Structure-function study of the C-terminal tail of Thioredoxin Reductase

Thioredoxin reductase (TR) is an enzyme that functions in maintaining cellular redox homeostasis and protecting the cell from oxidative damage. TR is the only enzyme that reduces the protein thioredoxin, which functions in further reducing proteins and other cellular substrates. This system works as an antioxidant that protects the cell from damaging molecules like hydrogen peroxide and oxygen metabolism byproducts. This project seeks to identify crucial amino acid residues present in TR that help orient the enzyme's unique C-terminal tail, which contains the adjacent cysteine residues responsible for thioredoxin reduction. Mutation of positively charged lysine (K) residues to the neutral amino acid alanine (A) at positions 26 and 121 of TR resulted in significantly decreased enzymatic activity towards lipoic acid, a substrate that mimics the C-terminus of TR. TR is a popular target for anti-tumor therapy, and understanding the full mechanism may further the development of anti-tumor drugs.