COMMENT

DUAL FUNCTION AND COMMON IDENTITY OF PROTEINS IN GLYCOGEN METABOLISM: REPLY TO A HYPOTHESIS

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Ryman and Whelan [1] have recently postulated that the enzymes involved in the control of liver glycogen metabolism might have a dual activity. Their hypothesis was partly based on results obtained in our laboratory and recently reviewed in this journal [2]. However, other facts included in the same review [2] were neglected, presumably because they were described in a very concise way; in the meantime, a more complete report of our work has been published [3].

Ryman and Whelan [1] have revived our previous hypothesis [4] that synthetase phosphatase exists in two forms. This enzyme is indeed inactive in a fresh liver Sephadex filtrate and becomes active within about 20 min upon incubation of the filtrate at 20° [4]. This latency had first been interpreted as the time required for the conversion of an inactive into an active form by a 'synthetase phosphatase activating enzyme' [4]; this hypothetical enzyme and phosphorylase phosphatase had so many properties in common that we suggested their identity [5]. Later on, it was found that liver phosphorylase *a*, which is present in a large amount in the fresh liver filtrate, is a strong inhibitor of synthetase phosphatase, whereas liver phosphorylase *b* is only slightly inhibitory [3, 6, 7]. The latency in the activation of glycogen synthetase could therefore be explained as the time required by phosphorylase phosphatase to convert phosphorylase *a* into phosphorylase *b* and it became unnecessary to postulate 2 forms of synthetase phosphatase. The assumption that synthetase phosphatase exists in 2 forms was finally disproved by the fact that antibodies directed against liver phosphorylase suppress the latency in synthetase activation [3, 7], making clear that synthetase phosphatase does not require a preincubation to become active. Although these antibodies were obtained against liver phosphorylase *a*, they do not distinguish between the *a* and *b* forms of the liver enzyme [3]. If, as suggested by Ryman and Whelan [1], phosphorylase *b* were identical to active synthetase phosphatase, the latter enzyme would have been inhibited by the antibodies. Their identity is further precluded by the fact that liver phosphorylase *b* slightly inhibits synthetase phosphatase [3].

Ryman and Whelan [1] have not only proposed that phosphorylase *b* would act as a synthetase phosphatase (see above) but also that the presence of ATP would reverse the relationship of enzyme to substrate, making synthetase *b* act as a phosphorylase *b* kinase. In order to check this hypothesis, we have measured the ratio of synthetase *b* to phosphorylase *b* kinase in a purified preparation [8] of liver synthetase *b* and found a value 35 times higher than in a crude liver homogenate. This finding precludes the possibility that synthetase *b* is identical to active phosphorylase *b* kinase; therefore synthetase *a* and inactive phosphorylase *b* kinase are different enzymes. It also appears unlikely from a theoretical point of view that the absence of ATP could be the signal for glycogen synthesis whereas its presence would induce glycogenolysis.

The only point in the Ryman and Whelan hypothesis that we could not submit to experimental control was the identity of phosphorylase *b* with phosphorylase *b* kinase phosphatase. It appears however unlikely that a single enzyme could catalyze a transglucosylation to a polysaccharide and the dephosphorylation of a protein.

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