Biofísica Magazine

July 2018
S2

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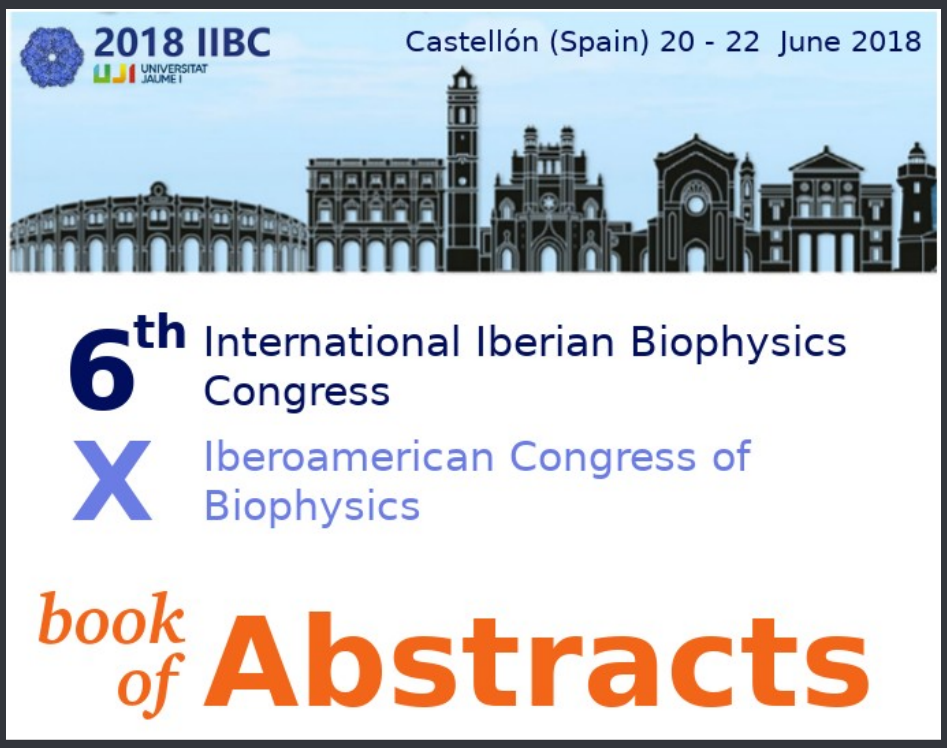

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June 2018

S3 | Channels, Receptors and Transporters

Hall **Auditorium**

Chair 1 João Morais-Cabral

Chair 2 Francisco Barros

Date: Thursday, June 21st
Time: 15:00–18:00
Sponsored by: The Spanish Ion Channel Initiative (SICI)

S3.1 Molecular function of α7 nicotinic receptors

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The α7 nicotinic receptor is expressed in brain and non-neuronal cells. Enhancement of α7 activity by positive allosteric modulators (PAMs) is emerging as a therapeutic strategy for cognitive and inflammatory disorders. We have focused on understanding α7 function and potentiation. We revealed that PAMs enhance α7 activation by increasing the open-channel lifetime and inducing prolonged activation episodes. Although α7 has been considered the homomeric member of the family, a novel $\alpha7\beta2$ receptor has been recently discovered in human brain. We generated $\alpha7\beta2$ receptors with fixed stoichiometry by two approaches comprising concatenated and unlinked subunits. We found that β2 can assemble with α7 subunits resulting in receptors with different stoichiometries, kinetic signatures and PAM selectivity. This information provides fundamental basis required to decipher the role of $\alpha7\beta2$ in native cells. In humans, there is a truncated α7 subunit (dupα7) that lacks part of the ACh-binding site and results from a partial duplication of the α7 gene. Its role remains unknown. We demonstrated that dupα7 acts as a negative modulator, cannot form channels, but can assemble with α7 into functional heteromeric receptors. Deciphering the molecular basis underlying α7 responses has implications for the design of novel therapeutic compounds.