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## 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

### CONTACT

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### 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 med

#### CATEGORIZED AS

- ▶ [Biotechnology](#)
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- ▶ [Medical](#)
- ▶ [Delivery Systems](#)
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#### RELATED CASES

2016-579-0

► 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

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	12,540,162	02/03/2026	2016-579
United States Of America	Issued Patent	11,732,008	08/22/2023	2016-579
European Patent Office	Published Application	3448872A	03/06/2019	2016-579

## RELATED MATERIALS

- "Chemoselective synthesis of functional homocysteine residues in polypeptides and peptides". Gharakhanian, E. G.; Deming, T. J. *Chem. Commun.*, 2016, 52, 5336-5339.
- Gharakhanian, E. G., & Deming, T. J. (2016). Role of Side-Chain Molecular Features in Tuning Lower Critical Solution Temperatures (LCSTs) of Oligoethylene Glycol Modified Polypeptides. *Journal of Physical Chemistry B*, 120(26), 6096-6101.

## ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Use Of Non-Ionic Copolyptide Hydrogels For Cell Suspension And Cell And Molecule Delivery
- Compositions Of Polyion Complex Polypeptide Hydrogels
- Chemoselective Side-Chain Modifications Of Methionine-Containing Elastin-Like Polypeptides

## Gateway to Innovation, Research and Entrepreneurship

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