A CHEMICAL BIOLOGY METHOD FOR THE SYNTHESIS OF PROTEIN SITE-SPECIFICALLY WITH LYSINE METHYLATION

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Research Interests

- Organic Chemistry
- Molecular Biology
- Protein Evolution
- Cell Biology

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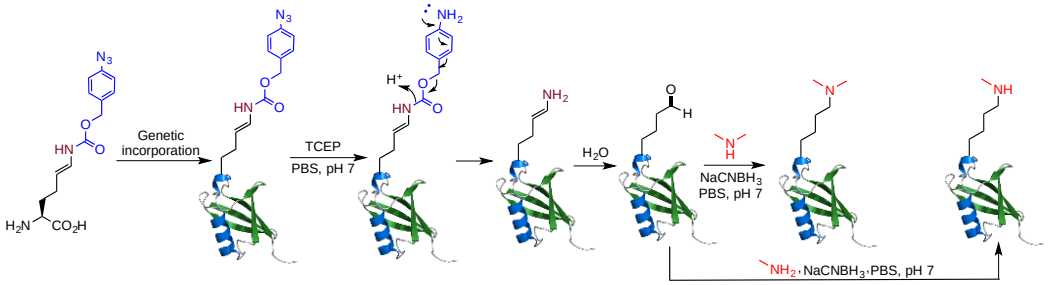
Overview

Protein lysine methylation is a wide spread posttranslational modification in mammalian cells that regulates epigenetic functions of proteins. However, there is a lack of a straightforward approach for the synthesis of proteins with lysine methylation

Technology

Using an evolved pyrrolysyl-tRNA synthetase and its cognate amber suppressor $tRNA^{Pyl}$, a precursor noncanonical amino acid is genetically encoded in E. *coli* by amber codon. Through simple mutagenesis to introduce amber mutation at a specific amino acid coding site in a protein coding gene and expression of this mutant protein in E. *coli* that codes our evolved pyrrolysyl-tRNA synthetase and $tRNA^{Pyl}$ in the presence of our noncanonical amino acid, a mutant protein that can be further converted to a protein with site-specific lysine mono- or dimethylation can be synthesized.



Advantages

- Both mono- and dimethylation of lysine can be selectively installed in proteins.
- There is no limitation on sites that can be installed with lysine methylation. Technically, any protein surface residues can be site-selectively mutated to be the one with lysine methylation.
- Proteins are expressed in E. coli. Large quantities can be easily obtained.
- The chemical processing to install lysine methylation is very simple which can achieve quantitation easily.
- The developed approach is applicable to all proteins that can be expressed in E. coli.

Applications

- The invention can be applied to synthesize mono- and dimethylated histones that are expensive commercial products for use in both academic research and industrial drug discovery.
- Further application of synthesized methyl-histones can be applied to synthesize methyl-nucleosomes that are hardly accessible and presumably expensive for researchers in both academia and industry.
- To synthesize other high interesting methylated proteins such as p53 as commercial products.

Stage of Development

The invention has been finalized.

Patent Status

Pending

Publications

Wang et al., Angew. Chem, Int. Ed., 2017, 56, 212-216.