sites. The structure reveals a ternary complex in which protein homo-dimerization is mediated by the specific arrangement of the two Ets-1 binding sites and demonstrates how Ets-1 transcription factor dimerizes by forming a central protein/DNA interface that involves several residues from a loop connecting the N-terminal autoinhibitory region and the ETS domain. Ets-1 variants, in which residues involved in protein-protein interaction are mutated, lose the ability for DNA-mediated dimerization and stromelysin-1 promoter transactivation. The X-ray structure of the Ets-1/DNA/Ets-1 complex formed on the stromelysin-1 promoter shows for the first time how Ets-1 transcription factor can function as a homodimer contrary to previous structures where Ets-1 was bound to DNA as a monomer or formed complexes with other transcription factors on DNA. Thus, our data unravel the molecular basis of the ability of Ets-1 to function as a facultative dimeric transcription factor and play an important role in the transcription regulation of the stromelysin-1 promoter.

Keywords: Ets-1, transcription regulation, protein-DNA complexes

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**Structure of the FOXO3a-DBD/DNA complex suggests the effects of post-translational modification**

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FOXO3a is a transcription factor of the FOXO family. The FOXO proteins participate in multiple signaling pathways, and their transcriptional activity is regulated by several post-translational mechanisms, including phosphorylation, acetylation and ubiquitination. Because these post-translational modification sites are located within the C-terminal basic region of the FOXO DNA-binding domain (FOXO-DBD), it is possible that these post-translational modifications could alter the DNA-binding characteristics. To understand how FOXO mediate transcriptional activity, we report here the 2.7 Å crystal structure of the DNA-binding domain of FOXO3a (FOXO3a-DBD) bound to a 13-bp DNA duplex containing a FOXO consensus binding sequence (GTAAACA). Based on a unique structural feature in the C-terminal region and results from biochemical and mutational studies, our studies may explain how FOXO-DBD C-terminal phosphorylation by protein kinase B (PKB) or acetylation by cAMP-response element binding protein (CBP) can attenuate the DNA-binding activity and thereby reduce transcriptional activity of FOXO proteins. In addition, we demonstrate that the methyl groups of specific thymine bases within the consensus sequence are important for FOXO3a-DBD recognition of the consensus binding site.

Keywords: FOXO3a, winged/helix, DNA complex

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**Crystal structure of the HRDC domain of human Werner syndrome protein, WRN**

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Werner syndrome is a human premature aging disorder characterized by chromosomal instability. The disease is caused by the functional loss of WRN, a member of the RecQ-helicase family that plays an important role in DNA metabolic pathways. WRN contains four structurally folded domains comprising an exonuclease, a helicase, a winged-helix, and a helicase-and-ribonuclease D/C-terminal (HRDC) domain. In contrast to the accumulated knowledge pertaining to the biochemical functions of the three N-terminal domains, the function of C-terminal HRDC remains unknown. Recently we determined the crystal structure of the human WRN HRDC domain (Kitano et al. J. Biol. Chem. 2007; 282 2717-28). The domain forms a bundle of alpha-helices similar to those of Saccharomyces cerevisiae Sgs1 and Escherichia coli RecQ. Surprisingly, the extra ten residues at each