



**Research Project Proposal**  
Academic year 2018-2019

**Project Nº40**

**Title:** *The primary cilium in brain tumor progression and therapeutics.*

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**Summary**

*In this project we will study the primary cilium respect to prognosis in glioblastoma (GB). 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 GB progress from less aggressive to more aggressive tumors. We suspect that most primary GB loose the primary cilium, while most secondary GB maintain the cilium and this fact makes them less aggressive.*

*As specific objectives, we propose: 1) to determine the incidence, morphology and length of the primary cilium in GB; 2) to determine the expression of molecules of the Shh pathway in GB; 3) to correlate the presence of the cilium and the activation of Shh with the histological and molecular groups of GBs and with variables of clinical evolution: recurrence, metastases, response to treatment; 4) to assay treatments against Shh, by inhibiting Smo (cyclopamine) and/or Gli (siRNA) in GB that express the cilium, and 5) to assay treatments, like tubastatin A, to restore the cilium in GB that do not present it.*

**References**

1. Castresana JS (2015) Cancer as a Ciliopathy: The Primary Cilium as a New Therapeutic Target. *J Carcinogenesis Mutagenesis* 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. *Oncotarget* 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. *Clinical Cancer Research* 18(9):2429-2435. doi: 10.1158/1078-0432.CCR-11-0755
- 4.

yes	X
no	

**Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?**