Docket #: S21-394

High-capacity Lentiviral Vectors

Technology Reference
CZ Biohub SF ref. no. CZB-230S
Stanford ref. no. S21-394

Researchers at Stanford have developed new lentiviral vectors that are able to deliver more genetic information than currently available vectors, aiding in the development of gene therapy.

Gene therapy is one of the most promising therapeutic avenues in translational medicine. This method involves the genetic engineering of cells in living humans to replace dysfunctional or pathogenic versions of genes. Several methods have been proposed for delivering gene therapy in patients, one of which is lentiviral vectors (LVVs). Lentiviruses are a group of retroviruses that can insert parts of their genetic material into a host cell's genome, including non-dividing cells. While LVVs have many advantages for use in gene therapy, one caveat of this approach is the limited capacity of these vectors. LVVs have approximately an 8-12 kilobase (kb) payload, which limits their delivery capacity to 1-2 genes. This physical limitation attenuates LVVs effectiveness in clinical gene therapy settings in which a larger payload capacity is needed to resolve genetic mutations.

Stage of Development
Research -

in vitro

Stage of Research
The inventors have devised a strategy to produce LVVs with roughly double the payload capacity of those currently available. Wild-type LVVs have two identical or nearly identical gRNAs. However, the full capacity of these gRNAs was not able to be utilized due to dimerization interactions between the two gRNAs that result in dimer linkage structure that is integral to viral packaging. The inventors have designed LVV structures that allow for the combining of the two gRNAs such that interactions

between like-gRNAs that would form homodimers are thermodynamically favored and stabilized, while interactions between unlike gRNAs that would form heterodimers are not thermodynamically favored and stabilized. Thus, these LVVs can form dimer linkage structures needed for viral packaging (homodimers) while avoiding heterodimers that would disrupt distinct sequences meant to be delivered as a payload into the genomes of human cells.

Applications

- Use of increased-capacity LVVs for gene therapy in vivo
- Use of increased-capacity LVVs as research tools

Advantages

- Roughly double the payload capacity of LVVs used under current methods
- Increased payload capacity makes these LVVs for broad use in a myriad of biomedical applications that require more than 1-2 genes to be modified.

Patents

- Published Application: WO2023212396
- Published Application: 20250290093

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