Stanford University

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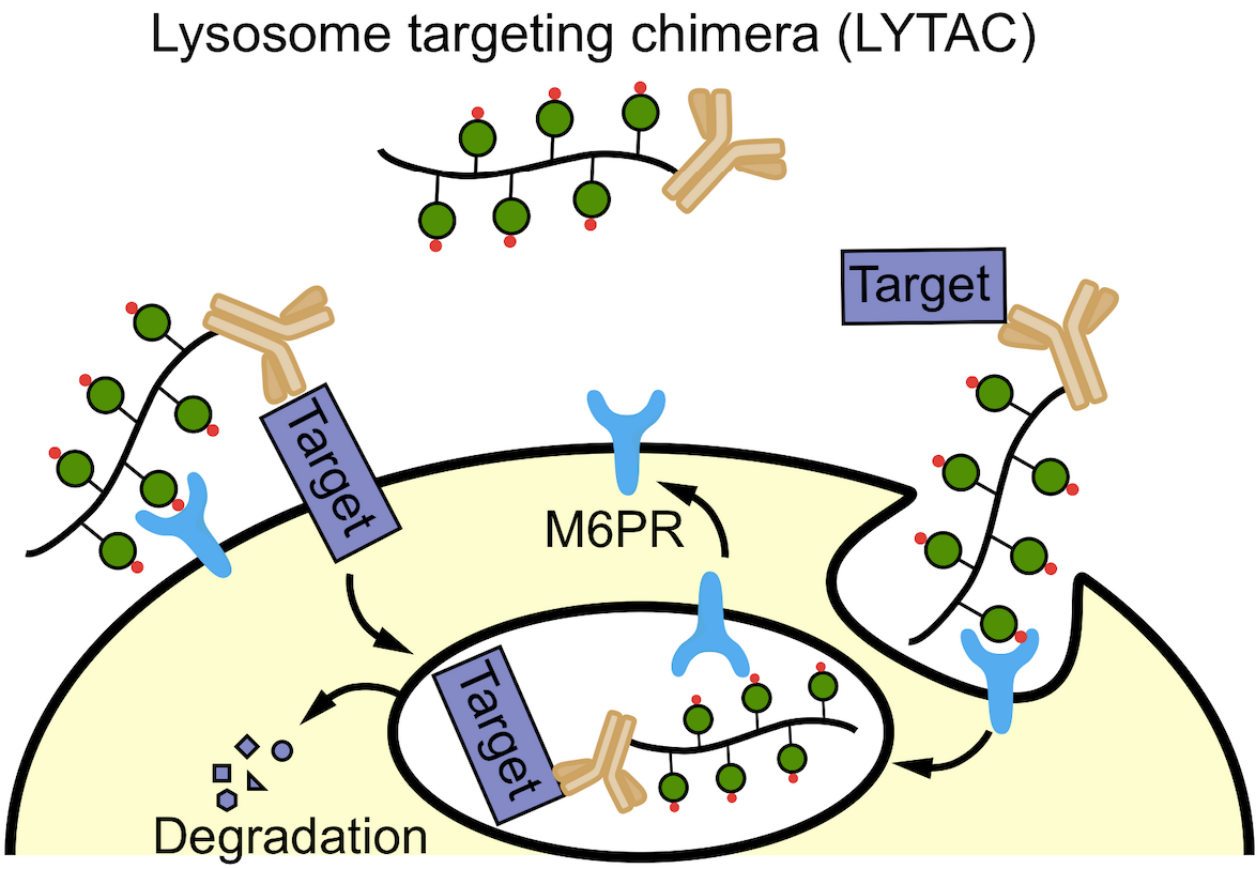
Lysosome targeting chimeras

Researchers at Stanford have developed a platform for targeted degradation of extracellular or cell surface proteins via the lysosomal pathway. Many protein-directed therapeutics act by obstructing target function or recruiting immune effectors. However, these mechanisms do not work for many potential therapeutic targets. Thus, new methods are needed for these "undruggable" targets. New protein degradation technologies have been developed to try and meet this need, but they only work on proteins with intracellular domains. Many secreted and membrane proteins play key roles in a variety of diseases. Thus, additional methods are needed to target extracellular and membrane proteins for degradation. To help meet this need the inventors have developed the lysosome targeting chimera (LYTAC) platform. LYTACs are conjugates capable of binding to the cell surface lysosome targeting receptor and the extracellular domain of a target protein. This platform enables depletion of secreted and membrane proteins and thus has the potential to dramatically impact human health.



LYTAC concept- a glycopolypeptide ligand for the lysosome targeting receptor (CI-M6PR) is conjugated to an antibody to traffic secreted and membrane proteins to lysosomes.

Stage of research

The inventors demonstrated that LYTACs mediate efficient degradation of apolipoprotein-E4, epidermal growth factor receptor (EGFR), CD71, and programmed death-ligand 1 (PD-L1).

Additional research
The inventors have developed additional research tools for investigating challenging proteins, see Stanford Docket S18-183.

If interested in this technology, please respond by August 5, 2019.

Applications

- Basic research
  - Study receptor trafficking and protein degradation
- Therapeutic development
  - Enables degradation of secreted and membrane proteins of therapeutic interest

Advantages

- Enables targeted degradation of secreted and membrane proteins
- Complements existing technologies directed to intracellular protein degradation
- Chemical tunability and modularity offer new opportunities in targeted protein degradation
- Potential to develop therapeutics directed to "undruggable" target

Publications

- S. Banik, K. Pedram, S. Wisnovsky, N. Riley, C. Bertozzi Lysosome Targeting Chimeras (LYTACs) for the Degradation of Secreted and Membrane Proteins *ChemRxiv* posted on 29.03.2019.

Related Web Links

- Bertozzi group

Keywords

protein degradation therapeutics, chimeric protein, discovery of new therapeutic targets, engineered protein fusion, fusion protein, lysosomal storage, protein activity control, protein degradation, protein delivery, protein interactions, protein research, research tool: protein analysis, research tool: reagent, therapeutic: platform technology, top pharma companies

Stanford Reference

Docket Number: S18-179

HIGHLIGHTS

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Reference

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