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The impact of donor diabetes on graft survival in Descemet membrane endothelial keratoplasty

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Abstract

Purpose : Considering the continued shift from PK to endothelial keratoplasty (EK) and nearly 33% of the corneas in the donor pool being derived from diabetic donors, in this study, we extended to study the transplant immunity in a non-diabetic EK mouse model transplanted with corneal tissue from diabetic donors

Methods : The central corneal endothelium and Descemet membrane were removed from the corneas of recipient BALB/c mice and replaced by a 1.5-mm donor graft of the posterior stroma and Descemet's membrane from either type 1 STZ-induced DM or non-diabetic mice. Graft recipients were not treated with any topical or systemic immunosuppression. At 4 weeks post-EK, the grafted corneas were harvested and assessed with flow cytometry. Additionally, we harvested the draining lymph nodes (DLNs) and assessed mature APCs ($CD45^+CD11b^+B220^-MHC\text{-}II^{high}$) and INF-$g^+$ $CD4^+$ T-cells frequencies using flow cytometry and ELISPOT assay, respectively. The remaining animals were assessed for corneal opacity (scored 0-5) and AS-OCT for 16 weeks.

Results : At 4 weeks post-EK, we also observed higher frequencies of alloreactive $CD4^+$ T-cells (p=0.032) in the transplanted tissue derived diabetic compared to non-diabetic donors. The hosts transplanted with tissue derived from diabetic donors showed three-fold higher frequencies of mature APC (p=0.048) and five-fold higher alloreactive IFN-g^+ $CD4^+$ cells (p=0.021) in DLNs compared to hosts that were transplanted corneal tissue from non-diabetic donors. We observed significantly lower endothelial cell density (p=0.0002) in the grafted tissue derived from diabetic compared to non-diabetic donors by week 4. We observed significantly increased central corneal thickness (p=0.0034)

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and lower allograft survival (0% vs. 75%, $p<0.0001$) in hosts that received corneal tissue from diabetic donors compared to hosts that received tissue from non-diabetic donors after 16 weeks.

Conclusions : These results extend from our previous observation in penetrating keratoplasty in diabetic donors, highlighting an amplified immune response against transplanted corneal tissue derived from diabetic donors for EK, resulting in high graft rejection rates.

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