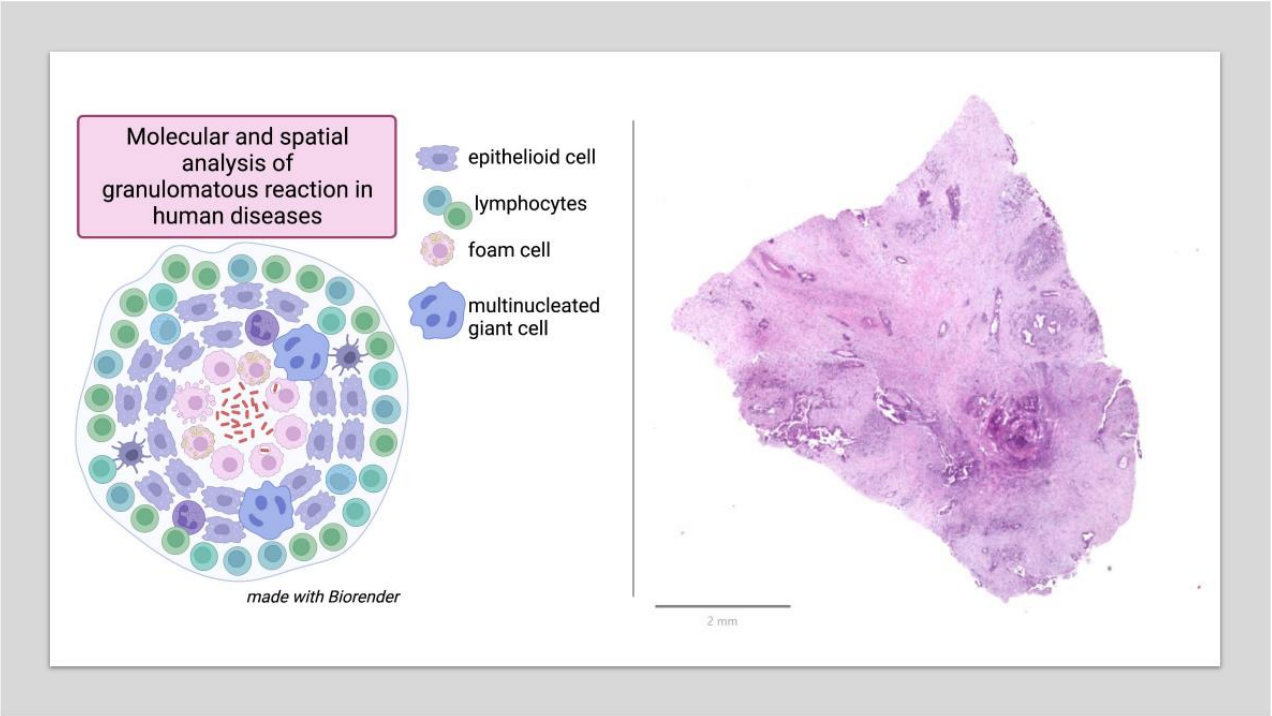
Molecular and spatial analysis of granulomatous reaction in human diseases

Tutor: Federica Marchesi, mat 17724

Cotutor: Massimo Locati, mat 15630 Federica.marchesi@unimi.it ; massimo.locati@unimi. Laboratory of Cellular Immunology HumanitasLaboratory of Leukocyte Biology ,Department of Medical Biotechnology and Translational Medicine



Granulomas are organized aggregates of macrophages, often with characteristic morphological changes, and other immune cells. These evolutionarily ancient structures form in response to persistent particulate stimuli—infectious or noninfectious—that individual macrophages cannot eradicate (1-2). Among the most frequent pathological conditions associated to granuloma formation, lung infection swith Mycobacterium tubercolosis is the most studied. In this project, we aim at combining artificial intelligence (AI)-aided histopathological approaches and hi-plex imaging tools to analyse the ecosystem of human granulomas on formalin-fixed, paraffin-embedded (FFPE) tissue specimens (3). Among other immune cells, particular attention will be dedicated to macrophages, based on solid literature pointing to their contribution to chronic inflammatioon and granuloma formation (4-5). The candidate will set up hi-plex staininng techniques and spatial transcriptomics to study relevant features of human granuloma in pathological conditions. Open source softwares will be used (inlcuding Qupath, Cytomap, R, Matlab). Key instruments include a slide scanner (AxioScan, Leyca), an imaging mass cytometer (Hyperion, StandarbioTools) and thr GeoMx platform (Nanostring)

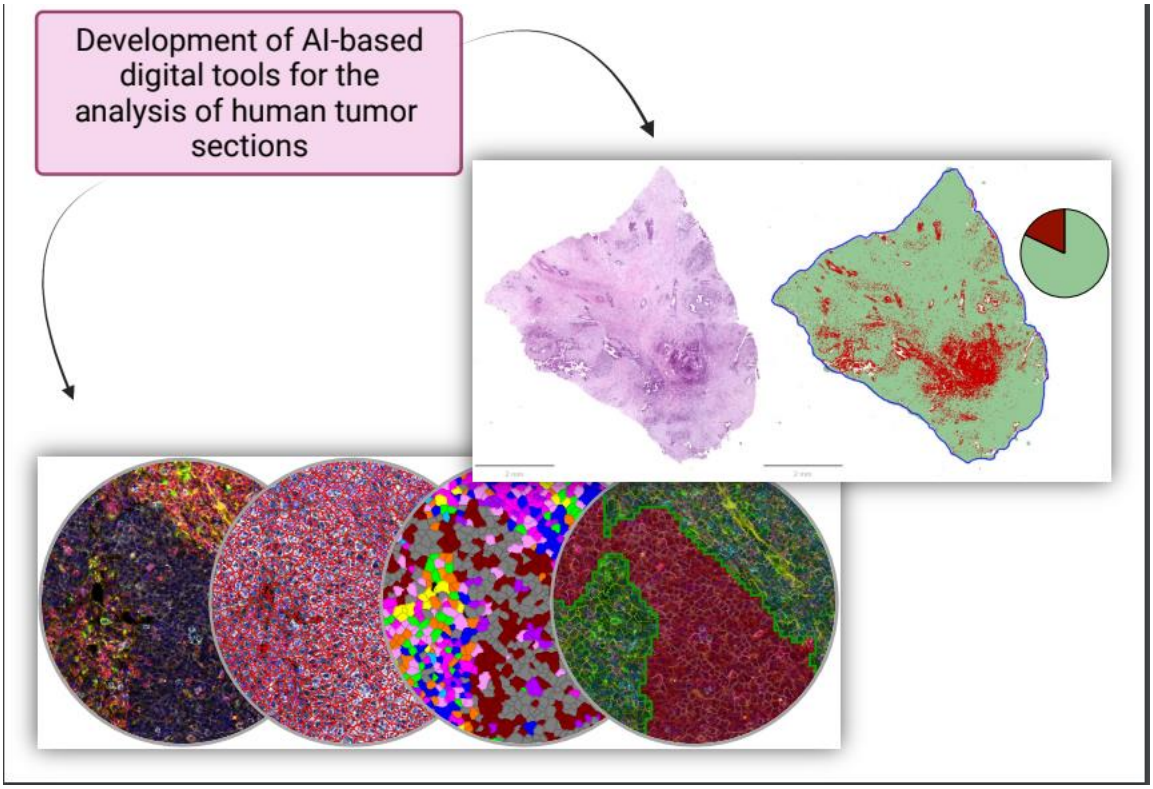
Development of AI based digital tools for the analysis of human tumor sections

Tutor: Federica Marchesi,

Co-tutor: Fabio Giavazzi

E-MAIL Federica.marchesi@unimi.it

LABORATORY DEPARTMENT Laboratory of Cellular Immunology-Humanitas Laboratory of Complex Fluids and Molecular Biophysics (https://sites.google.com/site/unimisoft) Department of Medical Biotechnology and Translational Medicine



Digital pathology coupled to artificial intelligence (AI)-powered approaches are becoming increasingly used in the oncoimmunology field as tools to extract sub-visual features and improve current diagnostic workflows (1). On the other hand, hi-plex approaches (e.g., CODEX, imaging mass cytometry, multiplex-IHC) are largely adopted to analyze the immune ecosystem of tumor specimens, allowing uto detect multiple markers on the same slide and appreciate an immune heterogeneity previously overlooked (2). In this project, we aim at combining AI-aided histopathological approaches and hi-plex imaging tools to analyse the ecosystem of human tumors on formalin-fixed, paraffin-embedded (FFPE) tissue specimens. The candidate will develop algorithms and computational tools to extract (from digitized slides of tumor tissues) features at both cell- and tissue-level. Open source softwares will be used (inlcuding Qupath, Cytomap, R, Matlab). Key instruments include a slide scanner (AxioScan, Leyca) and an imaging mass cytometer (Hyperion, StandarbioTools). Both hematoxilin & eosin slides and slides stained by multidimensional imaging will be used. Integrated analysis of the slides will be implemented to generate a collection of human interpretable features (HIFs) (3,4), which will be ultimately correlated with clinical variables. Beyond the most credited tumor cell morphological characteristics, such as nuclear size or number of mitotic cells, novel emerging HIFs will be analyzed, including spatial arrangement of tissue elements, leukocyte count or spatial distribution