

VASCULITIS SYNDROMES

Insights into the role of IL-21 in GCA

Despite advances in our understanding of the pathogenesis of giant cell arteritis (GCA), in terms of the involvement of type 1 T helper (T_H1) and type 17 T helper (T_H17) cell responses, the cytokines that control these pathways remain unknown. A paper in *Arthritis & Rheumatism* now identifies a key regulatory role for IL-21 in this process.

“We decided to undertake this project in order to find new molecular targets to cure vasculitis,” explains David Saadoun, one of the senior authors on this paper. “Based on recent findings from Cornelia Weyand and colleagues on T_H1 and T_H17 polarization in GCA we further explored the molecules driving these cells.”

First, using a multiparametric analysis of peripheral blood mononuclear cells, the authors described a cytokine signature that can be used to discriminate between patients with active and inactive disease. Next, they showed that numbers of T_H1 cells and T_H17 cells were higher and numbers of regulatory T cells were lower in peripheral blood from patients

with active disease than in age-matched controls. IL-21-producing $CD4^+$ T cells were also expanded in blood from patients with active disease, in direct correlation with the numbers of T_H1 and T_H17 cells.

Finally, the authors demonstrated that addition of IL-21 to cultures of $CD4^+$ T cells from patients with GCA resulted in the development of increased proportions of T_H1 cells and T_H17 cells, and that blockade of IL-21 (using an IL-21R/Fc chimeric construct) led to decreased proportions of these cells.

As Saadoun concludes, “We found that the level of IL-21 correlated with GCA disease activity and was critical to modulate T_H1 and T_H17 cell responses.”

Jenny Buckland

Original article Terrier, B. *et al.* IL-21 modulates T_H1 and T_H17 responses in giant cell arteritis. *Arthritis Rheum.* doi:10.1002/art.34327

Further reading Deng, J. *et al.* T_H17 and T_H1 T-cell responses in giant cell arteritis. *Circulation* 121, 906–915 (2010)