Phosphorylated STAT3 Protein as a Novel Biomarker of Graft Versus Host Disease

Graft versus host disease (GVHD) is a life-threatening condition with high mortality rates. Without prevention, 30-80% of allogeneic (from a donor) bone marrow transplant (BMT) recipients will develop GVHD. However, aggressive GVHD prevention measures can greatly increase the risk of cancer recurrence. Currently, the only risk factor available for physicians to consider when planning GVHD prevention is pre-transplant cancer risk. Our technology can distinguish BMT recipients that are low or high risk for developing GVHD based on levels of phosphorylated STAT3 protein in their white blood cells. Our test could help physicians select the optimal immunosupressive regimen to prevent GVHD while minimizing the risk of cancer recurrence.

COMMERCIAL OPPORTUNITY

- About 8,000 allogeneic bone marrow transplants are performed in the U.S. each year, all of which are at risk for GVHD (~30% if a donor is related to a recipient, or up to 80% if a donor is unrelated). Because GVHD is a life-threatening condition with high mortality rates, its prevention with immunosuppressive drugs (such as Methotrexate, cyclosporine, tacrolimus, or rapamycin) is currently standard allogeneic transplant care.
- Immunosuppressive drugs increase the risk of life-threatening infections and weaken the transplant and its ability to attack the malignancy (graft versus leukemia (GVL)), thereby increasing the chance of cancer recurrence. This is especially worrisome in patients with an already elevated risk of recurrence (such as high-risk malignancies with poor risk cytogenetic features, high fraction of blasts in the bone marrow, or the Philadelphia chromosome).
- Our technology would give physicians more confidence to taper the administration of immunosuppressive drugs to patients with low GVHD risk and a high-risk malignancy so that the GVL effect can be greater to eliminate the cancer, or to administer more intense immunosuppression to patients with high GVHD risk and a low-risk malignancy such as adding steroids to the regimen.
- Our technology could also identify the 20% of mismatched BMT recipients that don't develop GVHD and are routinely over treated with immunosuppressants, because there is no way to determine which patients will develop GVHD, and all of the patients are treated as if they will devleop GVHD.
- There are currently no FDA approved tests for risk of GVHD development. Our assay would require only a small amount of peripheral blood and utilizes standard immunostaining techniques which are inexpensive and easy to incorporate in a clinical diagnostic setting.

TECHNOLOGY

This technology utilizes the fraction of phosphorylated STAT3 protein in white blood cells (T-cells) obtained from the recipient's peripheral blood on day 21 following transplantation to determine the GVHD risk by day 100. In our cohort of 18 patients, all seven patients with phosphorylated STAT3 >48% developed severe (grade II-IV) GVHD. In contrast, only one patient (10%) developed severe GVHD with phosphorylated STAT3 <48%. Thus, the cut off of 48% can be used to separate the high and low GVHD risk groups. While promising, these pilot data will require validation in larger cohorts.

PUBLICATION/PATENT

- US Provisional patent application filed on 2/10/2014 for Dr. Brian Betts

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