

Patient-Driven Molecular Characterization of Rare and Refractory Germ Cell Tumors

Principal Investigator:

- Eliezer Van Allen, MD – The Broad Institute of MIT and Harvard

Co-Principal Investigator:

- David Solit, MD – Memorial Sloan Kettering Cancer Center

Abstract: Approximately 8,000 people in the U.S. are diagnosed with germ cell tumors (GCTs) each year. The vast majority are young men who develop testicular GCTs, although rarely patients develop GCTs in other anatomical sites, such as the ovaries or mediastinum. Most patients are cured with conventional chemotherapy, although 30% recur, and half of such patients ultimately succumb to their disease. GCTs exhibit an extreme burden of reciprocal loss of heterozygosity (RLOH), although the underlying molecular driver of RLOH and chemoresistance is largely unknown, and no single institution treats enough non-testicular or chemorefractory GCT patients to amass sufficient specimens for impactful discovery. Here, we propose to catalyze GCT translational discovery by creating a new mechanism to identify patients with this rare disease, and apply emerging sequencing strategies towards these tumors and germline to enable a deeper understanding of the molecular basis of these cancers in the chemosensitive and resistant states. Specifically, we will implement new technologies (whole genome/transcriptome of FFPE GCT samples) and computational algorithms to interrogate the underlying mechanism of RLOH and how this process evolves from chemosensitive to resistant states. We will also initiate a first-of-its-kind direct-to-patient strategy that leverages web-based approaches to identify patients with rare or refractory GCTs, and perform clinical molecular profiling with return of actionable results. This project will accelerate the clinical and molecular characterization of GCTs, explore the underlying biology driving this rare tumor type, and serve more broadly as an innovative model for studying rare cancers.