ADA2 encodes a component of three chromatin modifying histone acetyltransferasecomplexes: SAGA, SLIK, and ADA. These complexes function in positive and negative transcriptional regulation of numerous RNA polymerase II-transcribed genes; in addition, SLIK plays a role in the retrograde response. The three complexes each contain the histone acetyltransferase catalytic subunit Gcn5p, which interacts directly with Ada2p and preferentially modifies histones H3 and H2B. In vitro, Gcn5p acetylates N-terminal lysines on free histones, but acetylation of nucleosomal histone substrates also requires Ada2p and Ngg1p, which are found in a complex with Gcn5p. Ada2p has been shown to increase the HAT activity of Gcn5p, while Ngg1p plays a role in expanding the range of lysines that undergo acetylation.Independently of its interaction with Gcn5p, Ada2p has also been shown to function in transcriptional silencing at telomeres and ribosomal DNA. Ada2p binds telomeric chromatin and Sir2p to prevent the spread of silencing proteins Sir2p and Sir3p into subtelomeric regions.Null mutations in ADA2 confer slow growth in minimal glucose media, resistance to the toxic effect of the chimeric transcriptional activator GAL4-VP16, and silencing defects. The null mutant also grows poorly on low phosphate medium, and exhibits increased sensitivity to ethanol or caffeine. Microarray analysis indicates that 2.5% of S. cerevisiae open reading frames show a twofold or greater change in expression in the null mutant. The amino terminal region of Ada2p contains a ZZ-type zinc finger and a SANT domain, which is found in other proteins involved in chromatin remodeling, such as Swi3pand Rsc8p. Ada2p also contains a conserved central region, and a C-terminal SWIRM domain. Mutations in the Ada2p SANT domain confer growth and histone acetylation defects, indicating that this region is essential for the function of the HAT complexes. The amino terminal region of Ada2p is required for interaction with Gcn5p, whereas interaction with Ngg1p is mediated by the central region. Mutant analysis indicates that the central region is also required for full Gcn5p acetyltransferase activity and substrate specificity; in addition, it has been shown to bind phosphatidylserine. Ada2p is evolutionarily conserved among eukaryotes and orthologs have been described in several organisms, including Arabidopsis, Drosophila, and humans. The human ortholog ADA2b is a component of the SAGA-like complex STAGA and is recruited to p53-dependent promoters.