Preparation Of Functional Homocysteine Residues In Polypeptides And Peptides

Tech ID: 27543 / UC Case 2016-579-0

SUMMARY
UCLA researchers in the Department of Bioengineering and Department of Chemistry & Biochemistry have developed a novel method for efficient, chemoselective transformation of methionines in peptides and polypeptides into stable, functional homocysteine derivatives. This method provides a means of creation of new functional biopolymers, site-specific peptide tagging, and synthesis of biomimetic and structural analogs of peptides.

BACKGROUND
Methods for selective conversion of natural amino acids in peptides, polypeptides and proteins into different functional residues are desirable for many areas, including chemical biology, materials science, and pharmaceuticals. The introduced functionality can provide probes for tracking, mimicking of post-translational modifications, or a means to adjust biological and physical properties of biomacromolecules.

Thermoresponsive polypeptides possessing a lower critical solution temperature (LCST) respond to temperature in solution, especially in aqueous media. They have received much attention for a variety of applications such as stimulus-responsive assemblies, and as materials for potential use in medicine. In particular, short oligoethylene glycol (OEG) containing thermoresponsive polypeptides have been prepared using a variety of methods, using different core amino acid residues, and also with a wide range in number of ethylene glycol repeats and means of their attachment to different residues.

In order to introduce functionality at unique sites, it is essential that the natural residues are present in low abundance, which has focused much attention on cysteine, methionine, and N-terminal residues. While many methods are available for chemoselective modification of highly nucleophilic cysteine, some are potentially limited by racemization and moderate yields. Thus, there is a need for new methods to convert natural amino acids into different functional residues, and a need for new thermoresponsive polypeptides.

INNOVATION
Researchers at UCLA have developed a novel method for efficient, chemoselective transformation of methionines in peptides and polypeptides into stable, functional homocysteine derivatives. This process allows facile incorporation of a wide range of functional modifications for different uses. An example of this method is the modification of polypeptides via the thioether groups naturally present in methionine or in S-alkyl cysteine residues.

APPLICATIONS
- Synthesis of thermoresponsive polypeptides
- Drug delivery/carrier
- Therapeutics
- Functionalized protein coatings
- Scaffold for regenerative medicine

ADVANTAGES
- Uses easily handled, readily available reagents,
- Allows facile incorporation of a wide range of functional modifications
- Allows formation of more stable, charge neutral functional polypeptide products
- Charge neutral alkyl homocysteine derivatives: more biocompatible, better able to mimic various biological materials

STATE OF DEVELOPMENT
Successfully introduced azides, alkynes, sulfonates, phosphonates, carbohydrates, and amines to polypeptides

PATENT STATUS
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<td>Published Application</td>
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RELATED CASES
2016-579-0

INVENTORS
- Deming, Timothy J.

OTHER INFORMATION
KEYWORDS
Lower critical solution temperature, LCST, protein modification, methionine modification, chemoselective, homocysteine, oligoethylene glycol, OEG, thermoresponsive polypeptides, drug delivery, drug carrier, therapeutics, protein scaffold, regenerative medicine

CATEGORIZED AS
- Biotechnology
- Health
- Materials & Chemicals
- Polymers
- Medical
- Delivery Systems
- Therapeutics
- Research Tools
- Protein Synthesis


ADDITIONAL TECHNOLOGIES BY THESE INVENTORS
- Preparation Of Functionalized Polypeptides, Peptides, And Proteins By Alkylation Of Thioether Groups
- Nanoparticle Assembled Hollow Spheres
- Use Of Non-Ionic Copolymer Hydrogels For Cell Suspension And Cell And Molecule Delivery
- Initiators For Block-Copolymer Synthesis
- Amphiphilic Derivatives Of Thioether Containing Block Copolypeptides
- Compositions Of Polyion Complex Polypeptide Hydrogels
- Chemoselective Side-Chain Modifications Of Methionine-Containing Elastin-Like Polypeptides