Preparation Of Functionalized Polypeptides, Peptides, And Proteins By Alkylation Of Thioether Groups

Tech ID: 29945 / UC Case 2012-598-0

CONTACT

UCLA Technology Development Group
ncd@tdg.ucla.edu
tel: 310.794.0558.

INVENTORS

- Deming, Timothy J.

OTHER INFORMATION

KEYWORDS

drug delivery vehicle, cargo, polypeptide vesicles, polymer, nanotechnology/nanomaterial, cell-permeable, synthetic, gels

CATEGORIZED AS

- **Imaging**
  - Medical
- **Materials & Chemicals**
  - Biological
  - Chemicals
  - Nanomaterials
  - Polymers
- **Medical**
  - Delivery Systems
  - Imaging
  - Other
- **Nanotechnology**
  - NanoBio

RELATED CASES

2012-598-0

SUMMARY

UCLA researchers in the Departments of Chemistry, Physics, and Bioengineering, led by Dr. Tim Deming of the Bioengineering Department, have developed new methods for adding different functional groups on polypeptides. The UCLA researchers have used this method to create a platform to create and modify nanoscale vesicles and hydrogels for use in nanoscale drug delivery particles, injectable drug depots, imaging and detection, industrial biomaterials, and wound management.

BACKGROUND

Overview: Functionalized polypeptides and proteins are useful as drug delivery vehicles, composites and novel ligands. However, synthesis of complex polypeptides with defined modifications is a challenging task as functional side chains require complex and expensive methods to install. Additionally, current methods often introduce undesirable linkages or unnatural components that may affect use.

Platform to Create and Modify Nanoscale Drug Delivery Materials: With the rise of healthcare costs, the global pharmaceutical and biopharmaceutical industries have begun investing in alternative drug delivery technologies. In an effort to identify new and additional treatments, biologics and large molecules are becoming more important to pharmaceutical companies. For this reason, nanotechnology-enabled drug delivery mechanisms have received significant research and development over the past few years. These nanoscale systems offer the promise of minimizing toxicity, maximizing bioavailability, allowing for precise drug delivery, and controlled release of the payload.

Platform to Create and Modify Nanoscale Vesicles and Hydrogels for Use in Imaging and Detection: Biologic imaging is a key method for detection and analysis within the medical, pharmaceutical, and biotechnology industries. Core to the biologic imaging industry leaders' competitive strategy relies on acquiring unique imaging reagents based on nanotechnology. For this reason, nanotechnology-based imaging reagents have received significant research and development over the past few years. These nanoscale systems are promising for diagnostic applications including disease detection, augmentation of gold standard methods, and addressing the demand of a molecular approach toward personalized disease monitoring.

Platform to Create and Modify Nanoscale Particles and Gels for Use in the Industrial Biomaterials Market: Advanced materials play a critical role within a variety of industries across the globe. From construction, utilities, transportation and logistics, food and beverage, cosmetics, telecommunications, electronics, oil and gas, petrochemicals, and packaging, industries are heavily investing in advanced materials to address their needs. For this reason, nanoscale technologies have received significant research and development over the past few years. These nanoscale systems offer the promise of stability, synthetic, reproducible, and low cost.

Platform to Create and Modify Nanoscale Vesicles and Hydrogels for Use in Wound Management: With the increasing elderly population, the wound management market has been greatly affected, primarily due to the increase incidents of skin ulcers and surgical procedures. The wound management market has begun investing heavily in advanced dressing technologies as a means to address the rise in healthcare costs. These advanced dressing technologies include materials to deliver cells to the wound site; materials to deliver proteins, such as collagen, to the wound; and materials to act as artificial skin or as skin replacement. Many of these advanced materials are based on nanoscale gels and vesicles as a means to adhere to the wound at the cellular level.These nanoscale systems offer the promise of minimizing toxicity, maximizing bioavailability, and potentially reducing scarring.

INNOVATION

UCLA researchers in the Departments of Chemistry, Physics, and Bioengineering, led by Dr. Tim Deming of the Bioengineering Department, have developed a new method for adding different functional groups on polypeptides. Their approach is a simple one step addition of a wide range of functional modifications generating novel polypeptides. Their method utilizes stable thioether linkages on methionine residues by addition of epoxides in mild conditions followed by demethylation all in wet protic media. The process is highly efficient and yields of > 97% for conjugations were obtained. This new approach offers a cost-effective method for synthesizing functionalized polypeptides. This method has numerous applications, as discussed below.

The UCLA researchers have used this method to create a platform to create and modify nanoscale vesicles and hydrogels for use in nanoscale drug delivery particles, injectable drug depots, imaging and detection, industrial biomaterials, and wound management. The polypeptide-based platforms created by the Deming group are customizable in nearly all physical characteristics, can be tailored in size, be loaded with

hydrophobic and hydrophilic payloads, adaptable to specific delivery locations, low toxicity, are fully synthetic, possess highly reproducible properties, and are inexpensive to prepare compared to solid-phase peptide synthesis. The platform can be used to create novel, need-based nanoscale vesicles or injectable hydrogels, and can also be used to augment existing nanoparticles.

APPLICATIONS

- Nanoparticle carriers for drug delivery
- Injectable hydrogel drug depots
- Imaging and detection
- Industrial biomaterials
- Wound management

ADVANTAGES

- Able to load vesicles and hydrogels with hydrophilic and/or hydrophobic payloads
- Vesicles can penetrate cell membranes to intracellularly deliver payloads
- Potential low toxicity and biodegradability due to peptidic composition
- Surface chemistry is readily modified for specific cell and tissue type targeting
- Stable at high temperature (up to 80 °C in water)
- Vesicles can be engineered to various sizes (50 to 1000 nm)
- Inexpensive starting materials and process chemistry used to synthesize peptidic polymers
- Hydrogel is injectable
- Hydrogel version is thermo-responsive – an injectable liquid at room temp, solid at body temp
- Hydrogel possesses nano- and microscale network to allow cell attachment and proliferation
- Able to encapsulate macromolecules and other particles, including fluorescent and imaging probes
- Modifiable for specific cell and tissue type targeting
- Highly reproducible at manufacturing levels
- Easily forms as a coating

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	20150057433	02/26/2015	2012-598

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

UCLA Technology Development Group
10889 Wilshire Blvd., Suite 920,Los Angeles,CA 90095
tdg.ucla.edu
Tel: 310.794.0558 | Fax: 310.794.0638 | ncd@tdg.ucla.edu