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Linkage-specific di-Ubiquitin probes to illustrate ubqiuitin chain assembly

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The length and linkage types (K11, K48, K63, etc) of ubiquitin (UB) chains regulate the biological activities of proteins they modify. Synthesizing ubiquitin chains with defined linkage is challenging but vitally important for elucidating the signals encoded in protein ubiquitination. Here, we generated linkage-specific diUB probes with a thiol functionality at the linkage to enable its conjugation with E2, E3, and deubiquitinating enzymes (DUB) in the UB transfer pathways. We took advantage of unnatural amino acid (UAA) incorporation to substitute specific Lys residues in UB with N6-(thiazolidine-4-carbonyl) lysine (ThzK). We then converted ThzK to Cys-conjugated Lys (CysK) to enable the assembly of diUB probes by native chemical ligation. Our development of the diUB probe provides a new method to decode UB-mediated cell signaling.

Biography

Han Zhou has completed his bachelor and master degree from College of Pharmacy in Peking University Health Science Center. Now he is a fifth-year PhD candidate in Department of chemistry, Georgia State University under Dr Jun Yin. His main focus is chemcial biology and medicine chemistry in Ubiqiuitin transfer pathway.

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