

Research Project Proposal
Academic year 2015-2016

Project Nº 49* ASIGNADO

Title: Role of the metastatic protein TMPRSS4 in lung and breast cancer. Novel strategies for its inhibition.

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Summary

TMPRSS4 expression has been related to the acquisition of metastasis in several solid tumors, such as lung and breast. Moreover, its high expression correlates with poor prognosis in these tumor types. We have published several papers on the role of TMPRSS4 in lung cancer using both in vitro and in vivo assays. In this project we will focus on the role of TMPRSS4 in the acquisition of cancer stem cell (CSC) properties that may lead cells to metastatize. TMPRSS4 induces the process of epithelial to mesenchymal transition(EMT). Evidence suggests that cells with an EMT phenotype may also share properties with CSC. Therefore, it is possible that TMPRSS4 may also induce the development of CSC traits.

In this project we will use human cell lines from breast and lung cancer origin with and without TMPRSS4 expression. By using shRNA and overexpression strategies we will modify the endogenous expression of TMPRSS4 and analyse whether these cells change their ability to acquire CSC features, including self-renewal ability, tumorsphere formation, tumorigenicity in vivo, expression of CSC markers and metastasis.

Different techniques related to cell and molecular biology will be used, including RT-PCR, western blot, flow cytometry, immunofluorescence, cell culture, etc. Experiments in vivo using mouse models and luminometry will also be used.

References

-Larzabal L, Nguewa PA, Pio R, Blanco D, Sanchez B, Rodríguez MJ, Pajares MJ, Catena R, Montuenga LM, **Calvo A**. Overexpression of **TMPRSS4** in non-small cell lung cancer is associated with poor prognosis in patients with squamous histology.



-Larzabal L, de Aberasturi AL, Redrado M, Rueda P, Rodriguez MJ, Bodegas ME, Montuenga LM, **Calvo A. TMPRSS4** regulates levels of integrin $\alpha 5$ in NSCLC through miR-205 activity to promote metastasis.

-de Aberasturi AL, **Calvo A. TMPRSS4**: an emerging potential therapeutic target in cancer.

POSSIBILITY OF PhD

YES*

* (PhD grant required)