Lipid Peroxide Oxidation in Endoplasmic Reticulum Membranes, their Sub-fractions Isolated from Liver and Tumor Cells under the Effect of Phorbol Ester in Different Concentrations

Nadezhda Pal'mina[1], Elena Pinzar[2], Ian Pryme[3]

[1]Emanual Institute of Biochemical Physics RAS, Moscow, Russia;

[2]Laboratoire HP2 Hypoxie:physiopathologie respiratoire et cardiovasculaire UFR de Medecine Grenoble 1 France; [3]Department of Biomedicine University of Bergen, Norway.

It is known that phorbol esters are active modulators of the secondary messenger systems. Some of them, for instance,12-O-tetradecanoyl-phorbol-13-acetate(TPA), have the properties of tumour promotors. Lipid peroxidation (LPO) control system localized in cell membranes is very closly connected with cell proliferetion and tumour growth too. We have studied the effect of TPA and its inactive analogue 4-α-phorbol-12,13-didecanoate (DDP) in a wide range of concentrations (10^{-18}-10^{-4}M) on LPO in membranes and their sub-fractions isolated from the liver and tumor cells *in vitro*. It has been found that TPA inhibited LPO in microsomes from liver and tumor-host liver. Effect was dependent from concentration. DDP using in the same doses did not influence on LPO. Our experiments with tumor membranes isolated from ascitic Ehrlich tumour cells have shown that TPA are capable both – to inhibit and to activate LPO in dependence on TPA concentration, original saturation of membrane lipids and LPO intensity. Normal cells and tissues contain two sub-fractions of the endoplasmic reticulum (ER) membranes: smooth (S) and light rough (LR). ER of transformed cell lines: L-929, MPC-11, Krebs 11 can be separated into three sub-fractions: S, LR and heavy rough (HR). We have determined the LPO level in the lipids of these sub-fractions isolated from Krebs 11 ascites cells, treated with different concentrations of TPA (10^{-7}; 10^{-14} M). The capacity to oxidation in lipid extracts increases from S to LR and HR fractions. The initial level of lipid peroxidation products in S was equal to LR, but in HR was higher (more than in 2 times). There was a straight line correlation between the rate of lipid oxidation and relation PE/PC in these membranes. TPA(10^{-7}M) inhibited and promoted (10^{-14}M) LPO in lipids isolated from all type of ER sub-fractions. Such property as ability to modulate LPO is the characteristic feature for carcinogenetic and co-carcinogenetic substances. Obviously, this dual capacity of TPA to influence on oxidation could be significant for its promoting effect.