RESEARCH TOPIC MEM3

Expression analysis and functional characterization of CD25 on migratory dendritic cell in liver cancer
Curriculum MEM

Laboratory name
Laboratory of Cellular and Molecular Oncoimmunology, IRCCS Humanitas Research Hospital

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Abstract
CD25, encoded by Il2ra, constitutes the alpha subunit of the heterotrimeric receptors for interleukin (IL)-2 and IL-15. Preliminary data show that Il2ra, widely present in T lymphocytes, is highly expressed by an enigmatic intratumoral dendritic cell (DC) activation state, known as mDC or MregDC. Notably, mDC lack a functional IL-2 receptor due to the absence of Il2rb expression. Therefore, we hypotesise a potential involvement of mDC in IL-2 trans-presentation to effector cells. This PhD project, will aim at understanding the functional role of CD25 in mDC during tumor progression. The combination of newly generated gene-targeted mouse models, specifically lacking CD25 in mDC, and primary liver carcinogenesis coupled with single cell molecular profiling of the tumor infiltrate, will underpin mDC role in hepatic tumour microenvironment and in the orchestration of anti-tumour immunity. Finally, the axis CD25-mDC will be tested in human liver cancer by implementing a patient-derived tumor explant platform that will enable the functional characterization, the potential trans-presentation ability of mDC and its impact on cancer progression.

Main technical approaches
Genetically engineered mouse models, CRISPR, single cell RNA sequencing, flow and mass cytometry, analysis of patient derived tumor explants, histology, standard immunology techniques and bioinformatics.

Scientific references
Gerhard GM et al. Tumor-infiltrating dendritic cell states are conserved across solid human cancers. J Exp Med 2021

Pelly VS et al. Anti-inflammatory drugs remodel the tumor immune environment to enhance immune checkpoint blockade efficacy. Cancer Discovery 2021

Maier B et al. A conserved dendritic-cell regulatory program limits antitumour immunity. Nature 2020

Bonavita E et al. Antagonistic Inflammatory Phenotypes Dictate Tumor Fate and Response to Immune Checkpoint Blockade. Immunity 2020

Böttcher JP et al. NK cells stimulate recruitment of cDC1 into the tumor microenvironment promoting cancer immune control. Cell 2018

Type of contract

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