ANALYSIS OF NUCLEOSOME FORMATION POTENTIAL AND CONFORMATIONAL PROPERTIES OF HUMAN J1-J2 TYPE ALPHA SATELLITE DNA


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Summary

Motivation: The structure-forming function of alpha satellites in arrangement of the centromeric and pericentromeric heterochromatin implies the presence of certain contextual and conformational signals (codes) for compacting DNA of these regions into nucleosomes and chromatin structures of higher level. However, this aspect of informational content of primary DNA sequences of alpha satellites yet requires further studies.

Results: Computer analysis of nucleosome formation potential (NFP) was performed using a sample of J1–J2 type alpha satellites from the human genome. Several regions with the context favorable for several variants of nucleosome positioning were detected. Statistical analysis of distribution of DNA conformational properties, in particular, the property Wedge, demonstrates a superposition of the context-dependent and CENP-B-dependent nucleosome positionings.

Availability: The corresponding software packages are available at http://wwwmgs.bionet.nsc.ru/mgs/programs/recon/ (the method RECON) and http://wwwmgs.bionet.nsc.ru/mgs/programs/sitecon/ (the method SITECON).

Introduction

Tandemly repeated dimers of alpha satellites of the J1–J2 types whereon chain of nucleosomes are positioned represent the centromere-forming elements of nine human chromosomes. Each monomer has a length of ~171 bp and permits positioning of only one nucleosome (146 bp) with a short linker region, resulting in a supercompact DNA packaging in centromeric and pericentromeric regions (Gilbert and Allan, 2001). Characteristic of the monomers of J2 type is the presence of B box—the site for specific binding the centromeric protein CENP-B (Yoda et al., 1998). The event of CENP-B binding to B box determines an unambiguous nucleosome positioning within the dimer, as was demonstrated in in vivo (Ando et al., 2002) and in vitro experiments (Yoda et al., 1998). The experiments on in vitro reconstitution of nucleosomes in the absence of CENP-B protein showed that several equivalent translational positions for the entire chain of nucleosomes with retained fixed internucleosome interval were realized (Yoda et al., 1998). This fact suggests a sequence-dependent nucleosome positioning; however, the nature of this dependence is yet vague.

In this work, computer analysis of distribution of contextual and conformational nucleosome positioning signals in J1–J2 type dimers was performed. The results obtained agree well with the data on experimental nucleosome mapping.

Methods and Algorithms

Samples of actual J1 and J2 dimers differing in the context from the consensus not more than by 5% were used in the work. The sequences were extracted from the following genomic contigs: BX284928, AC069355, AC135046, AB005791, NC_000007, BX322613, AADD01123003, M58446, and AC135053.
The following sequence characteristics essential for nucleosome positioning were assessed: NFP by the method RECON (Levitsky et al., 2001) and distribution of 38 statistically significant conservative context-dependent DNA conformational and physicochemical properties by the method SITECON (Oshchepkov et al., 2004).

**Results and Discussion**

Shown in Fig. 1 are NFP profiles of J1 and J2 type alphoids constructed using the tool RECON (Levitsky et al., 2001). NFP value at each point corresponds to the probability of positioning the center of nucleosome at this point. The maximal NFP values within J2 type monomers, interpreted as the signals for translational nucleosome positioning, are observed at three positions, namely, 378, 414, and 449. The type J1 monomers contain four–five such signals. This result complies well with the data of experimental studies on nucleosome positioning in the absence of CENP-B (Yoda et al., 1998).

Analysis of the sample of J1 and J2 type alpha satellites using the tool SITECON (Oshchepkov et al., 2004) detected existence of several blocks of conservative properties, in particular, the property Wedge, which is a geometric sum of the angles Roll and Tilt and characterizes a total curvature of a free B DNA (Ulanovsky, Trifonov, 1987). The property Wedge illustrates well the distribution pattern of conservative properties along the J1–J2 monomers. The block of Wedge conservation in the J2 type monomer is localized to the region of B box, reflecting a high conservation of its context as a site for binding CENP-B protein (Yoda et al., 1998; Ando et al., 2002). However, the Wedge profile is insufficiently coordinated and hence, not additive. This means that the intrinsic curvature of the B box free of CENP-B protein is insignificant. Indeed, X ray structure analysis data demonstrate that B box as a DNA fragment with a length of 21 bp is bent to 60° only in the complex with CENP-B protein (Tanaka et al., 2001).

In the sample of J1 type monomers, the region 36–52, corresponding to the B box region in J2 type monomers, also displays a conservation of the property Wedge. However, unlike the genuine B box, increased Wedge values within this region are observed only in a 5-bp fragment, corresponding to a half-turn of the DNA helix (Fig. 2, above). Presumably, this is connected with a prominent intrinsic curvature of DNA within this region and reflects the linker function of the region, which, as a rule, is located between two nucleosomes positioned by the complex B box–CENP-B (see the layout in Fig. 1).
Fig. 2. Profile of the property Wedge along J1 type (above) and J2 type (below) monomers: firm line, the profile of mean values for the sample; gray area around the firm line, the range of standard deviation; the abscissa, nucleotide positions; and the ordinate, value of the property in degrees. Position of B box is shown.

Monomers of both types display conservation of the property Wedge over the region 97–105 as well. As is evident from Fig. 2, typical of this region are decreased values of the property in question, suggesting that DNA there is almost straight. It was demonstrated earlier that this particular conformation characterized the region of nucleosome dyad (Fitzgerald, Anderson, 1999); hence, this region may be assumed the center of nucleosome site, i.e., one of the preferable positions of the nucleosome dyad. Thus, the profile of the property Wedge along J1 and J2 type alpha satellites suggests a superposition of the context-dependent and CENP-B-dependent nucleosome positionings.

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