Cross-linking of Spectrin Increases the Permeability of the Erythrocyte Membrane's Lipid Domain

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The passive "ground" permeability of plasma membranes is assumed to involve, besides aqueous pores postulated by some investigators, the lipid domain of the membrane. To what extent this lipid domain forms a simple, unmodified bilayer is a matter of debate. In erythrocytes, the phospholipids are arranged asymmetrically and the asymmetry is influenced by spectrin, the major extrinsic membrane protein located as a network at the cytoplasmic surface (1). Cross-linking of spectrin - via disulfide bridges - by SH-oxidants (diamide, tetrathionate) induces reorientation of phospholipids from the inner to the outer layer due to an enhanced transversal mobility ((1) and Haest et al., this meeting).

In parallel to these effects treatment of erythrocytes with SH-oxidants enhances the simple nonmediated membrane permeability to non-electrolytes (erythritol, arabinose, mannitol, substituted glycerols and glycols), cations (Na^+, K^+, choline) and to anions (Cl^-, lactate, glycolate, acetate). The extent of acceleration increases with time of exposure and oxidant concentration, it is reversible upon treatment with reducing agents and can be suppressed by pretreatment of the cells with monofunctional alkylating SH-agents, which provides evidence for a causal role of the cross-linking of spectrin. The elevated permeability of the diamide treated membrane goes along with a decrease of the activation energy. At a given temperature, the relative increase of permeability is not related to the molecular weight of the test permeants but inversely related to their permeability in the unmodified membrane.

Changes of the overall membrane microviscosity, as probed by DPH (1,6-diphenyl-1,3,5-hexatriene), are not involved in the effect (polarization of control: 0.30, after diamide: 0.30). The "permeabilization" of the membrane produced by modification of the cytoskeletal network must therefore be due to more subtile changes of the lipid domain, e.g. lateral segregation of lipids leading to the formation of highly permeable "patches" or perturbation of the lipid-water interface.

(1) Haest, C.W.M., Plasa, G., Kamp, D. and Deuticke, B. (1978) Biochim. Biophys. Acta 509, 21 - 32.

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