ABSTRACT

The objective of this thesis is to investigate the role of Nkx2.5 gene dosage on electrophysiology of the mouse heart in prenatal stage of its development. The main goal of this work is to search for differences in conduction of electric impulses through the embryonic mouse hearts of different genotype. Special method of capturing the conduction of electric impulse through myocardium, called optical mapping, was used to visualize the electrical activity. Thanks to this method I was able to construct images and videos capturing the spread of the impulse with identification of the beginning of the activation and its direction in the heart. These outputs, or optical maps, help to define anomalies and defects in mutants compared with a normal functioning heart.

The thesis focuses on the expression of the transcription factor Nkx2.5 and regulatory components related with the correct formation and physiology of the heart until 9.5 days post coitum. Embryos at this developmental stage were optically mapped and analysed according to their genotype. While the wild type and heterozygote mouse embryos exhibited high degree of similarity, the homozygous mutants were dramatically different.

Considering this work as one of a few examining optical maps of Nkx2.5-null embryos in detail, the results may be a beginning of an elaborated search for abnormalities in phenotype correlating with gene dosage of this transcription factor. Defining the place of this gene in the complex regulatory network may help to deepen the understanding of congenital heart diseases, where the gene plays a significant role.