

ENZYMATIC INTRODUCTION OF THIOL HANDLE ON TYROSINE-TAGGED PROTEINS

Tech ID: 34061 / UC Case 2025-144-0

PATENT STATUS

Patent Pending

BRIEF DESCRIPTION

Site-selective covalent modification of proteins is key to the development of new biomaterials, therapeutics, and other biological tools. As examples in the biomedical field, these techniques have been applied to the construction of antibody-drug conjugates, bispecific cell engagers, and targeted protein therapies, among other applications. While many bioconjugation strategies, such as azide-alkyne cycloaddition or thiol-maleimide coupling, have become widely adopted, the improvement of existing techniques is a highly active area of chemical biology research, as is the development of new synthetic applications of these methods. Key focuses of such efforts include increasing reaction efficiency and ease, balancing selectivity with tag size, and expanding the modification options beyond traditional cysteine and lysine residues.

UC Berkeley researchers have developed compounds and methods using tyrosinase to couple small-molecule dithiols to tyrosine-tagged proteins, which effectively introduces a free thiol handle and provides a convenient method to bypass genetic incorporation of cysteine residues for bioconjugation. These newly thiolated proteins were then coupled to maleimide probes as well as other tyrosine-tagged proteins. The researchers were also able to conjugate targeting proteins to drugs, fluorescent probes, and therapeutic enzymes. This easy method to convert accessible tyrosine residues on proteins to thiol tags extends the use of tyrosinase-mediated oxidative coupling to a broader range of protein substrates.

SUGGESTED USES

- » making protein-protein conjugates for immunotherapy applications
- » making antibody-drug/antibody-protein conjugates

ADVANTAGES

- » simple way to functionalize tyrosine residues without generating cysteine mutants

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- [Site-Specific Coupling Of Biomolecules Using Orthoquinones And Thiols](#)
- [Compositions and Methods for Modification of Cells](#)

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OTHER INFORMATION

KEYWORDS

biopolymers, thiols, conjugate acid-base pairs

CATEGORIZED AS

- » **Materials & Chemicals**
- » Chemicals
- » **Medical**
- » Imaging
- » Therapeutics
- » **Research Tools**
- » Reagents

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