

# Chem 412 Seminar

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## *The Role of $\alpha$ -Helices in the Folding of the Thiol Protease Inhibitor Cystatin*

*Cystatin* is a member of a superfamily of thiol protease inhibitors with approximately 115 amino acid residues and is found in both extra- and intra-cellular forms. *Cystatins* appear to play a protective role in secretions such as saliva and tears. *Cystatin C* has also been identified as a co-component with amyloid  $\beta$  protein in the brains of Alzheimer's disease patients. The generic structure of the superfamily consists of 4  $\beta$ -strands [2 anti parallel pairs] and two helices. The second  $\beta$ -strand pair and shorter helix contains two disulphide bonds. We investigate the folding of this protein using a variety of biochemical and molecular biological approaches including Circular Dichroism, Nuclear Magnetic Resonance and protein denaturation using both the whole protein, truncated forms of the protein, and chemically synthesized peptides. Our studies indicate a pivotal role for  $\alpha$ -helix formation in the nucleation of folding of the protein. In the absence of such nucleation, high molecular weight  $\beta$ -strand aggregates are formed.