DOI:10.16262/j.cnki.1005-0841.2004.z1.027

Interaction of Neuronal Tau with DNA in Nano-Space

Qu M. H.[1,3] Hua Q.[1,3] Li H.[2,3] He R. Q.[1,3]

(1 Laboratory of Visual Information Processing, Ceter for Brain and Cognitive Science, Institute of Biophysics, CAS, Beijing 100101; 2 State Key Laboratory of Magnetism, Institute of Physics and Center for condensed matters, CAS, Beijing 100080; 3 Graduate School, CAS, Beijing 100039)

In this study, the binding of tau to DNA is investigated by the electrophoretic mobility shift assay. Using polynucleotide as probe, we find that tau bound to double-stranded DNA but not to single-stranded DNA. Formation of tau-polynucleotide complex is interfered at alkaline pH and high concentration of NaCl, but is not affected by dithiothreiotol. Electron microscopy reveals that the protein associated with the nucleic acid in a necklace manner. Nevertheless, DNA-cellulose chromatography and radioimmunodot-blot analyses show that calf thymus histone VI-S, VII-S and VIII-S could replace both recombinant human brain tau352 (tau-23) and tau441 (tau-40) from DNA. It appears that tau could bind to DNA reversibly in the presence of histones. The hyperchromic effect has been used to detect the effect of tau on the transition of double-stranded DNA to single-stranded DNA. It is shown that tau increases the melting temperature of calf thymus DNA from 67 to 81℃ and that of plasmid from 75 to 85℃. Kinetically, rates of increase in absorbance at 260 nm of DNA incubated with tau are markedly slower than those of DNA and DNA/bovine serum albumin used as controls during thermal denaturation. In contrast, rates of decrease in the DNA absorbance with tau are faster than those of controls when samples are immediately transferred from thermal conditions to room temperature. It reveals that tau prevented DNA from thermal denaturation, and improved renaturation of DNA. Circular dichroic spectra results indicate that there are little detectable conformational changes in DNA double helix when tau is added. Furthermore, tau shows its ability to protect DNA from hydroxyl radical (.OH) attacking in vitro, implying that tau functions as a DNA-protecting molecule to the radical.

In order to detect the length and the conformation of DNA interacting with tau, a series of different length and different sequence of complement strands nuclear tides were constructed. The result shows that one tau molecule just binds to a 13-bp polynucleotide without any discrimination. It means that tau molecular bind to DNA in one helix (in B-DNA 10bp make one helix and the length of a helix is 34nm). Furthermore, we find that protein tau can recognizes and associates with B-DNA (native DNA in high humidity and low Na^+ concentration), but not A-DNA [poly (dA-dT) · poly (dA-dT) and poly (dG-dC) · poly (dG-dC) in the same condition as above]. The result suggests that the interaction between tau and DNA depends on a strict conformation both protein and polynucleotides.

In addition, atomic force microscopy (AFM) is emerging as a versatile tool for allowing the visualization of protein, DNA, RNA, and protein-nucleic acid complexes at a nanoscale in the absence of stains, shadows and labels. Now researchers in the biological and biomedical sciences consider AFM as a potential (and potent) tool for their cell biological research. Here, Study by AFM shows that tau can induce DNA to form a kind of supercoiled conformation as its binding in vitro. This study indicates a reasonable interpretation for the function of tau in DNA protection and a structural regulation.