Poster Session Group II – Red TPS 26

Basic immunology

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Evaluation of exhausted T-cell subsets in patients with infectious mononucleosis

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Background: T-cell exhaustion may occur in the acute phase of infectious mononucleosis. Three major exhausted T-cells subsets: CD279 (PD-1)+, CD223 (Lag-3)+ and Tim-3 + exist. T cell immunoglobulin mucin-3 (Tim-3) is expressed by T-cells, interacts with galectin-9 and negatively regulates Th1 responses. Lymphocyte activation gene-3 (Lag-3) is important in the maintenance of tolerance to self and tumor antigens. Programmed cell death protein 1 (PD-1) is a cell surface receptor which promotes apoptosis of antigen specific T-cells and reduces apoptosis in T-regulatory cells.
Methods: Twenty-four patients with IM, confirmed by blood serum PCR analysis, were included in the study. Whole blood from 22 healthy volunteers matched by age and sex was used as control (C). Relative and absolute counts of exhausted CD3 + T-cell subsets were assayed in the acute phase and 3 months after discharge from the hospital using flow cytometric analysis. The Mann-Whitney U-test and Wilcoxon test were applied to compare two independent and two dependent groups respectively.
Results: The relative number of PD-1 + exhausted T-cells was 5 greater higher in patients with acute IM compared with the C (C – 0.61[0.35–0.96] %, IM – 3.09[1.11–3.57]%, $P = 0.005$), while the absolute CD3 + PD-1 + count was 8- fold greater (C – 15[6–18]cells/ul, 121[42–215] cells/ul, $P = 0.001$). Absolute counts of CD3 + Lag-3 + cells were elevated in the IM patients (C – 3[2–6] cells/ul, IM – 16[5–30] cells/ul, $P = 0.002$), while relative numbers showed no significant difference from the C ($P = 0.093$). Relative CD3 + Tim-3 + T-cell content was increased (C – 0.33 [0.13–0.48]%, IM – 0.53[0.35–0.91]%, $P = 0.033$). At 3 months after hospital discharge none of the exhausted T-cell counts studied were statistically different from C.
Conclusion: Accumulation of subsets of exhausted T-cells occurs during the acute phase of IM. Excessive proliferation of CD8 + cells occurs in IM with immune stimulation but also there is evidence of concurrent immunosuppression with elevation of exhausted T-cells which can inhibit immune responses.

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Liraglutide exerts an anti-inflammatory action in obese patients with type 2 diabetes

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Introduction: Liraglutide (L) an analogue of human glucagon-like peptide 1 which stimulates glucose-dependent insulin secretion can modify cardiovascular risk biomarkers such as hs-CRP, IL-6, and TNF-alpha. Treatment with L reduces TNF-alpha mediated expression of PAI-1, ICAM-1 and VCAM-1 expression in human vascular endothelial cells as well as TNF-alpha induced oxidative stress. The mechanisms of anti-inflammatory activities of L remain to be determined.
Methods: Fifteen obese patients with type 2 diabetes were studied, all using metformin (1–2 g/day) and sulfonylurea (glimiperide). All patients received L 1.2 mg daily add-on to stable therapy for 6 weeks. Blood samples were collected before, 6 weeks after start of treatment and after an overnight fast 6 weeks after stopping L. Samples were collected in Na-EDTA and carefully layered on a gradient, centrifuged with mononuclear cells (MNC) harvested. The mRNA expression of TNF-alpha, TLR2, TLR4, NOD1 and SIRT1 were measured in MNC by RT-PCR. All values were normalized to the expression of the housekeeping gene actin. Ceruloplasmin concentration was measured in plasma by photometric method with p-phenylendiamine.
Results: The mRNA expression in MNC of TNF-alpha, IkB, TLR2, TLR4, NOD1 fell significantly after 6 weeks of L. There was significant increase of SIRT1 mRNA expression. The plasma concentration of ceruloplasmin decreased significantly after 6 weeks of L. Surprisingly, the mRNA expression in MNC of TNF-alpha, IkB, TLR2, TLR4, NOD1, SIRT1 and ceruloplasmin concentrations reverted to baseline levels after L treatment.
Conclusions: Liraglutide has a potent anti-inflammatory effect as do GLP-1 agonists due to inhibition of NFkB pathways and up-regulate SIRT1 expression, down-regulating pro-inflammatory factors including cytokines (TNF-alpha), extra- and intracellular receptors (TLR2, TLR4, NOD1), and inflammation markers such as ceruloplasmin.

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Role of histamine H1 and H3 receptors in IL-27 synthesis by PBMC and dendritic cells

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Background: Recent investigations demonstrated that the immunoregulatory cytokine IL-27 is synergistic with IL-12 in activatimg antigen-presenting cells and CD4 + T cell precursors in their deviation to Th2 cells and production of gamma-IFN. Dendritic cells (DC) in vitro derived from peripheral blood mononuclear cells (PBMC) possess an independent activity for induction of immune response sand induce differentiation of naïve T- and B-cells. The goal of the study was the comparative investigation of IL-27 synthesis by PBMC and DC and the possible role of histamine receptors (H1 and H3 types) in IL-27 synthesis.
Methods: Peripheral blood was collected from healthy volunteers and isolated PBMC was cultivated within 48 h. DCs were derived from blood mononuclear cells in the presence of GM-CSF and IL-4. PBMC and DC from 9 healthy donors were cultivated with a specific H1 agonist (2-methylhistamine) and an H3 antagonist