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Review

A mini-review on the enzyme-mediated manipulation of proteins/peptides

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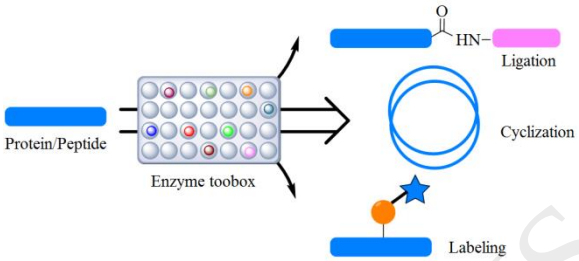
Graphical abstract



A number of enzymes are available in the toolbox facilitating the site-selective labeling, ligation, cyclization of proteins or peptides. In this review, some of the most important enzymes were discussed.

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ABSTRACT

Recent years have seen an ever increasing number of enzyme mediated protein/peptide modification reactions, which contribute significantly to the elucidation of related biological functions. The many available enzymes have, however, caused difficulties for practitioners in choosing the most appropriate enzyme for a certain purpose. This review surveyed the widely used enzymes (*i.e.*, sortases, butelase 1, subtiligase, formylglycine generating enzyme and farnesyltransferase) in the manipulation of proteins/peptides, and the application fields of these enzymes as well as the advantages and limitations of each enzyme are summarized.

1. Introduction

Proteins are among the most diverse and versatile class of molecules in nature. Building up on a defined group of monomers, *i.e.*, the 20 natural amino acids, proteins exhibit a vast array of functions in living systems, including mediating metabolic reaction [1], signal transduction [2, 3], molecule transportation [4-6], or simply as structural component [7]. Efficient strategies that add probes—site-selectively—to the proteins are indispensible to the study and control of their functions in complex settings [8-11]. Further, the increasing demands on proteins or peptides as drugs or functional materials have greatly speeded up the methodology development for protein/peptide ligation or modification [12-14]. Broadly speaking, there are two ways of manipulating proteins, *i.e.*, chemically or enzymatically. The chemical approaches usually harness the reactivity of protein side-chains of certain amino acid residues, *e.g.*, Cys, Lys or Tyr, and have contributed significantly in protein chemical biology [8, 9, 15, 16]. They are, however, in many cases either not highly site-selective or require an excess addition of the probe molecules [11, 17]. Enzyme-mediated protein modifications, normally based on recognition sequence motifs, are highly site-selective and have been increasingly applied [18-21]. The most important recent discoveries and advancements in applying enzymatic strategies for protein modification are covered in the current review, including sortases, butelase 1, subtilisin related ligases. Selected examples of prominent enzymes used for protein bioconjugation are also discussed. This is by no means an exhaustive list [22-25]; rather, the current review aims to serve practitioners in designing the most appropriate enzymatic approaches based on their research purposes and laboratory settings.

2. Sortases