Hematology/Oncology Research

Our pediatric hematology and oncology faculty members conduct research to identify and develop new medications and curative strategies for childhood blood disorders and cancers. In addition to our basic science research programs, our faculty participate in single-center and multi-center trials of novel therapeutic agents, supported by the Clinical & Translational Science Center (CTSC) and overseen by the Institutional Review Board of Weill Cornell Medicine.

Basic Science Research

The Lyden Lab
The laboratory of David C. Lyden, M.D., Ph.D., houses a leading research program focused on understanding the role of exosomes and tumor metastatic niches. Lyden Lab research has shown that growth factors secreted by a primary tumor prime certain tissues for tumor cell engraftment. In response to these soluble factors, tumor-associated cells, including hematopoietic progenitor cells, cluster at ‘pre-metastatic niches’, creating an environment conducive to tumor cell adhesion and invasion. At a pre-metastatic niche, newly recruited myeloid cells collaborate with other cell types residing in the tissue parenchyma. Together, these cells provide a platform of chemokines, growth factors, matrix-degrading enzymes and adhesion molecules, thereby accelerating assembly of the metastatic lesion. This model suggests that it may be beneficial for systemic therapies targeted at the metastatic microenvironment to be used early, perhaps even as an adjunct to the initial treatment of the primary tumor. Additionally, treatments may need to be tailored to each stage of metastatic progression: pre-metastatic, micrometastatic and macrometastatic, as well as to specific metastatic niches (lung, liver, brain and bone marrow). Notably, Lyden Lab collaborations have led to the development of a new interdisciplinary project bridging the fields of metastasis, tumor-secreted exosome research, lipid biology, and metabolomics.

Recent Lyden Lab research also involves the role of tumor-secreted microvesicles, known as exosomes, in cancer metastasis. The lab’s current studies focus on the molecular pathways activated by tumor exosome uptake at metastatic sites, as well as the identification of potential...
therapeutic targets to thwart metastasis. Recent findings have helped to explain why cancer metastasizes within certain organ sites, a process known as organotropism, as proposed by Stephen Paget in 1889.

**The Laboratory for Childhood Brain Tumor Research**

Investigations at the Laboratory for Childhood Brain Tumor Research, led by Praveen Raju, M.D., Ph.D., focus on medulloblastomas, the most common malignant brain tumor in children, and one of the leading causes of death in this age group. Over one-third of children with medulloblastomas die within five years of diagnosis, and the vast majority of survivors have significant neurological deficits due to the toxicity of combined surgery, radiation and chemotherapy. To improve survival and minimize side effects of current therapies, a more detailed understanding of the biology of medulloblastomas will better characterize their disease, as well as aid in prognosis and identification of novel treatments.

In addition to providing physiologically and genetically relevant preclinical mouse models for medulloblastoma subgroups, Laboratory for Childhood Brain Tumor Research efforts are also easily applicable to other pediatric cancers, including neural and non-neural tumors. Dr. Raju’s group actively improves animal models for pediatric brain tumors including Atypical Teratoid Rhabdoid Tumors (ATRT), Diffuse Intrinsic Pontine Gliomas (DIPG), and Subependymal Giant Cell Astrocytomas (SEGA), in order to identify improved therapies for patients that desperately need them.

**Oncology**

Lisa Roth, M.D., leads our basic oncology research program, in which her team has identified client proteins of the molecular chaperone Hsp90 to be altered in pediatric Burkitt lymphoma. They currently investigate the use of an innovative Hsp90 inhibitor as a novel therapeutic treatment, and data obtained from this proposal will contribute to the clinical development of targeted therapy for pediatric Burkitt lymphoma. Dr. Roth has received grant awards from the Lymphoma Research Foundation, the NIH Loan Repayment Program, the Rally Foundation for Childhood Cancer Research and the Sass Foundation for Medical Research.

**Education**

**Studies**

**Comprehensive Care in Patients with Thalassemia and Severe Congenital Anemias**

This observational, longitudinal study led by Dr. Sujit Sheth follows the natural history of patients with thalassemia and other severe congenital anemias, as well as patients with iron excess complications. Regular transfusion and iron chelation therapy are the standards of care for patients in this study. Treatment provided by the Weill Cornell Medicine New York Comprehensive Thalassemia Center includes baseline studies prior to the start of chelation therapy, and annual
monitoring thereafter.

PROMIS as a Novel, Patient-Reported Outcome (PRO) Tool in Adult Patients with Congenital Blood Disorders

This Patient-Reported Outcome Measurement Information System (PROMIS) initiative led by Dr. Sujit Sheth utilizes multiple question banks related to physical and social function, pain and other domains. PROMIS is free, and was developed based on a U.S. population with chronic illnesses. PROMIS is administered through computer-adaptive testing, which allows for rapid questioning and incorporation of multiple item banks into a single tool.