

Regulatory T lymphocytes and Transplantation

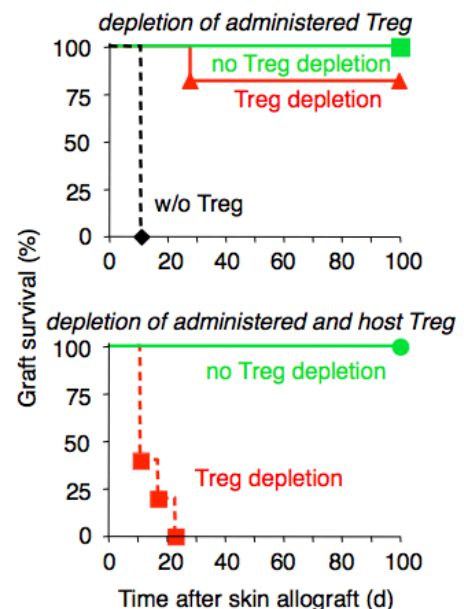
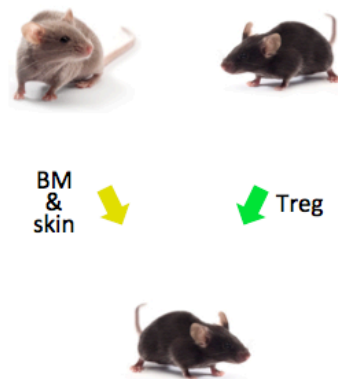


Prevention of chronic allograft rejection using regulatory T cells in the mouse

Joost van Meerwijk, Pathophysiology Centre of Toulouse Purpan (CPTP), Inserm U1043, CNRS, University of Toulouse, France

One of the major problems in transplantation medicine is the rejection of donor tissue by the patient's immune system. Immunosuppressive drugs inhibit acute rejection but they do not prevent chronic rejection and many patients will require subsequent transplantations. Moreover, these medicaments globally suppress immune responses and patients therefore develop opportunistic infections and cancer. We postulated that regulatory T cells should be able to prevent graft rejection. We indeed showed that they avoided rejection of bone marrow, skin, and heart allografts. Importantly, chronic rejection was fully prevented.

Moreover, a single injection of regulatory T cells was sufficient to prevent rejection, and we have investigated the mechanisms involved in this long-term persistence of donor-tolerance. It appears that administered regulatory T cells induce the emergence of similar cells of host-origin. The antigen-specificity of these host regulatory T cells



appeared instructed by the specificity of administered cells. Combined, these mechanisms ensure long-term tolerance to donor-tissue, and thus prevention of chronic rejection. Ultimate transposition to the clinic of the use of regulatory T cells to induce donor-tolerance should prevent chronic rejection and substantially increase the quality of life of millions of patients.