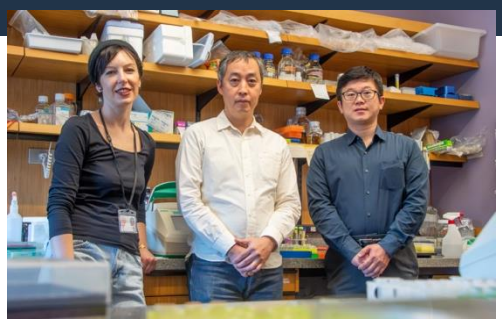
Seed Phase



Optimization of AAV vector production using riboswitch

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What is the problem?

Adeno-associated virus (AAV) vectors are emerging as a major class of gene therapy vectors used to deliver therapeutic genes to the patient's cells. However, manufacturing of AAV vectors is complex and expensive. One of the major challenges in AAV manufacturing is the high level of "empty capsids" or virus shells containing no genes (DNA) during production (Figure 1). These empty capsids necessitate costly purification processes and contribute to increased inflammation upon administration. Therefore, solutions to minimize empty capsids while improving full capsid yield will benefit both AAV manufacturers and patients.

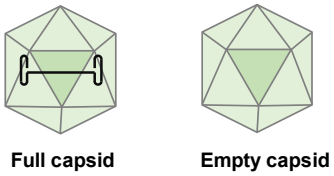
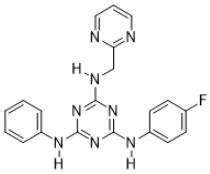


Figure 1

Figure 1. Full capsids contain single-stranded DNA that encodes therapeutic genes while empty capsids do not.



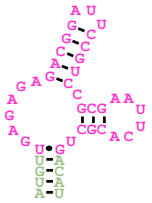


Figure 2. Small molecule (ASP2905) and the RNA aptamer (AC17-4) that are used to construct riboswitches that regulate gene expression.

What is your solution?

We aim to address the empty capsid problem by controlling the expression level and timing of viral proteins using "riboswitches." Riboswitches are gene switches that can induce protein expression in cultured cells by the addition of a small molecule. Our riboswitch technology is based on the new small molecule – RNA aptamer pair that was discovered in our group (Figure 2), which exhibits excellent switch characteristics. We believe that manipulating the expression of various viral genes during AAV production in cultured cells can result in efficient vector production while minimizing empty capsids.

Keywords: gene therapy, AAV, riboswitch, aptamer

Other resources

- Publication
- Publication
- Unit website

Contribution to SDGs

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