XLVIII Reunión Anual de la Sociedad Argentina de Biofísica

Libro de Resúmenes

SAB
XLVIII

27 al 29 de noviembre de 2019
Universidad Nacional de San Luis

XLVIII Reunión Anual de la Sociedad Argentina de Biofísica / compilado por Sebastián Andujar ...
[et al.]. - 1a ed . - Buenos Aires : SAB - Sociedad Argentina de Biofísica, 2019.
Libro digital, PDF

Archivo Digital: descarga
ISBN 978-987-27591-7-9

1. Biofísica. 2. Investigación. I. Andujar, Sebastián, comp.
CDD 570

Diagramación y Edición

M. Soledad Celej, Juan Pablo Acierno

Diseño de Tapa y Logo

Comité Organizador

Asistencia Técnica Web

Juan Pablo Acierno

Sociedad Argentina de Biofísica

Member of the International Union for Pure and Applied Biophysics

XLVIII Reunión Anual SAB

27-29 Noviembre 2019

San Luis, Argentina

XLVIII Annual Meeting SAB

27-29 November 2019

San Luis, Argentina

A Molecular Dynamic approach to the differential interaction between unsaturated free fatty acids and the nicotinic acetylcholine receptor

Obiol D[a], Amundarain MJ[a], Jaure O[a], Zamarreño F[a], Antollini S[b], Costabel M[a]
a - Instituto de Física del Sur (IFISUR), Departamento de Física, Universidad Nacional del Sur (UNS), CONICET
b - Instituto de Investigaciones Bioquímicas de Bahía Blanca (INIBIBB). Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS- CONICET), Bahía Blanca, Argentina

Free fatty acids (FFAs) are important cellular components that increase under certain pathological conditions. One of the effects of FFAs is a protection mechanism through the modulation of ion channels. The activity of the nicotinic acetylcholine receptor (nAchR) is blocked by certain FFAs and its binding site is located at the lipid-protein interface. The objective of this work was to determine, by means of molecular dynamics (MD), the possible points of contact and the effect produced by five different FFAs, located in annular and non-annular sites. The study was carried out on a system composed by a model of AChR from Torpedo marmorata (PDB ID: 2BG9) that was elaborated from PDB ID: 4COF as a template because the e-values were the lowest for each subunit and because it represented the closed desensitized state. The evaluation of the stereochemical parameters for the refined model was improved with respect to 2BG9. The refined model was incorporated into a lipid bilayer composed with a ratio of 1:1:3 of cholesterol, POPA and POPC respectively. We replaced three phospholipids from the lipid bilayer with three of the corresponding free fatty acids: cis-18:1ω-6, cis-18:1ω-9, cis-18:1ω-11, cis-18:1ω-13 and trans-18:1ω-9 in annular or non-annular areas. From the MD runs we obtained the most statistically relevant conformations of each FFAs in each of the systems, we determined the possible contacts with residues of the nAChR and the resulting profile of pore radius. In general, the results show that more contacts are established when FFAs are located in non-annular regions. As expected, contacts are established in a much greater proportion with non-polar residues. cis-18:1ω-11 in non-annular sites leads to conformations that open the pore of the channel, while in annular sites it stabilizes the desensitized state. With cis-18:1ω-13 a similar behavior is observed, although in non-annular sites it produces a pronounced constriction in the extracellular domain.

Acknowldegments

DO, MJA, OJ, FZ, SA and MC would like to thank CONICET and Universidad Nacional del Sur.