EXPERIMENTAL STUDY OF THE ANTITHYROID ACTION OF TUMOR CELL METABOLITES IN VITRO

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Experiments on rats have shown that ovarian tumor cells (strain OYa) produce substances sharply inhibiting the absorption of radioactive iodine by thyroid slices. The level of tissue respiration of the thyroid is unchanged.

Inhibition of thyroid function during growth of transplanted tumors has been reported several times [1, 2, 4-8], but the mechanism of this phenomenon remains unknown. My own suggestion is that inhibition of thyroid activity in animals with a transplanted tumor is due to the entry of one or several metabolites of the tumor cell, possessing antithyroid activity, into the circulating medium [3].

The object of the present investigation was to study whether tumor metabolites can act directly on thyroid cells.

EXPERIMENTAL METHOD

Experiments were carried out on 30 intact male rats weighing 150-180 g. The animals were divided into two equal groups and killed by exsanguination. The thyroid glands were quickly removed and thin slices were cut which were incubated in a Warburg apparatus for 1 h at 38° in an atmosphere of oxygen. The incubation medium for the control group was blood serum of intact rats and for the experimental group ascites fluid of strain OYa, freed from tumor cells by centrifugation. Immediately before the Warburg apparatus was placed in the water bath, radioactive iodine was added in a dose of 1 μ Ci. Oxygen absorption was determined manometrically and expressed as mm/mg dry weight of thyroid slices. Absorption of radioactive iodine by the thyroid slices from the incubation medium was investigated by means of a "Volna" PS-5M scintillation dosimeter and expressed as a percentage of the added dose. The numerical results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The results given in Table 1 show that incubation of thyroid slices of intact rats in ascites fluid of strain OYa is accompanied by maintenance of the initial level of respiration and by a sharp decrease in the ability of the thyroid parenchyma to absorb, and presumably to bind, radioactive iodine.

The decrease in the ability of thyroid slices to assimilate iodine from the incubation medium in the experimental group indicates damage to the mechanism by which the thyroid cell maintains its specific function — the synthesis of thyroid hormones. Hence it may be concluded that special metabolites, absent from the blood serum of intact rats, and apparently capable of exerting an antithyroid action directly at the cell level,

TABLE 1. Respiration and Absorption of Radioactive Iodine by Rat Thyroid Slices During Incubation in Blood Serum of Intact Animals and Ascites Fluid of Strain OYa

Group of rats	Oxygen (in ml)	I^{131} (in percent)
Control (incubation in serum of intact rats)	8.457± 0.836	22.93±2.10
Experimental (incubation in ascites fluid of strain OYa)	9.407±1.183 P > 0.01	11.58±1.03 P > 0.01

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are present in the ascites fluid of strain OYa, which is a product of the metabolism of the tumor cells and at the same time the medium in which they live. Consequently, there are no grounds for ruling out the possibility that these metabolites or what may be termed the antithyroid factor can pass from the peritoneal cavity, where ascites fluid collects during growth of strain OYa, into the general circulation. There are, therefore, no grounds likewise for ruling out the possibility of the direct action of the tumor antithyroid factor on enzyme systems of the thyroid cell responsible for absorption and assimilation of inorganic iodine into the iodine-containing hormones.

The following conclusions can thus be drawn from these results: 1) tumor cells of strain OYa produce metabolites with antithyroid action, and 2) the antithyroid effect of these metabolites is effected through their direct action on the thyroid gland cells.

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