Immunoprofiling after profound T cell depletion and minimization of
immunosuppression in pediatric kidney transplantation: A study of CCTPT/NIAID

William Harmon, MD¹, Fanny Benitez, MD¹, Nader Najafian, MD² and Mohamed Sayegh, MD¹,². ¹Transplantation Research Center, Children's Hospital Boston, Boston, MA, United States, USA and ²Transplantation Research Center, Brigham and Women's Hospital, Boston, MA, United States, 02115.

Despite excellent short-term outcomes for recipients of pediatric kidney transplantation, long-term success is compromised by complications of chronic immunosuppression and chronic allograft nephropathy. We thus undertook a study of minimal maintenance immunosuppression using a steroid-free, calcineurin inhibitor withdrawal protocol in 4 pediatric renal transplant centers. Campath-1H was used for induction and MMF and tacrolimus immunosuppression were used for 2-3 months, followed by withdrawal of tacrolimus and replacement with sirolimus. One-year acute rejection rate was 17% and only 2 grafts were lost, one due to recurrent FSGS and the other to medication non-adherence. There were no deaths and more importantly no cases of PTLD or other serious infections. Twenty-eight subjects had serial assessments of anti-HLA Class I and II antibody by Luminex up to 2 years post transplantation. Five subjects (18%) developed new anti-HLA antibody, 1 against Class I, 3 against Class II and 1 against both Class I and II. Twenty-three subjects had evaluation of lymphocyte recovery for at least one year post transplantation. Peripheral blood monocytes were monitored by flow cytometry and analyzed by FACSCalibur cytometry at 8 times point up to 24 months post transplant. Phenotypes examined in CD4+ and CD8+ T cell subsets included naive, Central memory and Effector memory; as well as T Regulatory Cells (Tregs). CD8+ T-cell percentages rebounded in 6 months, but CD4+ T-cells took 18 months to reach pre-transplant levels. Naive CD4+ cells rebounded more quickly than CD4+ memory and Central memory was more reduced than Effector memory. Patterns in CD8+ cells were similar. Percentages of Tregs increased immediately post transplant and remained high until at least 8 months. This pattern of recovery in children was different from the typical pattern in adults after profound T cell depletion in at least 2 ways: pediatric subjects had depletion of both memory and naive T cells with quicker recovery of naive cells, whereas adults typically have sparing of memory T cells in comparison to naive cells. Also, the memory T cells spared in children were mostly Effector rather than Central. Taken together with Tregs sparing, these observations suggest that this protocol could permit less maintenance immunosuppression in children.