THE EFFECT OF CHOLESTEROL ON "MOSAIC" NATURE OF THE LIPID BILAYER SURFACE

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The lipid bilayer structure is varied, and the distribution of hydrophobic properties on its surface is locally heterogeneous. Depending on lipids composing the bilayer, "mosaic" nature of this heterogeneity may vary, affecting protein-lipid interactions with the bilayer surface [1].

Cholesterol affects ordering of phospholipids and is an important participant of the protein's local lipid environment, which modifies structure and function of proteins, in particular, receptor tyrosine kinases (RTKs). However, little is known about the cholesterol's impact on hydrophobic properties of the lipid bilayer surface. Understanding of the phenomena underlying these processes will open up new perspectives in the study of lipid-protein interactions. RTKs often become therapeutic targets for cancer and other significant pathologies, therefore the study of these interactions is an urgent problem.

Using molecular dynamics simulations of lipid bilayers with varied hydrophilic "head" polarity, acyl chain length and saturation degree of phospholipids containing different amounts of cholesterol, we carried out a comparative analysis of the lipids geometric packing and the acyl chains order parameters in lipid bilayers with the experimental data from the literature in order to validate the results obtained. Based on the results of the analysis of hydrogen bonds, lipid density and geometric parameters of the simulated systems, we characterized the vertical and lateral distributions of cholesterol in bilayers of various compositions, which are consistent with the results of *in vitro* and *in silico* experiments from literature sources.

In this paper we show that adding cholesterol to lipid bilayers leads to a shift in the hydrophobicity of the bilayer surface towards neutral values. These changes are the result of reorganizing of phospholipids and most likely are not directly associated with cholesterol atoms present on the surface. The analysis of hydrophobic properties patterns of studied lipid bilayer surfaces shows that higher concentration of cholesterol may lead to the appearance of hydrophobic regions of higher area while areas of hydrophilic regions descend.

The results obtained will shed light on the mechanisms of modulating the activity of transmembrane proteins (in particular, RTKs) by influencing their membrane environment and the role of cholesterol in this process.

References.

1. *Polyansky A.A., Volynsky P.E., Arseniev A.S., Efremov R.G.* Adaptation of a membrane-active peptide to heterogeneous environment. II. The role of mosaic nature of the membrane surface // *Journal of Physical Chemistry B* Vol. 113, No. 4, 2009. Pp. 1120-1126.