Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2026-2027

Laboratory/Institute: LBFA ---> H2M **Director:** U. SCHLATTNER ---> R. TAMISIER
Team: Hypoxia – Muscles - Metabolism **Head of the team:** R. TAMISIER

Name and status of the scientist in charge of the project:
Drs. O. DORCHIES, CPJ-DR-Inserm, L. NEFF, CR-Inserm (CDD) **HDR: yes** ☐ **no** ☒
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Program of the Master's degree in Biology:

☐ Microbiology, Infectious Diseases and Immunology ☐ Biochemistry & Structure
☒ **Physiology, Epigenetics, Differentiation, Cancer** ☐ Neurosciences and Neurobiology

Title of the project: Efficacy and safety of HDAC6-targeting PROTACs in cell cultures

Objectives (up to 3 lines):

The project aims to determine efficacy and specificity and assess safety of PROTACs designed to reduce the levels of HDAC6, a protein that contributes to disease progression in Duchenne muscular dystrophy. The project is intended to continue with a PhD thesis on animal models of DMD.

Abstract (up to 10 lines):

Duchenne muscular dystrophy is a fatal genetic disease that affects boys. Patients develop muscle wasting, leading to progressive paralysis and death around 30 years of age by cardiac or respiratory distress. Our team is actively involved in understanding the mechanisms of the disease and developing innovative therapeutic options. Inhibiting HDC6 with tubastatin A (TubA) is efficacious in DMD mouse models. However, TubA is not orally available and requires daily injections – a no-go for fragile pediatric patients. We are developing orally-active TubA-based PROTACs that should lead to CRBN-mediated HDAC6 degradation by the proteasome. The master work will consist in validating 3-5 PROTACs in cell cultures: (i) efficacy at reducing HDAC6 levels, including dose-response; (ii) safety/toxicity for treated cells; (iii) specificity over other HADCs; (iv) downstream consequences on the acetylation of tubulin and tubulin network.

Methods (up to 3 lines):

The M2 student will use cell lines (e.g. HEK, C2C12), which will be treated with a panel of 3-5 PROTACs (synthesized by collaborators in Geneva). Cell survival will be assessed. Cell extracts will be prepared for quantification of HDACs and tubulin by western blots and immunofluorescence.

Up to 3 relevant publications of the team:

https://pubmed.ncbi.nlm.nih.gov/41022845/
https://pubmed.ncbi.nlm.nih.gov/38069776/
https://pubmed.ncbi.nlm.nih.gov/37739572/

Requested domains of expertise (up to 5 keywords):

Cell biology / Pathogenesis / Drug development / Animal models / Skeletal muscle