MECHANISM FOR BROAD SPECIFICITY IN NEUROPEPTIDASES. Jonathan M. Wagner, Nicholas Noinaj, David W. Rodgers, Department of Molecular and Cellular Biochemistry, Center for Structural Biology, University of Kentucky, 741 S. Limestone, Lexington, KY 50536.

We are interesting in understanding broad substrate specificity in a class of enzymes known as neuropeptidases, which metabolize bioactive signaling peptides. Crystal structures with the neuropeptidase, thimet oligopeptidase, show that substrate residues C terminal to the scissile bond interact with a specialized binding site that is distinct from the active site. The binding site on the enzyme is rich in aromatic and hydrophobic residues, and different peptide sequences position themselves somewhat differently on the surface to optimize contact. Side chains from the substrate deploy into shallow groves that can accommodate a number of residue types. We suggest that the unusual features of the binding surface are responsible for broad substrate recognition of these enzymes.