



Impact of The Research Programs We Support

Mount Sinai Hospital, New York, New York, Dr. Marla Dubinsky, MD

Funding supports translational research focused on prevention for IBD for those at risk now and those that might be in the future.

Dr. Dubinsky has been instrumental in bringing together a range of experts from across the Mount Sinai community and the country to work together on finding effective and long-lasting solutions to complex IBD problems. Her team is comprised of clinicians and researchers who excel in their chosen fields, which include medicine, genetics, genomics, microbiology, and immunology. With her colleagues across Mount Sinai, including Jean-Frédéric Colombel, MD; Judy Cho, MD; Jeremiah Faith, PhD; and Bruce E. Sands, MD, MS; Dr. Dubinsky is able to draw on a wealth of knowledge and research insights as well as share her own—increasing the impact of your funding.

A pivotal study investigated whether healthy siblings are the key to prevention. The study sequenced and analyzed fecal samples from 21 pediatric IBD patients and their first-degree relatives which were then processed to paint a picture of the microbial composition and metabolites (the substance the microbes produce) of genetically similar individuals both affected and unaffected by IBD. Genetic data was also acquired, with a focus on immunity-related genes.

This project represented the first IBD family study examining the microbiome ever done, leading to the most significant advances in IBD microbiome research in the world. In recognition of the relevance of this study, publication of this research, titled “A Disease-associated Microbial and Metabolomics State in Relatives of Pediatric Inflammatory Bowel Disease Patients” is forthcoming in *Cellular and Molecular Gastroenterology and Hepatology*.

Researchers at Mount Sinai then implanted human stool samples from both affected and unaffected members of the first family study in genetically-engineered humanized mice to observe the impact on the development of IBD. In short, researchers found that stool elicits the onset of disease. The Mount Sinai team is now working to identify which bacteria can protect patients from getting disease and which bacteria cause disease in order to develop targeted fecal transplant interventions.

Mount Sinai has now partnered with the Orthodox Jewish Community of New York, where IBD is very common within families. Analysis of samples from both affected and



unaffected family members will yield insights into the protective patterns that prevent certain family members from developing IBD. Dr. Dubinsky and her team will then follow family members to monitor which initially unaffected members eventually develop the disease. The ultimate goal is individualized intervention tailored to at-risk patients' specific microbial fingerprint. Imagine a day when someone at risk of IBD—say, an unaffected brother with a “pro-IBD” microbial profile whose sister is affected—may do something as simple as take a pill to restore his microbiome's homeostasis, thereby eliminating risk for the disease. A patient who today may develop IBD could tomorrow have the power of prevention in his or her own hands.

Cedars Sinai Medical Center, Los Angeles, CA, Dr. Shervin Rabizadeh, MD

The *Pediatric Inflammatory Bowel Disease Program at Cedars Sinai* is highly active in clinical, translational and basic science research to improve the care of children with inflammatory bowel disease. Research looks at mechanisms of action in the immune dysfunction in IBD, improving and individualizing treatment of children with IBD, and investigating novel treatments in pediatric IBD with participation and leadership in clinical trials. Current Projects include:

- Investigating why treatments are not successful in all patients, which includes defining drug levels, blood markers, stool inflammatory markers and ultrasound soon after initiating therapy. This helps to determine the appropriate dosing of anti-TNF therapy with the goal of higher success over long periods of time and minimization of side effects. This work will lead to better success of treatments.
- At Cedars, researchers studied the efficacy and side effects of Vedolizumab, one of the newest IBD drugs, in pediatric IBD patients. The Cedars program was the first to present data at the national gastroenterology meeting, DDW, on the usage of Vedolizumab in pediatric IBD. We continue to forge ahead with new treatments for refractory patients and to improve long term safety profile of medications for all pediatric IBD patients.
- The research program focuses on the prognostic factors of disease and various treatments as well as the long-term complications associated with the disease and treatments. We are also pushing forward in evaluating new treatments for pediatric patients with IBD. With the assistance of our generous donors, we continue to move towards our objective of helping children and their families deal with this difficult, frightening and at times life-threatening disease.