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Methods for Modifying Proteins and Peptides.

Production of alpha-N-methylated peptides for improved pharmacological properties.

IP Status: PCT Application Filed

Applications

- Generation of novel α-N-methylated peptide libraries
- Scaleup production of α-N-methylated peptides
- Modification of the pharmacological profile of therapeutic peptides

Key Benefits & Differentiators

- **Simpler, inexpensive engineering:** Requires fewer chemical steps, enzymes, and overall components for α-N-methylation of peptides.
- **Higher Yield:** Since it avoids chemical synthesis steps that produce low yields.
- **Tractable:** Amenable to rapid genomic changes in substrate peptides to generate libraries.

Novel method for α-N-methylation of peptides

A significant limitation in peptide drug design is the lack of methods that efficiently modify peptide backbones with functional groups that enhance the pharmacological properties of the peptides. Functional groups such as N-methylation are found in such as cyclosporin, where they confer useful biological traits, such as stability, membrane permeability, target selectivity, affinity, and oral bioavailability. However, it has been difficult to replicate N-methylation in synthetic peptides due to challenges in the synthesis process, high synthesis costs, and the inability to selectively methylate peptides. Novel solutions to these challenges would improve our ability to design new and effective peptide drugs.

Researchers at the University of Minnesota have developed a novel technology that efficiently produces an alpha-N-methylated peptide at high yield. Briefly, this technology leverages the borosin natural product pathway that utilizes ribosomally encoded and posttranslationally modified peptides (RiPPs) pathways to incorporate α-N-methylations on peptides. This new process separates the N-methyltransferase from the borosin precursor allowing both to be expressed and purified separately. Subsequently, selective α-N-methylation is enzymatically introduced into a therapeutically relevant peptide. Unlike current systems this method installs the methylation after the peptide bond is formed allowing for the synthesis of a repertoire of peptides for downstream modification. The engineering and synthesizing of modified peptides using this method is simpler requiring fewer chemical steps, enzymes, and overall components. Additionally, the method also reduces off-target modifications. Together, this method provides a starting place for engineering efficient drug design.

Phase of Development

TRL: 2-3
Early Development

Technology ID
20180338

Category
Life Sciences/Biologics
Life Sciences/Pharmaceuticals
Life Sciences/Therapeutics

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Researchers

- **Michael F. Freeman, Ph.D.**Biochemistry, Molecular Biology, and Biophysics

References

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