CRCHUM
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2e SÉMINAIRE DE RECRUTEMENT
AXE CANCER

Dominic Roy, PhD
Rosalind & Morris Goodman Cancer Research Centre, McGill University

Jeudi le 18 juin 2020 - 13 h à 14 h
Via Zoom

https://umontreal.zoom.us/j/98613607834?pwd=M0Vnb1dYQnduT25IZ0Z1Vmc5SDZDQT09
ID de réunion : 986 1360 7834 / Mot de passe : 211367

Metabolic regulation of T cells in infection and disease

T cells play a crucial role in immunity to infection and cancer. During immune challenge, T cells engage various metabolic pathways to meet the energetic and biosynthetic demands of clonal expansion and development of effector functions such as cytokine production. My work is focused on understanding how metabolism influences the proliferation and function of various T cell subsets in both normal and dysregulated immune responses.

I will be presenting my most recent work which, using metabolomics, identified methionine as a key nutrient affecting epigenetic reprogramming in CD4 T helper (Th) cells. We showed that methionine is rapidly taken up by activated T cells and serves as the major substrate for biosynthesis of the universal methyl donor S-adenosyl-L-methionine (SAM). We found that methionine was required to maintain intracellular SAM pools in T cells, and that methionine restriction reduced histone H3K4 methylation at the promoter regions of key genes involved in Th17 cell proliferation and cytokine production.

I will also present data from another recent study, in which the role of fatty acid oxidation in the generation of CD8 memory T cells was investigated using a genetic model to target Cpt1a specifically in T cells. Contrary to previous studies, we found that Cpt1a is largely dispensable for the generation of memory T cells. We also uncovered off-target effects of etomoxir, a widely used drug to study fatty acid oxidation in several experimental models.

Current and future work is aimed at 1) conducting metabolism-focused genetic screens in T cells to uncover metabolic pathways important in anti-tumor immunity and T cell exhaustion; 2) studying of how metabolism regulates oncolytic virus replication in tumor cells; as well as 3) the interplay between the impact of oncolytic virotherapy on the metabolism and function of tumor-specific T cells.
