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**Crystal Structure of the Human FOXK1a/DNA Complex and Its Implications on the Diverse Binding Specificity of Winged Helix/forkhead Proteins.** C.-D. Hsiao<sup>‡</sup>, K.-L. Tsai<sup>‡</sup>, C.-Y. Huang<sup>‡</sup>, C.-H. Chang<sup>‡</sup>, Y.-J. Sun<sup>§</sup>, and W.-J. Chuang<sup>‡</sup>, <sup>‡</sup>Inst. of Molecular Biology, Academia Sinica, Taipei, Taiwan 115, ROC, <sup>§</sup>Inst. of Bioinformatics and Structural Biology, National Tsing Hua Univ., Hsinchu, Taiwan 300, ROC, <sup>‡</sup>Dept. of Biochemistry, National Cheng Kung Univ. College of Medicine, Tainan 701, Taiwan.

Interleukin enhancer binding factor (ILF) is a human transcription factor and a new member of the winged helix/forkhead family. ILF can bind to purine-rich regulatory motifs such as the human T-cell leukemia virus long terminal region (HILV-1 LTR) and the interleukin-2 (IL-2) promoter. Here we report the 2.4 Å crystal structure of two DNA-binding domain of ILF (FOXK1a) binding to a 16-base pair DNA duplex containing promoter sequence. Electrophoretic mobility shift assay (EMSA) studies demonstrate that two ILF-DBD molecules bind to DNA in a cooperative manner. In addition to the recognition helix recognizes the core sequences through the major groove, the structure shows that wing 1 interacts with minor groove of DNA, and the H2-H3 loop region makes ionic bonds to the phosphate group resulting in affect the recognition of DNA. The structure also reveals that the presence of the C-terminal  $\alpha$ -helix in place of a typical wing 2 in a member of this family results in an alteration of the orientation of the C-terminal basic residues (RKRRPR) in binding to DNA outside the core sequence. These results provide a new insight into that how the DNA-binding specificities of winged helix/forkhead proteins may be regulated by their less conserved regions.