Drug Discovery & Development

Cyclic Peptide-Based Lysosome Targeting Degraders

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The Invention

UW-Madison researchers have developed a protein degrader that shuttles targeted extracellular protein into the lysosome using a cyclic peptide that binds to a cellular receptor attached to a binding molecule for a protein of interest. Once inside the lysosome, the target protein is released from the molecule and degraded. The shuttling molecule is released back outside of the cell where it can bind another target protein. The researchers tested this bifunctional molecule using a fluorescent label to ensure it entered and exited the lysosome. They labeled an antibody for the cancer target EGFR with the cyclic peptide and measured the presence of EGFR in HepG2, MCF7 and HeLa cells and noted a significant decreased in EGFR protein levels in cells dosed with the cyclic peptide labeled antibody suggesting that EGFR has been degraded in each of the three cell lines.

Peptide ligands that can bind to integrins have been extensively investigated for the delivery of anti-cancer drugs. The inventors tested the following cyclic peptide as the binder of RGD-binding integrins for the development of lysosome targeting degraders. cRGD = cyclo [-Arg-Gly-Asp-D-Phe-Lys] also known as c(RGDfK). The key residues are Arg-Gly-Asp or RGD, while Lys is part of the linker. This cyclic peptide has a strong affinity to αvβ3 isoform (2 nM), moderate binding to αvβ5, αvβ6, α5β1 (50-350 nM), and weak binding to αvβ8 and αIIbβ3 (>5,000 nM).

Additional Information

For More Information About the Inventors

- Weiping Tang

Tech Fields

- Drug Discovery & Development : Drug production & design
- Therapeutics & Vaccines : Oncology

For current licensing status, please contact Rafael Diaz at rdiaz@warf.org or 608-960-9847