



RESEARCH TOPIC MECM1

Investigating cholesterol metabolism in cancer and its impact on the tumor microenvironment and dendritic cell function

Curriculum MECM standard

Research Area

Immuno- Onco

Laboratory name

Cellular and Molecular Oncoimmunology

Research Supervisor

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Abstract

Conventional dendritic cells (cDCs) are pivotal antigen-presenting cells that capture environmental information and relay it to other leukocytes, thereby shaping both innate and adaptive immune responses. However, during tumor progression, cDCs often become dysfunctional, impairing their ability to cross-prime effector cells. The role of lipid metabolism in cDCs is emerging as a critical area of research. Within the tumor microenvironment (TME), the cholesterol and lipid composition profoundly affect the activation of cDCs by modulating the expression of key genes, including Bhlhe40. In cancer, cholesterol metabolism is frequently disrupted. This is especially pronounced in hepatocellular carcinoma, where tumor cells exhibit altered expression of Soat1 and Soat2, enzymes that serve as master regulators of free cholesterol esterification. This project seeks to investigate how the subverted cholesterol metabolism in tumor cells modifies the cholesterol and lipid content in the TME, ultimately influencing cDCs properties. Specifically, we will investigate the regulatory role of the transcription factors Bhlhe40 in these processes. By advancing our understanding of how impaired cDCs maturation affects tumor immunity, this research will contribute to bridging the gap between cancer cell lipid metabolism and immune responses, paving the way for novel immunotherapeutic strategies.

Main technical approaches

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

Scientific references

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Type of contract

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