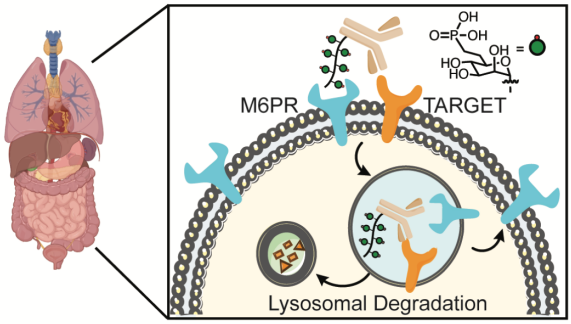
Docket #: S20-337

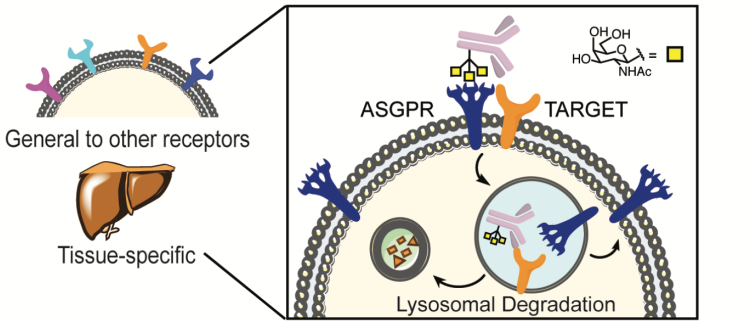
Polyspecific integrin-binding peptide (PIP)-LYTAC for degradation of integrins

Jennifer Cochran and Carolyn Bertozzi have collaborated to develop a bifunctional molecule called a polyspecific integrin-binding peptide (PIP)-LYTAC that can bind to integrins expressed on the surface of cancer cells and trigger their degradation via the lysosome.

Integrins are cell surface proteins that bind components of the extracellular matrix and play a critical role in facilitating tumor growth and metastasis. Many solid tumors express a variety of these integrins, making integrins a prime target for anti-cancer therapy. PIP-LYTAC molecules work by recognizing a variety of integrins, including ?v?1, ?v?3, ?v?5, ?v?6, and ?5?1 integrins, on the cell surface. The molecule can then link the engaged integrin to a lysosome targeting receptor and trigger its internalization and degradation. Removing integrins from cancer cells could slow tumor progression and prevent metastasis. The PIP-LYTAC can also be tailored to target organ- or tissue-specific lysosomal targeting receptors, allowing this molecule to be functionalized for specific tumor types. Integrins are also involved in viral infections, making PIP-LYTACs a potential antiviral therapy.



1st Generation Lysosomal Targeting Chimeras (LYTACs):
M6PR has broad tissue distribution



GalNAc-LYTACs:
ASGPR is exclusively expressed in hepatocytes.

Figure: LYTACs can hijack the asialoglycoprotein receptor (ASPGR) for targeted and cell-specific protein degradation. LYTACs targeting M6PR can degrade broadly expressed targets while LYTACs targeting ASPGR can degrade targets specifically on hepatocytes. Courtesy of Carolyn Bertozzi and Jennifer Cochran.

Related Technology: Stanford Docket 06-356: "Integrin Binding Peptides Based On Knottin Scaffolds"
Stanford Technology 18-179: "Lysosome targeting chimeras (LYTACs)"

Applications

- Cancer therapeutic for integrin-overexpressing cancers
- Antiviral therapy

Advantages

- Bifunctional: single protein can both target the integrin and trigger the degradation pathway
- Can be tailored for tissue- or organ-specific targeting
- Alternative to antibody approach

Publications

- Ahn, G., Banik, S., Miller, C.L., et al. "Lysosome Targeting Chimeras (LYTACs) That Engage a Liver-Specific Asialoglycoprotein Receptor for Targeted Protein Degradation." ChemRxiv. Preprint. (2020).

Patents

- Published Application: WO2022026906
- Published Application: 20230211001

Innovators

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