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Investigador responsable

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Extracellular matrix signaling in CD4+ T cell differentiation

Regulatory T (Treg) cells are an immunosuppressive subset of CD4+ T lymphocytes characterized by the expression of the master transcription factor forkhead box protein P3 (FoxP3). In health, Treg cells have a central role in maintenance of self-tolerance and immune homeostasis. In solid cancers, Treg cell accumulation in the tumor microenvironment (TME), including the sentinel lymph node, has been associated with poor prognosis and impaired response to immunotherapy, consistent with a potential Treg-mediated suppression of anticancer immunity. Accumulation of Treg cells in the TME is not only consequence of their recruitment from periphery; tumor-produced factors are also able to steer Treg cell differentiation from na.ve or even already differentiated CD4+ T cell subsets, to generate the so-called inducible Treg (iTreg) cells. The identification of factors that specifically influence Treg cell homeostasis and function is thus important to understand cancer pathogenesis and to design effective therapeutic strategies to manipulate of Treg cells in oncology patients, an unmet clinical need. In this project we propose that the composition of laminins (heterotrimeric extracellular matrix proteins) in the TME and the lymph nodes is a main determinant for hampering antitumor immunity by affecting Treg cell homeostasis and function. Along the stay, the students will become familiar with procedures involving the isolation, activation and differentiation of primary CD4+ T cells from mouse and human origin, the characterization of immune populations by FACS, functional assays to determine the effector and suppressive activity of different T cell subsets, basic principles of proteomics, immunohistochemical analyses in tissues derived from mouse tumors, as well as basic molecular and biochemical techniques. In addition, as part of a collaborative initiative, the candidate will have the opportunity to learn about quantitative spatially-resolved analyses, using the GeoMx DSP system, a leading edge technique for tissue profiling.