REAGENT TO LABEL PROTEINS VIA LYSINE ISOPEPTIDE B

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Technology description

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 theCorynebacterium 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 processesin vivoandin 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.

TheStaphylococcus 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 theCorynebacterium diphtheriae(C. diphtheriae) sortase enzyme catalyzes pilus polymerization via the formation of an isopeptide bond in vivo, the wild-typeC. diphtheriaeenzyme 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 theC. diphtheriaesortase enzyme so that it can be used as a bioconjugation reagent. Unlike the wild-typeC. diphtheriaeenzyme, 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 modifiedC. diphtheriaeenzyme can be used in concert with theS. aureussortase enzyme to modify multiple sites on a protein.

Application area

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

Institution

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