COENZYME A AND N-ACETYLTRANSFERASE ACTIVITY DURING GROWTH OF TUMORS

L. N. Bulovskaya and A. I. Kolosov

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Sulfadimidine acetylation activity in C57Bl/He mice, with low predisposition to cancer, was significantly lower than in C3H/Sn mice, with a high predisposition to cancer. Growth of melanoma B-16 in C57Bl/He mice led to increased sulfadimidine acetylation activity. These results, together with earlier observations, are evidence that the development of tumors is connected with changes in activity of the enzyme N-acetyltransferase. No difference in sulfanilamide acetylation was observed in the mice of these groups, indicating no differences at the coenzyme A level.

KEY WORDS: *coenzyme A; N-acetyltransferase; sulfanilamide; sulfadimidine; malignant tumors.*

Several biochemical processes which play an essential role in the development of malignant neoplasms (ATP formation, cholesterol synthesis, formation of steroid hormones, acetylation of amino groups of nuclear and ribosomal proteins) depend on the activity and direction of acetylation reactions. To study the activity of acetylation processes, the substances most commonly used as acetate acceptors have been sulfanilamide (streptocidum album) [10] and also sulfadimidine, sulfapyridazine, and sulfaethidole [3-5]. However, Lipmann showed some time ago that, if the coenzyme A level in the sample is the same, the quantity of sulfadiazine acetylated is only one-fifth that of sulfanilamide acetylated [10]. Further investigations showed that whereas the degree of acetylation of sulfanilamide is determined by coenzyme A activity [9], the degree of acetylation of sulfadiazine, sulfadimidine, and of certain other acetate acceptors depends on the activity of the enzyme N-acetyltransferase (EC 2.3.1.5) [7, 11].

The object of this investigation was to study different stages of the acetylation system in mice with high and low predisposition to cancer and during growth of experimental tumors.

EXPERIMENTAL METHOD

Female C3H/Sn and C57Bl/He mice (from the Rappolovo nursery, Academy of Medical Sciences of the USSR) were used. Melanoma B-16 was transplanted intramuscularly into female C57Bl/He mice. Acetylation activity was judged from the relative percentage of the acetylated form of sulfadimidine or of sulfanilamide in the blood 5 h after intraperitoneal injection of the corresponding preparation in a dose of 50 mg/kg. The percentage of acetylation [6] was determined in mice without tumors and 3 weeks after transplantation of melanoma B-16.

EXPERIMENTAL RESULTS AND DISCUSSION

Sulfanilamide acetylation activity in mice with high (C3H/Sn) and low (C57Bl/He) predisposition to cancer was identical; there were no changes likewise in the growth of melanoma B-16 (Fig. 1). This could be evidence of the absence of changes in coenzyme A activity during growth of melanoma B-16. The degree of acetylation of sulfadimidine in all cases was considerably lower than that of sulfanilamide acetylation. This confirms that acetylation of

Laboratory of Endocrinology and Laboratory of Experimental Therapy, Professor N. N. Petrov Scientific-Research Institute of Oncology, Ministry of Health of the USSR, Leningrad.
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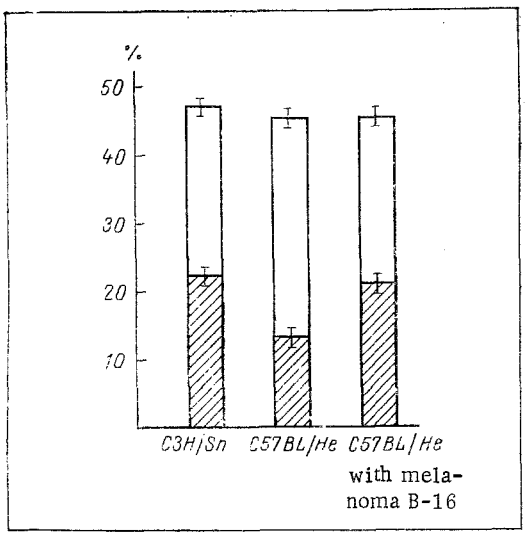

Fig. 1. Sulfanilamide (unshaded columns) and sulfadimidine (shaded columns) acetylation activity in mice with high (C3H/Sn) and low (C57Bl/He) predisposition to cancer under normal conditions and after transplantation of melanoma B-16. Ordinate, acetylation (in %). Values of M ± m given.

sulfadimidine is dependent on N-acetyltransferase activity, for the coenzyme A level (judging from the degree of sulfanilamide acetylation) can maintain a higher percentage of acetylation of the acceptor.

The degree of acetylation of sulfadimidine in mice with low predisposition to cancer was much lower than in the mice with high predisposition. Growth of melanoma B-16 in the C57Bl/He mice increased the sulfadimidine acetylation activity up to the level characteristic of C3H/Sn mice.

Changes in acetylation processes during tumor growth are thus connected with an increase in N-acetyltransferase activity. This increase evidently depends directly on malignancy, for the writers previously showed direct correlation between the degree of acetylation of sulfadimidine and the appearance, growth, and inhibition of growth of the malignant tumors [1].

With a longer course of tumor development, the increased N-acetyltransferase activity could perhaps lead to exhaustion of the coenzyme A reserves in the body [12].

The results show that by the use of different acceptors of active acetate it is possible to study different stages of the acetylation processes *in vivo*. With the aid of acceptors acetylated "monomorphically" (sulfanilamide, p-aminobenzoic acid [2]), activity of coenzyme A can be demonstrated, whereas by the use of acceptors acetylated "polymorphically" (sulfadimidine, sulfadiazine, isoniazid [2, 7, 8]) N-acetyltransferase activity can be studied. This must be taken into account when changes in acetylation processes are studied both *in vivo* and *in vitro* [8].

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