La Plata - 2018

XLVII Reunión Anual de la Sociedad Argentina de Biofísica

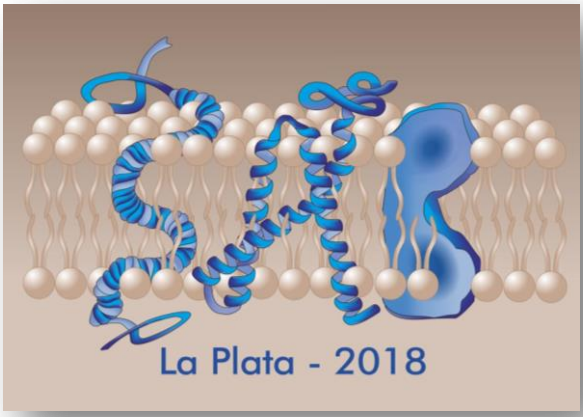
Libro de Resúmenes

5 al 7 de Diciembre 2018

Facultad de Ciencias Médicas de La Plata - UNLP

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

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Nicotinic receptors as therapeutic drug targets: Molecular bases of function, dysfunction and drug modulation

Bouzat C[a]
a - INIBIBB- UNS/CONICET- Bahía Blanca- Argentina

Nicotinic acetylcholine receptors (nAChR) are pentameric ligand-gated ion channels widely expressed in neuronal and non-neuronal cells in both vertebrates and invertebrates. In humans, dysfunction of nAChRs is associated with neurological, muscular and immune disorders. The nAChR operates as a molecular machine that transduces the binding of ACh into an electrical signal. Its molecular design has been tuned to function as a near perfect on-off switch that responds to ACh with the efficiency and speed required for proper cell function. We have combined mutagenesis, patch-clamp recordings, single-channel kinetic analysis and *in silico* studies to unravel the molecular mechanisms and structures underlying nAChR activation and modulation as well as to identify compounds with potential therapeutic use. For the muscle nAChR, a key protagonist in muscle contraction, we have postulated mechanisms that describe its activation and modulation, deciphered how mutations lead to congenital myasthenic syndromes, and explored worm receptors as antiparasitic drug targets. We have also focused on α7 nAChR, which is the homomeric member of the family and is involved in cognition, attention, memory and inflammation. We have revealed unique aspects of α7 activation as well as mechanisms and sites of action of positive allosteric modulators, which are promising therapeutic tools for schizophrenia and Alzheimer's disease. We have also identified the molecular function of novel heteromeric nAChRs containing the α7 subunit. Overall, our studies have allowed an integrated description of the nAChR, providing information of its molecular function in health and disease states and guiding rational therapy.