

Optimization of Precipitation Parameters for Purification of AAV5 Virus-Like Particles

Bachelor Thesis

General Information

PhD project started 01.2025

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Starting from **January/February 2026**

Positions available: 2 BSc positions

Language spoken: **English**

1. Introduction

Virus-like particles (VLPs) are nanostructures that mimic the organization and conformation of viruses, but they are noninfectious as they lack viral genetic material. Adeno-associated virus (AAV) vectors are among the most promising tools for gene therapy applications due to their safety and efficiency in gene delivery, but the production is challenging resulting in low yields and high costs. Previous research has demonstrated the potential of precipitation as capture step for VLPs. This project aims to optimize precipitation-based capture of AAV5-VLPs to improve recovery and purity through systematic parameter screening.

2. Research Objectives

- Screen different precipitants (e.g., PEG of various molecular weights, ammonium sulfate, etc.) for AAV-VLP precipitation.
- Evaluate the influence of pH and additives (including salts across the Hofmeister series) on precipitation efficiency and purity.
- Optimize precipitation conditions to maximize yield and minimize host cell protein and DNA contamination.
- Implement and validate an automated precipitation protocol on a robotic liquid handling platform.

3. Methodology

- Optional expression of AAV5-VP3 capsid proteins in *E. coli*.
- Design and execution of a precipitation screening matrix varying precipitant type, concentration, and buffer conditions.
- Use of the robotic liquid handling station (*Freedom EVO® 200*, Tecan Group Ltd.) to automate sample preparation and processing.
- Quantitative and qualitative analysis of VLP yield, integrity, and purity under different conditions using different analytical methods.

4. Analytics and Tools

- Robotic liquid handling station (*Freedom EVO® 200*, Tecan Group Ltd.)
- SDS-PAGE electrophoresis system, ELISA kit
- High Performance Liquid Chromatography, UV/Vis spectroscopy, Dynamic Light Scattering
- MATLAB or Python

5. Timeline

