SAB 2023
Córdoba

Sociedad Argentina de Biofísica

LI REUNIÓN ANUAL

SOCIEDAD ARGENTINA DE BIOFÍSICA

LIBRO DE RESÚMENES

29 - 30 de Nov. y 1 de Dic. 2023

Computational analysis of cholesterol:POPC bilayer interacting with α7 nAChR

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Nicotinic acetylcholine receptors (nAChRs) are ligand-gated ion channels composed of five transmembrane glycoprotein subunits organized pseudosymmetrically around a central pore or channel. Subtle changes in the lipid environment of nAChRs are highly relevant to their activity, producing significant effects on human biology. Lipids in the vicinity of the receptor can be located in annular or non-annular sites, with non-annular sites being in close contact with the receptor and exhibiting a low replacement rate, while annular sites are farther away and have a higher replacement rate. A receptor model based on a known structure (PDB: 7EKI) was inserted into a lipid bilayer composed entirely of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) lipids to create the control system, which lacks cholesterol molecules. Subsequently, systems with different cholesterol:POPC ratios in the membrane were generated, thus modifying the lipid environment of the nAChR. Atomistic Molecular Dynamics simulations were performed for these systems focusing on the cholesterol molecules surrounding the transmembrane domain (TMD) of homomeric α7 nAChR. Physicochemical properties of the membrane and the receptor were analyzed and compared with the results obtained for the control system. Furthermore, the mobility of cholesterol molecules in the membrane was studied, and also the residues involved in the interactions of these molecules with TMD.

Acknowldegments

This work was supported by Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) and Universidad Nacional del Sur (UNS).