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THU0009 ASSOCIATIONS BETWEEN CYTOKINE LEVELS AND TH17/TREG IMMUNE BALANCE IN PATIENTS WITH BEHCET'S DISEASE

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Background: Behcet's disease (BD) is a chronic systemic vascular inflammatory disease. Autoimmune imbalance associated with genetic and infectious factors promotes the immune response of neutrophils and T cells, which is BD's important pathogenesis. Several studies indicate the Th17/Treg immune imbalance may play an important role in BD pathogenesis^[1-2]. Although the proportion of Th17 cells was notably increased, which was accompanied by an increased levels of IL-17, IL-23^[1], whether other cytokines are associated with Th17/Treg immune balance is unclear.

Objectives: The aim of this study was to examine associations between levels of a broad selection of cytokines and Th17/Treg immune balance in patients with BD.

Methods: The study included 66 BD patients and 66 healthy controls. The absolute counts of lymphocyte subsets and CD4+T cell subsets were detected by flow cytometry for all participants. Serum levels of the following 6 cytokines were determined in the same samples using a cytometric beads array: Interleukin-2 (IL-2), Interleukin-4 (IL-4), Interleukin-6 (IL-6), Interleukin-10 (IL-10), Interferon- γ (INF- γ) and Tumor necrosis factor- α (TNF- α) for all BD patients. T tests were used to compare continuous measures. Correlations between levels of cytokines and Th17/Treg were assessed by Spearman's rank correlation tests.

Results: (1) Compared to healthy controls, the absolute counts of T cells were increased ($P=0.048$), the absolute counts of CD8+T cells were also increased ($P=0.031$) in BD group, the absolute counts of Th1 and Th17 cells were significantly increased ($P<0.05$) in BD group, the absolute counts of Th2 cells were decreased ($P<0.05$) in BD group, the ratio of Th1/Th2 was increased ($P<0.001$), and the ratio of Th17/Treg were increased ($P<0.001$) in BD group. There were no differences between the absolute counts of the two groups of B, NK, T+B+NK, CD4+T and Treg cells. (2) Among the investigated cytokines, the differences between the levels of IL-2, IL-6, INF- γ and normal range have statistical significance ($P<0.001$). Finally, two cytokines were positively correlated with Th17/Treg: i.e., IL-2 ($r=0.279, P=0.023$) and IL-4 ($r=0.260, P=0.035$) ($P\geq 0.2$ for all other cytokines).

Conclusion: Our research shows that T cell homeostasis perturbation, especially Th1 and Th17 expansion and Th17/Treg immune imbalance, is the cornerstone of BD pathogenesis. These findings suggest that immune responses associated with increased levels of IL-2 and IL-4 may promote Th17/Treg immune imbalance. This also highlights the role of IL-2 and IL-4 in maintaining a balance in the Th17/Treg ratio. Further studies are required to evaluate these preliminary findings in different patient populations and also examine the possible molecular mechanisms behind our observations.

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Abstract THU0009 Figure 1. Figure: The absolute counts of lymphocyte subsets in RA patients and healthy controls. Data are expressed as means $\pm$ SD (ABCDE). Correlation coefficient and regression line of Th17/Treg with IL-2 and IL-4 serum levels were represented as scatter plots (FG).

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THU0010 THE ANTI-INFLAMMATORY CYTOKINE INTERLEUKIN 37 IS AN ENDOGENOUS INHIBITOR OF TRAINED IMMUNITY

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Background: Trained immunity (TI) is a *de-facto* innate immune memory program induced in monocytes/macrophages by exposure to pathogens or vaccines, which evolved as a protective mechanism against infections. TI is characterized by rewiring of functional, epigenetic and metabolic programs of innate immune cells such as monocytes and macrophages, which sustain enhanced production of pro-inflammatory cytokines. Since aberrant activation of TI is implicated in inflammatory diseases, tight regulatory mechanisms are likely in place, but the mechanisms responsible for this modulation remain elusive.

Objectives: Scope of this study was to evaluate the role of IL-37, an anti-inflammatory cytokine that curbs inflammation as well as modulates metabolic pathways, as an endogenous regulator of trained immunity.

Methods: The effects of recombinant IL-37 were evaluated in a mouse model of TI induced by the administration of beta-glucan *in vivo* (survival to a lethal inoculum of infectious agents, production of inflammatory cytokines, recruitment of inflammatory cells at the sites of infection). Subsequently, the effects of IL-37 were evaluated *ex vivo* on bone marrow monocytes (production of inflammatory cytokines, metabolomic analysis of the activation status of the main pathways of cellular energy metabolism).