Chemoselective Side-Chain Modifications Of Methionine-Containing Elastin-Like Polypeptides

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SUMMARY

UCLA researchers in the Department of Bioengineering and Department of Chemistry & Biochemistry have developed a novel method for the introduction of various functional groups onto recombinant elastin-like polypeptides (ELPs), creating new compositions of ELPs that may be used for medical therapeutic or diagnostic applications.

BACKGROUND

Recombinant elastin-like polypeptides (ELPs) belong to a unique class of precision polymers with stimuli-responsive self-assembly properties for specific biomedical and biotechnological applications. ELPs are repeating sequences of [-Val-Pro-Gly-Xaa-Gly-] pentapeptide, where Xaa can be any amino acid except proline. ELPs exhibit a lower critical solution temperature (LCST), meaning ELP chains switch between fully soluble state and insoluble state in water when the temperature is below or above the LCST. Fully reversible solubility switch of ELPs is influenced by parameters such as the Xaa residue within the ELP repeats, the overall molecular weight, molar concentration of the ELP, and the ionic strength of the solution. The controlled self-assembly of individual ELP blocks has been explored to develop nanocarriers for drug-delivery systems. Tuning the LCST of temperature-responsive recombinant ELPs is usually achieved by designing different protein sequences, in terms of amino acid composition and length, implying tedious molecular cloning steps. Post-polymerization modifications of are mostly limited to conjugation of small organic molecules, oligonucleotides, drugs, or PEG to chain ends of ELPs. Modifications at the amino acid side chains within the ELP domain require modification of all the repeating functional groups in these sequences in high yield without affecting the amino acid backbone, C- and N-terminus, and side chain groups of other residues. This approach could be quite challenging for recombinant polypeptides, as it requires the incorporation of non-canonical amino acids.

INNOVATION

Researchers at UCLA have developed a novel method for introduction of various functional groups onto recombinant proteins by chemoselective alkylation of methionine. This method can be used to modify elastin repeat side chains and modulate the LCST of the polypeptides.

APPLICATIONS

- Drug carrier/delivery
- Scaffolds for regenerative medicine

ADVANTAGES

- Replaces tedious molecular cloning for introducing various functional groups onto recombinant ELPs
- Allows site-specific modification of the amino acid side chains within the ELP repeats

STATE OF DEVELOPMENT

- Successfully introduced methyl and benzyl groups to ELP repeats

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	10,526,396	01/07/2020	2015-607

CONTACT

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OTHER INFORMATION

KEYWORDS

elastin, elastin-like polypeptides, ELPs, lower critical solution temperature, LCST, recombinant protein modification, side-chain modification, chemoselective, drug delivery, drug carrier, therapeutics, protein scaffold, regenerative medicine

CATEGORIZED AS

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

RELATED CASES

2015-607-0

Japan	Published Application	2018525439	09/06/2018	2015-607
European Patent Office	Published Application	3328882	06/06/2018	2015-607
Canada	Published Application	WO2017021334	02/09/2017	2015-607

RELATED MATERIALS

- Kramer, J.R., Petitdemange, R., Bataille, L., Bathany, K., Wirotius, A., Garbay, B., Deming, T.J., Garanger, E., Lecommandoux, S. (2015) "Quantitative side-chain modifications of methionine-containing elastin-like polypeptides as a versatile tool to tune their properties" ACS Macro Letters 4:1283 – 1286.

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Use Of Non-Ionic Copolypeptide Hydrogels For Cell Suspension And Cell And Molecule Delivery
- Preparation Of Functional Homocysteine Residues In Polypeptides And Peptides
- Compositions Of Polyion Complex Polypeptide Hydrogels

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