Increased occurrence of faulty immunosuppressive cells in children with chronic arthritis could advocate new treatment approaches

Lovro Lamot*, Alan Šučur, Maša Filipović, Mandica Vidović, Ivana Radoš, Mirta Lamot, Vedran Katavić, Miroslav Harjaček. Sestre milosrdnice University Hospital Center and University of Zagreb School of Medicine

Juvenile idiopathic arthritis (JIA) is characterized by chronic joint inflammation lasting longer than six weeks, as opposed to the acute reaction in reactive arthritis (ReA) that develops in response to an infection, lasts shorter and usually ends with full resolution of symptoms, indicating different mechanisms responsible for those common forms of arthritis in children. A number of previous studies have indicated the critical role of adaptive immune system cells in the development of many immune-mediated diseases (IMD), including arthritis. Therefore, the objective of this study was to examine the differences in occurrence of various subsets of lymphoid cells in JIA and ReA patients: regulatory T (Treg) and regulatory B (Breg) cells as immunosuppressors, type 3 innate lymphoid cells (ILC3) associated with a wide range of inflammatory disorders by an increase in IL-17 producing T cells and Th17 cells that exhibit plasticity and can be shifted to produce IFN-γ.

Treg cells, Breg cells, ILC3 and Th17 derived Th1 cells were analyzed in whole blood of ten JIA and six ReA patients by flow cytometry, using directly conjugated monoclonal antibodies. The blood samples were collected during the first visit to Pediatric Rheumatology Clinic in Sestre milosrdnice University Hospital Center in Zagreb, Croatia, while the final diagnosis of JIA or ReA was made three months after. At each visit, juvenile arthritis disease activity score (JADAS-CRP) for each patient was calculated. The median ages of the JIA and ReA patients were 6.41 and 7.22, respectively.

In patients with JIA, the CD3+CD45+CD25+CD4+CD127-CD28- subpopulation of Treg cells was significantly abundant compared to ReA patients (P=0.04). No other significant differences in cell subpopulations among different patient groups were observed.

Although Treg frequencies account for only ~5% of the total CD4+ T-cell population, they have a massive role in the immune response. Particularly, CD28− Treg cells are characterized by reduced suppression of effector T cells yielding a pro-inflammatory cytokine profile characteristic for JIA.

Besides, they can be generated in vitro by stimulation of CD28+ Tregs with TNF-α, which is raised in JIA. Therefore, the increased occurrence of these cells in JIA patients found in our proof-of-concept study could partially explain the failure of the immunosuppressive mechanisms and the development of the chronic disease in JIA patients. This observation could have a broader clinical significance after confirmation in larger patient cohorts with multiple time points, considering Treg cells have already been shown as a novel therapeutic target in some IMDs.

Gut microbiota composition in children with adverse outcomes of immune-mediated disease

I Rados*, M Vidovic, M Cindric, A Hozić, M Harjacek, L Lamot. Sestre milosrdnice University Hospital Center, Zagreb, Croatia

The perplexing interactions between an organism and its gut commensal microbiota have both potentiating and detrimental effects on innate and adaptive immunity and consequently the development of several immune-mediated diseases. Juvenile idiopathic (JIA) and reactive arthritis (ReA) are two adverse outcomes of such disorder in children. This study aimed to assess the differences in the presence of subtypes of Escherichia coli (E.coli), one of the most abundant bacteria in the microbiota, in the stool of JIA and ReA patients.

Stool samples of 14 patients with joint swelling were collected during their first visit to Pediatric Rheumatology Clinic in Sestre milosrdnice University Hospital Center in Zagreb, Croatia. Three months later, the diagnosis of JIA was made in seven patients, while the others were classified as ReA. The samples were analyzed by mass spectrometry on nanoLC-Synapt G2 Si instrument. To identify the most abundant E.coli strains, samples were processed (X-ray of thoracic organs, ultrasound of the lungs and cervical spine, ventilation-perfusion scintigraphy), taking microbiological materials, empirical broad-spectrum antibiotic therapy is started. Invasive procedures such as surgical open drainage, lobectomy and/or percutaneous drainage are reserved for cases refractory to conservative treatment.