Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad – 500 046

Students' Annual Webinar

Tertiary structure stabilization of proteins using non-canonical long-range disulfide bonds

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Cysteine is unique among the 20 canonical amino acids in that it can form reversible disulphide covalent bonds in proteins. Disulfide bonds have been known to stabilize monomeric and subunit proteins and regulate protein activity. Hence, studies have utilized this idea and incorporated extra disulfides in proteins to stabilize their structures. However, the sites in proteins that can be cross-linked by a cysteine disulfide are constrained to a short distance of ~6.5Å (Cα-Cα). Thus, the relative long distances that might be required to bridge different protein sites for stabilization may preclude the introduction of canonical disulfide bond. Herein, we chemically synthesized three different non-canonical amino acids containing thiols which can form longer disulfide bonds ranging from 8Å - 14Å which would overcome the geometric constraints of cysteine disulfide. In this talk, I will discuss the chemical synthesis of these non-canonical amino acids and prospects of their incorporation into model proteins to improve their tertiary structure stability.

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5:00 PM