



Internship proposition  
One page max  
M2 OHNU 2026-27



Lab: CRCI2NA

team: 1 - ITMI

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Candidate:

Title of the internship:

Summary of the internship proposal:

In France, more than 50,000 new cases of lung cancer were reported in 2023. Among them, non-small cell lung cancers (NSCLC) are the most common. The KRAS oncogene is mutated in about 25 to 30% of NSCLC patients, with approximately half of these represented by the activating *KRAS* G12C mutation. For decades, targeting the KRAS protein has been a major therapeutic challenge in oncology, with little success. In recent years, multiple inhibitors specific to the G12C mutation have emerged, such as adagrasib. Unfortunately, the benefits for patients are modest, and all eventually develop resistance.

Our preliminary data, obtained through nanopore sequencing and CRISPR "activator" (CRISPRa) screening, highlight 3 long non-coding RNAs (lncRNAs) as potentially involved in the mechanisms of resistance to this inhibitor.

Our aim is therefore to elucidate the role of *LINP1* and *LINC01018* in the response to adagrasib, to propose new innovative targets for patients in treatment failure.

This project will combine the functional description of these lncRNAs in *in vitro* models and their evaluation as relevant targets in *in vitro* tumor spheroid and in *in vivo* PDX (Patient Derived Xenograft) models.

Our goal is to achieve a more comprehensive understanding of the molecular axis that governs the development of resistance to *KRAS* G12C inhibitors. This, in turn, will help refine therapeutic strategies, and propose new combination with conventional treatments.

Option(s) linked to the project:

- Hematology                      Immunology-Cancerology  
 Oncology                       Nuclear Medicine

Option(s) linked to the profile:

- Clinical Research Profile                       Data Analyst Profile  
 Experimental Biology Profile