



RESEARCH TOPIC MEM2

Dissecting the role of migratory dendritic cell in liver cancer Curriculum MEM

Laboratory name

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Abstract

The hepatic microenvironment is a site of complex immunological activities. The tolerogenic nature of the liver, can act as a barrier to anti-tumour immunity, foster cancer progression and resistance to immunotherapy.

Dendritic cells (DC) play a critical role in the maintenance of liver tolerance and in anti-tumour immunity. This PhD project will test the hypothesis that a recently identified activation state of conventional DC, termed mDC or MregDC, contributes to the regulation of anti-tumor immunity in the liver.

The primary aim of this PhD project is to unveil the cellular and molecular mechanisms controlling immune responses during liver carcinogenesis. By using a newly generated mouse model, enabling tracking or inducible depletion of mDC, we will dissect the ability of this enigmatic DC state to orchestrate anti-tumor responses. Moreover, we will study the crosstalk of mDC with other prevalent liver immune cells, such as natural killer cells, T cells and macrophages and the regulation of liver tolerance. Finally, the prognostic utility of mDC in human liver cancer will be tested and a liver tumor explant platform will be implemented to functionally characterize, ex vivo, the immunoregulatory properties of mDC from patients.

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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