

Research Project Proposal
Academic year 2016-2017

Project Nº 1
Title: The primary cilium in brain tumor progression and therapeutics.
Department/Laboratory: Department of Biochemistry and Genetics. University of Navarra School of Sciences
Director: Dr. Javier Sáez Castresana
Contact: jscastresana@unav.es
<p>Summary</p> <p>In this project we will study the primary cilium respect to prognosis in medulloblastoma (MB). The primary cilium is a structure on which activation of the sonic hedgehog (Shh) pathway can be produced. The cilium can suppress or activate the formation of tumors, depending on the absence or the presence of Shh ligand respectively. As a hypothesis, we think that the primary cilium disappears when MB progress from less aggressive (desmoplastic) to more aggressive (classic and anaplastic) tumors. We suspect that most MB of group Shh express the primary cilium, while most group 3 and 4 MBs would not express it or would do it as a shorter cilium or as an aberrant cilium, different to the optimal cilium needed to execute its function.</p> <p>As specific objectives, we propose: 1) to determine the incidence, morphology and length of the primary cilium in MB; 2) to determine the expression of molecules of the Shh pathway in MB; 3) to correlate the presence of the cilium and the activation of Shh with the histological and molecular groups of MBs and with variables of clinical evolution: recurrence, metastases, response to treatment; and 4) to assay treatments against Shh in MB, by inhibiting Smo (cyclopamine) and/or Gli (siRNA).</p> <p>References</p> <ol style="list-style-type: none"> 1. Castresana JS (2015) Cancer as a Ciliopathy: The Primary Cilium as a New Therapeutic Target. <u>J Carcinogenesis Mutagenesis</u> 6:e119. doi: 10.4172/2517-2518.1000e119. 2. Khan NA, et al. (2016) Identification of drugs that restore primary cilium expression in cancer cells. <u>Oncotarget</u> 7(9):9975-9992. doi: 10.18632/oncotarget.7198. 3. Hassounah NB, et al. (2012) Molecular pathways: the role of primary cilia in cancer progression and therapeutics with a focus on Hedgehog signaling. <u>Clinical Cancer Research</u> 18(9):2429-2435. doi: 10.1158/1078-0432.CCR-11-0755.



POSSIBILITY OF PhD:

YES¹

¹(PhD fellowship required)