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Erratum

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In "Induction of Single-strand Regions in Nuclear DNA by Adriamycin," by Melvin S. Center, pp. 1231-1238, through a printer's error, page 1235 was omitted. For the convenience of our readers, the correct pages 1235 and 1236 are reproduced on the following pages.

distinct phases. The nature of this reaction is unknown but it may represent the presence of high affinity binding sites which undergo a rapid strand separating process. As this occurs new binding sites may be exposed which results in the formation of extensive single-strand regions. This type of binding may represent the transmission of structural effects along DNA. Evidence for the transmission of allosteric effects in DNA has been described by Hogan et al. (10).

Additional studies have been carried out to examine the ability of adriamycin to induce the formation of single-strand regions in isolated chromatin. The assay carried out as with nuclei measures the formation of acid-soluble material after incubation of chromatin with adriamycin in the presence of Neurospora nuclease. The results obtained are closely similar to those with isolated nuclei. The formation of regions of chromatin which can be hydrolyzed to acid-soluble nucleotides occurs at optimium drug concentrations of 10-20 μg/ml (Figure 1C). The extent of hydrolysis of DNA occurring at various drug concentrations is however somewhat higher than that obtained with isolated nuclei. Although chromatin can be hydrolyzed to acid-soluble material in the presence of adriamycin and Neurospora nuclease a similar process does not take place when native T7 DNA is used as the substrate (Figure 1C). Similar results have been obtained when E. coli DNA is used as the substrate (not shown). As shown in Figure 1D, the kinetics of release of acid-soluble material in the presence of adriamycin and nuclease are also similar to the results obtained with isolated nuclei.

In addition to adriamycin several other antitumor agents which interact with DNA have been examined for their ability to induce single-strand regions in chromatin in isolated nuclei (Table 1). Of those studied thus far only daunomycin and ethidium bromide exert an effect similar to adriamycin. These compounds are capable of intercalation and this type of binding to DNA may possibly be a pre-requisite to the events leading to strand separation. Since this process does not occur with isolated native DNA (Figure 1C) it is indi-

TABLE 1

EFFECT OF VARIOUS ANTITUMOR DRUGS ON THE INDUCTION OF SINGLE-STRAND REGIONS IN NUCLEAR DNA

Reagent	Acid-soluble[a] material (CPM)	%Hydrolysis
NONE	0	0
Adriamycin	2200	4.6
Daunomycin	2710	5.6
Ethidium bromide	3100	6.4
Actinomycin D	0	0
CDDP[b]	0	0
Bleomycin	0	0
Camptothecin	0	0

(a) Assay for the induction of single-strand regions in nuclear DNA was carried out as described in Methods. All drugs were used at a final concentration of 20 µg/ml. Incubations were for 20 min at 37°C.

(b) CDDP, Cis-diaminedichloroplatinum II

cated however that other factors such as proteins associated with chromatin or chromatin conformation are also required for the formation of drug induced single-strand regions. It is of interest to note that Actinomycin D which can intercalate into DNA is without effect in this system when examined at drug concentrations of 20-100 µg/ml. The reason for this apparent selectivity of intercalating agents is currently under study. Other reagents such as cis-diaminedichloroplatinum II which introduces interstrand crosslinks in DNA (11), bleomycin and camptothecin which induce DNA strand breakage (12, 13) are not active in promoting the formation of nuclear DNA which is susceptible to nuclease cleavage.

Additional studies have been carried out to examine the effect of adriamycin and Neurospora crassa nuclease on the sedimentation properties of nuclear DNA. Figure 2 shows the results of an experiment in which nuclei containing [^{3}H]labeled DNA were incubated in the absence and presence of adriamycin (20 µg/ml) with nuclease for 5 min at 37°C. After lysis of nuclei and deproteinization of chromatin the DNA was centrifuged in neutral sucrose gradients. The results of these studies clearly demonstrate that in the presence of adriamycin nuclease treated DNA sediments with a sedimentation rate slower than that for DNA in-