

## Seminar

## Overcoming Folding Challenges of Chemically Synthesized Disulfide-rich Proteins Relevant to COVID-19, Malaria, and Diabetes

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Disulfide-rich proteins present significant challenges in chemical synthesis due to their complex disulfide combinations and folding pattern. The formation of correct disulfide pairings requires precise control over multiple competing pathways, as cysteines can theoretically form numerous bonds, but only one specific arrangement typically yields a biologically active My work addresses fundamental challenges protein. in disulfide-rich protein folding through systematic investigation of three therapeutically relevant protein targets that exemplify different aspects of these difficulties. Key findings demonstrate that calcium coordination is essential for LRAD3 domain folding, removal of aggregation-prone di-phenylalanine patches dramatically improved folding yields of RIPR N-terminal domain, use of organic co-solvent significantly improved folding yields by maintaining hydrophobic chains in solution during disulfide bond formation of insulin. These findings help advance practical strategies for the production of challenging disulfide-rich therapeutic protein targets.

*Tuesday, Jul 8<sup>th</sup> 2025 14:30 Hrs (Tea / Coffee 14:15 Hrs) Seminar Hall, TIFRH*