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Allochimeric MHC I-conditioned T cells attenuate chronic rejection in rat cardiac model system

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Background: We have shown previously that the mutated class I MHC molecules abrogate acute and chronic rejection and attenuate transplant vascular sclerosis (TVS) through the early changes (1-7 days post-transplantation) in T cell and dendritic cell molecular response. Here we studied a cohort of long-term (100 days) graft survival recipients for changes in T cell molecular response, and the role of regulatory T cells in the abrogation of chronic rejection in adoptive transfer experiments.

Methods: Heterotopic cardiac transplants were performed between donor Wistar Furth (WF) and ACI recipient rats. Controls received no treatment or 6 days therapeutic dose of cyclosporine (CsA 10mg/kg). The experimental group of primary ACI recipient received, peri-operatively, the allochimeric [[α]1h$^{l/u}$]-RT1.A^{a} MHC I molecule (1mg/kg) in conjunction with the sub-therapeutic dose of CsA for 3 days. Splenic T cells were isolated from ACI recipient at 100 days post-transplantation and either assessed for changes in the expression of chosen protein markers or, in adoptive transfer experiments; they were injected into lightly irradiated secondary ACI recipients grafted with WF hearts. Secondary cardiac grafts were harvested at 100 days of post-transplantation for assessment of chronic rejection, neointimal index (NI) and apoptosis.

Results: Secondary cardiac grafts from recipients exposed to allochimeric MHC I-conditioned splenic total T cells or CD4^{+} T cells showed significantly reduced NI and apoptosis, and were selectively infiltrated with CD4^{+}Foxp3^{+} (T regulatory, Treg) cells.

Conclusion: Adoptive transfer of allochimeric MHC I-conditioned T cells promotes development of Treg cells and attenuates chronic rejection in rat cardiac model system.

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