Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2015-2016

Project Nº 10
Title: Dissecting the functional role of dominant oncogene effectors in epithelial cancers
Department/ Laboratory Lab 1.02, Program in Solid Tumors and Biomarkers, Laboratory where the project will be carried out indicating Department, Area, Faculty, CUN, CIMA etc.
Director: Silvestre Vicent **Contact:** Lab 102, CIMA; 55 Pio XII Ave, Pamplona 31008 **Contact:** silvevicent@unav.es; 948194700 (Ext 1003)
Summary KRAS represents the dominant oncogene driving human tumorogenesis in 30% of human tumors. Mutations in KRAS are found in epithelial cancer types including lung, colorectal and pancreatic adenocarcinomas as well as cholangiocarcinomas. Given the uniqueness of KRAS as a target, it has remained refractory to therapeutic inhibition. Thus, a paradigm switch of this trend remains imperative to develop strategies designed to reach this unmet clinical need. The current proposal stems from a preliminary study aimed to identify KRAS-regulated genes. In this study an integrative cross-tumors analysis to identify genes specifically regulated by mutant KRAS was followed. This strategy identified FOSL1 as a gene representative of mouse and human cancers harbouring KRAS mutations, including lung adenocarcinoma (LAC), pancreatic ductal adenocarcinoma (PDAC) and colorectal cancer (CC). Follow-up functional experiments showed that FOSL1 is necessary for cell viability of KRAS-driven lung LAC and PDAC and a marker of poor survival in patients with these tumors. Thus, the goal of this proposal is to test the clinical and functional relevance of FOSL1 in other KRAS-driven epithelial tumors. A series of aims are planned to achieve this goal: a) Characterization of the expression levels of FOSL1 in IHCC human cancer specimens and their clinico-pathological implications. b) Characterization of FOSL1 expression levels in a genetically-engineered mouse model of IHCC. b) Functional dissection in vitro and in vivo of the role of FOSL1 in IHCC using a loss-of-function approach in cancer cell lines.

References References could be added (no more than three)

Malvezzi, M., Bertuccio, P., Levi, F., La Vecchia, C., and Negri, E. 2013. European cancer mortality predictions for the year 2013. Ann Oncol 24:792-800.
RAS oncogenes: the first 30 years. Malumbres M, Barbacid M. Nat Rev Cancer. 2003 Jun;3(6):459-65.

POSSIBILITY OF PhD

We anticipate that the findings derived from this project will open the possibility for the project to be continued with a Ph. D. (doctoral thesis).

YES*

* (PhD grant required)