Non-Natural Elements in the Exploration of Protein Structure and Function

The properties of biological systems can be dramatically changed and expanded by the incorporation of non-naturally occurring elements. I will discuss three areas of research involving the use of non-natural elements to study protein structure and function. Historically, a great deal of knowledge about protein folding and stability has come from studies of peptide model systems. Protein tertiary structural interactions often completely mask the contributions of individual secondary structure elements. Model systems allow one to study essentially pure secondary structural elements. I will discuss the development and use of model systems for β-sheet secondary structures, where non-natural turn-segments were developed to study the thermodynamics of folding in isolated β-sheets. I will go on to describe the development of a more complex experimental system to probe and select interactions within a coiled-coil protein architecture. The system involves the use of phage display to select for interactions between natural peptides displayed on the phage particles and immobilized synthetic peptides containing non-natural amino acids. Finally I will describe some experiments in live cells where bio-orthogonally reactive amino acids are used to selectively label and visualize newly synthesized proteins.

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