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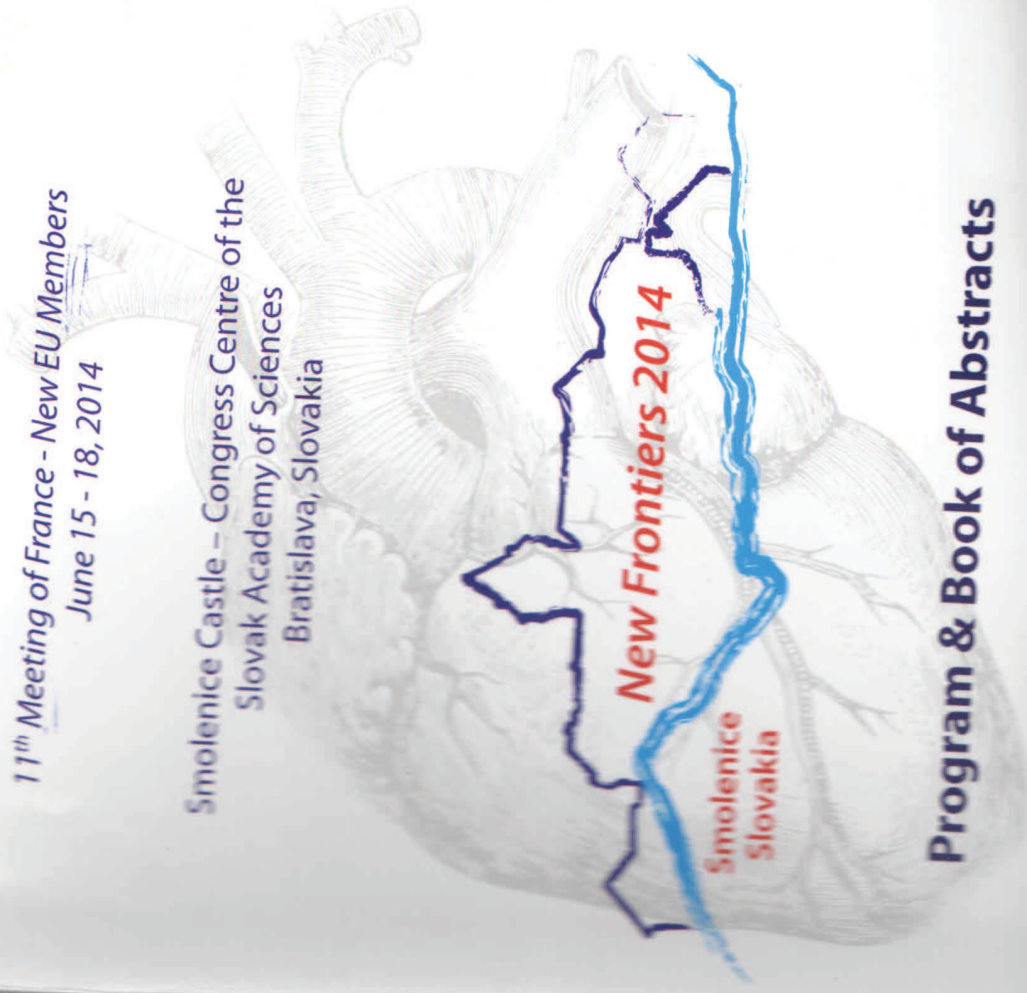
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Program & Book of Abstracts

RHO-KINASE ACTIVATION CONTRIBUTES TO HYPERTENSION IN RAT MODEL

G. A. Fülöp¹, T. Csíró¹, I. Rutkai², Á. Czikora³, A. Szalai⁴, R. Pórszász⁴, I. Édes⁵, Z. Papp¹, A. Tóth¹

¹ University of Debrecen Medical School, Institute of Cardiology, Division of Clinical Physiology, Debrecen, Hungary

² Tulane University, Department of Pharmacology, New Orleans, USA

³ National Institute of Health, Bethesda, USA

⁴ University of Debrecen Medical School, Department of Pharmacology and Pharmacotherapy, Debrecen, Hungary

⁵ University of Debrecen Medical Center, Institute of Cardiology, Debrecen, Hungary

Aims: Our aim was to characterize the spontaneously hypertensive stroke prone (SHRSP), and normotensive wistar kyoto (WKY) rat strains, to find possible differences in their blood pressure and cardiac system.

Methods: In our experiments, we detected the diameter changes of cannulated muscle arterioles, and the contractile force of the femoral artery. We measured the body and the heart weight, and the blood pressure.

Results: The body weight of the SHRSP rats (257±2g) was smaller than the weight of the WKY rats (361±10g, $p<0.01$). The heart/body ratio (0.0047), the systolic (210±12Hgmm) and diastolic (161±8 Hgmm) blood pressure of the SHRSP was significantly higher than in WKY rats (0.0027, 147±9Hgmm, 115±7Hgmm). The myogenic tone of the muscle arterioles was similar in the two groups. After pretreatment with Rho-kinase inhibitor fasudil (10 µM) the myogenic tone decreased more in the SHRSP group (82.5±6.2%) than in the WKY group (34.4±9.8 %). Treatment of femoral artery with 10-60mM KCl resulted in nearly the same contractile force, but after using fasudil, the contractile force of the SHRSP animals decreased significantly, while the control animals contractile force did not. Using serotonin we detected different reaction. (contraction for SHRSP: 14.33±1.44mN, which decreased to 9.25±1.5mN in the presence of fasudil, contraction for WKY: 8.17±1.88mN, which was 8.95±1.8mN after fasudil).

Conclusions: According to our results, Rho-kinase system probably plays an important role in the pathogenesis of high blood pressure. Better understanding the pathogenesis may lead to a more effective drug development.

AGE-RELATED CHANGES IN RESPONSE TO ISCHEMIA AND ADAPTATION IN MALE RAT HEARTS: POTENTIAL MOLECULAR MECHANISMS BEHIND

L. Griecsova¹, V. Ledvenyiova¹, V.K.M. Khandelwal¹, I. Gablovsky¹, I. Bernatova², Z. Tatarkova³, T. Ravingerova¹

¹ Institute for Heart Research, ² Institute of Normal and Pathological Physiology, Slovak Academy of Sciences and Centre of Excellence of SAS NOREG, Bratislava; ³

Department of Medical Biochemistry, Jessenius Faculty of Medicine, Comenius University, Martin, SR

Reduced tolerance to ischemia/reperfusion (IR) injury was shown in aged human and animal hearts, however, precise cellular mechanisms underlying this unfavorable phenotype are incompletely understood. Moreover, aging may interfere with the mechanisms of innate myocardial protection (preconditioning, PC) and cause defects in protective cell signaling cascades that may shift the balance from cell survival to cell death.

We studied effects of aging on myocardial function and response to ischemia, as well as selected molecular pathways in the hearts from juvenile (1.5 months), younger adult (3 months), mature adult (6 months) and senescent (24 months) male Wistar rats. In Langendorff-perfused hearts exposed to 30-min I/120-min R without or with prior PC induced by one cycle of 5-min I/5-min R, we measured the size of myocardial infarction (IS), susceptibility to ventricular arrhythmias and contractile function (LVDP). In parallel groups, LV tissue was sampled at baseline (BL) and after IR, for the detection of protein levels (WB) of protein kinase B (Akt, an effector of PI3-kinase), phosphorylated (activated) Akt (pAkt), its target endothelial NO synthase (eNOS) and protein kinase C ϵ (PKC ϵ) as "pro-survival" pathways linked with attenuation of apoptosis.

Maturation impaired heart response to lethal IR injury (increased IS) and promoted arrhythmogenesis, and these changes were more markedly evident in the younger groups of animals, while functional recovery was not affected by aging. PC suppressed the occurrence of malignant arrhythmias, reduced the IS and improved LVDP recovery in the younger animals, while its efficacy was attenuated in the mature ones. Loss of cardioprotective effects of PC was associated with reduced BL and post-IR levels of total Akt, pAkt, eNOS and PKC ϵ in the elder groups. Age-dependent decline in PC-induced upregulation of these proteins in the hearts of mature animals compared with younger adults was also observed.

In conclusion, aging-related alterations in myocardial response to ischemia may be caused by suppression of innate cardioprotection due to dysfunction of proteins involved in protective cell signaling.

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