Centre de recherche
CHU Sainte-Justine
Le centre hospitalier universitaire mère-enfant

Université de Montréal

PROGRAMME DE STAGES D'ÉTÉ
Initiation à la recherche biomédicale
au Centre de recherche du CHU Sainte-Justine
Été 2020

Humanized tumor model to better study immune cell interaction in mice

Numéro de l'offre de stage : No. 35

Équipe de recherche

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Programmes d'études ciblés

Biologie cellulaire, thérapie cellulaire, pharmacologie

Description du projet

Patient-derived xenograft models are currently considered the gold standard in trying to predict the efficacy of novel anti-cancer strategies. In this model, a patient-derived tumor is resected and injected into an immune-compromised mouse (i.e. NSG), allowing the growth of the tumor in absence of allograft rejection. One important limitation of this model is the absence of immune/inflammatory cells, affecting the response to the treatment and predictability in human. To address this issue, we developed novel and flexible humanized tumor mouse models. Briefly, fibroblasts are collected from adult or fetal healthy donors and transformed into tumor cells following their modification with defined oncogenes (hTERT, Ras^{V12}, SV40ER). These tumor cells are then injected into NSG mice immunologically reconstituted by either (1) adoptive transfer using PBMCs allogeneic or autologous to the transformed cells or (2) the transplantation of fetal hematopoietic stem cells and thymus. Using these models, our results have shown it is possible to reject heterotopic tumors in an autologous setting. We also have generated a diversity of autologous tumor cell types by first reprogramming healthy donor fibroblasts into induced pluripotent stem cells (iPSC) and then differentiating these cells into astrocytes and hepatocytes. We transformed these iPSC-derived cells using the same set of

oncogenes described above and also observed cancer progression and immune rejection in humanized mice. The objective of this project will be add to this model by adding autologous fibroblasts and endothelial cells to better mimic the compete humanized tumor stroma. The contribution of stromal cells to tumor response to immunotherapies will be studied. These results are expected to provide essential pre-clinical data for the development of improved anti-cancer therapies in humans. Our model will also extend our understanding of immune-based mechanisms of tumor evasion which will help in the development of new types of cancer drugs.

Rôle du stagiaire

The applicant will be ask to work with cell culture in vitro and to monitor tumor growth in vivo using a live imaging luminescence and fluorescence device. The applicant will also be initiated to histology (tumor samples) to monitor immune cells infiltration. It is expected students will present their data at lab journal club.

The ideal candidate will have high motivation and interest in cancer biology. Strong organization skill are also required. Ability to work with mice is highly recommended. Good interpersonal skills is a must.

Mots clés

Mice, tumor, iPSC, PBMCs