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Transplant tolerance in the human: Coming of age

Solid organ, tissue or cellular transplantation is the preferred therapy for multiple types of organ or system failures. However, the use of nonspecific immunosuppressive agents (IS) has been critical to prevent either host vs graft rejection or graft vs host disease. IS is costly; its long-term use leads to acute and chronic toxicities, opportunistic infections, malignancy, renal failure, and other organ damage. Since organs were first transplanted in humans, the field's elusive goal has been to establish donor-specific immunologic tolerance, a state where the transplant is accepted as "self," eliminating the need for IS.

Spontaneous "operational tolerance" resulting from the transplant recipient having stopped taking IS has been reported. Such spontaneous tolerance is rare and more organs are lost due to the non-compliance. Even though the participation of immunoregulatory cells has been reported, the various mechanisms operating in these rare patients as predictive biomarkers are elusive or at best inconclusive.

Based on a wealth of knowledge from experimental animal models, numerous *in vitro* and *ex vivo* assay systems, a number of groups have made deliberate attempts at inducing clinical transplant tolerance and have succeeded to some extent during the last decade. What all these studies have in common is the use of donor bone marrow derived cell infusions, which result in transient microchimerism or even prolonged macro or full donor chimerism. These early works will be briefly reviewed as a historical background. Then, an in-depth synthesis of new and ongoing studies will be made, with an emphasis on our own work in both HLA-identical and HLA-disparate kidney transplantations.

Biography

James M. Mathew, Ph.D. is currently an Associate Professor of Surgery and Microbiology-Immunology at Northwestern University in Chicago. He is also the Director of the Immune Monitoring Core of the Comprehensive Transplant Center at Northwestern. He received his Master's in Integrated Biology from Madurai Kamaraj University, Tamil Nadu, India in 1982, and then PhD in Immunology from the same institution in 1988. He had his post-doctoral training at Washington University, St. Louis in transplant immunology. Dr. Mathew was a faculty member in the Department of Surgery, Division of Organ Transplantation at the University of Miami, Florida and rose from Instructor to Associate Professor from 1994-2007. Then, he moved to Northwestern in 2007. He has reviewed for many journals, is on many editorial boards and currently is the Editor-in-Chief of the American Society for Histocompatibility and Immunogenetics Quarterly. Dr. Mathew has over 235 peer reviewed publications and has been funded by the NIH, VA and many pharmaceuticals and foundations.

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