Docket #: S22-275

Composition and Method of Universal Programmable Virus-like Particles (VLPs)

Stanford researchers have engineered retroviral and virus-like delivery systems for producing universal pseudotyped vehicles for cell and gene therapies. Binding moieties expressed on viruses and virus-like system can target desired specific cell types and bind off-the-shelf or custom antibodies in a plug-and-play manner.

Cell and gene therapies rely on successful delivery of therapeutic genetic payloads to specific cells or tissues. Retroviruses are used to directly integrate genetic payloads into the target cell for long-term, heritable, and stable expression of the gene. A major challenge in the field remains highly selective transduction to specific cell types. Stanford researchers have addressed the selectivity problem by developing a retrovirus that is decorated by a binding moiety that either directly binds the cell of interest through a cell binding domain (CBD) or binds an antibody/antibody fragment/ligand (ABD) that then binds the cell. The system is expandable to virus-like particles (VLPs).

Figure

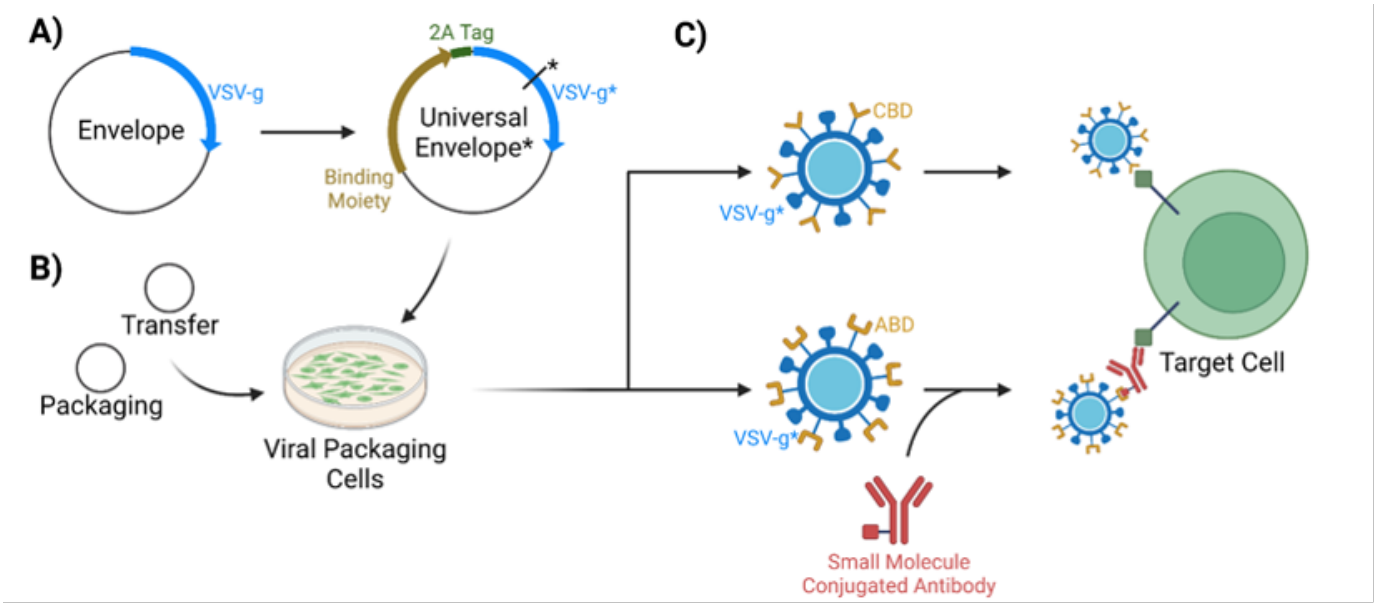

Figure description: **A)** Universal retroviruses are created by engineering the envelope or packaging plasmid with a binding moiety (envelope version shown). The cognate envelope protein (VSV-g shown) can further be mutated to no longer recognize its cognate ligand. **B)** Transfected with the other retroviral packaging plasmids into viral packaging cells, retroviruses are generated that are decorated with the binding moiety. **C)** The binding moiety can contain either a cell binding domain (CBD, top) or an antibody/antibody-fragment/ligand binding domain (ABD, bottom). In the CBD case, the binding moiety directs the virus toward a very specific protein, enabling it to transduce the cell type. In the ABD case, the binding moiety binds a secondary binder such as an antibody, which together transduces specific cell types. (*image credit: inventors*)

Stage of Development

Proof of Concept: Researchers have demonstrated the CD7 version of CBD and the FITC and biotin versions of the ABD for delivery into various types of immune cells including T cells, NK cells, and monocytes.

Applications

- Cell and gene therapy

Advantages

- Increases retroviral transduction space and specificity
    - Can engineer cells that cannot be transduced by traditional lentiviruses, such as CD4+ T cells, CD8+ T cells, NK cells, and monocytes.
- Universal: one virus design can be conjugated with any antibody to target any cell
- Facile
- Modularly switchable cell specificity
- Minimal off-target transduction
- ABD/CBD not integrated to host cell genome ensures no downstream problems
- System can be integrated into virus like particles (VLPs)

Patents

- Published Application: WO2024059569

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