CHARACTERIZATION OF N-TERMINAL METAL BINDING DOMAIN 5-6 OF WILSON DISEASE PROTEIN

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Wilson protein is a P-type copper-transporting ATPase found in the copper secretory pathway in the liver and kidney. It contains 6 cytosolic N-terminal metal binding domains that contain the conserved motif MXCXXC. We have cloned and expressed residues 485-633, corresponding to metal-binding domains 5 and 6 of Wilson protein (WD5-6). Unique features of this multi-domain construct is that two of the disease causing mutations in the N-terminal metal binding domain occur one in each of the domains and the presence of a short amino acid linker between domains, relative to the longer intervening sequences between the other Wilson metal-binding domains. Similar domain-domain spacing is found in orthologs with only two metal-binding domains and also in the final two domains of orthologs with multiple metal-binding domains. Therefore WD5-6 provides a good model to test the influence of one domain on another. Results of spectroscopic and structural studies will be presented.