Multiple Conformations in the Ligand-Binding Site of the Yeast Nuclear Pore Targeting Domain of NUP116P

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The yeast nucleoporin Nup116p plays an important role in mRNA export and protein transport. We have determined the solution structure of this protein's C-terminal 147 residues, the region responsible for targeting the protein to the nuclear pore complex (NPC). The structure of Nup116p-C consists of a large beta sheet sandwiched against a smaller one, flanked on both sides by alpha-helical stretches, similar to the structure of the human homologue hNup98. In unliganded form, Nup116p-C exhibits evidence of exchange among multiple conformations, raising the intriguing possibility that it may adopt distinct conformations when bound to different partners in the NPC. We have additionally shown that a peptide from the N terminus of the nucleoporin Nup145p-C binds Nup116p-C. This previously unknown interaction may explain the unusual asymmetric localization pattern of Nup116p in the NPC. Strikingly, the exchange phenomenon observed in the unbound state is greatly reduced in corresponding spectra of peptide-bound Nup116p-C, suggesting that the binding interaction stabilizes the domain's conformation. These studies offer a high resolution view of a yeast nucleoporin structural domain and may provide insights into NPC architecture and function.