RESEARCH TOPIC MECM_1

Targeting macrophage recruitment and metabolic reprogramming to counteract liver metastases (MARVEL)

Curriculum

MECM Standard

Research Area

Onco - Immuno

Laboratory name

Lab of Macrophage Dynamics

Research Supervisor

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Abstract

Liver metastases represent a major cause of cancer-related mortality, particularly in colorectal cancer (CRC) and pancreatic ductal adenocarcinoma (PDAC). The tumor microenvironment (TME) of liver metastases is highly immunosuppressive and dominated by macrophages, including Kupffer cells (KCs) and monocyte-derived macrophages (MoMs), which promote tumor progression and immune evasion.

This PhD project aims to dissect and therapeutically target two key mechanisms underlying macrophage-driven immunosuppression: (i) monocyte recruitment to the metastatic niche, and (ii) macrophage metabolic reprogramming. By integrating genetic mouse models, pharmacological interventions, and advanced metabolic and immunological profiling, the study will investigate how modulation of metabolic–epigenetic pathways can reprogram macrophages toward an anti-tumor phenotype.

Using a combination of genetic mouse models, pharmacological inhibition, and advanced metabolic and immunological profiling, the project will evaluate how acting on metabolic-epigenetic reprogramming can lead to anti-tumor phenotype.

Translational validation will be performed using patient-derived samples and spatial transcriptomics approaches to assess clinical relevance.

Overall, this project seeks to develop innovative immunometabolic strategies to reprogram the liver metastatic niche and enhance anti-tumor immunity, ultimately contributing to improved therapeutic approaches for metastatic cancer

Main technical approaches

In vivo mouse models of CRC and PDAC liver metastasis
Conditional knockout models
Flow cytometry and immune profiling
Immunohistochemistry and multiplex imaging
Metabolomics (LC-MS, MALDI imaging)
Seahorse metabolic assays

Spatial transcriptomics (Visium HD)
Single-cell analysis and bioinformatics integration
Patient-derived organoids and tissue models

Scientific references

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Type of contract

PhD scholarship of € 21.000 gross per year awarded by Humanitas University. This sum is exempt from IRPEF income tax according to the provisions of art. 4 of Law no. 476 of 13th August 1984 and is subject to social security contributions according to the provisions of art. 2, section 26 and subsequent sections, of Law no. 335 of 8th August 1995 and subsequent modifications.

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