

Proposed Mechanisms of Function of Taf14-Containing Nuclear Complexes Involved in Transcriptional Regulation of *Saccharomyces cerevisiae*

Aakanksha Gundu

Understanding transcriptional regulation in *Saccharomyces cerevisiae* has key implications for cancer treatment because cancer is caused by abnormalities in transcription and the DNA-repair response. YEATS-domain proteins play an essential role in transcriptional regulation of the yeast genome by reading histone post-translational modifications. As a YEATS-domain protein, Taf14 is involved in the DNA-repair pathway, plays a role in the heat response pathway, influences cytoskeleton organization, and has the ability to read histone lysine acetylation. Overall, Taf14 is a nuclear hub that plays a fundamental role in the control of DNA processes. This protein recognizes transcriptional coactivator proteins of 6 nuclear complexes: RSC, SWI/SNF, TFIIF, TFIID, NuA3, and INO80. These nuclear complexes have functions ranging from histone modifications to chromatin remodeling to transcriptional factors. Recent research has discovered a conserved binding motif on each of these complexes that is recognized by Taf14 to induce protein-protein interactions.

The purpose of this research project is to propose mechanisms of function of the TFIIF and TFIID complexes and how they may be involved in the DNA-repair pathway. After mutating the conserved binding sequences recognized by Taf14 on the complexes, the mutant strains, such as Taf2, Tfg1-1M4, and Tfg1-2M4, were grown in the presence of DNA-damaging agents, including hydroxyurea, camptothecin, methyl methanesulfonate, and a caffeine stressor. The pathways by which the DNA-damaging agents act sheds light on the role of proteins involved in these complexes. The results suggest that TFIIF may be playing a role in DNA repair by increasing the concentration of available deoxyribonucleotides for DNA synthesis because the Tfg1-2M4 mutation prevents the yeast strain from growing in hydroxyurea. Strikingly, although Tfg1-2M4 did not grow in hydroxyurea, the strain's ability to grow in the presence of camptothecin suggests that there is some mechanism present in the cell that counteracts the effect of camptothecin inhibiting DNA topoisomerase I activity. Future directions of this project include extending the research to the other nuclear complexes that interact with Taf14, testing the growth of the mutant strains with other DNA-damaging agents, and finding further evidence of the mechanisms of TFIID and TFIIF in yeast.

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