

Crystal Structure of Yeast Esa1 Suggests a Unified Mechanism for Catalysis and Substrate Binding by Histone Acetyltransferases

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Esa1 is the catalytic subunit of the NuA4 HAT complex that acetylates histone H4, and is a member of the MYST family of HAT proteins that includes the MOZ oncoprotein and the HIV-1 Tat interacting protein Tip60. We have determined the X-ray crystal structure of the HAT domain of Seleno-Met derivatized Esa1 bound to coenzyme-A using MAD. We have also investigated the protein's catalytic mechanism. Our data reveals that Esa1 contains a central core domain harboring a putative catalytic base, and flanking domains that are implicated in histone binding. Comparisons with the Gcn5/PCAF and Hat1 proteins suggest a unified mechanism of catalysis and histone binding by HAT proteins, whereby a structurally conserved core domain mediates catalysis, and sequence variability within a structurally related N- and C-terminal scaffold determines substrate specificity.

References: Yan, Y., Barlev, N. A., Haley, R. H., Berger, S. L. and Marmorstein, R. "Crystal Structure of Yeast Esa1 Suggests a Unified Mechanism for Catalysis and Substrate Binding by Histone Acetyltransferases." (2000) *Mol. Cell*, in press (November issue)

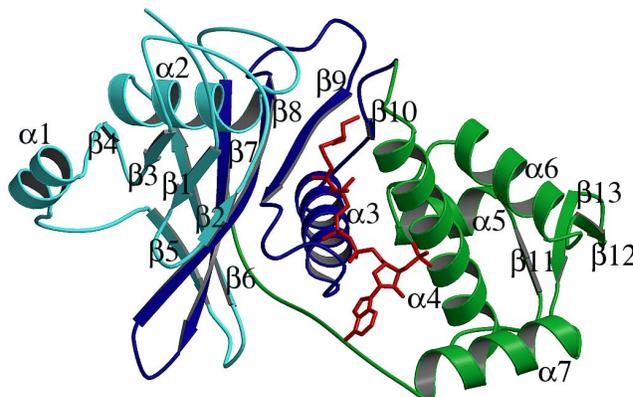


Figure. Structure of the Esa1/CoA complex. The central core domain is colored in blue, the N-terminal subdomain is colored in aqua and the C-terminal subdomain is colored in green. Coenzyme-A is shown as a stick figure in red.