# Developmental mechanisms of arrhythmias - role of connexins in arrhythmogenesis

**MUDr.Jiří Beneš**

**Abstract**:

**Objective**: The aim of this study is an improvement of our knowledge concerning the role of connexins in arrhythmogenesis. The main focus is on the role of *connexin40* (Cx40) in heart development in mice and changes in *connexin43* expression in volume overload heart failure rat model.
**Methods**: The infuence of Cx40 on heart develoment was studied on transgenic mouse Cx40:GFP model using the method of optical mapping. Volume overload heart failure was examined in the rats with aortocaval shunt. Morphological changes in hearts were examined using imunofluorescence microscopical techniques.
**Results**: In the atria, Cx40 is important especially during the early stages. Cx43 can partially substitute its function from 12.5 embryonic day on. Cx40 deficiency leads to decreased conduction velocity and ectopic sites of activation. Absence of Cx40 in ventricular conduction system leads to the development of right bunde branch block. Volume overload in rats leads to excentric hypertrofy and later to heart failure. We described morphological as well as microscopical changes in failing hearts. Without the presence of fibrosis, the main arrhythmogenic substrate we found was reduced amount of Cx43 and its dephosphorylation.
**Conclusions**: This study decribes in detail the impact of Cx40 deficiency on the development of cardiac condution system during cardiogenesis and evaluates the changes during volume overload heart failure that can function as arrhytmogenic substrate.

**Key words**: *connexin40*, *connexin43*, optical mapping, cardiac hypertrophy, heart failure, arrhythmogenesis, mouse, rat