

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

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SUMMARY

UCLA researchers in the Department of Chemistry and Biochemistry have developed a new method to increase the rate of ligation catalyzed by the S. aureus Sortase A enzyme

BACKGROUND

The sortase A (SrtA) enzyme from Staphylococcus aureus is widely used as a tool to catalyze in vitro ligation reactions that join biomolecules and create antibody-drug conjugates. SrtA functions as a transpeptidase that joins via peptide bond two peptides, a peptide containing the sequence LPXTG (where X can be any amino acid) and a peptide containing penta-glycine (GGGGG) at its N-terminus. SrtA has been used in industry and academia to generate a variety of bioconjugates including: antibody-drug conjugates, nucleic acid-protein fusions, PEGylation/lipidated proteins, cyclized proteins, protein fusions, and to add proteins to solid supports. However, these ligation reactions are often very slow in vitro and can take days to achieve high yield. The development of a novel method or strategy to improve in vitro rates of SrtA ligation would facilitate the generation of a wide variety of bioconjugates.

INNOVATION

Prof. Robert T. Clubb and colleagues at UCLA have developed a new substrate-fused SrtA enzyme that dramatically enhances in vitro ligation rates. This was achieved by fusing the penta-glycine substrate to the enzyme, yielding an 18-fold in vitro rate enhancement. This method may allow for rapid generation of a variety of bioconjugates.

APPLICATIONS

- ▶ Used as a tool to rapidly generate bioconjugates including: antibody-drug conjugates, nucleic acid-protein fusions, PEGylation/lipidated proteins, cyclized proteins, protein fusions, and solid-support protein fusions.

ADVANTAGES

- ▶ 18-fold rate enhancement over other SrtA mediated ligation strategies
- ▶ Simplifies reaction because fewer components are required as substrate is fused to the enzyme

STATE OF DEVELOPMENT

Researchers have used this strategy to create NMR silent solubility tags for protein NMR applications.

RELATED MATERIALS

- ▶ [Rapid addition of unlabeled silent solubility tags to proteins using a new substrate-fused sortase reagent. Amer BR, Macdonald R, Jacobitz AW, Liauw B, Clubb RT. J Biomol NMR. 2016 Mar;64\(3\):197-205. doi: 10.1007/s10858-016-0019-z. Epub 2016 Feb 6. PMID: 26852413](#)

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	10,766,923	09/08/2020	2016-404

CONTACT

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



INVENTORS

- ▶ Clubb, Robert T.

OTHER INFORMATION

KEYWORDS

protein mediated ligation, sortase, SrtA, peptide ligation, intein ligation, intein, antibody-drug conjugate, bioconjugates, silent tagging, transpeptidation, and enzyme mediated ligation

CATEGORIZED AS

- ▶ **Biotechnology**
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 - ▶ Other
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 - ▶ NanoBio
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RELATED CASES

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ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

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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

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