

## **The Aspartic Proteinase from *Saccharomyces Cerevisiae* Fold its own Inhibitor into a Helix**

*M. Li, L. Phylip, W. Lees, J. Winther, G. Dunn, A. Wlodawer, J. Kay, and A. Gustchina (NCI-FCRDC)*

Abstract No. li8527

Beamline(s): **X9B**

Aspartic proteinase A from yeast is specifically and potently inhibited by a small protein called IA3 from *Saccharomyces cerevisiae*. Although this inhibitor consists of 68 residues, we show that the inhibitory activity resides within the N-terminal half of the molecule. Structures solved at 2.2 and 1.8 Å, respectively, for complexes of proteinase A with full-length IA3 and with a truncated form consisting only of residues 2-34, reveal an unprecedented mode of inhibitor-enzyme interactions. Neither form of the free inhibitor has detectable intrinsic secondary structure in solution. However, upon contact with the enzyme, residues 2-32 become ordered and adopt a near-perfect  $\alpha$ -helical conformation. Thus, the proteinase acts as a folding template, stabilizing the helical conformation in the inhibitor, which results in the potent and specific blockage of the proteolytic activity.