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Human DNA helicase IV is nucleolin, an RNA helicase modulated by phosphorylation

(Unwinding enzyme; cdc2; casein kinase; nucleolus; pre-ribosome assembly)

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SUMMARY

The cDNA encoding human DNA helicase IV (HDH IV), a 100-kDa protein which unwinds DNA in the 5′ to 3′ direction with respect to the bound strand, was cloned and sequenced. It was found to be identical to the human cDNA encoding nucleolin, a ubiquitous eukaryotic protein essential for pre-ribosome assembly. HDH IV/nucleolin can unwind RNA-RNA duplexes, as well as DNA-DNA and DNA-RNA duplexes. Phosphorylation of HDH IV/nucleolin by cdc2 kinase and casein kinase II enhanced its unwinding activity in an additive way. The Gly-rich C-terminal domain possesses a limited ATP-dependent duplex-unwinding activity which contributes to the helicase activity of HDH IV/nucleolin.

INTRODUCTION

The different DNA helicases unwind duplex DNA in an ATP-dependent fashion and thus play essential roles in DNA replication, repair, recombination and in some cases transcription (Matson et al., 1994; Thommes and Hübscher, 1992). Specific functions in different aspects of DNA metabolism have been ascribed to most of the prokaryotic, yeast and viral DNA helicases, whereas the in vivo functions of animal cell helicases are still unclear, including those present in human cells. In this context we have purified to homogeneity from HeLa cells and characterized five human DNA helicases (HDH), namely HDH I, HDH II, HDH III, HDH IV and HDH V (Tuteja et al., 1990; 1991; 1992; 1993; 1994). Recently, we have identified HDH II as Ku, an autoantigen recognized by sera of scleroderma and lupus erythematosus patients (Tuteja et al., 1994). The aim of the present study was to clone and sequence the *HDH IV* gene and eventually identify its function. We could thus observe that HDH IV is in fact human nucleolin (NUC), i.e., a ubiquitous protein of eukaryotic organisms which has a certain, if yet not fully understood, role in the maturation, as well as in nucleo-cytoplasmic transport processes, of rRNA; in this context, NUC is capable of destabilizing rRNA/rRNA helices, a property residing in its C-terminal domain (Ghisolfi et al., 1992a). Also, NUC is known to be a substrate for two different protein kinases, even

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Abbreviations: aa, amino acid(s); Ab, antibody(ies); bp, base pair(s); cdc2, cell division control protein; cDNA, DNA complementary to RNA; CK, casein kinase; DTT, dithiothreitol; HDH, human DNA helicase; *HDH*, gene encoding HDH; kb, kilobase(s) or 1000 bp; nt, nucleotide(s); NUC, nucleolin; *NUC*, gene (DNA, RNA) encoding NUC; r-, ribosomal; *UTR*, untranslated region(s).

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