Deciphering the roles of MAF in the regulation of T cell responses in cancer

Despite considerable progress in immunotherapy against metastatic cancers, we are still far from being able to manipulate selectively the immune system to restore immune responses potent enough to eradicate metastatic tumors in high percentages of patients. The tumor microenvironment creates a highly suppressive contexture that favors the recruitment of suppressive immune cells, such as regulatory T cells, and strongly inhibits classical T cells. Cancer induces T cells that phenotypically and functionally strongly differ from “classically activated T cells”, i.e. the ones known to protect from disease. These cells are poorly functional, so-called “exhausted”. Even though most of the studies have focused on CD8 T cells, both CD8 and CD4 T cells are affected by this process. Molecular pathways regulating the polarization of T cells in tumors are still only partially understood. Our aim is to deeply characterize the roles of the transcription factor MAF, which we have identified as regulators of T cell polarization/dysfunction during melanoma development.

We have already shown that MAF is a key transcription factor modulating CD8 T cell activity in melanoma. For this project, we will focus more on its function in CD4 T cells and particularly in regulatory T cells as well as on its impact on transcriptional regulation. As we have identified that MAF plays a critical role in T cells from the colon to regulate homeostasis, we will study the importance of MAF expressing CD4 T cells during the development of colon cancer in a chemically induced and genetically induced model.

Our project will provide both novel basic scientific knowledge and clinical insights. Our findings will likely have implications for future developments of immunotherapy, not only for melanoma but also for other frequent cancer types (such as lung, bladder/urinary tract or colon cancers), as illustrated by the recent progress in immunotherapy of cancer patients.