Technical Papers

Nucleodepolymerase Activity of Precancerous Rat Liver[1]

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Evidence has been obtained in this laboratory (*1*) of the occurrence of an irreversible liver cirrhosis, indicative of a preneoplastic state, in rats fed cooked polished rice and *p*-dimethylaminoazobenzene during 120 days. It is not clear how the azo dye operates to produce an altered equilibrium at the precancerous level in the economy of the liver cell.

The part played by nucleic acids in tumor production has been demonstrated by Caspersson and Santesson (*2*). Whether the altered desoxyribonucleic acid equilibrium in precancerous liver cells is the first step toward cellular malignancy or is only an accompanying phenomenon is not evident. Nevertheless, desoxyribonucleic acid synthesis appears intimately bound to the mitotic mechanism and to cellular division, so that any quantitative change in the desoxyribonucleic acid synthesis may well be the cause of abnormal cellular proliferation. Because studies of the chemical and enzymatic pattern of the nucleic acid in cancer tissue have revealed the net results of altered metabolism of nucleic acid, it was felt that similar studies during the transition period of carcinogenesis would help to elucidate the evolution nucleic acid metabolism may be undergoing during carcinogenesis.

TABLE 1

NUCLEODEPOLYMERASE ACTIVITY OF PRECANCEROUS RAT LIVER

Time, days	0	30	60	90	120	150
Ribonucleodepolymerase*	.09	.11	.13	.23	.18	.13
Desoxyribonucleodepolymerase†	9.4	10.7	13.9	16.5	13.5	11.1

* In terms of increase of mg acid soluble P after 2 hr incubation at 37° C, of a mixture of 1 ml of a 3% Na ribonucleate, 1 ml of tissue extract containing 0.40 mg N acid 1 ml of veronal acetate buffer at pH 7.

† In terms of decrease of viscosity, after ½ hr of incubation at 30° C, of a mixture of 3 ml of 1% Na desoxyribonucleate and 3 ml of tissue extract containing 1.23 mg N/ml.

Investigation of nucleodepolymerase activity was carried out according to the method described by Greenstein (*3*), who reported no change in depolymerase activity in normal liver and in transplanted hepatoma. We find no reference in the literature to the nucleodepolymerase activity of precancerous tissue and particularly of precancerous cirrhotic liver in rats fed *p*-dimethylaminoazobenzene. In view of the importance of these enzymes in the altered metabolism of nucleic acid, we have investigated the depolymerase activity of preneoplastic tissue.

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Albino white rats (Carworth Farms) were fed a diet of cooked polished rice with *p*-dimethylaminoazobenzene (0.06% concentration) supplemented with 1 g of fresh carrots per day. The nucleodepolymerase activity of rat liver was determined according to method described by Greenstein, at 30-day intervals, for a period of 150 days on the basic diet. The ribonucleodepolymerase activity in normal rat liver was 0.09, which is a value similar to Greenstein's. The desoxyribonuclease, on the other hand, was found to be slightly higher (9.4), compared to 7.0 reported by Greenstein (*4*).

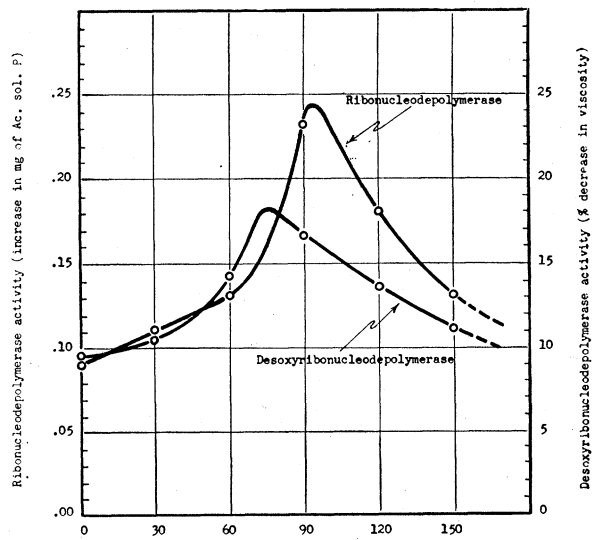

FIG. 1. Nucleodepolymerase activity of precancerous rat liver (time, days).

Our results to date on this precancerous cirrhotic liver indicate that the nucleodepolymerase activity varies appreciably in comparison with that of normal rat liver. The enzymatic activities of both depolymerases show a progressive increase up to maximum activity at 90 days, followed by progressive decrease to 150 days (Table 1).

The period of increased activity of the depolymerases (90–120 days) corresponds to the precancerous cirrhotic liver stage. It would appear that, once this transition stage of carcinogenesis has been reached, the depolymerase activity decreases and finally drops with the occurrence of the hepatoma to a normal level (Fig. 1). These findings indicate that the enzymes of nucleic acid metabolism behave differently during the transition stage of carcinogenesis than in the true neoplastic stage.

References

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