Retinoic acid-induced gut tropism improves the protective capacity of Treg in acute but not in chronic gut inflammation.

Abstract:

Treg are endowed with immunosuppressive activities and have been proposed as promising targets for the therapy of autoimmune diseases. As the suppressive capacity of Treg depends on their migration into the affected tissues, we tested here whether modulation of Treg homing would enhance their capacity to suppress inflammation in mouse models of inflammatory bowel disease. Retinoic acid (RA) was used to induce the gut-specific homing receptor alpha(4)beta(7) efficiently and, to some extent, the chemokine receptor CCR9 on in vitro expanded Treg. Upon transfer, RA-treated Treg were indeed more potent suppressors in an acute, small intestinal inflammation model, compared with Treg stimulated without RA. By contrast, the efficacy of Treg to resolve an established, chronic inflammation of the colon in the transfer colitis model was not affected by RA-treatment. In the latter model, a rapid loss of RA-induced alpha(4)beta(7) expression and de novo induction of alpha(4)beta(7) on previously negative cells was observed on transferred Treg, which implies that Treg acquire gut-seeking properties in vivo under inflammatory and/or lymphopenic conditions. Together, our data show that the induction of appropriate homing properties prior to transfer increases the protective potential of adoptively transferred Treg in acute, but not in...
chronic, inflammatory disorders of the gut.

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