Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2025-2026

Laboratory/Institute: Institute for Advanced Biosciences **Director:** Christophe Arnoult
Team: RNA splicing, Cell Signaling and Response to Therapies **Head of the team:** Béatrice Eymin

Name and status of the scientist in charge of the project: Béatrice EYMIN
HDR: YES x **no** ☐
Address: Centre de Recherche UGA / Inserm U 1209 / CNRS UMR 5309 Institut Pour l'Avancée des Biosciences Site Santé - Allée des Alpes 38700 La Tronche

Phone: +33 (0)4 76 54 94 76 **e-mail:** beatrice.eymin@univ-grenoble-alpes.fr

Program of the Master's degree in Biology:

☐ Microbiology, Infectious Diseases and Immunology ☐ Biochemistry & Structure
X **Physiology, Epigenetics, Differentiation, Cancer** ☐ Neurosciences and Neurobiology

Title of the project: Exploring the role of tumoral circRNAs on endothelial cells behavior and tumor neo-angiogenesis: towards clinical applications to fight resistance in lung cancer

Objectives (up to 3 lines):

In this project, we want to decipher whether and how two circRNAs we recently found to be overexpressed in lung cancer cells, notably those with acquired resistance to platinum salts, regulate endothelial cells behavior and by the way tumor neo-angiogenesis which could contribute to escape from therapies.

Abstract (up to 10 lines):

Lung cancer is a major public health problem. Counteracting acquired resistance to therapies remains a major goal to cure patients. circRNAs belong to a new category of mainly non-coding RNAs which role in tumorigenesis has emerged in recent past years. In the lab, we recently identified two circRNAs that are overexpressed in lung cancer cell lines and in lung cancer patients having received chemotherapy. We found that these circRNAs modulate the secretome of lung cancer cells, including pro-angiogenic chemokines and inflammatory cytokines. We postulate that these circRNAs could modulate endothelial cells behavior. Based on these results, the objectives of this Master M2 internship will be: (1) to investigate in direct or indirect (conditioned medium) co-cultures as well as in microfluidic systems the consequences on endothelial cells behavior (proliferation, survival, migration) of the neutralization (by using siRNA) or overexpression (using cells we already engineered in the lab) of these circRNAs in lung cancer cells; (2) to develop nanovectors based on gold nanoclusters, in collaboration with chemists at IAB, that will be used to deliver siRNA against circRNAs in tumor/endothelial cells.

Methods (up to 3 lines):

Cell culture and co-cultures, siRNA transfection, proliferation/migration/survival phenotypic assays, confocal microscopy, immunofluorescence studies, microfluidic systems

Up to 3 relevant publications of the team:

1. Khalife M*, Jia T*, Caron P*, Shreim A**, Genoux A**, Cristini A, Pucciarelli A, Leverve M, Lepeltier N, Garcia-Rodriguez N, Dalonneau F, Ramachandran S, Fernandez Martinez L, Marcion G, Lemaître N, Brambilla E, Garrido C, Hammond EM, Huertas P, Gazzeri S, Sordet O, Eymin B. SRSF2 overexpression induces transcription/replication-dependent DNA double-strand breaks and interferes with DNA repair pathways to promote lung tumor progression. *NAR Cancer*, Apr 2;7(2):zcaf011 (2025). */** contributed equally.

2. Gazzeri S*, Zubchuk N, Montaudon E, Nemati F, Huot-Marchand S, Berardi G, Pucciarelli A, Dib Y, Nerini D, Oddou C, Pezet M, David-Boudet L, Ardin C, de Fraipont F, Maraver A, Girard N, Decaudin D, Toffart AC, Eymin B*. PPP3CB overexpression mediates EGFR-TKI resistance in lung tumors via calcineurin/MEK/ERK signaling. *Life Sci. Alliance*; 1;7(12):e202402873 (2024). * co-corresponding authors

3. Jia T, Jacquet T, Dalonneau F, Coudert P, Vaganay E, Exbrayat-Héritier C, Vollaire J, Josserand V, Ruggiero F, Coll JL, Eymin B. FGF-2 promotes angiogenesis through a SRSF1/SRSF3/SRPK1-dependent axis that controls VEGFR1 splicing in endothelial cells. *BMC Biology*; 19(1):173 (2021).

Requested domains of expertise (up to 5 keywords):

. Cell Culture and Co-Culture experiments
. Cell survival, migration and viability assays
. Biochemistry (Western-blot)
. Epifluorescence microscopy
. General knowledge on circRNAs and endothelial cells biology