INTERROGATION OF STAT3 ACTIVATION IN PATIENTS WITH POLYARTICULAR JUVENILE ARTHRITIS

Stephanie Wood[1], Justin Branch[2], Priscilla Vasquez[2], Marietta M. DeGuzman[2], Amanda Brown[2], A. Carmela Sagcal Gironella[2], Siamun Singla[2], Andrea Ramirez[2], Tiphanie P. Vogel[2]

[1] Baylor College of Medicine, Department of Pediatrics, Rheumatology

[2] Baylor College of Medicine and Texas Children's Hospital, Pediatrics, Rheumatology

Keywords:

Background: Juvenile idiopathic arthritis (JIA) affects 1:1000 children. Untreated, JIA can cause pain, disability, and deformity, but early disease control allows for improved outcomes. The polyarticular JIA (polyJIA) subset is the most clinically similar to adult rheumatoid arthritis (RA), yet its pathogenesis remains poorly understood. One inflammatory pathway of interest in polyJIA is STAT3 signaling. STAT3 is a transcription factor critical to the development of inflammatory T helper 17 (Th17) cells, as well as modifying the T regulatory cell (Treg) lineage. Previous studies have demonstrated elevated Th17 cells and activated STAT3 in blood and synovial fluid of adult patients with RA. However, little is known about T cell subsets or STAT3 activation in polyJIA. We hypothesized Th17 cells and STAT3 activation will be increased in treatment naïve polyJIA patients compared to pediatric healthy controls.

Materials/Methods: Blood from 13 patients with polyJIA was collected at initial diagnosis (treatment naïve) and serially until remission was achieved. Adult and pediatric healthy controls were also collected. Peripheral blood mononuclear cells (PBMCs) were isolated and T cell subsets and STAT activation (phosphorylation) was evaluated using flow cytometry.

Results: Regulatory T cells from patients with polyJIA were found at similar levels as pediatric controls. However, treatment naïve polyJIA patients had increased Th17 cells compared to pediatric controls (0.15% v 0.44%, p=0.0371). We identified high interleukin (IL)-17, interferon-y dual positive T cells (non-classical Th1 cells) appearing in the post-treatment samples of several polyJIA patients. After activation (using IL-6, IL-27 or IFN-a), compared to adult controls a subset of polyJIA patients had highly elevated activated STAT3, but not STAT1 or STAT5, in CD3+CD4+ T cells.

Conclusions: A better understanding of the mechanisms behind polyJIA is necessary to provide more efficient and effective clinical care. Although multiple therapeutics to treat polyJIA exist, a data-driven approach to determine the best treatment does not. Patients with polyJIA have increased Th17 cells and a subset have highly activated STAT3. These immunologic features may identify patients that would benefit from tailored treatment using non-traditional first line therapeutics that target this pathway.

Images / Graph / Table: No image uploaded