Internship proposition 2025-2026

(One-page max)

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

Lab: Target, inserm umrs1089

Team: Translational Gene Therapy for Muscular Diseases

Name and position of the supervisor: Nicolas Wein, Associate Professor

Email of the supervisor: Nicolas.wein@inserm.fr

Candidate (if internship filled): TBD

Title of the internship: alternate delivery of adeno-associated virus

Summary of the internship proposal:

Background: Neuromuscular Disorders (NMDs) are mostly genetic, rare diseases affecting the muscles and nervous system (NS) system. The societal burden of these diseases is huge, as many remain without therapeutic options. Gene therapy using adeno-associated virus (AAV) has been explored in clinical trials, showing safety and promising improvement in NMDs patients.

Multiple strategies are currently in clinical trials using either intramuscular (IM) or intravascular (IV) delivery of the vector. Despite promising initial results, the effect is only local for IM treatment or requires a large amount of virus for IV delivery. In contrast to children, AAV therapies become more problematic for the treatment of teenagers or adults due to high vector production costs as well as potential safety due to high doses. In addition, *many muscular disorders also display pathology of the NS*. Therefore, efficient simultaneous targeting of both the muscle and NS would likely enhance therapeutic outcomes. Our preliminary data demonstrated that muscles and NS are targeted following cerebral spinal fluid (CSF) in wild type mice (manuscript in preparation). In this project, we proposed here to test CSF dosing rodent models of Duchenne Muscular Dystrophy to ensure that muscle damage does not alter vector spreading. We will then use larger animal such as the Golden Retriever Muscular Dystrophy dog and wild type pigs. This project will provide preclinical proofs of concept that aletnative way to inject AAV can improve muscle function and help other organs such as NS, which are usually overlooked.

Profiles linked to the project:

■ Experimental Biology *(Recherche expérimentale)*

☐ Clinical Research *(Recherche clinique)*