



Research Project Proposal
Academic year 2018-2019

Project Nº 29

Title: Exploring the tumor microenvironment and novel immunotherapy strategies in pre-clinical mouse models of B cell lymphomas

Department/ Laboratory

Onco-Hematology Program at CIMA, Laboratory of Lymphoproliferative Syndromes (Lab 1.03)

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Summary

BACKGROUND: Considerable advancement in our understanding of the pathogenesis and progression of B-cell lymphoma has been achieved through the molecular dissection of the malignant cells. However, it has become increasingly evident that tumors comprise not only the malignant cells but also a plethora of non-malignant cells and extracellular matrix — the tumor microenvironment. Supporting this notion, we have recently generated several multi-transgenic mouse models in the lab that recapitulate the molecular, cellular and tumor microenvironment of aggressive human B-cell lymphomas.

We work with the hypothesis that B-cell lymphomas distort intercellular signals to promote immunosuppression and escape anti-tumoral responses, which could potentially be reverted through immunotherapy.

GOALS: Our translational proposal aims to comprehensively characterize the lymphoma microenvironment and evaluate the therapeutic potential of novel immunotherapy strategies in our pre-clinical mouse models.

METHODOLOGY: To achieve this we propose to use cytometry, computational immunology tools, immunohistochemistry, and other cellular and molecular techniques to characterize the landscape of immune cell types in the murine tumor microenvironment, as well as to assess morphology, distribution and expression of co-inhibitory/co-stimulatory molecules on tumor-infiltrating immune cells. Importantly, we will also design and explore novel in vivo immunotherapy strategies in our mouse models, involving monoclonal antibodies and immunomodulatory drugs, which will require that the student obtains the 'official approval' to work with animals offered in the MIB.

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Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?