Research Project Proposal
Academic year 2015-2016

Project Nº 29
Title: Genocopy models of lung cancer metastasis for targeted therapies
Department/ Laboratory Division of Oncology Solid Tumors and Biomarkers Adhesion and Metastasis Lab Center for Applied Medical Research (CIMA)
Director 1 Fernando Lecanda **Contact:** flecanda@unav.es 　　　　　Ph: 948 194 700 Ext 1001

Summary

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 autochtonous 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 ladscape 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-mided, highly motivated young scientist with strong organizational and excellent communications skills.

References

1. K Valencia, C Ormazábal, C Zandueta, D Luis-Ravelo, I Antón, MJ Pajares, J Agorreta, LM Montuenga, S Martínez-Canarias and **F Lecanda** (2012) Inhibition of Discoidin

Domain Receptor-1 (DDR1) Reduces Cell Survival, Homing and Colonization in Lung Cancer Bone Metastasis. Clin Can Res 18(4); 969–80.

2. Luis-Ravelo, Iker Antón, Carolina Zandueta, Karmele Valencia, Cristina Ormazábal, Susana Martínez-Canarias, E. Guruceaga, N. Perurena, S. Vicent, J. De Las Rivas, **F Lecanda** (2013) A Gene Signature of Bone Metastatic Colonization Sensitizes for Tumor-Induced Osteolysis and Predicts Survival in Lung Cancer. Oncogene Oct 23;33(43):5090-9

3. K Valencia, D Luis-Ravelo, N Bovy, I Antón, S Martínez-Canarias, C Zandueta, C Ormazábal, I Struman, S Tabruyn, V. Rebmann, J De Las Rivas, V Segura, E Bandrés, and 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)