LIPMO : Lipid modulation of synovial myeloid cells in osteoarthritis - Marie-Astrid Boutet, RMeS

Osteoarthritis (OA) is a leading cause of disability worldwide, yet no disease-modifying treatment is currently available. Prior to cartilage degradation, the synovial tissue undergoes significant inflammatory changes, strongly associated with pain and radiographic severity. We previously described that the diffuse-myeloid (DM) synovial histopathotype, characterized by myeloid cell infiltration and lipid metabolism gene signatures, appears in ~40% of OA patients. Interestingly, the infrapatellar fat pad (IFP), a rich adipose structure in direct contact with the synovium, may influence synovial immune cells through paracrine lipid mediators. However, the crosstalk between these tissues and its impact on myeloid cell phenotypes remains poorly defined. The **LIPMO project** aims to decipher how lipid mediators from the IFP shape the regulatory or pathogenic functions of synovial myeloid cells in DM synovitis, thereby informing patient stratification and the development of targeted therapies. This interdisciplinary effort brings together complementary expertise in joint immunopathology, myeloid cell biology, and lipidomics:

Objective 1 will characterize myeloid cell diversity in matched DM synovial and IFP tissues using spectral cytometry and multiplex immunofluorescence.

Objective 2 will explore the effects of lipid mediators on myeloid cell function through lipidomic profiling, in vitro modeling with monocyte-derived cells, and functional modulation using siRNA-loaded lipoplexes.

This project will provide new insights into the immunometabolic regulation of OA, contribute to personalized therapeutic strategies, and foster an emerging collaboration within the ImmuNE Labex.