CONNECTIVE TISSUE DISEASES

Oral anti-CD3 antibodies for SLE

Defects in the number and function of regulatory T (T_{REG}) cells are thought to have a key role in the pathogenesis of systemic lupus erythematosus (SLE). Research by Howard Weiner and colleagues shows that oral administration of anti-CD3 antibodies to lupus-prone SNF1 mice results in the development of an inducible subset of $CD4^+CD25^-LAP^+$ T_{REG} cells, and blocks disease development and progression in this animal model.

Mice that received anti-CD3 antibodies developed less-severe glomerulonephritis and produced lower levels of pathogenic autoantibodies targeting double-stranded DNA (dsDNA) than control mice. In addition, this treatment led to increased numbers of suppressive $CD4^+CD25^-LAP^+$ T_{REG} cells, which produced more transforming growth factor β than comparable cells from control mice. Reduced numbers of inflammatory $IL\text{-}17^+CD4^+ICOS^+CXCR5^+$ follicular helper T cells, $CD138^+$ plasma cells and $CD73^+$ mature memory B cells were detected in anti-CD3-treated mice in comparison with control mice. In animals with established disease, anti-CD3 treatment reduced the levels of anti-dsDNA autoantibodies and improved survival.

"Clinically applicable strategies to generate inducible T_{REG} cells *in vivo* could have beneficial effects in the treatment of SLE," explains Henry Yim Wu, the corresponding author. "Our positive results in animals with ongoing disease raise the possibility that oral anti-CD3 antibodies might be an effective immunomodulatory therapy for SLE that could be easily and rapidly applied to human subjects."

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Original article Wu, H. *et al.* Suppression of murine SLE by oral anti-CD3: inducible $CD4^+CD25^-LAP^+$ regulatory T cells control the expansion of $IL\text{-}17^+$ follicular helper T cells. *Lupus* **18**, 586–596 (2009).