Photochemical Access to Unnatural Amino Acids and Modified Peptides

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New synthetic methodologies that provide site-selective or site-specific amino acid/peptide modifications under sustainable conditions are essential for drug development, especially for drug programs based on the modification of proteins, antibodies, and DNA. Nowadays, classical approaches generally rely on higher-energy systems, either through highly reactive organometallic reagents or UV-irradiation, to achieve the desired reaction outcome. On the other hand, contemporary synthetic methodologies have focused on achieving selective and mild conditions. Visible-light-mediated catalytic methodologies have offered an innovative solution to forge similar bonds as enabled by classical methodologies but with the advantages of using a low-energy source, allowing for selective and controlled reactions (Figure 1).

In this regard, we will present our recent findings on photochemical strategies for the synthesis of non-canonical amino acids and amino acid derivatives (1-4). Additionally, the discussion will include a side-selective solid-phase metallaphotoredox N(in)-arylation of peptides (5). These reaction systems demonstrated remarkable chemoselectivity and tolerance toward a variety of substrates integrated into pharmacologically active molecules, as well as affinity- and labeling tags, and bioconjugation handles.

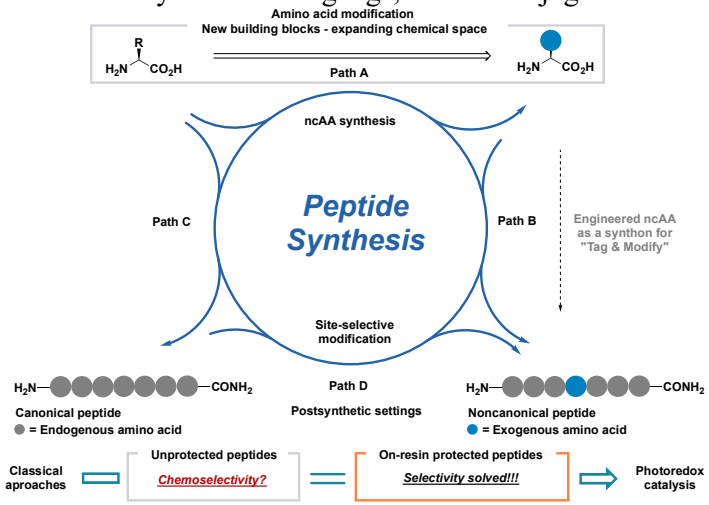

Figure 1.

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