Selective SHIP-1 Phosphatase Inhibitor as a Novel Therapy for Tissue Graft Failure and Blood Cancers

This technology is a new use of a compound as an inhibitor of a novel target in the treatment of graft vs. host disease (GvHD) and blood cancers. SHIP-1 (Src Homology Inositol Phosphatase-1) protein regulates the function of the immune cells that mount graft rejection, as well as promotes growth of malignant blood cancer cells. Current immunosuppressive therapies for preventing and treating GvHD and graft failure are used at significant financial and health costs to the transplant patient. Our lead compound in preclinical development shows efficacy in preventing GvHD and treating multiple myeloma in mice without toxicity or adverse events.

COMMERCIAL OPPORTUNITY

- Over 20,000 hematopoietic cell transplants and 750,000 tissue transplants are performed annually in the US alone; in 2012, there were over 68,000 new cases of leukemia and myeloma reported in the US, suggesting a very large market opportunity from these combined patient populations.
- The US cost of immunosuppressive drugs and the monitoring required by their administration has been estimated at >$30,000 in the first year after transplantation, and ~ $15,000 per year thereafter for the prevention and treatment of tissue/graft failure and GvHD with some patients remaining on therapy for the remainder of their lives following the procedure.
- Side effects of effective immunosuppression by current therapies include nephrotoxicity, diabetes, anemia, cytopenias, hypertension, neuropathy with over-immunosuppression increasing the risk for infection and blood cancers.
- Mouse studies of our lead compound demonstrated statistically significant suppression of cells responsible for graft failure and GvHD without toxicity to key vital organs. A xenograft mouse model study of multiple myeloma also showed a statistically significant increase in survival with lead compound treatment.

TECHNOLOGY

An increase in the myeloid immunoregulatory cell (MIR) population is sufficient to suppress the allogeneic T-cell response that leads to GvHD and transplant organ rejection. Our lead compound increases this MIR population by 5-6 fold in the spleen and lymph nodes of treated mice compared to vehicle-treated and untreated mice ($p < 0.0001$). Similar effects were observed with human peripheral blood mononuclear cells in cell culture. Also, lead compound treatment in mice challenged with multiple myeloma cells resulted in significantly reduced percentages of circulating myeloma in blood and increased survival of treated mice ($p=0.01$). Preliminary toxicity studies of our lead compound in mice demonstrated no evidence of lung, heart, kidney, intestine, brain, or liver pathology or adverse events, nor a decrease in body weight associated with 5-week treatment with the lead inhibitor.

PUBLICATION/PATENT

- R. Brooks, et al. (2010) *J. Immunol*. 184(7):3582-9; G.M. Fuhler, et al (2012) *Mol. Med*. 18:65-75
- US non-provisional patent application filed on 4/13/11 for Dr. William Kerr

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