

GRAL MSc RESEARCH SCHOLARSHIP 2020-2021 RESEARCH INTERNSHIP PROPOSAL

Institute / Group

IRIG / BCI - IMAC

Supervisor

Nadia Cherradi

E-mail

nadia.cherradi@cea.fr

Phone

+33 4 38 78 35 01

Research Project Title

Role of N-myc Downstream Regulated Gene member 4 (NDRG4) in adrenocortical cancer aggressiveness

Description of the project

Adrenocortical carcinoma (ACC) is a rare but highly aggressive tumor of the adrenal cortex, in which overexpression of a panel of microRNAs has been associated with malignancy. In addition, we have found that miR-139-5p overexpression in ACC is involved in tumor aggressiveness. We subsequently identified NDRG4 as a direct target gene of miR-139-5p in ACC. NDRG4 is markedly under-expressed in ACC cell lines as well as in tumors from ACC patients. The NDRG family of proteins has been shown to relay several oncogenic signalling pathways in cancer cells. However, their role in adrenocortical tumorigenesis is unknown. The aim of the internship is to determine NDRG4 function in adrenocortical cancer cells, particularly in relation to the Wnt/ β -catenin signaling pathway which is frequently activated in ACC. Using pull-down and reporter gene assays, we will investigate whether NDRG4 interacts with molecular complexes of the Wnt/ β -catenin pathway (Frizzled receptor complex and β -Catenin destruction complex) to attenuate downstream signalling. The role of NDRG4 downregulation in promoting ACC cancer cell traits will be determined (proliferation, migration, invasion) in 2D and 3D heterotypic co-culture models (cancer cells and vascular endothelial cells).

Keywords

Adrenocortical cancer - MicroRNA - MicroRNA target genes – Wnt/ β -Catenin signalling pathway – 3D heterotypic co-culture models

Relevant publications of the team

Rataj F, Planel S, Denis J, Roelants C, Filhol O, Guyon L, Feige JJ, Cherradi N. Targeting Aurich elements-mediated mRNA decay with a truncated active form of the zinc-finger protein TIS11b/BRF1 impairs major hallmarks of mammary tumorigenesis. *Oncogene*. 2019 Mar 26. doi: 10.1038/s41388-0190784-8.

Agosta C, Laugier J, Guyon L, Denis J, Bertherat J, Libe R, Boisson B, Sturm N, Feige JJ, Chabre O, Cherradi N. MiR-483-5p and miR-139-5p promote aggressiveness by targeting Nmyc downstream-regulated gene family members in adrenocortical cancer. *International Journal of Cancer*. 2018 Aug 15;143(4):944-957. doi: 10.1002/ijc.31363.

Cherradi N. MicroRNAs as potential biomarkers in adrenocortical cancer: progress and challenges. *Frontiers in Endocrinology*, 2016, 6 (195), 1-15. Doi:10.3389/fendo.2015.00195.
