Furan- and Triazolinedione-based Chemistries for Bio-orthogonal Protein Modification

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Within OBCR, we have developed a highly selective and efficient singlet oxygen mediated crosslink technology which is applicable to peptide-protein, peptide-nucleic acid and nucleic acid interstrand crosslink scenarios.[1] For this purpose, a furan 'warhead' is introduced into one of the biomolecular partners and subsequently activated by means of an oxidation trigger such as singlet oxygen which induces generation of a nucleophile-sensitive keto-enal moiety.[2] The overall procedure allows spatiotemporal control of the crosslinking event.

In the context of peptide ligand-receptor interactions, we have described, in live cells under normal growth conditions, spontaneous enzymatic activation and crosslinking of furan-modified peptide ligands to their membrane GPCR with zero toxicity, high efficiency and spatio-specificity.[3] Furan introduction into peptide and protein ligands and subsequent covalent modification of their natural targets was achieved after triggering photocatalytic singlet oxygen generation.[4]

Different furan[5] and triazolinedione[6] based building blocks were further developed for versatile and site-selective modification of proteins and synthesis of bioconjugates. The talk will highlight selected specific examples of these cross-linking and conjugation methodologies.

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