

## INVITED LECTURE T7

### **How winged helix/forkhead proteins using less conserved residues to regulate diverse DNA sequence**

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Winged helix/forkhead proteins have shown to have similar binding specificity to the core sequence. In addition, these proteins have conserved amino acid sequences in the putative recognition helix. This raises an intriguing question as how proteins use conserved residues to recognize distinct core sequences. To date, more than 200 winged helix/forkhead proteins have been identified but only two forkhead protein/DNA complexes have been reported. Prior to this study, little is known about how winged helix/forkhead proteins recognize diverse DNA sequence. We report here a 3-D crystal structure of human FOXK1a (DNA binding domain of ILF) bound to a 16-base pair DNA duplex containing promoter sequence. This complex structure provides a new insight into that how the DNA-binding specificities of winged helix/forkhead proteins may be regulated by their less conserved regions. The present structural study also offers the first view of a cooperative binding of ILF to DNA that contains the core sequence. The cooperativity of ILF can arise through DNA conformability in the absence of strong protein-protein interactions. The structural evidence present here was also consistent with our biochemical data.