



Designing Ubiquitin Oligomers

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing a chemical approach to synthesizing well-defined oligomers of the ubiquitin protein.

Overview

Ubiquitin (Ub) is a small protein composed of 76 amino acids and found throughout the cells of eukaryotic organisms. It folds into a compact globular structure, often as part of a complex of proteins. Ub is attached, or 'conjugated,' to other proteins' lysine residues via a covalent bond.

This process is called ubiquitylation, and research suggests nearly five percent of the human genome is dedicated to coupling and removing Ub and Ub-like molecules from proteins. Given its central role, misregulation of Ub is associated with myriad diseases like cancer, neurodegeneration and congestive heart failure.

Ubiquitylation can involve single Ub molecules or polymeric chains. Ub itself contains seven lysine residues, each of which may link to other Ub molecules. Synthesizing these different, important types of linkages for research has been a challenge.

The Invention

UW-Madison researchers have developed methods for synthesizing oligomers of Ub and Ub-like polypeptides with a well-defined number of Ub units. The oligomers are constructed using thioether groups rather than the natural isopeptide linkages. The thioether groups may be designed to closely mimic the native isopeptide or may be varied.

Methods for preparing and coupling Ub building blocks (i.e., monomers) also are provided.

Applications

- Synthesized oligomers can be used to study the role of ubiquitin in cellular physiology and human disease.
- Developing a new line of ubiquitin-based research tools

Key Benefits

- Method is efficient and precise.

Publications

- Trang V.H., Valkevich E.M., Minami S., Chen Y.C., Ge Y. and Strieter E.R. 2012 Nonenzymatic Polymerization of Ubiquitin: Single

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