Fiche proposition de stage - *Internship offers 2025-26*

Offre pour / Offer for (you can make offers for both level, if the subjects are different, please use a new form)

- ○ **Master 2 (from end January)**
- ○ **Master 1 (from mid January)**

Intitulé du stage *Title*	Microbial metabolites in gut homeostasis and their potential as cancer therapeutics
Laboratoire d'accueil *Host laboratory*	Institut de Recherche en Cancérologie de Montpellier (IRCM), INSERM U1194, Team " "Epitranscriptomics and Cancer Adaptation" https://www.ircm.fr/sommaire1.html
Nom du responsable *Name of the PI*	Alexandre David
Nom d'encadrant *Supervisor*	Kuldeep Lahry
Description (3 phrases) *Description (3 sentences)*	Microbial metabolite **queuine (Q)** is salvaged by mammals and site-specifically incorporated into a subset of cytoplasmic and mitochondrial tRNAs by the host **tRNA-guanine transglycosylase (QTRT1/QTRT2)**. Queuosine modification at the wobble-position G34 stabilizes tRNAs and modulates mRNA decoding efficiency at defined codon sets. Although Q is dispensable for cell viability under standard culture conditions, **hypomodification of Q-tRNAs correlates with proliferative disorders (including cancer) and has been implicated in development, differentiation, aging, and neuroprotection.** Building on our recent unpublished findings (Zhang W*., **Lahry K*.**, *et al.* Nature Cell Biology, in press), we have discovered that the upstream microbial precursor **pre-queuosine1 (preQ1)** exerts **anti-proliferative activity in both human and mouse cells**. In vitro and in vivo data show that **preQ1 is bioavailable in plasma and tissues and becomes incorporated into host tRNAs.** Mechanistically, preQ1 incorporation leads to **selective depletion of its cognate tRNA species**, driving **translational repression** that disproportionately impacts

	housekeeping gene expression. We further identify **IRE1 RNase activity** as a mediator of **ribosome-associated, selective degradation of preQ1-modified tRNAs**, independent of canonical unfolded protein/stress signaling. This Master's project will dissect molecular and cellular mechanisms by which the **Q/preQ1 axis couples the microbiota to host physiology programs**, with emphasis on **intestinal epithelial homeostasis and cancer progression.** The host team focuses on the contribution of **RNA modifications on cancer cell adaptation** using genetic studies in living cells and animals, together with **RNA mass spectrometry**, **next-generation sequencing** and **AI-based approaches**.
Durée prevue (2 à 6 mois) Duration (2 to 6 months)	6 months
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