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

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 PN5 activity. Accordingly, they conclude that PN5-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 PN5, 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, phosphofructokinase and adenylate kinase. These results allowed us to conclude that: (1) PN5 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 PN5 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 PN5-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 PN5 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 PN5 and adenylate kinase activities [2], which showed partial recovery after the addition of β-mercaptoethanol to the RBC incubation medium containing H2O2.

References
