THE POSTNATAL DEVELOPMENT OF MITOCHONDRIAL TYROSINE AMINOTRANSFERASE IN RAT LIVER

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Tyrosine aminotransferase (TAT) activity is absent or very low in the cytoplasm of rat liver at delivery. During the ensuing few hours, the synthesis of soluble TAT proceeds rapidly, reaching maximal levels approximately twelve hours after natural birth or premature delivery [1,2]. A complex sequence of hormonally mediated events appears to be responsible for the postnatal synthesis of this enzyme [3]. In a recent report from this laboratory [4], the same authors have suggested that cytosol TAT consists of three different forms, the synthesis of each being under different hormonal control. Mitochondrial TAT [5] has been shown to be completely separable from the soluble enzyme by the use of isoelectric focussing in a pH gradient. It hence became of interest to us to investigate the postnatal development of mitochondrial TAT, which appears to be a fourth form of this enzyme.

Livers were homogenized in 0.25 M sucrose (1 g/9.0 ml). The homogenates were centrifuged at 850 *g* for 10 min to remove nuclei and cell fragments, and the pellet washed once. Mitochondria were pelleted by centrifugation of the combined supernatant and pellet washings at 6000 *g* for 15 min, washed once and resuspended in sucrose. The final suspension contained the mitochondrial content of 1.0 g (wet weight) of liver per 1.0 ml of 0.25 M sucrose.

TAT activity was determined by the method of Sereni, Kenney and Kretchmer [1]. 200 μl Aliquots of the mitochondrial suspension were incubated with the substrate for 30 min at 37°.

Premature delivery of animals and their subsequent maintenance were as previously described [6].

Fig. 1 shows the activity of mitochondrial TAT in early postnatal liver compared to that found in the adult liver. It can be seen that the activity slowly increases following delivery, approximating adult levels by 2 days after birth.

Table 1 shows the effect of actinomycin D on the postnatal development of the enzyme. The high degree of repression obtained with this drug suggests that DNA-directed RNA synthesis is a prerequiste for the postnatal appearance of this enzyme. The increase

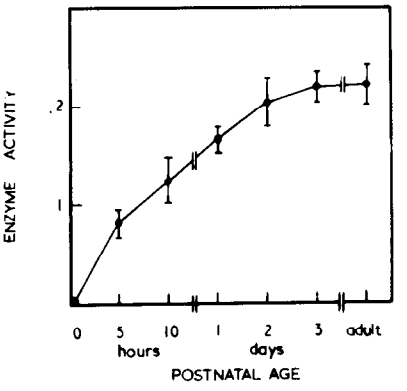

Fig. 1. For the determination of mitochondrial TAT activity in their first 10 hr after delivery, animals were delivered by uterine section. Four litter mates from each of four litters were sacrified at the times shown. The activity at 1, 2, and 3 days postnatal was assayed on pooled liver samples of 4 animals from each of 4 litters delivered normally. Adult mitochondrial TAT activity was determined in 4 animals.

The values shown on the graph represent the mean ± S.D. of the determinations. Enzyme activity is expressed as μmoles *p*-hydroxyphenylpyruvate/hr/g wet wt. liver.

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Table 1

Litter	TAT activity		
	Test	Control	% Repression
(1)	0.15	0.76	80
(2)	0.23	0.91	75
(3)	0.12	0.60	87

Litter mates delivered by uterine section were immediately injected with actinomycin D (3.5 μg) or saline, and sacrified 5 hr later. Each result shown was obtained on pooled liver samples from four animals. Mitochondrial TAT activity is expressed as μmoles *p*-hydroxyphenylpyruvate/hr/g wet wt. liver.

in the activity of TAT in the early postnatal period hence appears to be the result of *de novo* enzyme synthesis.

Little is known of the control of the synthesis of mitochondrial TAT, save the fact that large increases in the activity of the soluble enzyme are generally mimicked by slower and smaller increases in the activity of the mitochondrial form [7]. The results presented above bear out this observation. During the first 10 hr following delivery, the activity of soluble TAT increases from approximately zero to 20–60 units/g liver. The activity falls to adult levels (20–30 units/g) by approximately 24 hr after birth [1,2]. The fact that the postnatal increase in the activity of mitochondrial TAT shows different kinetics to the soluble enzyme suggests that the synthesis of each of the forms is under the control of different inductive mechanisms.

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