La Plata - 2018

XLVII Reunión Anual de la Sociedad Argentina de Biofísica

Libro de Resúmenes

5 al 7 de Diciembre 2018

Facultad de Ciencias Médicas de La Plata - UNLP

XLVII Reunión Anual de la Sociedad Argentina de Biofísica: libro de resúmenes / Soledad Celej ... [et al.]. - 1a ed. - Buenos Aires: SAB - Sociedad Argentina de Biofísica, 2018.
Libro digital, PDF

Archivo Digital: descarga y online
ISBN 978-987-27591-6-2

1. Biofísica. 2. Investigación. I. Celej, Soledad
CDD 571.4

Diagramación y Edición

M. Soledad Celej, Juan Pablo Acierno

Diseño de Tapa y Logo

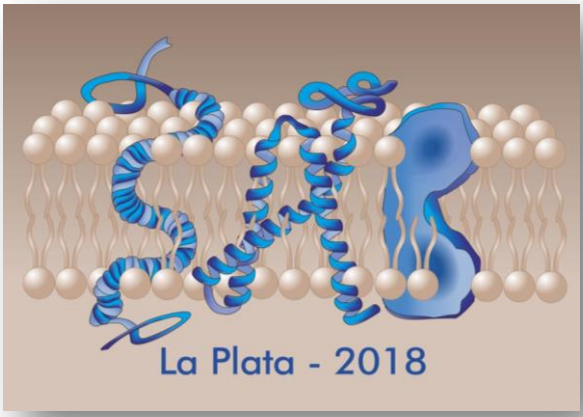
Mario Raúl Ramos

Asistencia Técnica Web

Juan Pablo Acierno

Sociedad Argentina de Biofísica

Member of the International Union for Pure and Applied Biophysics



XLVII Reunión Anual SAB

5 – 7 Diciembre 2018

La Plata, Argentina

XLVII Annual Meeting SAB

5 – 7 December 2018

La Plata, Argentina

Molecular Modulation of Human α7 Nicotinic Receptor by Amyloid-β Peptides

Lasala M[a], Fabiani C[a], Corradi J[a], Antollini S[a], Bouzat C[a]
a - Instituto de Investigaciones Bioquímicas de Bahía Blanca (INIBIBB-CONICET)

Amyloid β peptide (Aβ) is a key player in the development of Alzheimer disease (AD). It is the primary component of senile plaques in AD patients and is also found in soluble forms. Cholinergic activity mediated by α7 nicotinic receptors has been shown to be affected by Aβ soluble forms. To shed light into the molecular mechanism of this effect, we explored the direct actions of oligomeric $A\beta_{1-40}$ and $A\beta_{1-42}$ on human α7 by fluorescence spectroscopy and single-channel recordings. Fluorescence measurements using the conformational sensitive probe crystal violet (CrV), which shows different affinities for resting and desensitized states, revealed that Aβ induces α7 concentration-dependent conformational changes. At 100 pM, Aβ displaces CrV Kd value for the resting state towards that of the desensitized state from which α7 is still reactive to carbamycholine (Carb). These observations are compatible with the induction of active/desensitized states as well as of a novel conformational state in the presence of both Aβ and Carb. At 100 nM Aβ, α7 adopts a resting-state-like structure which does not respond to Carb, indicating the stabilization of α7 in a blocked state. In real time, we found that Aβ is capable of eliciting α7 channel activity either in the absence or presence of the positive allosteric modulator PNU-120596. Activation by Aβ is favored at picomolar or low nanomolar concentrations and is not detected at micromolar concentrations. At high Aβ concentrations, the durations of the activation episodes elicited by ACh are significantly reduced, an effect compatible with slow open-channel block. We conclude that Aβ directly affects α7 function and acts as an agonist and a negative modulator: activation of α7 by low Aβ concentrations may be involved in beneficial physiological effects, and the reduced α7 activity in the presence of higher Aβ concentrations may contribute to the cholinergic signaling deficit and may be involved in the initiation and development of AD.