Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2015-2016

Project Nº 24
Title: In vivo validation of NatB as a new antitumoral target
Department/ Laboratory Laboratory of Protein Modifications (4.04). Gene Therapy and Regulation of Gene Expression. CIMA
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Summary Most eukaryotic proteins are aminoterminally acetylated although the function of this modification has not been clearly elucidated. One of the enzymatic complexes that catalyze this reaction is the NatB complex, being this enzyme necessary for a proper actin cytoskeleton function and organization. We have observed that this enzyme is upregulated when hepatocarcinoma is developed in mice and humans and its overexpression is associated with poor prognosis in several other human tumors like: lung, colorectal, breast, bladder, myeloma and melanoma. Similarly, the inhibition of this enzyme blocks cellular proliferation and tumor growth in xenograft models. Therefore we are interested in deciphering if NatB can be a new antitumoral target. Meantime, we have generated conditional hepatocyte NatB knock-out animals that present hepatocyte proliferation deficiency, hepatocyte polarization defects and deregulation of several relevant signaling molecules like □-catenin and TRIM-24 trascription regulators. In order to determine the relevance of NatB inhibition to block tumor growth and dissemination we will genetically promote liver and lung tumor development activating KRas-G12D oncogene expression and inactivating p53 antioncogene. We want to analyze if NatB knock-out makes animals are more resistant to tumor development and spreading, analyzing the molecular mechanisms that govern this effect. We will start analyzing the relevance of NatB regulated molecular pathways: actin cytoskeleton, □-catenin, Hippo-YAP and TRIM-24, on tumor development. Moreover, we will test if tumors developed in NatB knock-out animals are more sensitive to antitumoral treatments like Cisplatin and Doxorubicin as consequence of promoted autophagy when NatB is inhibited.

POSSIBILITY OF PhD

YES*

* (PhD grant required)