



**MGH Cancer Center Harvard Medical School** 

## RTICC SEARCH COMMITTEE SEMINAR

6<sup>th</sup> August

- 4th Floor seminar Room, The Ruth and **Bruce Rappaport Faculty of Medicine** 
  - · Light refreshments will be served

## "Targeting T cell Dysfunction to Sensitize **Tumors to Immunotherapy"**

Cancer immunotherapy, based on unleashing the immune system against cancer, has revolutionized the treatment of metastatic malignancies and achieved durable responses in many patients. Despite those advances, immunotherapy resistance develops in roughly half of the patients and is ultimately fatal. A key driver of this resistance is the development of dysfunctional and exhausted CD8+ T cells within the tumor microenvironment. Chronic antigen stimulation and a range of suppressive factors, including inhibitory signals, hypoxia, an altered extracellular matrix, and immunomodulatory metabolites, compromise T cell function and limit therapeutic efficacy.

My research focuses on deciphering the mechanisms of T cell exhaustion in response to immunotherapy and developing strategies to restore T cell function. Building from clinical observations, I combined in-depth mechanistic studies with translational approaches using Patient-Derived Organotypic Tumor Spheroids (PDOTS), a clinically relevant ex vivo human tumor model for testing of therapeutic efficacy. This work identified therapeutic avenues to promote effector T cell expansion and function, prevent exhaustion, and ultimately overcome resistance to immunotherapy.