



Cluster of Excellence

- "From Regenerative Biology to Reconstructive Therapy"

Special Lecture

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**„New experimental approaches for the
diagnosis and therapy of cardiac arrhythmias“**

Wednesday, March 27th 2013

lecture hall H, 5 pm c.t.

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rebirth - "From Regenerative Biology to Reconstructive Therapy"

Abstract: New experimental approaches for the diagnosis and therapy of cardiac arrhythmias

Cardiac arrhythmias are common disorders affecting the rhythmicity of the heartbeat and can lead to hypotension, syncope, and even sudden cardiac death. My current research focuses on identification of new methods for diagnosis, treatment and understanding the mechanisms of cardiac arrhythmias using optogenetics and patient-specific induced pluripotent stem cells.

Bradycardic arrhythmias are typically treated by the implantation of a cardiac pacemaker, which stimulates the heart electrically. My group has developed an alternative, optogenetic method to stimulate cardiomyocytes by light (Bruegmann T et al. Nature Methods 2010). We showed that light can be used for artifact-free, uniform and long-lasting stimulation with high spatio-temporal precision in cardiomyocytes in vitro as well as in mouse hearts in vivo. To analyse mechanisms of cardiac pacemaking we have developed new optogenetic methods for modification of IP3 and cAMP intracellular signaling cascades in pacemaker cells with light. Currently we are using optogenetic technologies to understand mechanisms of arrhythmia generation but also try to explore as to whether some of these approaches can be translated into clinical applications.

Ventricular tachycardia are common causes of death after a heart infarct. We showed that transplantation of electrically coupling cardiomyocytes in the infarct scar reduces the incidence of arrhythmia and using optogenetic methods we could prove that the transplanted cells electrically couple with the native myocardium (Roell W et al. Nature 2007).

Ventricular tachycardia can be also caused by inherited mutations of cardiac ion channels that lead to the "Long QT Syndrome" (LQTS). To investigate LQTS in cardiomyocytes in vitro, my lab uses induced pluripotent stem (iPS) cells, which can be obtained from skin biopsies and differentiated into cardiomyocytes. We have generated LQTS 3-specific iPS cells with a human mutation of the sodium channel and differentiated these into cardiomyocytes (Malan D et al. Circ Res 2011). In these cells electrophysiological patchclamp recordings showed the known mutation-specific biophysical effects on sodium current and pathological prolonged action potentials at slow pacing rates. Thus we showed that an inherited arrhythmia can be investigated in the culture dish using cardiomyocytes from iPS cells.

We are extending this line of research and are investigating how patient-specific drug testing can be performed with automated electrophysiological analysis of cardiomyocytes from iPS cells using a planar patch clamp technologies as well as optogenetic stimulation of cardiomyocytes on micro-electrode arrays.