

Detection of impending infections in immunocompromised cancer patients

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Abstract: This application focuses on cancer patients undergoing allogeneic hematopoietic stem cell transplantation (allo-HCT), specifically the impact of the intestinal microbiome and associated metabolome on treatment-related complications and mortality. MSKCC and Weill Cornell investigators have established the infrastructure and experience to collect serial fecal and plasma samples from allo-HCT patients and have profiled the intestinal microbiome using 16S rRNA and shotgun metagenomic sequencing. Collectively, our >20,000 sample biobank from >1,500 allo-HCT patients is accompanied by detailed clinical metadata established correlations between the microbiome and clinical events with unprecedented temporal resolution. We have demonstrated that loss of commensal, particularly obligate anaerobic species, is associated with increased risk of bacteremia, *Clostridium difficile* colitis, graft-versus-host disease and mortality, in patients undergoing allo-HCT.

Our preliminary studies demonstrate that loss of health-promoting commensal bacterial species and microbiome domination by antibiotic-resistant pathogens results in marked changes in the intestinal and plasma metabolome. This creates an opportunity for their early detection and appropriate interventions. The assembled group of investigators brings together experience in mass spectrometry metabolomics, microbiome, infectious disease and microbial metabolism. We will leverage this multi-disciplinary experience to develop a Mass Spectrometric approach that can rapidly stratify cancer patients into categories of infectious risk by their microbiota composition. Patients with a loss of essential commensal bacterial species, or with intestinal domination by antibiotic-resistant pathogens, will be identified from fecal and plasma biomarkers. Our work has the potential to better inform the selection of infectious disease treatments and to guide microbiome reconstitution efforts following cancer treatments and thereby improve outcomes and survival.