IMMUNOLOGY AT THE CONFLUENCE OF MULTIDISCIPLINARY APPROACHES

ABSTRACT BOOK

Institute for Biological Research "Siniša Stanković" National Institute of Republic of Serbia
University of Belgrade

Immunological Society of Serbia

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Poster presentation

THE DECREASE OF TOLEROGENIC ILC3 AND TREG CELLS IN SMALL INTESTINE CORRELATES WITH THE PROGRESSION OF TYPE 1 DIABETES IN MICE

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Type 1 diabetes (T1D) is a chronic autoimmune disease characterized by the imbalance between the CD4 or CD8 T effector (Teff) cells and the FoxP3$^+$CD4 T regulatory cells (Tregs) that leads to pancreatic beta-cells destruction causing insulin deficiency. Environmental factors, diet and microbiome are associated with the recent rise in T1D incidence. Intestinal immune cells must maintain a tolerogenic response in the gut that involves the development of Tregs. Recent data show that IL-2-producing type 3 innate lymphoid cells ILC3s (IL-2$^+$ILC3) in the small intestine are essential for maintaining FoxP3$^+$ Tregs and oral tolerance to dietary antigens and reveal the previously unknown direct communication between ILC3s and Treg cells in the gut. We investigated the frequencies of small intestine lamina propria IL-2$^+$ILC3s and FoxP3$^+$ Tregs during transition from prediabetes to diabetes in young and old female NOD mice. 20 weeks old, diabetic NOD mice had higher frequencies of Lin^{neg}CD45$^+$RORγt$^+$CD127$^+$ ILC3s in small intestine lamina propria compared to 4 weeks of age-young NOD mice. However, the frequencies of IL-2-producing ILC3s and CD4$^+$CD25^{hi}FoxP3$^+$ Tregs were significantly lower in diabetic NOD mice compared to young, prediabetic mice. We next investigated how microbiota change before diabetes induction is reflected on Treg and ILC3 populations. Male C57BL/6 mice were treated with broad spectrum antibiotics (ABX) for 14 days and then T1D was induced by multiple low doses of streptozotocin (STZ). *Ex vivo* cell analyses was done on day 10 after the first STZ injection. The significantly higher incidence of T1D observed in ABX-treated mice correlated with significantly lower frequencies of IL-2-producing ILC3s and FoxP3$^+$Tregs in small intestine lamina propria compared to mice treated with STZ only. The obtained findings show that the decrease of tolerogenic ILC3s and FoxP3$^+$Tregs in small intestine is associated with the progression and higher incidence of T1D.