Multiple sclerosis (MS) is the most common cause of neurological disability in young adults following trauma. It is thought that MS is triggered by environmental agents in genetically-susceptible persons, a combination which will lead to auto-inflammatory processes. Several immunomodulatory drugs, possibly slowing MS progression, are now available. However, there is no cure for the disease. This situation most likely reflects the fact that one does not know precisely the cause(s) of MS. Important improvement has been obtained in the understanding of the function of individual actors of the immune response. For instance, it is well established that T cells are key features in MS pathogenesis. Over the past years, my Laboratory has focused on the CD8+ T cell response towards Epstein-Barr virus (EBV), which is a recognized environmental factor of MS. We show that the EBV-specific CD8+ T cell response is dysregulated in MS patients, either in the blood, or in the CSF. Yet, the mere characterization of a single cell type will not allow obtaining a comprehensive view of the complex immunopathogenesis of MS.

Recently, to examine what stands upstream from T cell activation, we have studied in detail the phenotype and activation level of different antigen-presenting cells (APCs: B cells and monocytes). Here, we will thus discuss how dysregulated is the ex-vivo profile of APCs that may significantly influence the phenotype and activation profile of T cells. In parallel, to eventually obtain a chance to look at what stands downstream from T cell activation, i.e. what happens in the CNS, we have developed the induced-pluripotent stem cells (iPSC) technology which allows us to gain access in vitro to neural cells directly derived from MS patients. Our ultimate goal is to develop a “brain-in-a-dish” model, a tool opening a broad new field of investigations in human MS: an overview of the applications will finally be given.

Selected Publications: