RESEARCH TOPIC MECM_27

Integrative approaches for the digital spatial profiling of immune and inflammatory microenvironment in multi-drug resistant rheumatoid arthritis.

Curriculum

MECM Data Science

Research Area

Immuno

Laboratory name

Rheumatology - Multiscale and Nanostructural Imaging Unit

Research Supervisor

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Abstract

Rheumatoid arthritis (RA) is a chronic autoimmune disorder affecting approximately 1% of the global population and is characterized by persistent inflammation of synovial joint tissue driven by immune cell infiltration [1]. Increasing evidence indicates that the pronounced cellular heterogeneity within inflamed joints plays a critical role in mediating resistance to current therapeutic strategies, a phenomenon observed in up to 40% of patients [1,2]. Within the framework of the MDR-RA consortium, which aims to elucidate the molecular determinants of multi-drug resistance in RA, this PhD project is designed to investigate the cellular and microenvironmental landscape of RA at high resolution. The primary objective is to identify cellular states, molecular signatures, and signaling pathways associated with disease progression and clinical outcomes. To achieve this, the project will employ single-cell and spatially resolved omics approaches to comprehensively characterize synovial tissue architecture. In particular, it will involve the integration of spatial proteomics data obtained through Imaging Mass Cytometry (IMC) with spatial transcriptomics platforms, including Visium, Xenium, and GeoMX. The combined use of these technologies will enable cross-validation of transcriptomic findings at the protein level while preserving spatial context and single-cell resolution [3,4]. Furthermore, the project will include the development of advanced computational pipelines and bioinformatic workflows for multi-omics data integration. Artificial intelligence (AI)–based models will be implemented to combine molecular, imaging, and clinical datasets, with the aim of improving patient stratification, refining treatment selection, and supporting clinical decision-making. The candidate will benefit from the interdisciplinary expertise available within the MDR-RA consortium and the Multiscale and Nanostructural Imaging Unit. This environment will provide comprehensive training in experimental and computational methodologies, including IMC sample processing, high-

dimensional data analysis, and integrative bioinformatics, fostering a multidisciplinary approach to complex biomedical research questions.

Main technical approaches

Image analysis – Imaging mass cytometry - Development of bioinformatics pipeline with R and python – Immune cell profiling

Scientific references

1. Rivellese, F. and Pitzalis, C., "Cellular and molecular diversity in Rheumatoid Arthritis", Semin. Immunol., 2021, 58, doi: 10.1016/j.smim.2021.101519

2. Lewis, M. J. et al., "Molecular portraits of early Rheumatoid Arthritis identify clinical and treatment response phenotypes", Cell Rep., 2019, 28(9), doi: 10.1016/j.celrep.2019.07.091

3. Erreni, M. et al., "Depicting the cellular complexity of pancreatic adenocarcinoma by Imaging Mass Cytometry: focus on cancer-associated fibroblasts", Front Immunol. 2024, 7, doi: 10.3389/fimmu.2024.1472433

4. Allen, R. O. et al., "Combining Xenium in situ spatial transcriptomics and Imaging Mass Cytometry on a single tissue section", BiorXiv, 2026, doi: 10.64898/2026.02.18.700929

Type of contract

Scholarship of € 24.500 gross per year awarded by Istituto Clinico Humanitas. This sum is subject to IRPEF income tax and exempt from social security contributions.

Borsa di studio pari a € 24.500 annui lordi erogata da Istituto Clinico Humanitas. Importo soggetto a tassazione IRPEF ed esente da contribuzione previdenziale.

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