FRI0423 DECREASED PERIPHERAL T CELL REACTIVITY IN ANKYLOSING SPONDYLITIS AFTER TREATMENT WITH ETANERCEPT

L. Pang[1], L. Wang[2], T. Suo[1], H. Hao[2], X. Fang[1], J. Zhang[2], J. Jia[1], F. Huang[2], **J. Tang**[1]
[1]Center for Infection and Immunity, National Laboratory of Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, [2]Rheumatology, Chinese PLA General Hospital, Beijing, China

Objectives: To study the effect of TNF-alpha antagonist (etanercept) treatment on the peripheral T cell reactivity of ankylosing spondylitis (AS) patients.
Methods: Peripheral blood mononuclear cells (PBMC) were collected from 40 patients with AS at baseline, after two and six weeks of etanercept treatment or placebo treatment, and from 10 healthy controls. The number of monocytes that secrete TNF-alpha and the number of T cells that secret interferon γ(IFN-γ) and interleukin 2 (IL-2) after anti-CD3/anti-CD28 stimulation were detected by ELISPOT. CD4+ and CD8+ T cell proliferation after stimulation were assayed with WST-1 live cell staining method. In addition, the change of myeloid dendritic cells (mDC) cell and regulatory T cells (Treg) were analyzed by FACS.
Results: ASAS20 responses were achieved in 57.1% and 71.4% of etanercept treated AS patients on week 2 and 6, compared to only 15.8% and 5.2% in placebo group ($P<0.05$). BASDAI50% improvements were observed in 28.6% and 47.6% in etanercept group as compared to 15.8% and 10.5% in placebo group ($P<0.05$). After 2 and 6 weeks of etanercept treatment, the number of TNF-α secreting monocyte was decreased ($P<0.05$). Although the T cell proliferation rate was not reduced, the number of T cells secreting IL-2 and IFN-γ after anti-CD3/anti-CD28 stimulation was significantly decreased ($P<0.001$ for both cytokines). This change in T cell function is correlated with a significant increase in MHC Class II positive mDC cells in circulation. Increased Treg cell numbers was also observed. No changes were observed in the number of MHC Class I positive mDC cells.

Conclusion: Six weeks of etanercept treatment in AS patients reduced the TNF-α production by monocytes. The reduction of TNF-α level led to blockage of the MHC Class II positive mDC maturation. This in turn enhanced the regulatory T cell level and reduced the cytokine secretion from effector T cells.