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Non-canonical amino acids as building blocks for designer proteins

Non-canonical amino acids are not encoded by the genetic code, but they can participate in protein translation under controlled conditions. Most of the non-canonical amino acids carry unusual side chains such that their translation into a target protein sequence can provoke structural, chemical, or functional modifications normally not found in nature. Non-canonical amino acids with bioorthogonal reactive handles are of particular interest because they facilitate the selective conjugation with other molecules at a pre-defined position in the protein. This results in the directed chemical modification of proteins with superior control. The introduction of non-canonical amino acids into proteins in residue- or site-specific manner offers an extension to classical genetic engineering approaches for protein modification, which has gained increasing popularity in the academic environment. Nevertheless, it faces specific challenges upon upscaling, which still hamper its industrial application.

In my presentation, I will highlight our recent research, which includes the manipulation of enzyme activity with non-canonical amino acids; the tuning of protein-ligand interactions using tryptophan analogs; the site-selective chemical modification of sugar-binding proteins via reactive non-canonical amino acids; the improvement of the incorporation efficiency and the the biosynthesis of amino acid analogs from inexpensive precursors. The latter is essential to substantially lower the costs for protein engineering with non-canonical amino acids, which is particularly important for the scalability of the approach in industrial biotechnology.