

# Site-Specific Protein Modification via Copper(I)-Catalyzed 1,2,3-Triazole Formation and Its Implementation in Protein Microarray Fabrication

Po-Chiao Lin(林伯樵)<sup>1,2</sup>, Shau-Hua Ueng(翁紹華)<sup>1</sup>, Mei-Chun Tseng(曾美郡)<sup>1</sup>, Jia-Ling Ko(柯嘉玲)<sup>1,3</sup>, Kuo-Ting Huang(黃國庭)<sup>1</sup>, Sheng-Chieh Yu(余聖潔)<sup>1</sup>, Avijit Kumar Adak<sup>1</sup>, Yu-Ju Chen(陳玉如)<sup>1,2</sup>, and Chun-Cheng Lin(林俊成)<sup>1,2\*</sup>

1. Institute of Chemistry and Genomic Research Center, Academia Sinica, Taipei, Taiwan

2. National Tsing Hua University, Hsinchu, Taiwan and Chemical Biology and Molecular Biophysics, Taiwan International Graduate Program, Academia Sinica, Taipei, Taiwan

3. Department of Chemistry, National Taiwan Normal University

\*corresponding authors: [cclin66@mx.nthu.edu.tw](mailto:cclin66@mx.nthu.edu.tw)

Effective and site-specific modification of proteins by target molecules is an essential yet challenging step to research in biochemistry and biophysics. In this report, we combined the intein fusion protein expression system with Cu(I)-catalyzed 1,2,3-triazole formation to demonstrate specific modification of protein C termini. This protein modification method was validated using various types of molecules including fluorescent FITC, biotin, carbohydrate, peptide and even a covalently linked homodimeric protein by a diazido linker. The method, when applied to the fabrication of protein microarrays, showed that site-specific covalent bond formation retains higher protein activity on a solid surface compared with techniques that rely on random amide bond formation.

