A Novel Glycopolymer to Enhance Protein Stability

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BACKGROUND

Proteins have found utility for numerous commercial and clinical purposes, including use in biochemical and chemical processes, and as agents for the treatment and prevention of human and veterinary disease. A major challenge associated with the use of proteins is their inherent instability. Many proteins rapidly degrade in response to "environmental stresses," such as changes in temperature, pH, light, and desiccation, which has implications for their production, transport, use and storage. Attachment of poly(ethylene glycol) to therapeutic proteins, a process commonly referred to as PEGylation, has been used successfully to increase their stability in vivo by reducing both protease degradation and renal clearance. However, PEGylation does not necessarily increase protein stability in response to environmental stresses. The development of a technology that enhances the stability of proteins to such stresses would dramatically increase the number of proteins that could be used commercially, reduce costs associated with protein production, storage and transportation, and increase protein shelf-life.

INNOVATION

Dr. Heather Maynard and colleagues at UCLA have developed a novel glycopolymer to enhance the stabilization of proteins in response to various environmental stressors, including lyophilization and heat. The glycopolymer incorporates the disaccharide trehalose, which is frequently used as a preservative in foods and is Generally Regarded As Safe. The trehalose-based polymer developed by the Maynard group is prepared in such a way to have end-groups that the polymer can, if desired, be directly attached to the biomolecule. Direct attachment of the trehalose-polymer to proteins increases protein stability using lower polymer concentrations. Moreover, the method of synthesis allows for the preparation of trehalose-based polymers with a narrow molecular weight distribution, something that has not been achievable using methodologies developed by others. Studies are underway to determine whether the attachment of the trehalose-based polymer to the biomolecule also confers properties that are similar or superior to PEGylation, such as enhanced protection from proteolytic degradation and extended in vivo circulation time

APPLICATIONS

- Increased stability of proteins (e.g. enzymes and antibodies) or other biomolecules (e.g. siRNA) against environmental stressors, reducing the need for controlling such factors in their production, storage, and transportation.
- A possible substitute for PEGylation.

ADVANTAGES

- Glycoconjugate can be directly attached to biomolecule, allowing lower concentrations of the glycopolymer to be used to increase biomolecule stability.
- Method of synthesis allows for preparation of a polymer with narrow molecular weight distribution, which is significant when seeking regulatory approval for an agent incorporating such a polymer.

STATE OF DEVELOPMENT

Ongoing work focuses on validation of protection to other stressors. Experiments are underway to determine in vivo stability of this glycoconjugate.

PATENT STATUS

Country	Type	Number	Dated	Case

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OTHER INFORMATION

KEYWORDS

protein stability, protein chemistry, protein degradation, biologics, protein storage, environmental stressors, protein therapeutics, protein delivery, vaccines, protein polymers, drug delivery, antibody, nutraceuticals, food technology

CATEGORIZED AS

- **Agriculture & Animal Science**
  - Nutraceuticals
- **Biotechnology**
  - Food
  - Health
- **Materials & Chemicals**
  - Chemicals
  - Polymers
- **Medical**
  - Delivery Systems
  - New Chemical Entities, Drug Leads
  - Therapeutics
  - Vaccines
- **Research Tools**
  - Antibodies
  - Protein Synthesis
  - Reagents

United States Of America	Issued Patent	11,951,176	04/09/2024	2012-422
United States Of America	Issued Patent	10,899,879	01/26/2021	2015-112
United States Of America	Issued Patent	10,543,280	01/28/2020	2012-422
Switzerland	Issued Patent	2807177	11/13/2019	2012-422
Germany	Issued Patent	2807177	11/13/2019	2012-422
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France	Issued Patent	2807177	11/13/2019	2012-422
United Kingdom	Issued Patent	2807177	11/13/2019	2012-422
Ireland	Issued Patent	2807177	11/13/2019	2012-422
Italy	Issued Patent	2807177	11/13/2019	2012-422
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United States Of America	Issued Patent	10,273,333	04/30/2019	2015-602
United States Of America	Issued Patent	9901648	02/27/2018	2012-422
Japan	Issued Patent	6195848	08/25/2017	2012-422
European Patent Office	Published Application	EP 3723814	10/21/2020	2012-422

RELATED CASES

2012-422-0, 2015-112-0, 2015-602-0

RELATED MATERIALS

- Trehalose glycopolymers for stabilization of protein conjugates to environmental stressors. J Am Chem Soc. (2012)
- Trehalose Glycopolymers as Excipients for Protein Stabilization

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- PolyProtek: Platform for Delivering and Stabilizing Therapeutic Biologics, Vaccines, and Industrial Enzymes
- Dual-Enzyme Responsive Peptides
- A Novel Basic Fibroblast Growth Factor Conjugate for Broad Therapeutic Application
- Update To Degradable Trehalose Glycopolymers
- Noncrushable/Nonabusable Pill Formulations
- Trehalose Hydrogels For Stabilization And Delivery Of Proteins

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