Methods to avoid Graft-versus-Host Disease after allogenic transplant

Brief Technology Description

Methods to prevent or reduce GI tract inflammation by modulating the gut microbiome and immune system

Technology Overview

Despite substantial advances in hematopoietic stem cell transplantation (HSCT), graft-versus-host disease (GvHD) is a major contributor to morbidity and mortality after allogenic HSCT. The intestinal epithelial cells (IECs) in the gastrointestinal (GI) tract plays a critical role in driving the pathogenesis of acute GvHD, which occurs within the first few months following transplantation. Dr. Geoff Hill’s group has developed methods of reducing the risk of GvHD by (i) modulating the subject’s microbiome via administration of antibiotics, probiotics, or fecal transplant, and/or (ii) by reducing the activity of an inflammatory cytokine by administering cytokine inhibitor(s), and/or (iii) by reducing the expression of MHC II on intestinal epithelial cells in the subject by administering innate defense regulators and host defense peptides. These methods are developed based on the finding that IECs presented alloantigen to CD4+ T cells, which is crucial in initiating GvHD. Additional in vivo mouse experiments demonstrate that inhibition of microbiota-driven IL-12 pretransplant was sufficient to attenuate MHC class II expression by IECs and prevent acute GvHD lethality. In order to reduce the risk of GVHD in a transplant recipient, a composition addressing the above approaches can be administered to the subject before transplantation and preferably prior to conditioning therapy.

Applications

- Reduce risk of GvHD following allogenic HSCT, BMT
- Reduce risk of acuate GVHD following organ transplantation

Potential Advantages

- Multiple strategies can be applied together to maximize results
- Therapeutic Interventions target the underlying immunopathobiology without deleting macrophages or dendritic cells

Market Overview: Acute GvHD will affect up to 70% of patients and approximately half of these patients will develop acute GvHD of the GI tract.