

Research Project Proposal
Academic year 2016-2017

Project Nº 33
Title: Genocopy models of lung cancer metastasis for targeted therapies
Department/ Laboratory Division of Oncology. Solid Tumors and Biomarkers. Lab 1.02. Center for Applied Medical Research(CIMA)
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<p>Summary</p> <p>Lung cancer metastasis represents the most devastating consequence of cancer associated with dismal prognosis. Yet, current efforts to dissect critical determinants and molecular mechanisms of tumor cell dissemination have been hampered by the paucity of experimental available models. This project aims: (1) To develop several GEMMs (genetically engineered mouse models) of autochthonous lung tumors with complex genocopies of humans tumors (The Cancer Genome Atlas) by using genome editing CRISPR/Cas9 technology (2) To implement the multistep metastatic cascade and its multi-organ tropism observed in human tumors by using multimodal strategies (3) To dissect the contribution of changes in the phenotypic and genomic mutational landscape to the pre-metastatic niche, to early and late steps of dissemination and to organ tropism. The approach will heavily rely on cutting-edge technologies of genome editing, GEMMs, the use of adeno, retro and lentiviral transduction systems, cell and molecular biology techniques (RT-qPCR, Western, cloning by homologous recombination, and functional assays (CHIP, kinase assays, a deep seq) image analysis (microCT scans, X-rays, microPET, bioluminescence in vivo), bioinformatic and computational tools. This approach will preserve immunosurveillance and tumor-stromal interactions ideal to unveil critical targets for the development and evaluation of targeted anti-metastatic therapies. We look for an open-minded, highly motivated young scientist with strong organizational and excellent communications skills.</p> <p>References</p> <ol style="list-style-type: none"> 1. K Valencia (...) and F Lecanda (2012) Inhibition of Discoidin Domain Receptor-1 (DDR1) Reduces Cell Survival, Homing and Colonization in Lung Cancer Bone Metastasis. <u>Clin Can Res 18(4); 969–80.</u> 2. Luis-Ravelo, (...) F Lecanda (2013) A Gene Signature of Bone Metastatic Colonization Sensitizes for Tumor-Induced Osteolysis and Predicts Survival in Lung Cancer. <u>Oncogene Oct 23;33(43):5090-9</u>



3. K Valencia, (...) **F Lecanda** (2014) miRNA cargo within Exosome-like Vesicles (ELV) Influences Metastatic Bone Colonization Molecular Oncology 8(3):689-703

POSSIBILITY OF PhD

YES*

* (PhD grant required)