Complex Interplay of Forkhead BoxP3, Interleukin 22, and Interleukin 17 in Multiple Sclerosis Patients on Disease Modifying Therapy

Gezahegn B[1], Vaitaitis GM [1,2] Wagner DH [1,2]
[1] University of Colorado School of Medicine, Aurora, CO [2] Webb-Warring Center, Denver, CO

Multiple Sclerosis (MS) is an autoimmune disease affecting the central nervous system, characterized by immune-mediated destruction of myelin. The balance between regulatory and inflammatory cytokines guides disease progression. We investigated Interleukin 22 (IL-22), a cytokine with regulatory and inflammatory activity, Forkhead Box P3 (FoxP3), a regulatory transcription factor, Interleukin 17 (IL-17), an inflammatory cytokine, and T helper 40 (Th40) cells, a subset of CD4+ T cells, in MS, along with the potential of TGF Beta, a cytokine with neuroprotective function, as a therapy. These biomarkers have anti and pro-inflammatory activity and have not been investigated in MS patients on Disease Modifying Therapy (DMT). Tracking these biomarkers can help track progress of illness and personalize DMT.

Samples were collected from MS patients on Disease Modifying Therapy (DMT). Lymphocytes were isolated, stimulated, and analyzed for Th40 levels and CD3, CD4, IL-17, IL-22, and FoxP3 expression after treatment with IL-22, IL-17, or TGF Beta.

Th40 cells remained elevated in MS despite DMT, with cell stimulation leading to increased Th40 levels. FOXP3 levels were lower in untreated and stimulated MS samples compared to controls. IL-17 and IL-22 levels were decreased in MS samples. TGF Beta treatment resulted in higher levels of FOXP3 and IL-22 relative to other treatments.

DMT regulated inflammation by downregulating IL-22 and IL-17 but had no impact on Th40 cells. Further, anti-inflammatory activity was not targeted by DMT and should be considered as alternative targets in DMT. Lastly, TGF Beta treatment showed promising increase in anti-inflammatory activity but requires further investigation to yield significant impact.