Reagent to Label Proteins via Lysine Isopeptide Bonds

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INVENTORS

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OTHER INFORMATION

KEYWORDS

bioconjugation; isopeptide bonds; Corynebacterium diphtheriae; pilus polymerization; in vitro protein ligation; in vitro peptide ligation

CATEGORIZED AS

- **Materials & Chemicals**
  - Biological
- **Medical**
  - Research Tools
- **Research Tools**
  - Antibodies
  - Other
  - Reagents

RELATED CASES

2018-463-0

SUMMARY

Researchers in the UCLA Department of Chemistry and Biochemistry and the University of Texas-Medical Center, Houston Department of Microbiology and Molecular Genetics have modified the *Corynebacterium diphtheriae* (*C. diphtheriae*) sortase enzyme so that it can be used as a bioconjugation reagent *in vitro*.

BACKGROUND

Sortase enzymes have been used to catalyze various processes *in vivo* and *in vitro*, including antibody-drug conjugate construction, protein engineering, and biosensing. *In vivo*, sortase enzymes catalyze pilus polymerization in many strains of Gram-positive bacteria. Pili are protein polymersexpressed on the cell envelope of bacteria and are critical for bacterial virulence. *In vitro*, bacterial sortase enzymes can be employed to ligate not only their natural protein substrates but also many other peptides and proteins.

The *Staphylococcus aureus* (*S. aureus*) sortase enzyme is a commonly used bioconjugation reagent *in vitro*, but it preferentially attaches molecules to proteins via a peptide bond as opposed to an isopeptide bond. Isopeptide bonds present numerous advantages over peptide bonds, allowing for more protein sites to be linked and creating more stable linkages with increased resistance to proteolysis. Although the *Corynebacterium diphtheriae* (*C. diphtheriae*) sortase enzyme catalyzes pilus polymerization via the formation of an isopeptide bond *in vivo*, the wild-type *C. diphtheriae* enzyme is not active *in vitro*.

INNOVATION

Researchers in the UCLA Department of Chemistry and Biochemistry and the University of Texas-Medical Center, Houston Department of Microbiology and Molecular Genetics have modified the *C. diphtheriae* sortase enzyme so that it can be used as a bioconjugation reagent. Unlike the wild-type *C. diphtheriae* enzyme, the modified enzyme can ligate proteins and peptides *in vitro*. The modified enzyme enables peptide and protein linkage in high yield via the formation of lysine isopeptide bonds, which are less susceptible to proteolysis and therefore more stable than their peptide bond counterparts. Furthermore, the modified *C. diphtheriae* enzyme can be used in concert with the *S. aureus* sortase enzyme to modify multiple sites on a protein.

APPLICATIONS

- Antibody development
- Antibody-drug conjugates
- Bioconjugation and protein engineering
- Biosensing and biocatalysis
- Selective domain labeling for biophysical studies
- Cell-specific labeling
- Construction of immune-PET (positron emission tomography) reagents for non-invasive imaging
- Lipid modification of proteins
- Targeted therapeutic delivery
- Immobilization of proteins to biacore sensor chips

ADVANTAGES

- Enables peptide and protein linkage via side chain lysine isopeptide bonds in high yield
- Less susceptible to proteolysis than peptide bonds

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	11,634,699	04/25/2023	2018-463

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- New Method to Increase the Rate of Protein Ligation Catalyzed by the S. Aureus Sortase A Enzyme

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