

## DNA binding by the TATA-binding protein (TBP)

### PDB 1CDW

When a DNA sequence needs to be 'read' to make new proteins, specific proteins are recruited to the right position in the DNA in order to 'read' it. However, for those proteins to be recruited, the right sequence must be recognised. This is the role of the TATA-binding protein (TBP): eukaryotes typically have, before their genes, the sequence T-A-T-A-T/A-A-A/T (although there are many variations), to which TBP binds. TBP then recruits the machinery that 'reads' genes to make more proteins.

Load PDB 1CDW, which contains TBP in complex with DNA.

*Describe the secondary structure of TBP (i.e. number of  $\alpha$ -helices,  $\beta$ -strands, etc.).*

*The TATA-binding protein contains 4  $\alpha$ -helices, a 9-strands  $\beta$ -sheet and 14 loops (or coil regions).*

*Which secondary structure elements in TBP interact with DNA?*

*TBP binds to DNA via its  $\beta$ -sheet.*

*Does DNA keep its double-helical structure when bound to TBP?*

*The stretch of DNA bound by TBP slightly unravels and loses its double-helical structure.*

Display the side chains of the following residues: **Arg-192**, **Arg-199**, **Arg-290**, **Lys-221** and **Lys-312**.

*What role does the structure suggest for these residues? (You can display the DNA as sticks to see more clearly).*

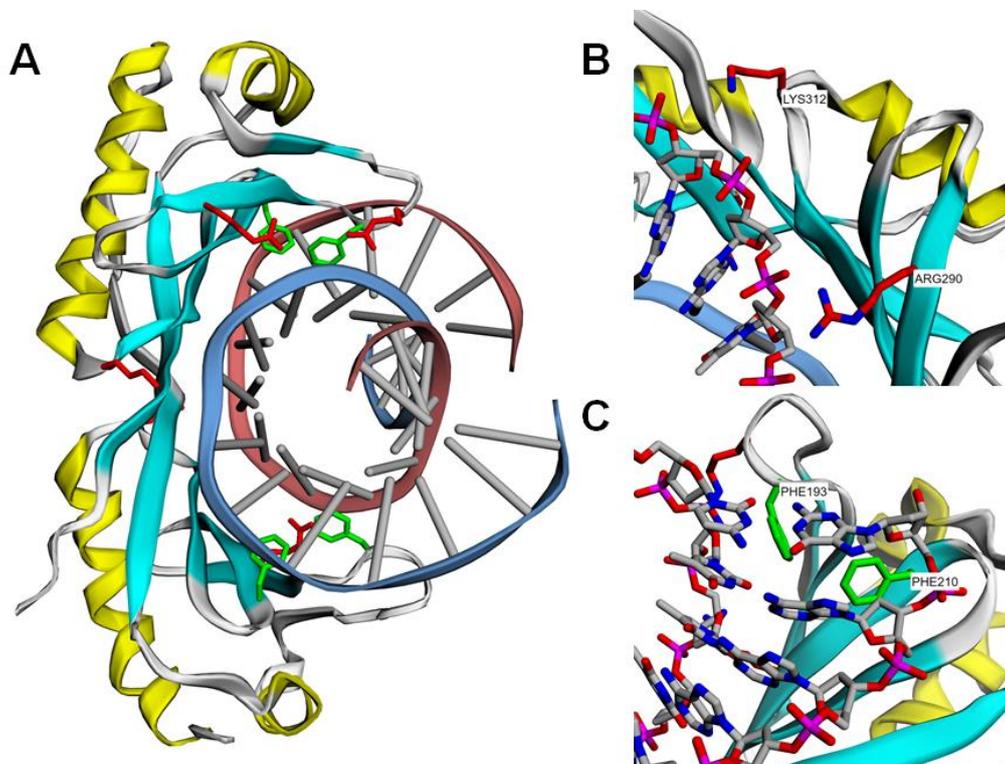
*These positively charged residues are close in space to the negatively charged backbone of DNA, suggesting that they are responsible for DNA binding through electrostatic interactions.*

Display the side chains of **Phe-193**, **Phe-210**, **Phe-284** and **Phe-301**.

*What role does the structure suggest for these residues?*

*These bulky, aromatic residues are inserted between the bases, suggesting a role in disrupting the double helix.*

Make a figure showing the residues mentioned above (arginine, lysine and phenylalanine residues) to show how their position in the protein is key for their functions, using Figure 8 as an example.



**Figure 8** | The TATA-binding protein (TBP). **A.** The overall protein with  $\beta$ -sheets in cyan and  $\alpha$ -helices in yellow. The DNA is shown as a cartoon. **B.** DNA binding by TBP: the two positively charged residues labelled are in close proximity with the sugar-phosphate backbone of DNA (only one strand is displayed). **C.** Phe-193 and Phe-210 are inserted between DNA bases, disrupting the double-helical structure.