Effects of Anticancer Drugs on Transcription *in vitro*

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The effects of DNA interacting drugs on: (1) total RNA synthesis catalyzed by *E.coli* and T7 RNA polymerase; (2) synthesis of the initiating dinucleotide (pppApU) by *E.coli* RNA polymerase ("abortive initiation"); (3) elongation of RNA chains synthesized by T7 RNA polymerase on pT7-7 plasmid DNA bearing T7 RNA polymerase promoter ϕ 10 with human Cu/Zn superoxide dismutase coding sequence, (4) interaction of transcription factor Sp1 and its binding site were studied. Intercalating ligands which form quickly dissociating complexes with DNA (anthracyclines, proflavine, ethidium bromide) are compared with the slowly dissociating drug of d(G·C) specificity (actinomycin D), the non-intercalating, d(A·T) specific pyrrole antibiotics (netropsin and distamycin A) and covalently binding to DNA 1-nitroacridine derivative (nitracrine). The obtained results indicate that rapidly dissociating ligands, proflavine and ethidium bromide, inhibit total RNA synthesis *in vitro* and the abortive initiation to a similar extent while they do not induce discrete elongation stops of RNA polymerase. Actinomycin D and nitracrine exhibit a high inhibitory effect on total RNA synthesis and induce stops of RNA polymerase while not affecting abortive initiation. Pyrrole antibiotics primarily inhibit the initiation, while no elongation stops are induced. Actinomycin D inhibits complex formation between nuclear proteins and the Sp1 binding site. Netropsin, ethidium bromide, proflavine and other intercalating acridines do not affect Sp1 binding. The results indicate that the effects primarily depend on sequence specificity and secondarily on the dissociation rate of ligands from their complexes with DNA.