

A188 ANAKINRA EFFECTS ON T CELLS IN PATIENTS WITH REFRACTORY IDIOPATHIC INFLAMMATORY MYOPATHIES

Mei Zong,¹ Vivianne Malmström,¹ Ingrid E Lundberg¹ ¹Rheumatology Unit, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden

10.1136/ard.2010.149013.31

Background and objectives Interleukin 1 (IL-1) is overexpressed in muscle tissue of inflammatory myopathies. A clinical response to IL-1 blockade with anakinra was seen in 7/15 patients with refractory myositis, but the biological explanation for improvement has not been clarified nor has predictors of response been identified (Dorph *et al*, Abstract ACR 2009). IL-1 is a multifunctional cytokine, and anakinra therapy could affect many cell types. The authors have here focused on its role in mediating T cell differentiation into Th17-like cells. The authors have here explored possible predictive biomarkers for anakinra therapy response, and investigated changes in effector T cell function and phenotype.

Materials and methods 15 refractory myositis patients were included in a 12-month open-label study (100 mg anakinra per day). Serum creatine kinase (s-CK) was measured as a surrogate

marker for clinical response. Peripheral blood samples were collected before and after 6 months.

Serum levels of IL-1 receptor antagonist (IL-1Ra) were detected by a commercial ELISA, and T cells were studied by flow cytometry. To assess systemic immune activation, the proportions of naïve versus memory T cells were determined. The effector function of in vivo primed T cells was assessed by re-stimulating cells with anti-CD3 for 6 h and performing intracellular cytokine staining for interferon γ (IFN γ), tumour necrosis factor α and IL-17A.

Results Before treatment the patients demonstrated elevated levels of serum IL-1Ra (n=14, mean=2559 pg/ml, range 467–6937 pg/ml) compared to healthy controls (mean=354 pg/ml, range 11–839 pg/ml, Son *et al*, *Intern Med*, 2000). 10/14 patients were still on anakinra therapy at 6 months and thus displayed significantly elevated IL-1Ra (mean=19 571 pg/ml, range 19 572–18 844 pg/ml, p=0.005).

Viable cells from peripheral blood were available at baseline for eight patients and following 6 months of therapy for six subjects (three responders and three non-responders). When dissecting the pool of naïve versus activated/memory T cells, a strong negative correlation was seen between baseline level of CD4 CD45RO T cells and changes in CK levels after 6 months (R=-0.9, p=0.001).

The levels of IFN γ -secreting CD4 T cells (mean=1.1%, range 0.08–4.96%) increased after 6 months, while IL-17 producing T cells (mean=0.16%, range 0.03–0.4%) decreased in 2/3 responders.

Conclusions Patients with myositis may respond to anakinra treatment. This functional assay indicates that anakinra might favour T cell differentiation into Th1 rather than Th17 as indicated by more IFN γ and less IL-17A secretion. Furthermore, a high level of CD4 activated memory T cells might indicate a worse clinical outcome as demonstrated by less decreased CK levels.