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Relative Metabolic Activities of Normal and Tumorous Liver Nucleoproteins Indicated by Radiophosphorus.*

TRUMAN P. KOHMAN AND HAROLD P. RUSCH.

From the Chemistry Department and the McArdle Memorial Laboratory for Cancer Research, University of Wisconsin.

The observations that tumors are high in arginase¹ and mono- and polynucleotidase² activities, and recent studies with radiophosphorus,^{3,4} indicate rapid metabolism of the nuclear substance of neoplastic tissues. However, in these experiments, except those comparing lymphoma with normal lymph node,⁴ it has been necessary to contrast cancer cells with various kinds of normal cells of different types. The liver carcinoma which can be produced by feeding azo dyes⁵ is admirably suited to such experiments since the analogous normal tissue is readily available.

In Experiment I three groups of stock albino rats were used, one receiving a semi-synthetic diet (dextrin 79, casein 10, butter 5, salts 4, yeast 1, cod liver oil 1), another receiving in addition 0.06% dimethylaminoazobenzene (DAAB), and the third receiving 10% whole dried liver in addition to the basal ration and the azo dye. In Experiment II two groups of stock albino mice were used, one receiving a stock diet,⁶ and the other in addition 0.05% p-aminoazotoluene (AAT). The rats were kept on the diet for 5 months and the mice for 7 months before the experiments, at which time all the animals receiving the azo dyes but no liver had developed hepatomata. Of 10 rats receiving both the azo dye and whole liver, only one developed liver tumors, and was discarded.

Each animal received subcutaneously 0.5 cc of a neutral radiophosphate solution. After 24 hours the animals were killed and the livers extracted 2-3 times with cold 0.01-2 N NH_4OH . The entire protein fraction was precipitated with cold trichloroacetic acid, and

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¹ Edlbacher, S., and Merz, K. W., *Z. physiol. Chem.*, 1927, **171**, 252.

² Edlbacher, S., and Kutcher, W., *Z. physiol. Chem.*, 1931, **199**, 200.

³ Marshak, A., *Science*, 1940, **92**, 460.

⁴ Tuttle, L. W., Erf, L. A., and Lawrence, J. H., *J. Clin. Invest.*, 1941, **20**, 57.

⁵ Kinoshita, R., *Trans. Soc. Path. Japan*, 1937, **27**, 665.

⁶ Steenbock, H., *Science*, 1923, **58**, 449.

the precipitate washed several times each with cold dilute trichloroacetic acid, acetone, alcohol at 70°, and ether, in order to remove all non-nucleic phosphorus. The residue was then wet-ashed, the total phosphorus determined colorimetrically, and the radioactivity measured with a Geiger-Müller counter.

For each animal we have calculated the fraction of the activity administered per gram of animal which was found per milligram of phosphorus in the isolated fraction. The results (Table I) show that the tumorous livers exhibit an increased uptake of labeled phosphate in the nucleoprotein fraction compared to the controls. This increase amounted to $44 \pm 11\%$ with the rats and $46 \pm 7\%$ with the mice. If the increased activity resides only in the cancer cells, the actual activity of the latter must be considerably greater than that observed, since they constitute only a fraction of the liver bulk. The increased activity of the liver-fed group ($22 \pm 7\%$) is probably due in part to the better health and food consumption of these animals and in part to their fatty condition which caused their weights to be high without a correspondingly high phosphorus content.

Since these experiments provide a comparison between normal and cancer cells derived from the same primordial cells and located in the same part of the body, they indicate that the nucleoprotein metabolism is increased in neoplastic tissue.

TABLE I.
Twenty-four-hour Uptake of Radiophosphorus by Normal and Tumorous Liver Nucleoproteins of Rats and Mice.

Exp. animals P ³¹ inj. P ³² inj.	I. Rats .015 mg 35,000 counts/min			II. Mice .065 mg 25,000 counts/min	
	Semi-synth.	Semi-synth. + DAAB	Semi-synth. + DAAB + 10% liver	Stock	Stock + AAT
Avg wt (g)	258	146	318	20.6	24.2
Condition of livers	Normal	Tumorous	Normal	Normal	Tumorous
Activity of liver nucleoprotein	.179	.250	.272	.081	.128
	.205	.253	.275	.104	.132
	.223	.287	.280	.108	.156
	.234	.297	.286	.112	.160
	.236	.304	.286	.116	.160
	.275	.319	.300	.122	.161
	.309	.353*	.302		.161
		.400	.316		.167
		.423			.175
		.427*			
Avg activity	.237	.341	.290	.107	.156
Standard error	$\pm .016$	$\pm .021$	$\pm .005$	$\pm .006$	$\pm .005$

*Avg value for 2 rats whose liver nucleoproteins were accidentally mixed.
Weight = 2.