Pyrimidine 5'-Nucleotidase Acquired Deficiency in Beta-Thalassaemia: Involvement of Enzyme-SH Groups in the Inactivation Process

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David et al. [1] have recently published an interesting article in this journal, suggesting that the most probable mechanism for the faster inactivation of pyrimidine 5'-nucleotidase (PN5) in thalassaemia involves enzyme-SH group oxidation by red blood cell (RBC) membrane lipid peroxidation products. This assumption is documented by the demonstration that monofunctional aldehydes produced by lipid peroxidation are powerful inhibitors of P5N activity. Accordingly, they conclude that P5N-SH groups are much more sensitive to monofunctional aldehydes than other thiol enzyme-SH groups.

In 1988, using a hydrogen peroxide (H₂O₂)-sodium azide (NaN₃) in vitro system [2], we have demonstrated that incubation of human RBCs in the presence of increasing concentrations of H₂O₂ exerted a highly sensitive inhibitory effect on P5N, which was strongly correlated (r = 0.987) with an increase in malonyldialdehyde (MDA) production by RBCs. A similar but less intense effect was also observed for glucose-6-phosphate dehydrogenase, phosphofructo-kinase and adenylate kinase. These results allowed us to conclude that: (1) P5N was highly sensitive to the effect of RBC peroxidation, probably through the peroxide radicals involved in the production of MDA, and (2) the assay system used provided a means for measuring the sensitivity of the different RBC enzymes to an oxidative threat. In addition, our results supported the hypothesis of a probable in vivo oxidative stress mechanism as the cause of the acquired P5N deficiency observed in β -thalassaemia trait [3]. Although the evidence presented by David et al. [1] strongly confirms our results, no mention has been made of our paper, published in Enzyme

one year ago [2]. In our opinion, the results of David et al. [1] stress the fact that P5N-SH groups are more sensitive to 4-hydroxynonenal than to other aldehydes, but neither the importance of these compounds in β -thalassaemia nor their possible in vivo effect on P5N activity has been elucidated. Conversely, they are in accordance with the different effect of in vitro peroxidation observed on pyruvate kinase activity when compared to P5N and adenylate kinase activities [2], which showed partial recovery after the addition of β -mercaptoethanol to the RBC incubation medium containing H₂O₂.

References

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