

SÉMINAIRES ET CONFÉRENCES



Grégoire Altan-Bonnet, Ph.D.

**Section Head - Immunodynamics Group
Deputy Chief - Laboratory of Integrative Cancer Immunology
Center for Cancer Research - National Cancer Institute - Bethesda MD**

“ Navigating the high-dimensional space of T cell activation, using robotics and machine learning “

Cancer immunotherapies elicit highly variable outcomes in patients and genetically identical mouse models, suggesting a strong intrinsic stochastic component. Using thousands of well-controlled ex vivo immunoassays, we show that leukocyte activation and tumor cytotoxicity display macroscopic variability that follows a shifted Poisson distribution. This variability arises from stochastic activation of a rare subpopulation of T cells (“Spark T cells”) coupled to a paracrine IFN- γ -driven positive feedback. By integrating these quantitative insights into a custom machine-learning pipeline with single-cell resolution, we phenotypically and functionally identify Spark T cells in murine naïve T cells and in human T cell blasts used for adoptive cell therapy, and demonstrate their role in shaping heterogeneous immunotherapy responses [PMID: 41650970]

Building on this framework, we investigate how receptor-level signal integration modulates T cell potency and specificity. While chimeric antigen receptor (CAR) T cells show strong cytotoxicity but limited specificity in solid tumors, endogenous T cell receptors (TCRs) provide exquisite antigen discrimination with reduced efficacy. Deploying our high-throughput platform and mathematical modeling [PMID: 35587980], we reveal inhibitory and cooperative crosstalk between co-expressed TCRs and CARs: strong TCR-antigen interactions enhance CAR activation, whereas weak interactions antagonize it. Leveraging this crosstalk, we engineer dual TCR/CAR T cells targeting neoantigens and HER2 that exhibit enhanced antitumor activity with minimal off-tumor toxicity in a humanized solid tumor mouse model [PMID: 40220754]

Together, these results show how stochastic T cell activation and receptor-level signal integration jointly govern variability, potency, and precision in cancer immunotherapy.”



Faculté de médecine
Département de biochimie
et médecine moléculaire

Université 
de Montréal

Le vendredi 1^{er} mai, 12h30

Pavillon Joseph-Armand-Bombardier, Salle : 1035

et

[Zoom](#)

invité de Paul François
paul.francois@umontreal.ca