Induction of regulatory T cells and their role in cutaneous immune responses

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Compelling evidence exists for the presence of an immunomodulatory T cell, the Treg. While implicated in down regulating immune responses to self antigens and organ transplants, the definitive characterization of these cells has been difficult, with various groups reporting the presence or exclusion of unique markers in individual model systems. We have established a transgenic mouse model in which we are able to study regulatory T cells at cutaneous sites. Our studies indicate that alloreactive T cells (BM3) are unable to mediate skin graft rejection when the alloantigen (GPI-tethered H-2Kb) is expressed exclusively in basal epithelial cells. Furthermore, T cells in our system can mediate the acute rejection of skin grafts that bear wild type H-2Kb but are rendered tolerant if given prior exposure to the mutant H-2Kb-GPI expressed off the Ker 14 promoter. We found that 85% of mutant skin grafts onto BM3 recipients are accepted. This compares with an acute rejection rate of 88% for the skins expressing the wild type H-2Kb. When first engrafted with H-2Kb-GPI, 55% of the wild type grafts are then accepted. The tolerated skin grafts are infiltrated with T cells. Ongoing immunohistochemical and FACS analyses are being undertaken to characterize the tolerizing lymphocytes in this system.