

CAN WE GET RID OF IMMUNOSUPPRESSANTS?

*M. Siemionow*1*

1Cleveland, OH, USA

Clinical application of composite tissue allografts requires introduction of minimal immunosuppressive or tolerance inducing protocols. Working for the past 20 years on the strategies for tolerance induction in composite tissue allografts using a standard 7-day limb transplantation model across major histocompatibility barrier, we have established a protocol for tolerance induction under alpha-beta selective blocking antibody TCR combined with IL-2 blocker cyclosporine A therapy.

Application of this combined alpha beta TCR/CsA therapy for 7 days resulted in induction of tolerance in fully allogenic and semi-allogenic limb allograft transplants, which was maintained for over 720 days without need for lifelong immunosuppression. Induction and maintenance of tolerance correlated with induction of donor-specific chimerism and maintenance of chimerism over the time of allograft survival. Based on this experience, as well as experience with vascularized skin allograft transplants, we have found that the bone marrow component of the allograft is essential for tolerance induction.

To test this hypothesis, we have used a model of vascularized bone allograft transplantation and compared this model with composite vascularized skin / vascularized bone and face transplantation model for chimerism and tolerance induction. To make these studies clinically applicable, we have tested the injection of crude and processed bone marrow directly into the bone of the recipients of the skin allografts and compared it with the conventional intravenous transplantation of the bone marrow.

Finally, we have established a protocol for cellular therapy based on creation of donor / recipient chimeric cells which resulted in good engraftment and survival of vascularized skin allografts supported by donor chimerism.

The lecture will summarize the results of the above experimental models and will discuss the correlation between chimerism and tolerance. Potential clinical application of this protocol will be presented. A new approach to bone marrow-based cellular therapeutics with chimeric cells will be introduced and discussed.