Title: A Study of Thiol Redox Status in Allogeneic Transplantation to Determine if it can be Predictive of Graft Versus Host Disease

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Synopsis:
This is a two year prospective observational study in 12 - allogeneic transplant patients and 8 - autologous transplant patients to monitor the temporal relationship between changes in redox profile of plasma and lymphocyte to development of GVHD. Although the sample size is modest, the prospective nature and intra-subject repeated measures design would allow investigators to validate metabolic biomarkers as sensitive indicators of GVHD. Successful completion of this study would allow clinical translation of the findings to help identify a subset of patients predisposed to development of GVHD.

The specific aims are:

1. To characterize the amino acid metabolome profile in plasma and leukocytes of patients undergoing hematopoietic stem cell transplantation.

   The metabolomic and redox profile of plasma and leukocytes in patients undergoing autologous and allogeneic HSC transplantation will be determined at baseline and at regular time points over the course of 2 years. The temporal changes in plasma and leukocyte metabolomic profiles in allogeneic HSC transplantation in patients with grade 2-4 GVHD (GVHD+) will be compared to patterns observed in patients who do not develop GVHD (GVHD-). The candidate biomarkers will then be validated by comparison with the current gold standard (histopathology) for GVHD. Additionally, the pre-BMT metabolomic profiles between the two groups will also be compared to identify metabolic factors that may increase GVHD risk.

2. To determine the cytokine profile and T cell effector subset representation in allogeneic transplantation patients Using flowcytometry techniques, the cytokine profile and T cell effector subset representation in allogeneic transplantation patients (GVHD- and GVHD+) will also be determined. T cells are the primary mediators of GVHD and correlating the plasma and lymphocyte metabolomic profile to the dominant T cell profile will give investigators additional mechanistic insights into disease pathology. TNF-α, and IL-2 receptor levels will be determined in both cohorts of patients (GVHD- and GVHD+) by ELISA. Investigators anticipate that compromised redox status will correlate with temporal changes in pro-inflammatory cytokines. Other secondary endpoints to be assessed would include graft failure, neutrophil/platelet engraftment, chimerism (in T, B and myeloid cell fractions), and 1 year survival in the patient population.