be reliable markers of mortality following T/HS.

P.C.15.07
The involvement of H3 histamine receptors in the synthesis of cytokines and chemokines by mononuclear and dendritic cells

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Introduction: Histamine via its H1-H4 receptors expressed in different immune cells, induces multiple immunological responses. The most important cells expressing this receptors are peripheral blood mononuclear cells (PBMC) as well as dendritic cells (DCs). The goal of this study was to study the differences in the synthesis and secretion of the main cytokines and chemokines by PBMC and DCs and the role of H_3 histamine receptors in this processes.
Materials and Methods: DCs from 10 healthy donors and PBMC were cultivated in the presence of dual H3/4 histamine receptor antagonist Ciproxifan. The concentrations of cytokines and chemokines in 48- hour cultures have been investigated by Multiplex assays.
Results: It have been shown that cultivation of PBMC with H3/4 antagonist significantly increases the secretion of IL-4, IL-13, IL-18, IL-27 and IP-10. Ciproxifan causes a noticeable inhibition of the secretion of SCF, GM-CSF, LIF, IL-2, 5, 6, 7, 9, 15, 31 and increases the synthesis of IL1a by PBMC. At the same time H3/4 antagonist significantly increased the secretion of SCF, GM-CSF, IL1-α and IL-5, but decreases the secretion of IL-2, IL-6, IL-15 and LIF by DC. Inhibition of H3/4 receptors causes a significant increase in secretion of main chemokines by PBMC (Eotaxin, RANTES, MIP-1α, MIP-1β) and DC (MCP-1 and RANTES).
Conclusions: 1. H_3 histamine receptors are involved in the regulation of cytokines and growth factors synthesis both in PBMC and DC.
2. H3/4 antagonist Ciproxifan differently influence on the synthesis and secretion of cytokines and chemokines by PBMC and DC.

P.C.15.08
Anti-IL-20 monoclonal antibody suppresses prostate cancer growth and bone osteolysis in murine models

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Interleukin-20 (IL-20) is a proinflammatory cytokine belonging to the IL-10 family. IL-20 is involved in several diseases, such as psoriasis, rheumatoid arthritis and osteoporosis. However, there is little known about the role of IL-20 in prostate cancer. We explored the function of IL-20 in prostate cancer tumor progression. Immunocytochemical staining showed that IL-20 and its receptors were expressed in human prostate cancer cell line (PC-3). In vitro analysis, anti-IL-20 monoclonal antibody 7E suppressed prostate cancer cell proliferation, migration, and colony formation. IL-20 upregulated N-cadherin, $STAT_3$, vimentin, fibronectin, RANKL, cathepsin G, and cathepsin K, and also promoted soluble RANKL protein production, and phosphorylation of P-38, Erk1/2, Akt and NFκB in PC-3 cells. In vivo, we evaluate the therapeutic potential of 7E in prostate cancer tumor growth model and in prostate cancer-induced osteolysis. 7E reduced tumor growth, suppressed tumor-mediated osteolysis, and protect the bone mineral density in mice injected with prostate cancer cells. In conclusion, our results suggest that IL-20 plays pivotal roles in the tumor progression of prostate cancer. Anti-IL-20 mAb 7E reduced tumor growth, and decreased osteolytic bone lesion. Therefore, IL-20 may be a novel target and anti-IL-20 mAb may have a therapeutic potential in prostate cancer.

P.C.15.09
Interleukin-4 (IL-4) gene polymorphism is associated with febrile seizure in Iranian children

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Febrile seizures (FS) are the most common childhood convulsive disorders and a number of genetic mutations contribute to FS manifestation. Genetic mutations, in addition to the association of fever with seizures, suggest the possibility of proinflammatory and anti-inflammatory cytokines involvement in the pathogenesis. As IL-4 has inhibitory role in production of proinflammatory, related gene polymorphisms were investigated in Iranian patients suffering from FS in this study. 82 patients with FS were participated, compared to 139 controls. The allele and genotype frequency of 3 single-nucleotide polymorphisms (SNPs) in IL4 gene were assessed using SSP-PCR method. In the patients group the frequency of IL4-590/C allele was significantly higher comparing control group ($P < 0.0001$) while the frequency of IL-4 (–590) TC (rs2243250) and IL-4 (–33) TC (rs2070874) genotypes was significantly lower in patients compared to controls ($P = .0001$ and 0.001, respectively). The most frequent IL-4 haplotype in FS group was TCC ($P < 0.0001$). However, frequencies of GCC ($P = 0.01$), TTT ($P = 0.009$), and TTC ($P = 0.0007$) haplotypes were significantly lower in patients. Therefore, definite alleles, genotypes, and haplotypes in the IL-4 gene were overrepresented in Iranian patients with FS, which could predispose individuals to the disease and may contribute to the development of FS.

P.C.15.10
Strain differences in sterile inflammation and immune suppression induced by acute cadmium administration in rats depend on the affected activity and tissue

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Introduction: Conflicting data (suppression, augmentation, no effect) exist concerning cadmium (Cd) effects on immune system depending on activity and tissue examined. This study investigates responses to acute Cd intoxication in three compartments (peripheral blood, spleen and lungs) in Dark Agouti (DA) and Albino Oxford (AO) rats, which are differently susceptible to variety of stimuli.
Materials and Methods: Systemic (IL-6, TNF, acute phase proteins) and tissue responses [cell stress (metallothionein/MT gene expression), CD11b expression, and cytokine (IFN-γ, IL-17, IL-10) production and mRNA expression] were measured following intraperitoneal (1 mg/kg) Cd administration.
Results: Cd induces systemic inflammatory response with similar intensity in both rat strains. Increase in Cd spleen content and MT expression evident in both strains (higher in DA compared to AO rats) was followed by increase in neutrophil infiltration and CD11b expression (with same intensity). Although in both strains Cd caused decreased IFN-γ, unchanged IL-17 and lower IL-10 responsiveness (compared to respective control), decrease of IFN-γ was more intense in DA compared to AO rats. In lungs of both strains increased Cd deposition and MT expression (higher in AO) as well as neutrophil infiltration and CD11b expression (greater in DA) was observed. While decreased IFN-γ was noted in both strains, lower IL-17 and IL-10 (vs. controls) were evident in DA rats solely.
Conclusions: Acute Cd intoxication exerts strain-related effects (both inflammatory and immunosuppressive) depending on tissue and activity investigated, but the effects are more pronounced in DA rats.
Funded by Ministry of Education, Science and Technological Development of Serbia (Grant#173039).

P.C.15.11
Molecular dissection of signaling pathways initiated at IL-33/ST2 axis in human cord blood derived mast cells

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Introduction: Interleukin-33 (IL-33) is a newly discovered Interleukin-1 (IL-1) family of cytokine. It binds with ST2 receptor on immune cells to mediate allergy and asthma. Here, we dissect the intracellular signaling pathways initiated at IL-33/ST2 axis in human cord blood derived mast cells (hCBMCs) using in vitro approaches.
Materials and Methods: hCBMCs were differentiated from CD34+ haematopoietic progenitor-cells harvested from umbilical-cord blood. Immunoglobulin E (IgE) primed hCBMCs were pretreated either with selective pharmacological inhibitors or small-interferring RNAs (siRNAs) for Sphingosine Kinase (SphK), Phospholipase D (PLD) and Extracellular Signal-Regulated Kinase (ERK) and were subsequently administered with various concentrations of rhIL-33 at different time points. We have used Multiplex ELISA as well as QPCR arrays to assess various cytokines and chemokines and other intracellular signaling molecules triggered by IL-33/ST2 axis in hCBMCs.
Results: In IgE-primed hCBMCs, the IL-33 stimulates various signaling molecules including SphK1, PLD1, ERK1/2 and transcription factors such as NFkB to drive the transcription of a range of cytokines and chemokines. Importantly, the inhibition of SphK1, PLD1 and ERK1/2 attenuated the release of several proinflammatory cytokines as well as chemokines and reduced the degranulation of mast cells.
Conclusions: IL-33/ST2 pathway is essential for the initiation, maintenance and propagation of allergic responses initiated through IgE/FcεRI receptor in hCBMCs. Hence, the intracellular signaling pathways involving signaling molecules such as SphK1, PLD1 and ERK1/2 are some of the essential mediators of allergic responses initiated through this axis in hCBMCs.