LABEX IGO – 2023 INTERNAL CALL FOR PROJECTS FOR YOUNG INVESTIGATORS

Project title:
The role of B cells in immune checkpoint inhibitor related adverse events in cancer patients

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Abstract:
Advances in treating patients with immunotherapy have dramatically changed cancer morbidity and mortality. Immune checkpoint inhibitors drugs purposely release immune regulatory controls and consequently increase immune antitumor activities; however, this release also provokes a significant risk of immune-related adverse events (irAE), which can lead to autoimmune-like events affecting multiple organs that present with a wide spectrum of clinical manifestations, ranging from mild to fatal forms, such as dermatitis, hepatitis, thyroiditis and colitis, and less frequently but clinically important, hypophysitis, myocarditis, pneumonia and arthritis. Although the exact pathophysiology underlying irAE has not been fully elucidated, several mechanisms have been considered as potential players in the immune pathogenesis of irAE, such as the activation of self-reactive T cells, the increase of inflammatory cytokines and chemokines, the contribution of genetic factors and microbiota, or direct toxicity of immune checkpoint inhibitors to healthy tissue. Recently, several studies suggested a contribution of B cells in the pathophysiology of irAE, such as changes in circulating B subsets, a defect of regulatory B cells, and an accumulation of B cells in damaged organs. The goal of this project is to investigate the functional orientation of B cells towards an activating (or pro-inflammatory) or a regulating (or anti-inflammatory) profile at the onset of irAE in damaged organs, such as skin, colon, and liver tissues. The expression of cytokines in B cells will be quantified using a simultaneous detection of proteins and transcripts by Imaging Mass Cytometry™ based on the RNAscope™ *in situ* hybridization protocol coupled with antibody staining.