

significant change. UBSM contraction in response to β -Ala8-NKA(4-10) did not differ in Ga12/13-KO mice but was sensitive to the Rho-kinase inhibitor Y-27632. Interestingly, withdrawal of extracellular calcium, or inhibition of L-type voltage dependent calcium-channels by nifedipine both altered smooth muscle contraction adversely. NKA-induced contraction of UBSM is mediated by NK2 receptors and Gq/11 proteins. Downstream signaling appears to involve both IP3R-mediated intracellular Ca^{2+} -release and influx of extracellular Ca^{2+} through L-type calcium channels. Surprisingly, PLC β does not seem to contribute to NKA-signaling, which may indicate the importance of alternative PLC enzymes in the IP3 generation. Finally, Gq/11-mediated activation of Rho-kinase significantly contributes to NKA-induced UBSM contraction, probably via inhibition of myosin phosphatase.

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P3.4 Morphological and molecular changes after application of ionizing radiation on the rat myocardium

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One of the most widely used methods of treating oncological patients is ionizing radiation therapy. Radiation beam causes damage to the cancer cells which can reduce cancerous mass and leads to recovery of the oncological patients. On the other hand, irradiation of nearby tissues like myocardium can cause some damage leading to the heart ischemia and heart failure.

The aim of this work was to study the morphological changes and changes in molecular markers six weeks after irradiation with a single dose of 25 Gy, applied to mediastinal region of Wistar male rats. Irradiated myocardium was examined for Peroxisome Proliferator-activated Receptor alpha (PPAR-alpha) and miRNA gene expression levels. Changes in ventricular myocardium were studied using electron microscopy. Levels of Connexin-43 (Cx-43) expression in irradiated and non-irradiated rat heart tissue were assayed by immunoblotting analysis.

Six weeks after chest irradiation, electron microscopy revealed increased left ventricular capillary density and endothelial cells oedema, activation and/or degeneration of endothelial cells and presence of inflammatory cells. Immunoblotting analysis of left ventricular tissue showed three forms of myocardial Cx43 (two functional phosphorylated and one non-phosphorylated form). In irradiated rats, significantly increased expression of total Cx43 was detected compared to normal control rats indicating that irradiation has the ability to up-regulate myocardial Cx43 in heart tissues. The irradiated rats exhibited lower expression of PPAR-alpha than the control ones. This indicates a shift in substrate preferences from fatty acids to glucose. Expression of

microRNA-15b in irradiated rat myocardium was significantly decreased compared with that in normal hearts. Therefore, it can be assumed that 6 weeks after radiation hearts were probably protected by activation of some adaptive mechanisms.

Despite of deleterious effects of irradiation on the myocardium, the results indicate that protective mechanisms maintaining the physiological function are activated in early phase of radiation injury.

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P3.5 Different characteristics of diabetic cardiomyopathy in rat models

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Purpose: Diabetic cardiomyopathy, a cardiac manifestation of diabetes mellitus (DM), is characterised by specific structural, molecular and functional alterations of the myocardium. Upon this concept we investigated whether type-1 or type-2 diabetes lead to different alterations in cardiac function or histological and molecular changes.

Methods: Our experiments were carried out in a rat model of type-1 (streptozotocin induced) and type-2 DM (Zucker Diabetic Fatty rats). Left ventricular (LV) function was characterised using a pressure-volume (P-V) conductance catheter system. Load independent indices of LV contractility (preload recruitable stroke work (PRSW)) and indices of LV relaxation (time constant of LV pressure decay(Tau)) and stiffness (LV end-diastolic pressure (LVEDP)) were calculated, respectively. In addition to our functional measurements TUNEL assay was carried out to evaluate degree of apoptosis. Myocardial gene expression analysis was performed by qRT-PCR. Cardiac remodelling was investigated by histological and immunohistological techniques.

Results: In comparison to the control, type-1 DM resulted in decreased LV systolic performance: decreased systolic pressure, maximal dP/dt and PRSW (45.39±2.45 vs 76.44±4.06 mmHg). Type-2 DM was associated with increased LV stiffness (LVEDP: 9.4±0.5 vs 7.7±0.4 mmHg) while systolic indices were altered only to a lower extent. We found cardiac hypertrophy and degeneration with histomorphological examination. More pronounced nitro-oxidative stress, DNA damage and cardiac fibrosis were observed in type-1 DM compared to type-2 DM. Overexpression of c-fos and c-jun and downregulation of eNOS were seen in type-1 diabetic rats. On the other hand TGF- β 1 and ANF mRNA-levels were significantly higher in type-2 diabetic model.

Conclusions: Diabetic cardiac alterations are characterised by decreased systolic performance and impaired relaxation in type-1 diabetic rats, while diastolic dysfunction was more pronounced in type-2 DM. In the background of diabetic