

Abstract

Group of specialized cells that form cardiac conduction system is responsible for generation and coordinated propagation of the electrical impulse in the heart. Changes in its development can be connected with arrhythmias; therefore, a good level of knowledge is necessary and relevant for basic science and clinical practice. For correct development of the conduction system are important genes coding gap junctions proteins, ion channels, transcription factors and other molecules involved in signaling cascades (endothelin, neuregulin). Development of conduction system is determined in addition to genetic factors also by epigenetics and environmental factors. This thesis with its individual papers on which it is based is addressing different aspects of conduction system development, which appears to be a complex process. Another feature which is linking all papers together, is the methodological approach enabling us to study function of the conduction system - optical mapping.

In the first publication we studied by the means of *in vitro* organ culture the impact of work load without interfering hemodynamics on the conduction system maturation in the chick embryonic heart. The phenotype observed during experiments was developmental regression of conduction system maturation together with changes in trabecular morphology. Experimental design was extended by a series of rescue experiments with artificial work load, which was achieved by injection of a droplet of silicon oil into primitive ventricle of the looped heart. Mechanical stretching of the cardiac myocytes is an important epigenetic factor in the early conduction system development.

The following publications were focused on Cx40 absence and its impact on function of conduction system. This analysis would not be possible without description of normal conduction system development in mouse from the physiological point of view. Absence of gap junctions protein - Cx40, which is expressed in the ventricular conduction system and atrial myocardium with the exception of the sinoatrial node, resulted in decrease of functional right bundle branch in the late developmental phase. Our conclusion is that in the earlier phase of development the function of right bundle branch is independent of Cx40. Activation of Cx40 - null atria is from the 12th embryonic day originating from an ectopic site localized in the right atrial appendage. Activation time is prolonged in the case of activation originating from ectopic site and is dependent on Cx40 genotype, with the longest activation time of both atria in complete Cx40 absence.

The last publication was dedicated to functional analysis of the mouse line with suppression of KvLQT1 protein with phenotype similar to long QT syndrome. Function of cardiac conduction system was disrupted; in late developmental phase right bundle branch block we observed together with left ventricular activation time prolongation.