Internship proposition 2025-2026

(One-page max)

Master 2 GP Medicine 4R (Repair, Replace, Regenerate, Reprogram)

Lab: TaRGeT, INSERM UMR1089

Team: Virus to vector (V2V)

Name and position of the supervisor: Audrey Bourdon, PhD (Ingénieure de recherche)

Email of the supervisor: audrey.bourdon@univ-nantes.fr

Candidate (if internship filled):

Title of the internship: Tracing the journey of Adeno-Associated Virus-derived vectors using an *in vitro* cellular platform

Summary of the internship proposal:

Adeno-associated virus-derived vectors (AAV) have become standard tools for *in vivo* gene therapy. Despite the variety of natural AAV serotypes and tissue tropisms, vector targeting remains broad, reducing transduction specificity and efficiency. Very high doses of vectors are therefore required, which inevitably increase the risk of adverse events. In this context, the AAV vector capsid engineering has been extensively explored in order to develop better AAV vectors to achieve therapeutic expression levels with lower vector doses. With more new AAV variants available, it's critical to screen and validate the potency of these vectors by assessing the key steps of AAV trafficking using relevant *in vitro* cellular models. When AAV reaches the cells, it binds to receptors/co-receptors, followed by uptake in endocytic vesicles. It then travels towards the trans-Golgi network (TGN) and escapes into the cytosol. The capsid is imported through the nuclear pore complex into the nucleus for vector genome uncoating.

Our team has initiated the setup of a methodology to address the journey of rAAV vectors *in vitro* using molecular assays and cell imaging, adaptable to any cellular model. Our molecular assays are designed to measure (1) the binding to cell membrane, (2) the uptake in cytosol, (3) the nuclear entry and (4) the uncoating of rAAV vectors. We also visualize the rAAV genome after RNAscope assay and rAAV capsids by immunocytochemistry and confocal microscopy. It allows us to trace the path of rAAV through the cell and colocalize rAAV particles in cell compartments such as early endosomes, lysosomes, TGN and nuclear membrane. In this context, the main purpose of the internship is to contribute to the setup of the molecular assays and cell imaging to study the rAAV vectors trafficking in cellular models.

Profile(s) linked to the project:

x Experimental Biology *(Recherche expérimentale)*

☐ Clinical Research *(Recherche clinique)*