Laurence Buisseret – Project description

Breast cancer is a complex and heterogeneous disease of which the classification has been significantly detailed in recent years through the development of gene expression signatures that currently identify at less four clinically distinct types of neoplasm: Luminal A and B, triple negative and HER2+. However, significant disparity in clinical outcome still remains within each disease entity leading investigators to continue searching for more refinement. The first generation of molecular analyses based on gene expression profiling gave rise to several prognostic signatures that improved breast cancer taxonomy (ex. GGI, Mammaprint, Oncotype) and are currently used in clinical practice. These signatures focus principally on the malignant cell, which is reflected in their assessment of genes regulating the cell-cycle and proliferation. In recent years, attention has turned to the various non-neoplastic cells present in tumors, including stromal cells and infiltrating leukocytes, whose interactions with tumor cells can significantly influence an individual patient's ultimate outcome. A correlation has been established between immune gene signatures, which capture signals from infiltrating leukocytes, and clinical outcome with the strongest correlation observed in triple negative and HER2+ breast cancer. Recent reports have further shown that a significant association exists between the presence of specific subsets of immune cells and clinical outcome. Extensive CD8+ T cell infiltration in tumors was strongly associated with patient survival, whereas the presence of macrophages or FOXP3+ CD4+ regulatory T (Treg) cells surrounding the breast tumor bed was associated with a worse clinical outcome. Immune cell infiltration has also been associated with a benefit from chemotherapy by predicting response to preoperative chemotherapy.

The principal aims of this project are to further investigate the presence and role that leukocytes play in organized immune responses generated in breast cancer (BC)-associated tertiary lymphoid structures (TLS). Specifically, this project will focus on the role B cells play within the tumor-infiltrating lymphocytes (TIL), determine the TIL-TLS prevalence among the different BC molecular subtypes as well as in metastatic disease and correlate these data with clinical outcome in both primary and metastatic BC. This project is an important component of the overall efforts by the Breast Cancer Translational Laboratory (BCTL) and Molecular Immunology Unit (MIU) to understand the critical elements of effective anti-tumor adaptive immune responses, how they affect different therapeutic responses and to identify powerful prognostic and/or predictive immune-related biomarkers that can be exploited in the development of novel immune therapeutic BC strategies.