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Research interests:

1. Neuronal communication, calcium homeostasis and regulatory mechanisms.
2. Neuronal calcium channels
3. Neuronal nicotinic receptors
4. Animal models of neurodegenerative diseases (amyotrophic lateral sclerosis, Alzheimer's disease, Huntington's disease)

For the last three decades, my research interest has been focused to the elucidation of the basic mechanisms that regulate the phenomena of excitation-secretion coupling, in which Ca^{2+} acts as key second messenger. To this aim, we use the chromaffin cell of the adrenal medulla, isolated in primary cultures or in situ in slices, as our main experimental model. We have characterized the subtypes of voltage-activated calcium channels (VACC) expressed by chromaffin cells of different animal species and the fine mechanisms that control the cellular calcium homeostasis and the exocytotic release of catecholamines, as well as endocytosis. These experiments carried us to the formulation of a “functional triad” hypothesis, that includes the VACC, the endoplasmic reticulum (RE) and the mitochondria in the regulation of the exo-endocytosis and calcium signals. More recently, we have applied this basic knowledge to different mouse models of neurodegenerative diseases, such as Alzheimer's disease (AD), amyotrophic lateral sclerosis (ALS), and Huntington's disease (HD). Our data in these models suggest the existence of an alteration of the functional triad that controls the calcium and the exo-endocytotic signals in chromaffin cell, that are reflected by alterations of the kinetics of the pore of fusion, which controls the final stages of the exocytotic neurotransmitter release. Ultimately, in collaboration with organic chemists of the ITH we are aimed to the search of new neuroprotective medicines capable of delaying the progression or these neurodegenerative diseases.

Selection of publications

- 1.-Nanclares, C., Gameiro-Ros, I., Méndez-López, I., Martínez-Ramírez, C., Padín-Nogueira, J.F., Colmena, I., Baraibar, A.M., **Gandía, L.** and García, A.G. Dual antidepressant duloxetine blocks nicotinic receptor currents, calcium signals and exocytosis in chromaffin cells stimulated with acetylcholine. **J. Pharmacol. Exp. Ther.** 2018; 367: 28-39.
- 2.-Martínez-Ramírez C, Baraibar AM, Nanclares C, Méndez-López I, Gómez A, Muñoz MP, de Diego AMG, **Gandía L**, Casarejos MJ, García A.G. Altered excitability and exocytosis in chromaffin cells from the R6/1 mouse model of Huntington's disease is linked to overexpression of mutated huntingtin. **J. Neurochem.** 2018;147: 454-476.
- 3.-Baraibar, AM, De Pascual, R, Camacho, M, Domínguez, M, Machado, JD, **Gandía, L** and Borges, R. Distinct patterns of exocytosis elicited by Ca^{2+} , Sr^{2+} and Ba^{2+} in bovine chromaffin cells. **Pflugers Arch. Eur. J. Physiol.** 2018; 470: 1459-1471.
- 4.-Lajarín-Cuesta, R, Arribas, R, Nanclares, C, García-Frutos, E, **Gandía, L** and De Los Rios, C. Design and synthesis of multipotent 3-aminomethylindoles and 7-azaindoles with enhanced protein phosphatase 2A-activating profile and neuroprotection. **Eur. J. Med. Chem.** 2018; 157: 294-309.
- 5.-Nanclares, C, Baraibar, AM and **Gandía, L.** L-type calcium channels in exocytosis and endocytosis of chromaffin cells. **Pflugers Arch. Eur. J. Physiol.** 2018; 470: 53-60.
6. Punzón E, García-Alvarado F, Maroto M, Fernández-Mendívil C, Michalska P, García-Álvarez I, Arranz-Tagarro JA, Buendia I, López MG, León R, **Gandía L**, Fernández-Mayoralas A, García AG. Novel sulfoglycolipid IG20 causes neuroprotection by activating the phase II antioxidant response in rat hippocampal slices. **Neuropharmacology.** 2016; 116: 110-121.

7. Calvo-Gallardo, E, De Pascual, R, Fernández-Morales, JC, Arranz-Tagarro, JA, Maroto, M, Nanclares, C, **Gandía, L**, De Diego, AMG, Padín, JF and García, AG. Depressed excitability and ion currents linked to slow exocytotic fusion pore in chromaffin cells of the SOD1^{G93A} mouse model of amyotrophic lateral sclerosis. **Am. J. Physiol.** 2015; 308: C1-C19.
8. García, AG., Garcia-De-Diego, AM, **Gandía, L**., Borges, R. and García-Sancho, J.: Calcium signalling and exocytosis in adrenal chromaffin cells. **Physiol. Rev.** 2006; 86: 1093-1131.
9. López MG, Montiel C, Herrero CJ, García-Palomero E, Mayorgas I, Hernández-Guijo JM, Villarroya M, Olivares R, **Gandía L**, McIntosh JM, Olivera BM, García AG. Unmasking the functions of the chromaffin cell α_7 nicotinic receptor by using short pulses of acetylcholine and novel selective blockers. **Proc. Natl. Acad Sci USA** 1998; 95: 14184-14189.
10. García, A.G., Sala, F., Reig, J.A., Viniegra, S., Frías, J., Fonteriz, R. and **Gandía, L.**: Dihydropyridine BAY-K-8644 activates chromaffin cell calcium channels. **Nature** 1984; 309: 69-71.