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Mapping protein binding stability on nucleosomal DNA by single-molecule approach

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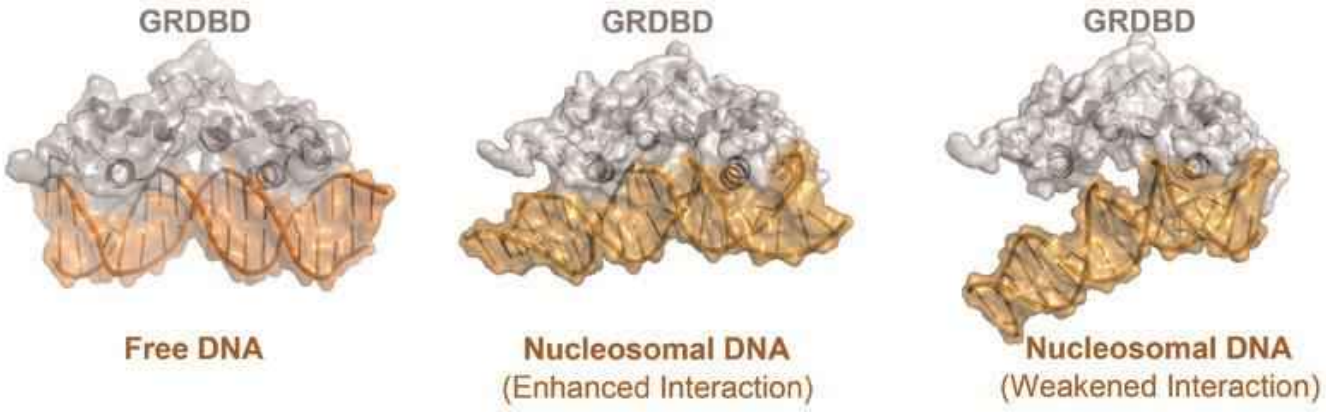
The conformation of nucleosomal DNA is significantly different from that of a canonical B-form double stranded DNA (dsDNA), and is generally regarded to be less flexible and less accessible than free dsDNA due to the tight association of histone cores. Previous studies have demonstrated that the key mechanism involved in nucleosomal DNA-protein interaction is the protein accessibility to the DNA binding site. In this work, we used single molecule assays to measure the stability of two transcriptional factors (glucocorticoid receptor DNA binding domain (GRDBD) and estrogen receptor DNA-binding domain (ERDBD)) bound to their binding sites on different positions of the nucleosomal DNA. Interestingly, the results demonstrated that the nucleosomal DNA-GRDBD binding is not always consistent with the histone shielding effect, but adjusted by additional structural changes. Furthermore, the changes of these DNA-GRDBD interaction profiles were confirmed using molecular modeling and docking approaches based on their crystal structures. Very differently, ERDBD essentially is unable to bind to the nucleosomal DNA anywhere including the unblocked positions. We thus have concluded that the nucleosomal DNA-protein interaction is regulated not only by the histone shielding of the DNA binding sites, but also by the conformational changes of the nucleosomal DNA.



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