System to Produce Biotinylated Proteins

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SUMMARY

UCLA investigators from the Department of Molecular and Medical Pharmacology have developed a system that allows the metabolic biotinylation of secreted proteins in vivo by biotin ligase, both secreted and ER-retained. This process is an improvement over traditional in vitro chemical methods, and does not alter biological functions and reduces the chance of protein degradation.

BACKGROUND

Biotin (vitamin H) is an essential coenzyme that is also used to tag proteins for detection, labeling, and purification purposes. The process of adding biotin to proteins is called biotinylation. Biotin labeling has also been applied to drug targeting and viral gene therapy vector-targeting strategies. Traditionally, biotin labeling has been performed in vitro by chemical methods. The problem with these chemical methods is that the random and heterogeneous modifications can lead to the inactivation of biological function after mixing with streptavidin or avidin. Antibody biotinylation especially leads to heterogeneous conjugates. Therefore, there is a need for a method that will uniformly biotinylated proteins without altering binding properties and resulting in loss of affinity.

INNOVATION

UCLA researchers have developed a system that allows metabolic biotinylation of secreted proteins in vivo by both versions of biotin ligase (secreted and ER-retained). The system is a general approach for production of site-specific biotinylated proteins for streptavidin/avidin-biotin technology. The biotinylation technology also shortens and streamlines the lengthy process of traditional methods and reduces the chance of protein degradation during in vitro biotinylation by exogenous ligase. Not only is this system a significant improvement over traditional chemical methods, the system produces uniformly biotinylated proteins without altering biological functions or binding specificity. Researchers also generated a stable cell line expressing ER-retained BirA, the biotin protein ligase of E. Coli

APPLICATIONS

- Produce uniformly biotinylated secreted proteins for in vivo by both versions of biotin ligase, secreted and ER-retained
- May be used for streptavidin/avidin-biotin technology
- Stable cell line expressing ER-retained BirA (biotin protein ligase of E. Coli) can be generated for research purposes

ADVANTAGES

- Any protein, antibody, or antibody fragments can be biotinylated post-translationally
- Shortens and streamlines the current process of protein biotinylation by eliminating the need to purify and treat secreted proteins with exogenous reagents
- Biotinylation efficiency is >90%
- Reduces chance of protein degradation

STATE OF DEVELOPMENT

Investigators have tested the system to biotinylated proteins in vivo by biotin ligase.

RELATED MATERIALS

CONTACT

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



INVENTORS

- Work, Anna W.

OTHER INFORMATION

KEYWORDS

system, process, biotinylated, biotin, vitamin H, coenzyme, ligase, protein, antibody, streptavidin, avidin, stable cell line

CATEGORIZED AS

- **Biotechnology**
  - Other
- **Research Tools**
  - Cell Lines
  - Expression System
  - Other
  - Reagents

RELATED CASES

2008-501-0

▶ Metabolic biotinylation of recombinant antibody by biotin ligase retained in the endoplasmic reticulum. Biomolecular Engineering 24 (2007)

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	8,043,830	10/25/2011	2008-501

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ A Novel Immuno-PET Tracer for Imaging of CD20
- ▶ A Novel Renilla-Derived Luciferase with Enhanced Activity and Stability
- ▶ Humanized Antibodies to the Extracellular Domains of Human N-Cadherin
- ▶ Fully Human Antibodies and Fragments Recognizing c-Met

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

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