CeMMP Centre for Cryo-electron Microscopy of Membrane Proteins

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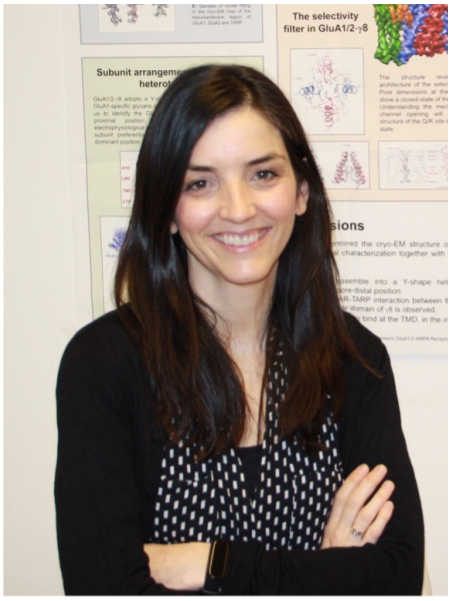

Beatriz Herguedas is a "Ramón y Cajal" fellow at the BIFI institute in Zaragoza (Spain). She obtained her degree (2006) and PhD in Biochemistry (2007-2011) at the University of Zaragoza in Spain working on the structure of electron-transfer proteins under the supervision of Milagros Medina and Marta Martínez. During her PhD she did research stays in the labs of Juan Hermoso and Ignacio Fita at the Spanish National Research Council, where she specialized in X-ray crystallography. In 2011 she joined the group of Ingo Greger at the MRC Laboratory of Molecular Biology to work on AMPA Glutamate Receptors (AMPARs), combining crystallography and cryo-EM to get insights into AMPAR heteromerization. In 2019 she was awarded a "Ramón y Cajal" fellowship from the Spanish Research Agency, allowing her to start her independent career at the BIFI institute, where she is now focused on the structure and dynamics of calcium permeable AMPARs and their complexes with auxiliary proteins

Structural studies of heteromeric AMPA Glutamate receptors

AMPA Glutamate Receptors (AMPARs) are ion channels located at post-synaptic neurons, where they mediate fast-excitatory neurotransmission. AMPARs are tetrameric receptors composed of different combinations of four subunits, GluA1 to GluA4, which also interact with auxiliary subunits, such as TARPs, cornichons or GSG1L. Here I will summarize the recent advances in the structural biology of AMPAR complexes, focusing on the gating cycle of the GluA1/2-TARP-g8 complex. I will describe the structural features of the receptor in different functional states and dissect the impact of TARP-g8 in the modulation of the channel properties. Combining structural data with electrophysiology and molecular dynamics simulations we show how TARP-g8 extracellular domains interact with the receptor ligand binding domain to modulate AMPAR function. We also analyze how receptor gating is coupled to changes in the selectivity filter, which determines cation selectivity, as well the role of TARP-g8 in the modulation of receptor rectification.