducers and a MAP (monophasic action potential) electrode. Experiments in isolated atria are offered for detailed studies of pharmacological interventions with regard to effects on heart rate and atrial contractility.

## Detailed physiological studies in primary cardiac and non cardiomyocytes

We offer the isolation of primary adult or neonatal mouse cardiac myocytes for mechanistic studies. The core unit is equipped to allow simultaneous studies of intra-cellular calcium and contractility in isolated myocytes using wide-field microscopy (Two photomultiplier-based Ionoptix myocyte calcium and contractility recording systems and a camera-based PTI RatiomasterTM system).

Multiple applications including the determination of local ion concentrations or FRET measurements are enabled in cardiomyocytes or other cell types using laser-scanner- and spinning disc-based confocal microscopy (Zeiss LSM710, Yokogawa CSU-X1). Two patch clamp stations allow the comprehensive assessment of electrical alterations in isolated cardiac myocytes (measurement of action potential and underlying ion currents).



*Action potential recorded from a patched mouse ventricular cardiac myocyte (photo)*

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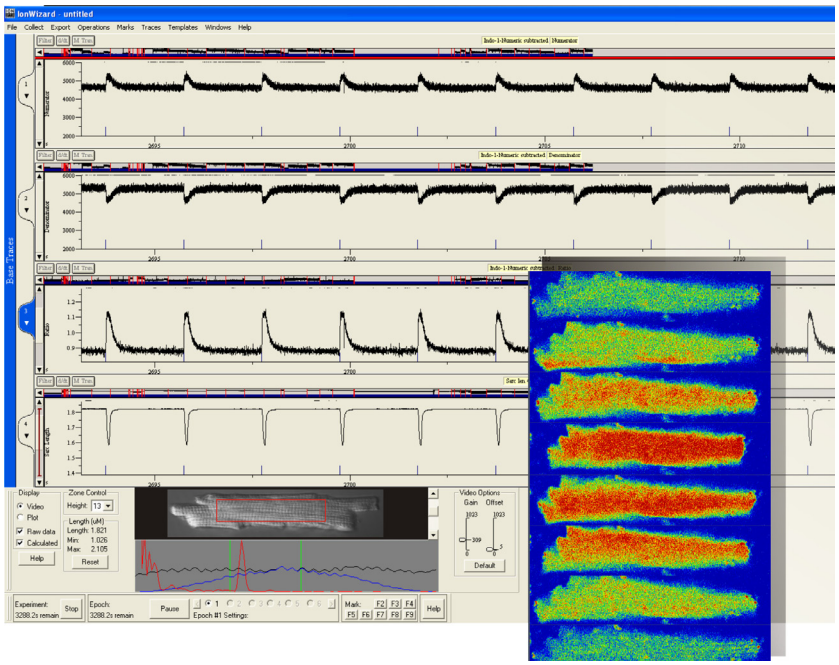

*Simultaneous registration of calcium transient amplitude and sarcomere shortening using wide-field microcopy or confocal live cell imaging (inset)*

## Representative Publications


Kido-Nakahara M, Buddenkotte J, Kempkes C et al. (2014) Neural peptidase endothelin-converting enzyme 1 regulates endothelin 1-induced pruritus. J Clin Invest doi:10.1172/JCI67323 (Epub ahead of print)

Stegemann A, Sindrilaru A, Eckes B et al. (2013) Tropisetron suppresses collagen synthesis in skin fibroblasts via alpha 7 acetylcholine receptor and attenuates fibrosis in a scleroderma mouse model. Arthritis Rheum 2013 65: 792-804.

Kirchhefer U, Wehrmeister D, Postma AV, et al. (2010) The human CASQ2 mutation K206N is associated with hyperglycosylation and altered cellular calcium handling. J Mol Cell Cardiol 49: 95-105.

Lewin G, Matus M, Basu A, et al. (2009) Critical role of transcription factor cyclic AMP response element modulator in β1-adrenoceptor-mediated cardiac dysfunction. Circulation 119: 79-88.

Kirchhefer U, Klimas J, Baba HA, et al. (2008) Triadin is a critical determinant of cellular Ca cycling and contractility in the heart. Am J Physiol Heart Circ Physiol 293: H3165-74.


## Getting started

The investigator is requested to meet with the facility staff to discuss specific needs and to design the project.


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