Transforming Growth Factor-? and All-Trans Retinoic Acid Generate Ex Vivo Transgenic Regulatory T Cells With Intestinal Homing Receptors

Moore, C.

Sauma, D.

Morales, J.

Bono, M. R.

Rosemblatt, M.

Fierro, J. A.

CD4+CD25+Foxp3+ regulatory T cells (Treg) mediate immunologic self-tolerance and suppress immune responses. In the gut, a subset of dendritic cells is specialized to induce Treg in a transforming growth factor-? (TGF-?)- and retinoic acid (RA)-dependent manner. The aim of this study was to establish if RA synergizing with TGF-? induced antigen specific CD4+ CD25high Foxp3+ Treg portraying gut homing receptors. Splenic CD4+CD25- Foxp3- naïve T cells from DO11.10 mice were cocultured with splenic CD11c+ dendritic cells from Balb/c mice in the presence of TGF-?, RA, and low levels of an antigenic peptide. After 5 days of culture, cells were analyzed for the expression of Foxp3 and the gut homing receptors CCR9 and ?4?7. The number of Foxp3+ T cells generated with TGF-? and RA was at least 3 times higher than in the cultures with TGF-? alone and 15 times higher than in controls without exogenous cytokines. Also, supplementation of the cultures with RA induced the expression of the intestin