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Memory T cells are significantly increased in rejecting liver allografts in rhesus monkeys

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Introduction: In kidney, heart and islet transplantation the rhesus monkey (*Macaca mulatta*, RM) has been shown to be an excellent preclinical model that can provide the basis for new immunosuppressive protocols for clinical studies. However, there remain relatively few liver transplant (LT) models in nonhuman primates. In this study, we analyzed the immune cell populations of PBMC and secondary lymphoid organs along with livers of normal rhesus monkeys and compared them to those of rejecting liver transplanted recipient's following withdrawal of immunosuppression.

Methods & Results: We undertook six allogeneic ABO compatible orthotopic LT in monkeys using six normal donor monkey livers. We collected tissues including lymph-node, spleen and blood from which we isolated immune cells for FACS analysis along with the liver from the recipient. We found that CD4 or CD8 naïve T cells were normally seen at low levels (13.89±8.67 or 1.50±1.44 respectively) and memory T cells were seen at high levels (76.12±11.40 or 98.0±1.60) in the liver rather than lymphoid organs or PBMC. However, regulatory cells such as CD4+FoxP-3+ T cells and CD8+CD28- cells remained in high numbers (0.77±0.54 and 34.99±6.40) in the liver but not in lymph node or PBMC. These results demonstrate that the liver has rather unique immunological properties compared to other organs. We also compared CD4/8 T sub-populations in normal or rejected livers and the various tissues showed that naïve cells were dramatically decreased in spleen, lymph node and PBMC of rejected transplanted monkeys but rather their memory cells were increased in all tissues and PBMC.

Conclusion: We have shown that the normal liver has large numbers of C4Tregs or CD8+CD28- or MDSC which are the known immune suppressive cells at much higher levels than other lymph node or peripheral blood. Memory T cell populations in rejected livers or lymphoid organs were expressed at significantly higher levels than those seen in normal tissues including as seen in the peripheral blood.

Biography

During the course of my Ph.D. I studied therapeutic anti-inflammatory effects of human mesenchymal stem cells on traumatic brain injury and studied the role of stem cells in human brain tumor development using SD-rat model. As a post Doc my focus was to study therapeutic strategies towards successful xenotransplantation. I was involved in two main projects related to the development of the first pre-clinical nonhuman primate study of solid organ xenotransplantation. This was done using genetically engineered pigs expressing multiple human complement and coagulation regulatory proteins in order to overcome the immunological and physiological barriers against successful xenotransplantation.

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