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2001 Program  
Investigator Initiated (2-year project)

**Project Title:** Bone marrow derived stem cell repopulation of transplanted lungs

**Project Summary:** Many patients undergo lung transplantation as a treatment for advanced tobacco-related lung disease. The objective of this project was to determine the degree of lung repopulation by type II pneumocyte descendents of adult bone marrow-derived stem cells, and to assess the relationship between the degree of repopulation and rejection history in lung transplant recipients. Recut sections were obtained from lung biopsies and autopsy lung tissues from seven male recipients of transplanted lungs from female donors, and four female recipients of transplanted bone marrow from male donors. Sequential immunohistochemistry and fluorescence in situ hybridization was performed on each section to evaluate for Y-chromosome-containing type II pneumocytes. As a result, Y-chromosome-containing type II pneumocytes were found in 9/25 biopsies from 5/7 gender-mismatched male lung transplant recipients, and accounted for 0-1.746% of type II pneumocytes in the eight cases in which the total number of pneumocytes could be determined. Y-chromosome-containing type II pneumocytes were also found in one biopsy from a bone marrow transplant recipient. There was no evidence of polyploidy to suggest cell-cell fusion. In the lung transplant patients, the number of type II pneumocytes of male karyotype showed a statistically significant relationship with the cumulative number of episodes of acute cellular rejection and patient age, but not the interval between biopsy and transplantation or the cumulative number of episodes of lymphocytic airway inflammation. Type II pneumocytes containing a Y-chromosome were found in patients with and without chronic airway rejection.

**Project Successes:** Lung and bone marrow transplant recipients develop low levels of pneumocyte repopulation by bone marrow-derived stem cells or their progeny. These cells contribute minimally to the type II pneumocyte proliferation that is often present in these patients as a sequel to alveolar injury. This suggests that stem cell populations intrinsic to the adult lung may be more important to lung regeneration than circulating bone marrow-derived stem cells. Repopulation does not appear to protect against chronic airway rejection.

**Publications from BRP funded research in Peer Reviewed Journals:**

**Zander DS**, Baz MA, Jorgensen M, Visner GA, Theise ND, Crawford JM: Bone marrow-derived stem cell repopulation contributes minimally to the type II pneumocyte pool in transplanted and native lungs. *Mod Pathol.* 2004;17:345A.

**Presentations from BRP funded research:**

**Zander DS.** *Bone Marrow-Derived Stem Cell Repopulation of Transplanted Human Lungs.* Gainesville, Florida University of Florida Shands Cancer Center Stem Cell Symposium; 2002.

**Zander DS.** *Research on Lung Injury and Repair After Transplantation.* Houston, Texas:University of Texas Health Science Center at Houston Medical School; 2002.

**Zander DS**, Baz MA, Jorgensen M, Visner GA, Theise ND, Crawford JM. *Bone marrow-derived stem cell repopulation contributes minimally to the type II pneumocyte pool in transplanted and native lungs*. Vancouver, British Columbia: 93rd Annual Meeting of the United States and Canadian Academy of Pathology; March, 2004.