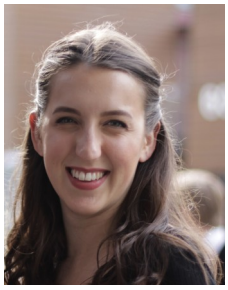
ImmunoTools *multiplex* Award 2022



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Cytokine expression in bone marrow plasma of multiple myeloma patients to identify immune profiles related to survival

Multiple myeloma (MM) is caused by malignant plasma cells (myeloma cells) that accumulate in the bone marrow and cause symptoms such as bone destruction, anemia, kidney failure and frequent infections. While treatment usually works well initially, patients eventually relapse, and treatment gets less efficient at later stages. Although new drugs have increased the survival of patients, MM is still an incurable disease. Survival in MM is highly variable ranging from aggressive disease with overall survival (OS) of a few months to patients with a chronic disease for more than two decades. Whereas many clinical variables and tumor genomic aberrations are associated with risk, little is known about how the immune environment in the bone marrow affects tumor progression and response to treatment. The focus of this study is to investigate cytokines in bone marrow plasma in patients with long-term disease control (LTDC) (>5 years between diagnosis and relapse or OS>8 years) versus patients with short aggressive disease (short-term disease control (STDC))(OS<2 years), and compare the immune profiles of these two patient groups.

Currently we have a study going that aims to investigate the immune microenvironment in the bone marrow in longitudinal samples from LTDC and STDC patients, and compare abundance of immune cell subtypes such as different subsets of innate immune cells, T cells, and B cells in the two patient groups. These

experiments are conducted using mainly Cytometry by Time-Of-Flight (CyTOF), which is a form of mass cytometry, with a panel consisting of 37 markers to identify different subsets of immune cells and cytokines/chemokines. The panel is currently very focused on different subsets of T cells, as these have been shown to be of high importance in the anti-tumor immune response. Thus far, data from the CyTOF analysis indicates a difference in abundance of specific $CD8^+$ T cell subsets in LTDC and STDC patients. It is well known that the expression of various cytokines and chemokines is also important in the development and maturation of immune cells such as T cells. *Zheng et al.* (2013) have previously demonstrated specific cytokine patterns in the plasma of healthy donors, donors with monoclonal gammopathy of undetermined significance (MGUS), which is a condition that precedes MM, and donors with MM at various disease stages (active disease, on treatment, or in remission). They found that the cytokines expressed in patients with MM were heavily shifted toward an anti-inflammatory, pro-tumorigenic response, and that this cytokine pattern remains even when patients enter remission.

Thus, given previous investigations of cytokine patterns in MM as well as indications from our current work, we think a broader investigation of cytokines and chemokines would be highly valuable to further this research and get a more detailed picture of the tumor immune microenvironment, and how this might differ in patients with short aggressive disease versus those with long-term disease control.