Drug Discovery & Development

Peptide Mimics Last Longer, Target Protein-Protein Interactions

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WARF: P140148US02

Inventors: Samuel Gellman, James Checco

The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing modified Z-domain scaffold peptides that are smaller, cheaper to synthesize and less susceptible to enzyme degradation.

Overview

The ability to modulate interactions between proteins is an attractive goal for both research and therapeutic applications. Developing modulating agents using traditional small-molecule approaches is quite challenging due to the large and irregularly shaped interfaces inherent in protein-protein interactions.

Synthetic peptides are promising candidates because of their relatively large size and ability to mimic natural protein surfaces with high affinity and selectivity. One method uses a staphylococcal bacteria protein as a scaffold that can be modified to bind to a desired protein target. This so-called “Z-domain” scaffold is a relatively stable three-helix bundle, and has been used to create peptides that bind to tumor antigens as well as growth factors.

Several efforts have focused on truncating the three-helix scaffold to a two-helix scaffold, which offers advantages in synthesis, labeling and therapeutic administration. Either way, like most small peptides, Z-domain peptides are susceptible to degradation by proteolytic enzymes in the body. This severely hinders their therapeutic utility.

The Invention

UW–Madison researchers have developed modified Z-domain peptides that last longer *in vivo* while retaining strong binding properties. The researchers removed one of the helices and stabilized the remaining two with a disulfide bond. They substituted some residues with alpha and beta amino acid residues; the latter helps resist degradation by proteolytic enzymes.

The α/β-peptide mimics (or foldamers) can be tailored to target a variety of different proteins and protein-protein interactions. Given their small size (39 amino acids) relative to full-length Z-domains (59 amino acids), the new peptide mimics are easier to synthesize and modify.

Applications

- Peptide mimics for research and therapeutics

Key Benefits

- Method truncates, stabilizes and enhances bioavailability of the peptides.
- Peptides are more resistant to proteolytic degradation.
- Show high affinity/specificity
- Easier to synthesize and modify

- Easier to administer therapeutically

Stage of Development

The researchers have created peptides that bind to two proteins associated with cancer and other diseases, VEGF and TNFα.

Additional Information

For More Information About the Inventors

- Samuel Gellman

Related Technologies

- WARF reference number P02125US describes protein foldamers containing alpha, beta and gamma amino acids.

Tech Fields

- Drug Discovery & Development : Drug production & design

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