Maddur MS, Vani J, Hegde P, Lacroix-Desmazes S, Kaveri S and Bayry J. (2011). Inhibition of differentiation, amplification, and function of human T_H17 cells by intravenous immunoglobulin. *J Allergy Clin Immunol*., 127:823-830

Background: TH17 cells play a critical role in the pathogenesis of several autoimmune and allergic diseases. Intravenous immunoglobulin (IVIg), a therapeutic preparation of polyclonal IgG that is increasingly used in the treatment of diverse autoimmune and allergic diseases, might target TH17 cells to exert therapeutic effects.
Objective: We sought to examine whether IVIg interferes with the development and function of human TH17 cells.
Methods: TH17 cells were differentiated from naive human CD41 T cells in the presence of TGF-ß and IL-21. TH17 cells were amplified by stimulating memory CD41 T cells in the presence of IL-1b and IL-6. The effect of IVIg was examined on the differentiation and amplification of TH17 cells, expression of the TH17 lineage-specific transcription factor retinoic acidrelated orphan receptor C, secretion of TH17 effector cytokines, and phosphorylation of signal transducer and activator of transcription 3, a transcription factor that plays an important role in TH17 cell development and function.
Results: IVIg inhibits the differentiation and amplification of human TH17 cells, as well as the production of their effector cytokines IL-17A, IL-17F, IL-21, and CCL20. The inhibitory effects of IVIg on TH17 cells are F(ab9)2 dependent and involve interference with the expression of retinoic acid-related orphan receptor C and activation of signal transducer and activator of transcription 3. Also, IVIg significantly enhanced forkhead box protein 3–positive regulatory T cells among the memory CD41 T cells.
Conclusion: These results reveal a novel mechanism of action of IVIg in achieving a therapeutic effect in autoimmune and allergic diseases, in which TH17 cells play a key modulatory role in sustaining the chronic inflammatory response. Our results also suggest a reciprocal regulation of TH17 and regulatory T-cell populations by IVIg.