Imaging mass cytometry for the identification of disease-defining BOB.1-expressing T- and B-cell subsets in Chronic Lung Allograft Dysfunction.

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Although significant advances have been made in the field of organ transplantation, the long-term survival and function of transplanted lungs are limited by the development of bronchiolitis obliterans syndrome (BOS), an irreversible obstructive disease that results in a progressive loss of airway structure. It is proposed that repeated injuries from alloimmune and autoimmune responses drive inflammation and fibrosis of the bronchiolar walls, yet, exact molecular pathways underlying BOS pathogenesis remains unknown. In this project, we will apply imaging mass cytometry on the Hyperion Imaging System to capture and quantify different immune and stromal compartments at subcellular resolution in tissue biopsies obtained from lung transplant recipients that developed BOS as compared to recipients with stable lung function (STA). As we have strong evidence that the lymphocyte-restricted transcriptional regulator BOB.1 is a crucial molecular switch controlling pathogenic immune responses in multiple autoimmune and chronic inflammatory diseases, including BOS, we will quantify BOB.1 expression in BOS versus STA lungs and identify and localize BOB.1-expressing subsets within lung microenvironments that correlate with clinical outcomes following lung transplantation. The work will be performed at CRTI UMR 1064 in close collaboration with Sophie Hillion and Christophe Jamin at Brest University Hospital (IGO partners at UMR 1227). The overall goal of our translational research is to leverage an exceptional bio-platform consisting of unique lung tissue samples and cutting-edge imaging mass cytometry to establish a path towards stratified medicine by defining and characterizing the hierarchy and cross-talk between different cellular and molecular players involved in chronic tissue inflammation and remodelling in BOS.