AAV-Factory: Synthetic Viral Nanosystem for Highly Efficient AAV Production for Gene Therapy

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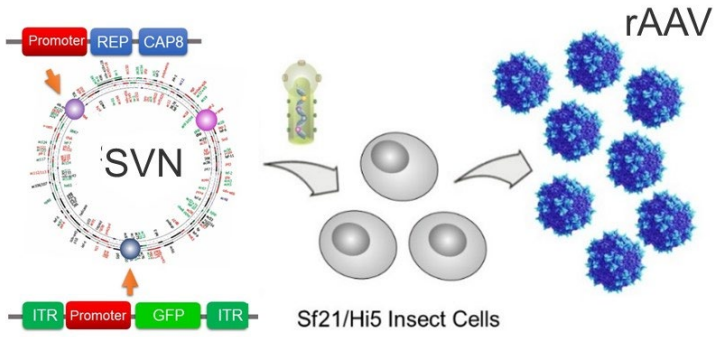

Synthetic viral nanosystem producing rAAV for gene therapy

Project description:
Gene therapy is one of the fastest growing fields in the pharmaceutical industry. The first approved gene therapy utilized a recombinant AAV vector (rAAV), and dozens more rAAVs are currently in clinical trials. rAAV gene therapy drugs are priced in the region of €500'000 and above, partially a result of currently highly complex production processes combining multiple components, requiring multiple separate GMP production runs. In the present project, we intend to introduce the first scalable, single-virus rAAV production platform to resolve this bottleneck. The resulting significant reduction of manufacturing complexity will lower the price of future rAAV gene therapies and deliver additional, currently unaddressed or unaffordable rAAV treatments for genetic diseases into the clinic by providing scientists at laboratory R&D stage with more user-friendly and productive tools. Benchmarking the prowess of our platform, we will produce high-quality rAAVs for correcting steroid resistant nephrotic syndrome (SRNS), a devastating childhood congenital disease.

Our innovative rAAV production platform will rely on a reengineered baculovirus, a small, non-human, non-pathogenic virus. We already created a partly synthetic prototype, SynBac, and will now exploit a step-changing, AI-powered synthetic genomics approach, combined with state-of-the-art DNA assembly technologies, to evolve, scramble and optimize SynBac for our purpose. We will hardwire into SynBac modalities encoding functional rAAVs and comprehensively query the baculovirus genomic space for sustained, high-quality, high-level rAAV production, followed by biochemicl and biophysical validation. Best rAAVs thus produced with the best SynBac variant will be rigorously tested for structural and functional integrity using state-of-the-art approaches including Cryo-EM, and validated in cell and mouse models for rectifying the SNRS disease phenotype.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.