



**Research Project Proposal**  
Academic year 2021-2022  
MÁSTER EN INVESTIGACIÓN BIOMÉDICA

**Project Nº 02**

Title: Spatial analysis of tissues: cellular positioning and cell-cell interactions in multiplexed histological images

Immunopathology Lab, Department of Pathology, CUN

Director: Carlos E de Andrea, MD, PhD

Contact: ceandrea@unav.es

Co-director: José Echeveste, MD, PhD

Contact: jiecheves@unav.es

Summary: Recently developed approaches for multiplexed imaging have revealed complex patterns of cellular positioning and cell-cell interactions with important roles in both cellular- and tissue-level physiology. The spatial structure of the tumour and its microenvironment establishes spatial interactions among cell types as phenotypes of tumour-host interactions. Understanding the mechanisms by which these interactions are generated has the potential to aid the development of new therapeutics.

Methods: A customized histo-cytometric multidimensional analysis pipeline will be used to evaluate the complex microenvironment of tumours. This method to characterize the distinct spatial features of a tumour will be used to investigate the interplay between neutrophils and NETs and CD8+ T cells and NK cells in the tumour microenvironment. We have been using computational pathology strategies to construct a topological map of cell types within a tumour. Using deep learning algorithms for image analysis, we are able to study the spatial structure of the tumour microenvironment, referred to as topological tumour graphs. Recently, using this approach, we were able to recognize two stromal features, namely stromal clustering and stromal barrier, which represented the melanoma stromal microenvironment. Tumours with increased stromal clustering and barrier were associated with reduced intratumoural lymphocyte distribution and poor overall survival independent of existing prognostic factors. Similar deep learning algorithms will be used to dissect the stromal architecture of solid tumours allowing the quantification of neutrophils, CD8+ T cells and NK cells and their spatial relationship.

yes		Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?
no	X	