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A novel method for prolongation of allogeneic skin graft survival

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Despite the effectiveness of skin autotransplantation, the high degree of immunogenicity of skin precludes the general use of allogeneic skin grafts. Systemic immunosuppression is generally felt to be inappropriate for isolated skin grafts. This study examines the potential to create an allogeneic skin transplant that delays rejection by inducing localized immunosuppression. Specifically, IDO (indoleamine 2 3-dioxygenase) expressing fibroblasts are introduced into the dermis and subcutaneous area of donor subjects to provide a tryptophan depleted environment and therefore local immune suppression toward the graft. Four-days post injection of the cells, grafts with regular and IDO fibroblast were transplanted to the allogeneic recipients and monitored until graft rejection. Additionally, IDO-expressing cell survival, migration and interaction with recipients' dendritic cells (DCs) in the allogeneic environment were studied. Skin transplantation studies demonstrate that IDO expressing grafts remain viable for significantly longer than control allogeneic grafts ($p=0.01$). Following injection of the IDO cells to the allogeneic full-thickness graft, average survival graft rate in IDO group increased up to 35-days in comparison to 13-days in the control group ($p<0.001$). DCs which were isolated from skin draining lymph nodes of IDO-expressing graft recipients expressed significantly higher levels of PDL-1 and PDL-2 molecules when compared with control groups. These data suggest that local immunosuppression can be provided by the delivery of IDO-expressing fibroblasts in allogeneic skin transplantation. The potential of this research goes far beyond the promising role for skin transplantation. This cell-based approach to localized immunosuppression can also provide potential opportunities to autoimmune skin disorders such as alopecia areata.

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