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51.5 ± 6.3% in normoxic controls. Infliximab did not change infarction in normoxic rats (53.0 ± 3.9%) but blunted the infarct size-limiting effect of CCH (44.9 ± 2.1%). These data suggest that TNF- α is involved in the induction of the cardioprotective mechanism of CCH. Supported by grants GAAV IAAX01110901 and GAČR 303/12/1162.

18. Effect of Cd36 on cardiac ischemic tolerance and adrenergic signaling in spontaneously hypertensive rats

Martina Klevstig^{1,2}, Dmitry Manakov³, Jan Šilhavý⁴, Jiří Novotný³, Michal Pravenec⁴, František Kolář⁴, Olga Nováková¹, František Novák¹, Jan Neckář⁴
¹Department of Cell Biology, Faculty of Science, Charles University in Prague, Prague, Czech Republic; ²Department of Biochemistry, Faculty of Science, Charles University in Prague, Prague, Czech Republic; ³Department of Physiology, Faculty of Science, Charles University in Prague, Prague, Czech Republic; ⁴Institute of Physiology, Academy of Sciences of the Czech Republic, Prague, Czech Republic

Cd36 fatty acid translocase plays a key role in supplying heart with its major energy substrate, long-chain fatty acids (LCFA). We have found that the spontaneously hypertensive rat (SHR) harbors a deletion variant of *Cd36* gene that results in reduced transport of LCFA into cardiomyocytes and predisposes the SHR to cardiac hypertrophy. In the current study, we analyzed the effects of mutant *Cd36* on susceptibility to ischemic ventricular arrhythmias and myocardial infarction in adult SHR-*Cd36* transgenic rats with wild type *Cd36* compared to SHR controls. Using an open-chest model of coronary artery occlusion, we found that SHR-*Cd36* transgenic rats exhibited profound arrhythmogenesis resulting in increased duration of tachyarrhythmias and total number of premature ventricular complexes. On the other hand, transgenic SHR showed reduced infarct size. Similar differences were observed in isolated perfused hearts, and the increased susceptibility of transgenic SHR to arrhythmias was abolished by reserpine, suggesting the involvement of catecholamines. Furthermore, the SHR-*Cd36* transgenic strain had higher β -adrenoceptor density (29.8±2.6 vs. 18.8±3.5 fmol/mg protein), phosphorylated protein kinase A (PKA) expression (by 43%), indicating higher PKA activity, as well as increased forskolin-stimulated activity of adenylyl cyclase (401±9 vs. 268±10 pmol cAMP/mg/min). It can be concluded that *Cd36* plays an important role in modulating the incidence and severity of ischemic and reperfusion ventricular arrhythmias and myocardial infarct size induced by coronary artery occlusion. The proarrhythmic effect of *Cd36* transgene appears to be related to increased adrenergic stimulation. Supported by grants GAUK 429611, GAAV IAAX01110901, MSM 0021620858 and GAČR P303/12/1162.

19. Effects of aging and high-fat diet on myocardial ischemic tolerance in mice with AMP-activated protein kinase alpha2-subunit deficiency

Kristýna Slámová¹, Petra Janovská¹, František Papoušek¹, Jan Kopecký¹, František Kolář¹
¹Institute of Physiology, Academy of Sciences of the Czech Republic, Prague, Czech Republic

AMP-activated protein kinase (AMPK), a crucial sensor and regulator of cellular energy status, plays an important role in metabolic regulation under stress conditions,

and inadequate AMPK signaling may be also involved in processes associated with aging. AMPK is rapidly activated during myocardial ischemia and can be implicated in improved ischemic tolerance. The aim of our study was to find out whether alpha2-subunit deficiency can influence heart function and ischemic tolerance of aged mice. We compared infarct size in transgenic AMPK alpha2^{-/-} (TG) and wild type (WT) male and female mice at the age of 6 and 18 months. In addition, effects of high-fat diet during aging (from 12th to 18th month of age) were examined in females. Isolated Langendorff-perfused hearts were subjected to 45-min global no-flow ischemia and 60-min reperfusion. Infarct size normalized to the size of the left ventricle (LV) was similar in both strains and sexes at the age of 6 months. Aging did not significantly affect infarct size in males, whereas 18-month-old WT females exhibited markedly improved ischemic tolerance compared with age-matched TG mice and 6-month-old mice of both strains and sexes. The high-fat diet increased infarct size in aged WT females without affecting infarction in TG animals. The main echocardiographic parameter of heart function, fractional shortening was significantly lower in TG males and females compared with WT and this difference was more pronounced after high-fat feeding. No difference in AMPK alpha1 protein level was detected between the strains. On the other hand, AMPK alpha2 level and AMPK phosphorylation status were decreased in old WT hearts. These results suggest that AMPK alpha2-subunit deficiency can negatively influence changes in heart function and ischemic tolerance associated with aging and high-fat diet.

20. Differential response of older adult male and female rat hearts to ischemia-reperfusion injury

Veronika Ledvényiová¹, Dezider Panca¹, Jana Matejková¹, Iveta Bernátová², Taťána Ravingerová¹

¹Institute for Heart Research, Slovak Academy of Sciences, Centre of Excellence SAS NOREG, Bratislava, Slovakia; ²Institute of Normal and Pathological Physiology, Slovak Academy of Sciences, Centre of Excellence SAS NOREG, Bratislava, Slovakia

Great attention has been paid to hypertension, dyslipidemia, diabetes mellitus and other risk factors (RF) of cardiovascular diseases (CVD) as the leading cause of death in developed countries. However, impact of these RF on CV system has been mainly studied separately, while their incidence in population is often cumulative. Gender is one of the major aspects of differences in cardiovascular morbidity and mortality in human population, where men are at higher risk than age-matched premenopausal women. Maturation is an important RF of CVD related to the highest mortality rate in the elderly. The study aimed to investigate the role of maturation in response of male (M) and female (F) hearts to ischemia/reperfusion injury and to explore a potential role of PI3K/Akt in the hearts of older M and F rats. Langendorff-perfused non-preconditioned and preconditioned (IPC) hearts of 12- and 18-week-old M and F Wistar rats were subjected to 30-min regional ischemia and 2-h reperfusion with or without prior perfusion with PI3K inhibitor wortmannin (W, 100nM) for the evaluation of arrhythmias and infarct size (IS). IPC reduced IS in 12-week-old M and F and suppressed arrhythmias only in M. Inhibition of PI3K/Akt during IPC did not modify arrhythmogenesis in 12-week-old