Abstract (in English):

The aim of the work was to perform in-depth analysis of M_2KO mice both at baseline and upon a challenge with a cold stress and to explore the role of opposing receptors (i.e. adrenoceptors) in adaptation to lacking M_2-receptors in the heart. We have performed receptor binding studies, study of receptor gene expression, echocardiography, telemetric monitoring of heart rate, body temperature and activity, heart rate variability and biorhythm analysis, analysis of heart rate response to the application of drugs (carbachol, atropine, isoprenaline, propranolol), assessment of adenylyl cyclase and NO synthase activity, measurement of catecholamine blood concentration and gene expression of catecholamine-synthesizing enzymes. We have found that the disruption of M_2-receptor gene caused a compensatory decrease of cardiostimulatory β_1-adrenoceptors and β_2-adrenoceptors with corresponding down-regulation of the gene expression, M_3-receptors were down-regulated as well. Missing M_2-receptors were functionally replaced by the main cardioinhibitory β_3-adrenoceptors that were up-regulated, not by cardioinhibitory M_4-receptors. β_3-adrenoceptors were found to signal through adenylyl cyclase instead of NO synthase. All these changes were found in the left ventricle only, so heterologous regulation is likely to be the responsible mechanism. Slightly higher basal heart rate and lower basal body temperature of M_2KO animals underscore the importance of telemetric measurement to avoid biased recordings. Despite all the changes found the overall cardiac function was unaltered.

Key words: M_2KO mice, adrenoceptors, muscarinic receptors, heart, stress, adaptation