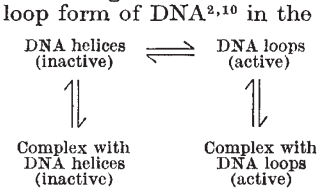
BIOCHEMISTRY

Correlation of the Binding to DNA Loops or to DNA Helices with the Effect on RNA Synthesis

RECENT investigations have revealed that template DNA is found natively in the form of single-stranded loops during the active transcription of selected portions of the genome in higher organisms[1,2]. Conversely, during repression of such transcription the DNA is found natively in the form of double-stranded helices[1,2]. A variety of organic molecules which function *in vivo* as inhibitors or stimulators of RNA synthesis within pre-selected portions of the genome[2] have been shown to be capable of a reversible physical binding to DNA *in vivo* or *in vitro*. Each of these inhibitors or stimulators binds preferentially to either single-stranded or to double-stranded DNA. In every case for which adequate data are available (Table 1), a strong correlation exists between the form of DNA preferred for binding and the effect of the ligand on RNA synthesis within pre-selected portions of the genome. These strong correlations suggest that such ligands may exert their characteristic effects on RNA synthesis by preferentially stabilizing either the inactive helical form or the active loop form of DNA[2,10] in the equilibrium:



The mechanisms of such preferential binding to either double-stranded helical DNA or to single-stranded loop DNA are little understood. Preliminary thermodynamic analyses have revealed that the equilibrium between the helical and the loop forms of DNA can be shifted during binding by an effect of the ligand on one or more of the physical forces existing within the DNA-solvent system. These forces include: (*a*) the hydrophobic solute-solvent interactions between DNA and water[19]; (*b*) the hydrogen bond interactions between the complementary bases of opposing DNA strands[20]; (*c*) the electrostatic charge interactions between the phosphate groups of the same or opposing DNA strands[21]; (*d*) the stacking (van der Waal's) interactions between the successive bases of the same or opposing DNA strand[22]. In addition, the ability of particular ligands to (*e*) cross-link opposing DNA strands[23] or to (*f*) fit sterically into certain regions of the DNA molecule[23] is of importance in the inhibition or stimulation of RNA synthesis. Thus, both histone-type inhibitors and actinomycin-type inhibitors bind preferentially to double-stranded helical DNA by utilizing properties (*e*) and (*f*)[23]. In addition, histones alter physical force (*c*)[3], while actinomycins may alter forces (*a*), (*c*) and (*d*)[6]. By contrast, both testosterone-type stimulators and oestrogen-type stimulators bind preferentially to single-stranded loop DNA by utilizing property (*f*)[24], and by altering physical forces (*a*) and (*d*)[24]. Before such inhibitors or stimulators can bind to DNA and alter the rates of RNA synthesis they must often be first concentrated within the particular sensitive tissue by specific, non-DNA binding agents[12,25].

Table 1. CORRELATION OF THE PREFERRED FORM OF DNA FOR BINDING WITH THE EFFECT ON RNA SYNTHESIS

Ligand	Preferred form of DNA for binding	Effect of ligand on RNA synthesis
Histones	Double-stranded (ref. 3)	Inhibition (refs. 4, 5)
Polylysine	Double-stranded (ref. 3)	Inhibition (ref. 5)
Actinomycin *D*	Double-stranded (ref. 6)	Inhibition (ref. 7)
Acridine orange	Double-stranded (ref. 8)	Inhibition (ref. 8)
Chloroquine	Double-stranded (ref. 9)	Inhibition (ref. 9)
Testosterone	Single-stranded (ref. 10)	Stimulation (ref. 11)
Oestradiol	Single-stranded (ref. 10)	Stimulation (ref. 12)
Methylcholanthrene	Single-stranded (ref. 13)	Stimulation (ref. 14)
RNA polymerase	Single-stranded (ref. 15)	Stimulation (ref. 16)
Complementary RNA	Single-stranded (ref. 17)	Stimulation (ref. 18)

All the foregoing inhibitory or stimulatory ligands (Table 1) except complementary RNA are molecules which are capable of reacting with all portions of the DNA genome non-selectively. RNA by contrast is capable of a selective interaction with specific portions of the DNA genome[17]. It is this selective ability which appears to be the basis for its role as the agent of specific de-repression of RNA synthesis during selective transcription of the genome[1,2,18]. In a similar fashion, polyoma viral DNA binds preferentially to single-stranded host DNA[26]. The result of such oncogenic viral DNA interaction with the host DNA genome is a de-repression of host DNA synthesis and of host enzyme synthesis[27,28]. A concurrent selective de-repression of host RNA synthesis is also likely[27].

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Isolation and Amino-acid Sequence of β-LPH from Sheep Pituitary Glands

SEVERAL adenohypophyseal hormones have been demonstrated to possess *in vitro* lipotropic activity; these include growth, adrenocorticotropic, thyrotropic, α-melanocyte-stimulating and β-melanocyte-stimulating hormones. Recently, Rudman, Astwood and their colleagues reported the preparation of Fraction *H*, peptides I and II, and showed these preparations to be lipotropic agents[1,2].