DNA loops and semicatenated DNA junctions

ABSTRACT

Our data strongly support a model of Form X consisting in a DNA loop at the base of which the two DNA duplexes cross, with one of the strands of one duplex passing between the strands of the other duplex, and reciprocally, to form a semicatenated DNA junction also called a DNA hemicatenane.

INTRODUCTION

Background Alternative DNA conformations are of particular interest as potential signals to mark important sites on the genome, contrasting with the rather uniform structure of the classical B-form DNA double helix which shows little variation as a function of its nucleotide sequence. The structural variability of CA microsatellites is particularly pronounced. These are repetitive poly (CA) · poly (TG) DNA sequences spread in all eukaryotic genomes as tracts of up to 60 base pairs long, sometimes longer, which are particularly abundant in the human genome where they are present in about 105 copies. Because of this abundance, combined with their frequent length variability between different individuals, they have served as a very useful source of markers in human genetics. Many in vitro studies have shown that the structure of poly (CA) · poly (TG) can vary markedly from the classical right-handed DNA double helix and adopt diverse conformations (for a review see e.g. and references therein), the best known of which being left-handed Z-DNA. In the course of our work with DNA fragments containing this repetitive sequence we have observed the formation of several alternative structures which appeared as retarded bands upon gel electrophoresis. While some of them have been shown to correspond to multistranded complexes, a series of closely spaced bands initially named 'bands X' were drawn to our attention for two reasons. First, they migrated near the regular double-stranded form of the fragment, suggesting that they might correspond to double-stranded, not multi-stranded, structures. Second, they were bound with high affinity by proteins HMG1 and HMG2, two abundant non-histone nuclear proteins for which no double-stranded DNA substrate with such a high affinity was known. Here we describe a mechanism of formation of these structures, and their characterization as DNA loops at the base of which the DNA duplexes form a unique knot in which one of the strands of one duplex passes between the strands of the other duplex, and reciprocally, to form a semicatenated DNA junction, also called a DNA hemicatenane.

CONCLUSION

Conclusions An alternative DNA structure named Form X, which was observed previously by polyacrylamide gel electrophoresis of DNA fragments containing a tract of the CA microsatellite poly (CA) · poly (TG) but had not been characterized, has now been identified as a DNA loop maintained at its base by a semicatenated DNA junction (Fig. 6). Structures containing DNA hemicatenanes had been previously suggested to exist in the cell but had not been isolated before. The possibility to prepare such structures, combined with their remarkable stability, should allow one to study their evolution and their possible function when introduced into living cells.