IS THE FLUID-MOSAIC MODEL OF BIOLOGICAL MEMBRANES FULLY RELEVANT? STUDIES ON LIPID ORGANIZATION IN MODEL MEMBRANES

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The basic concept of the fluid-mosaic model [Singer and Nicolson, Science 175 (1972) 720], an essential point of which is that the membrane proteins are floating in a sea of excess lipid molecules organized in the lipid bilayer, may be misleading in terms of understanding the movement of membrane components in biological membranes which show distinct domain structure. It seems that the lipid bilayer is an active factor in the formation of the membrane structure, and that the lipid composition is responsible for the presence of domains in the membrane. The main role in the process of domain formation is played by cholesterol and sphingolipids. The presented results show that in the binary mixture of cholesterol and an unsaturated phospholipid, cholesterol is segregated out from the bulk unsaturated liquid-crystalline phase, forming cholesterol-enriched domains or clustered cholesterol domains due to the lateral nonconformability between the rigid planar ring structure of cholesterol and the rigid bend of the unsaturated alkyl chain at the C9-C10 carbon position. These cholesterol-enriched domains may be stabilized by the presence of saturated alkyl chains of sphingomyelin or glycosphingolipids, and also by specific proteins which selectively locate in these domains and stabilize them through protein-protein interaction. Such protein-rich domains are called “rafts”, and have been proved to be responsible for signal transduction to and from the cell, and for protein sorting. It was also interesting to check whether polar carotenoids, compounds showing some similarities to cholesterol (common first stages of biosynthesis and similar effects on membrane properties), could also promote domain formation and locate preferably in one of the lipid phases. Our preliminary data show that in the presence of cholesterol, lutein (a polar carotenoid) may segregate out from saturated lipid regions (the “liquid ordered” phase) and accumulate in regions rich in unsaturated phospholipids, forming carotenoid-rich domains there. To address the issue of the molecular organization and dynamics of the raft-constituent molecules and the raft itself in the membrane, conventional and pulse EPR (electron paramagnetic resonance) spin labeling techniques were employed.