Effect of Infection and Acute Cellular Rejection on T Cell Populations in Post-Lung Transplant Biopsy Specimens
K Suzue MD PhD1, SM Bhorade MD2, M Tretiakova MD PhD3, Can Gong3, YX Fu MD PhD3 and AN Husain MD3
1Department of Pathology, Mount Sinai Hospital, Chicago, IL
Departments of 2Medicine and 3Pathology, The University of Chicago Medical Center, Chicago, IL

Background
• Approximately half of lung transplant recipients will suffer from graft dysfunction within 5 years after transplantation.
• Episodes of infection and acute rejection are risk factors for subsequent chronic lung transplant rejection. A better understanding of the inflammatory milieu within lung allografts is crucial for improving immunosuppressive regimens and survival in lung transplant (LTx) recipients.
• Recent studies have shown the presence of regulatory T cells (Tregs), which are CD3+CD4+CD25+ T cells which can inhibit the CD8+ anti-cellular T cell response and induce immunotolerance. A major goal in organ transplantation is to be able to harness tolerance processes and to minimize the need for immunosuppressive drugs.
• This study assessed the populations of T cells present in LTx biopsy specimens.

Design
• We evaluated 21 LTx transbronchial biopsy specimens, which were divided as:
  Group 1 (n=5) positive for acute cellular rejection (A1BX, A1BX, A2B0, A2B0, A2B2)
  Group 2 (n=8) positive for viral infection (CMV, influenza, RSV)
  Group 3 (n=8) negative for infection and acute cellular rejection
• We confirmed these diagnoses on H&E sections and by clinical history. We then immunostained for CD3, CD4, CD8, CD20 and FoxP3 and examined the interstitial and perivascular infiltrates.
• Scored: 0 for no positive cells; 1 for 1 cell/40X; 2 for 2-8 cells/40X, 3 for >8 positive cells at 40X and 4 for diffusely positive cells at 4X

Results
• All 21 cases contained a higher proportion of CD8+ T cells in the interstitium, relative to CD4+ T cells.
  • In group 1 (acute cellular rejection group), 1-10% (mean 8%) of interstitial T cells were FoxP3+, and the perivascular FoxP3+ T cell infiltrate was 10%-20% FoxP3+ T cells.
  • In contrast, in group 2 (viral infection group), rare to absent (0-4%; mean 1%) (p=0.002) interstitial FoxP3+ T cells were seen despite a 3+ to 4+ level of CD3+ T cell infiltration.
  • In group 3 (no rejection or infection), analysis of T cells was difficult due to the minimal inflammatory cell infiltrate.

Conclusions
• This preliminary study illustrates the difference in T cell populations in LTx allografts in patients with acute cellular rejection vs. infection.
• Specifically, viral infections led to lower numbers of FoxP3+ T cells and may be a mechanism by which viral infections contribute to chronic lung allograft rejection. Evaluation of regulatory T cells as well as other immunologic mediators and markers will contribute to our understanding of lung transplant immunopathology. Indeed, manipulation of specific T cell subsets may be an effective strategy for inducing lung transplant tolerance.