Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2026-2027

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 DR2 INSERM Team Leader

HDR: yes x no ☐

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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 interplay between DNA repair and splicing machineries in Drug Tolerant Persister cells (DTPs) that escape EGFR-TKI targeted therapy.

Objectives (up to 3 lines):

Our aim is to deepen the molecular mechanisms that contribute to lung cancer cells escape to targeted therapies (EGFR-TKIs) that are currently used in clinic to treat lung cancer patients. More specifically, we aim to further understand the functional links exisiting between the DNA repair pathways and the spliceosome machinery that controls RNA splicing.

Abstract (up to 10 lines):

Lung cancer is the most lethal cancer worldwide and therefore a major health problem. Advances in basic and clinical research have led to the development of drugs, such as Epidermal Growth Factor Receptor (EGFR)-tyrosine kinase inhibitors (EGFR-TKIs), that target mutated, constitutively active EGFR. These inhibitors show high therapeutic efficacy. However, some cells (Drug-Tolerant Persisters, DTPs) escape treatment and lead to the development of secondary tumors resistant to these inhibitors. With the aim of counteracting the appearance of secondary tumors, we are interested in factors that promote genome instability and the dysregulation of the DNA damage response in DTPs. Remarkably, recent findings from the lab showed a closed interplay between DNA repair pathways and splicing factors such as SRSF2. Moreover, our recent RNA-Seq studies highlighted RNA splicing as being one of the most significantly dysregulated process in DTPs. The aim of this Master M2 internship will be to validate some of the targets identified in these transcriptomic analyses as well as to deepen the functional consequences of their dysregulation in DTPs.

Methods (up to 3 lines):

The candidate will subject lung cancer cells to treatment with osimertinib, an EGFR-TKI, and will analyze by RT-qPCR and RT-PCR the mRNA levels of the identified targets, as well as will modulate their expression by using either siRNA or overexpression in order to assess their functional roles on DNA genomic instability, DNA repair pathways and cell survival.

Up to 3 relevant publications of the team:

1. Xian X, Gong R, Rong S, Zhang Z, Jia F, **Eymin B**[*], Jia T[*]. Unraveling the FGFR-RNA Splicing Axis: Mechanisms, Oncogenic Crosstalks and Innovations for Therapeutic Purpose. *Acta Pharmaceutica Sinica B (APSB)*. Accepted. * Co-corresponding authors.

2. 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** (2025) SRSF2 overexpression induces transcription/replication-dependent DNA double-strand breaks and interferes with DNA repair pathways to promote lung tumor progression. *NAR Cancer.* 7(2):zcaf011 (2025). */** contributed equally.

3. Gazzeri S*, Zubchuk N, Montaudon E, Némati F, Huot-Marchand S, Barardi 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*** (2024) PPP3CB overexpression mediates EGFR-TKI resistance in lung tumors via calcineurin/MEK/ERK signaling. *Life Sci Alliance.* 7(12): e202402873. * co-corresponding authors.

Requested domains of expertise (up to 5 keywords):

. Cell Culture experiments
. Cell survival (flow cytometry) and viability assays
. Molecular biology (RT-qPCR, PCR) and Biochemistry (Western-blot)
. Epifluorescence microscopy
. Knowledge on genome stability and splicing machinery