

Supplementary Note 3

Different transplanted tissues are differentially affected by Treg-specificity

Interestingly, whereas Treg specific for directly and indirectly presented alloantigens fully protected all three tested tissues (bone marrow, skin, and heart), cells specific for directly presented alloantigens differentially affected their rejection. When the latter cells were administered, bone-marrow allografts showed indefinite survival; skin grafts showed signs of chronic rejection (eosinophil and macrophage infiltration), but without widespread tissue destruction; and cardiac allografts were heavily infiltrated and extensive tissue-destruction associated with fibrosis was observed. This observation suggests that rejection of the three tested tissues is mediated by distinct mechanisms, differentially affected by Treg specific for directly presented alloantigens but all inhibited by cells activated by the direct and indirect pathways. More work will need to be done to assess the rejection mechanisms involved and to understand the differential Treg-specificity requirements to control them.