Tracking T Cell-Antigen Presenting Cell Contacts within Tumors in vivo

Principal Investigator:

- Gabriel Victora, PhD – The Rockfeller University

Co-Principal Investigator:

- Nir Hacohen, PhD – The Broad Institute of MIT and Harvard

Abstract: T cell responses to tumors begin with presentation of tumor antigens by antigen presenting cells (APCs) to CD4+ and CD8+ T cells. Maximal effectiveness is attained when APCs interact efficiently with both T cell lineages. Despite the importance of these dynamics to successful tumor immunity, little is known about how APC-T cell interactions change during the response to solid tumors in vivo. The Victora lab has developed a system for labeling cell-cell interactions in mice in vivo, which allows us for the first time to determine the history of interactions between APCs and T cells during an immune response. Relying on the Hacohen lab's expertise in tumor immunology and APC function, we propose to use this labeling system to (i) characterize the dynamics of interaction of APCs with CD4+ T cells within the tumor and in draining lymph nodes, (ii) determine the functional state of APCs that interact with T cells by single-cell RNA-seq, and (iii) determine how these interactions change upon treatment with chemotherapy and immunotherapy. We expect to gain insight into what populations of APCs are responsible for antigen presentation during the antitumoral response; how interaction with T cells may change the functional profiles of these APCs; and how immuno- and chemotherapy change how APCs and T cells interact, and what this means in terms of the effectiveness of these treatments. Detailed knowledge of the nature of APC-T cell interactions in steady state and after therapy may improve our ability to trigger effective immune responses to tumor antigens.