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Methods: Murine bone marrow cells were isolated from wild-type and PI3K β mice and differentiated into osteoclasts in vitro in the presence of M-CSF and RANKL. For survival assays cells were stained with annexin-V-phycoerythrin and 7-aminoactinomycin-D, necrosis and apoptosis markers, and analysed by fluorescence-activated cell sorting. For actin ring formation assays, cells were fixed, permeabilized and stained with Alexa488-Phalloidin. MicroCT analysis was used to study the trabecular bone of the distal femoral metaphysis of the mice.

Results: In vitro differentiation of murine progenitors to multinucleated osteoclasts was strongly reduced in case of the PI3K β -/- cultures. Disruption of PI3K β decreased the resorptive capacity of osteoclasts too. PI3K β was not required for the survival of preosteoclasts, but it was needed for actin ring formation in mature osteoclasts. PI3K β -/- mice had significantly higher trabecular bone volume than wild type mice. The number of trabecules was higher in the KO mice, there was no significant difference in the trabecular thickness between the two genotypes.

Conclusion: Based on our results we can state that the PI3K β is important for osteoclast development, function and in vivo bone resorption likely by regulating the organization of the osteoclast cytoskeleton.

B/3. EFFECTS OF MUSICAL ENVIRONMENTAL ENRICHMENT IN NEW BORN RATS

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Keywords: musical enriched environment, monosodium-glutamate, neurobehavioral development, retina

Introduction: Our research group examined several neuroprotective agents and some environmental factors in nervous system lesions previously. We already described the positive effects of environmental enrichment in some animal models. About musical enrichment we have not found any results on the early neurobehavioral development, so we started to examine it. The aim of the present study was to investigate whether musical enriched

environment has any effects on the neurobehavioral development of newborn rats, and is able to attenuate retinal injury induced by neonatal monosodium glutamate (MSG) treatment.

Methods: We used two types of musical enrichment: classical and heavy-metal music from 6PM till 6AM daily. We examined the animals every day to investigate their neurobehavioral development: eye opening, incisor eruption, negative geotaxis, and some reflex performances: placing, grasping, crossed extensor, sensory reflexes. Retina degeneration was induced by early postnatal subcutaneous MSG injection.

Results: Our results show that musical enriched environment has no significant effects on the normal development. We found only slight differences between the two music groups: the heavy-metal group showed some reflex earlier than the classic. On the other hand we found significant differences between the groups in the glutamate-induced retina degeneration: the metal animals had more severe degeneration than the classical music rats.

Conclusion: These results show that musical environmental factors just slightly influence the early development of the nervous system, but in case of injuries the effects of the musical environmental influences will have significant effects in the size of the injury and the dynamism of the regeneration. We hope that our results could be bridge between the rehabilitation, clinical practice and base science in the future.

B/4. ROLE OF THE SOMATOSTATIN SST4 RECEPTOR IN INFLAMMATORY, NEUROPATHIC AND POSTOPERATIVE PAIN MODELS OF THE MOUSE

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Keywords: sst4 receptor, J-2156, acute inflammation, neuropathic hyperalgesia, chronic postoperative hyperalgesia

INTRODUCTION: Inhibitory effects of somatostatin on hormon production and tumor growth are well known, however, its

anti-inflammatory and analgesic effects were proved by our workgroup. These effects are mediated through the activation of the somatostatin receptor subtype 4 (sst4). Our research aimed at exploring the role of the sst4 receptor in mouse models of acute inflammation, chronic postoperative and neuropathic hyperalgesia.

METHODS: Acute inflammation was induced by intraplantar injection of carrageenan, traumatic mononeuropathy was produced by partial ligation of the sciatic nerve and chronic postoperative pain was evoked by meniscectomy in sst4 receptor gene-deleted (sst4^{-/-}) and wildtype (sst4^{+/+}) mice. The mechanonociceptive threshold of the paw was determined with dynamic plantar aesthesiometry. The role of the selective sst4 receptor agonist J-2156 was examined in these models.

RESULTS: Carrageenan caused 40% decrease of the mechanonociceptive threshold in wildtype mice, this hyperalgesia was significantly greater among sst4^{-/-} animals. J-2156 inhibited hyperalgesia in sst4^{+/+} mice, yet it was ineffective in the knockout group. The 45% hyperalgesia measured following the nerve ligation did not change significantly in the absence of the sst4 receptor, but J-2156 inhibited hyperalgesia in sst4^{+/+} mice. Both groups developed a 70% hyperalgesia after the meniscectomy, which decreased to 40% during the experiment. J-2156 was ineffective in this model.

CONCLUSIONS: The endogenous activation of the sst4 receptor is analgesic in acute inflammation, however, it does not have a protective role in chronic neuropathic and postoperative pain. The exogenous activation of the receptor effectively decreases hyperalgesia both in acute inflammation and chronic neuropathy.

B/5. DISPARATE AGE-RELATED ALTERATIONS IN CHOLECYSTOKININ (CCK) EFFECTS ON ENERGY HOMEOSTASIS

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Keywords: cholecystokinin, energy homeostasis

Obesity of the middle-aged is followed at old age by anorexia and cachexia. Complex age- and body composition-related alterations in the regulation of energy homeostasis may be assumed in the background. Energy homeostasis involves both body weight- and thermoregulation. Age-related changes in the responsiveness to catabolic brain-gut axis peptide cholecystokinin (CCK) possibly contribute to variations in energy balance during aging.

Male Wistar rats of different age-groups (2-, 3-, 6- or 12- and 18-24 months corresponding to juvenile, young adult, early or late middle-aged and old) were injected intraperitoneally (5 µg, to test anorexigenic effects on 48-h fasting-induced re-feeding) or intracerebroventricularly (500 ng, to test thermoregulatory actions) with CCK. Calorie-restricted 12-month (40% reduction) and high-fat diet-induced obese (60% fat calories) 6-month old groups were also established. Food intake was recorded in a FeedScale system, thermoregulatory analysis was performed using thermocouples (recording core- and tail skin temperatures) and measuring oxygen consumption in an indirect calorimeter (Oxymax).

CCK suppressed re-feeding in young adult, early middle-aged and old, but not in juvenile and late middle-aged animals. CCK-resistance of late middle-aged rats was prevented by life-long calorie-restriction. Conversely, in the obese early middle-aged rats anorexigenic CCK effects were diminished. Disparate age-related alterations were found in thermoregulatory responsiveness: strong hyperthermic effects in young rats diminished with aging.

Thus, age-related changes in responsiveness to CCK may contribute to the explanation of age-related obesity as well as aging anorexia. CCK-responsiveness is also influenced by body composition: calorie-restriction prevents the development of resistance to CCK.



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Balatonfüred, 19 August 2012



**Istvan Somkuti M.D. PhD.
President of HMAA**