

# TFM offers 2026-2027

**Project title:** Development of a platform to engineer small extracellular vesicles for peptide-based therapies targeting AAT deficiency.

**Summary:** The **working hypothesis** is that small extracellular vesicles (**sEVs**) can serve as an **efficient delivery** system for **therapeutic proteins** and peptides, which can be **endogenously loaded** by engineering the donor cell lines. Specifically, the present proposal focuses on developing an innovative therapeutic approach that employs small extracellular vesicles (sEVs) as a delivery system for functional alpha-1 antitrypsin (**AAT**) to protect alveoli from enzymatic degradation in patients suffering of AAT deficiency. This **innovative treatment can be administered via inhalation**, directly to the lungs.

Building on this hypothesis, the **primary goal** of the project is to **design endogenous loading** strategies by expressing recombinant **fusion proteins** composed of **hATT** and **sEVs specific markers**. To achieve this goal, the proposal identifies **four milestones** that address key challenges in the development of EV-based therapeutics: **a)** achieving efficient protein (AAT) loading on/into EVs, **b)** overcoming limitations in scalable and efficient EV purification methods, **c)** ensuring effective delivery of EVs to pulmonary tissue, and **d)** establishing a robust, scalable biomanufacturing process for EV production. To achieve this goal, we have defined three specific objectives:

The **first objective** focuses on the engineering of HEK293 cells to produce esEVs efficiently loaded with AAT. This objective involves the expression of **AAT fused to LAMP2B or TSG101**. The strategy includes the **expression of cleavable HisTag/StrepTag** on the esEV surface to facilitate **esEVs purification**.

This proposal belongs to the project **TherPeEVs** kindly funded by the Ministerio de Ciencia e Innovación (Plan Estatal de Investigación Científica y Innovación). The student will work within a research group together with a Polish PostDoc researcher, so a good level of English is essential.

**Supervisor:** Dr. Martí Lecina, Associate professor

**Laboratory:** Bioprocessing, Department of Bioengineering

**Contact email:** [marti.lecina@iqs.url.edu](mailto:marti.lecina@iqs.url.edu)