

Supplementary Note 2

Evidence that Treg with indirect specificity may prevent allograft rejection

The hypothesis we postulated in this report stating that Treg specific for indirectly presented alloantigens could prevent chronic allograft-rejection is consistent with previously published data showing that tolerance to allografts induced by blockade of costimulatory molecules, which is known to be mediated by Treg¹, requires host MHC class II². Also other evidence supports the notion that Treg specific for indirectly presented alloantigens may be involved in prevention of allograft-rejection³⁻⁶, e.g. by inhibiting production of alloantibodies⁷.

1. Taylor, P.A., Noelle, R.J. & Blazar, B.R. CD4+CD25+ Immune Regulatory Cells Are Required for Induction of Tolerance to Alloantigen via Costimulatory Blockade. *J. Exp. Med.* **193**, 1311-1318 (2001).
2. Yamada, A. *et al.* Cutting Edge: Recipient MHC Class II Expression Is Required to Achieve Long-Term Survival of Murine Cardiac Allografts After Costimulatory Blockade. *J. Immunol.* **167**, 5522-5526 (2001).
3. Hara, M. *et al.* IL-10 Is Required for Regulatory T Cells to Mediate Tolerance to Alloantigens In Vivo. *J. Immunol.* **166**, 3789-3796 (2001).
4. Wood, K.J. & Sakaguchi, S. Regulatory T cells in transplantation tolerance. *Nat. Rev. Immunol.* **3**, 199-210 (2003).
5. Lechler, R.I., Sykes, M., Thomson, A.W. & Turka, L.A. Organ transplantation--how much of the promise has been realized? *Nat. Med.* **11**, 605-613 (2005).
6. Golshayan, D. *et al.* In vitro-expanded donor alloantigen-specific CD4+CD25+ regulatory T cells promote experimental transplantation tolerance. *Blood* **109**, 827-835 (2007).
7. Callaghan, C.J. *et al.* Abrogation of antibody-mediated allograft rejection by regulatory CD4 T cells with indirect allospecificity. *J. Immunol.* **178**, 2221-2228 (2007).