Tumors grow within a complex microenvironment composed of immune cells, fibroblasts, endothelial cells and other non-malignant cells. The study of the composition of tumor microenvironments has led to classifications with prognostic and theranostic values, as well as to treatments modulating its composition and its functional orientation.

Immunotherapy is aimed to substitute or activate the patient’s immune reactions to its tumor in order to control the disease in the long run. It has already revolutionized the management of several deadly and major cancers. Evaluating the tumor microenvironments allows the most appropriate selection of patients for an immunotherapeutic approach, to unveil mechanisms of resistance and provides novel therapeutic targets. In Colorectal Cancer, the molecular and immune classifications confirmed that not only Microsatellite instable (MSI) tumors, but also a subgroup of Microsatellite Stable (MSS) tumors, are characterized by a favorable immune contexture with high Th1/cytotoxic infiltration. Other subtypes exhibited poor immune infiltration or, in the worst prognostic case, high T cell infiltration in the context of a major inflammatory, angiogenic and desmoplastic reaction which should be addressed differently in terms of immunotherapy. In clear cell Renal Cell Cancer, we identified a poor prognosis subgroup with high infiltration of CD8 T cells which express check-point inhibitors in the presence of PDL-1 and/or PDL-2 expressing tumor cells. We characterized the lymphocyte populations that concur to poor prognosis and could be targeted by appropriate immunotherapeutic approaches.