

Docket #: S24-004

Genetically Encoded Lysosome Targeting Chimeras for Cell-mediated Delivery

Researchers at Stanford have developed fully genetically-encodable lysosome-targeting chimeras which allow for the targeted delivery of various proteins into receiver cells.

Lysosome-targeted degradation is an emerging therapeutic modality that facilitates the degradation of membrane and soluble extracellular proteins. Compared to traditional therapeutic modalities, such as small molecule or antibody-based inhibitors, targeted protein degradation offers increased potential potency and broadens the druggable proteome. These techniques generally use bifunctional molecules to recruit proteins of interest to either lysosome trafficking receptors or plasma membrane-associated ubiquitin ligases. The main drawback of the first generation of this technology, called lysosome-targeting chimeras (LYTACs), is that they contain synthetic glycopeptides that cannot be genetically encoded, thereby limiting cell-mediated delivery applications.

Stage of Development

Research - in vitro

Stage of Research

The inventors have developed fully genetically-encodable lysosome-targeting chimeras (GELYTAC), which allow for integration into therapeutic cells for targeted delivery at desired tissue sites. This comprises fusion polypeptides containing a target binding domain and an IGF2R-binding portion of a human IGF2 protein.

Applications

- The engineered GELYTAC construct can secret from human cells, including primary T-cells, to drive the uptake of various proteins into receiver cells and act on local targets.
- Administration to a human in need with a condition requiring targeted protein degradation in an appropriate dosage to ameliorate or treat at least one symptom.
- Application with a pharmaceutically acceptable carrier that can enhance, stabilize or facilitate the preparation of the expression cassette encoding the fusion polypeptide.

Advantages

- Improved potency by mutations in the IGF2 protein in the engineered GELYTAC.
- Integration of therapeutic proteins into the genomes of therapeutic cells for targeted delivery at diseased sites.
- Broad cell-mediated delivery applications.
- Spatially-selective targeted protein degradation.

Patents

- Published Application: [WO2025259950](#)

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