



Research Project Proposal
Academic year 2018-2019

Project Nº 50

Title: *Understanding the cellular and molecular layers of organization that define the stem cell niche at a single cell resolution.*

Department/ Laboratory *Lab 1.02, Center For Applied Medical Research, Hematology-oncology..*

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Summary: *The importance of ancillary cells in tumor biology has been demonstrated in multiple tissues and the bone marrow (BM) is not an exception. In leukemia, whether the BM microenvironment provides the necessary conditions for mutant stem cell clones to arise or flourish or whether the neoplastic cells remodels the niche to facilitate their outgrowth is still a mater debate. Nevertheless, it is plausible to predict that understanding the complex interphase between leukemic cells and their niches will facilitate the development of novel curative approaches for these diseases. Hence, using the mouse bone marrow niche in homeostasis and during neoplastic transformation we aim to unravel the cellular and molecular interactions that defines the tissue behavior using a multi-omics approach based on single-cell-RNA sequencing and single-cell-ATAC-sequencing. Computational and mathematical modeling will then be applied in order to understand the complex network of events that govern tissue homeostasis and transformation. We will subsequently validate experimentally the interaction networks drew by our system biology approach using advanced mouse genetics, multiparametric flow cytometry and multi-omics. Information gathered from these experiments will also provide a list of molecular candidates for therapeutic intervention in aging and leukemia. We will validate those candidate cell populations and genetic pathways by means of gain and loss-of-function assays in vitro and in vivo using murine models and primary human samples. If successful, we will provide a complete transcriptional and cellular wiring of the BM tissue in homeostasis and neoplasia revealing the heterotypic interactions that define its nature.*

yes

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

no