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Empowering Ideas

Thioamide-modified peptides for stabilized therapeutics and drug development

Natural bioactive peptides and hormones with thioamide substitutions at cleavage sites for improved pharmacokinetics

Inventor

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STAGE OF DEVELOPMENT

- *In vitro* and *in vivo* testing

INTELLECTUAL PROPERTY

PCT pending (PCT/US2015/28008)

DESIRED PARTNERSHIPS

- License
- Co-development

REFERENCE MEDIA

Goldberg, J.M. et al. Journal of the American Chemical Society, 2014. 136(5), pp 2086-2093.

Wissner, R.F., et al. Journal of the American Chemical Society, 2013. 135(17), pp 6529-6540.

Goldberg, J.M., et al. Journal of the American Chemical Society, 2010. 132(42), pp 14718-14720.

APPLICATIONS

- Peptide therapeutics for diseases including diabetes, hypertension, and congestive heart failure
- Stabilized, bioactive hormone analogs
- Delivery of therapeutically active proteins
- *In vivo* pharmacology studies

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Problem

Natural bioactive peptides are attractive lead pharmaceutical compounds, but peptides are subjected to rapid proteolysis in vivo. The majority of the time spent in peptide biologic drug development seeks to reduce this protein degradation, while maintaining activity.

Solution

Researchers in the Petersson lab have developed a straightforward strategy to modify bioactive peptides in a minimally invasive manner. A single atom thioamide (O-to-S) substitution at the cleavage site of the peptide can decrease proteolysis rates up to 1000x to improve stability while maintaining peptide activity and function. The researchers applied this strategy to the incretin hormone glucagon-like peptide 1 (GLP-1), which stimulates insulin and suppresses glucagon secretion. GLP-1 is inactivated in vivo by dipeptidyl peptidase (DPP-4). The thioamide-substituted version of GLP-1 has a 100x increase in stability and is not significantly disruptive to the protein's secondary structure or activity in cell-based assays. Thioamide GLP-1 was shown to be active and modulate glucose levels in mice. Other DPP-4 substrates are involved in the treatment of diabetes, obesity, stress, growth and development, or congestive heart failure; thioamide-stabilized versions of these peptides are being synthesized and tested.

Advantages

- Maintain proteolytic resistance
- Improve pharmacokinetics
- Increase peptide half-life for sustained circulation time
- Reduce drug development time