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### Research interests:

1. Drug Design and Synthesis
2. Pharmacological neuroprotection

My current work focuses on the validation of new therapeutic targets for the treatment of central nervous system diseases. During the latest years, it has been stated that the most accepted hypothesis to explain the development of Alzheimer's disease have not given the expected crops. For this reason, new approaches have to be aimed. Since I started my scientific career as a independent investigator, I have focused on drug discovery on alternative biological targets to treat neurodegenerative diseases, like the mitochondrial Na/Ca exchanger (NCLX), the phosphoprotein phosphatase PP2A, and the newly discovered calcium channel CALHM-1. In my lab, we are designing and synthesizing new compounds able to selectively act over these targets. We have discovered the first organic ligand capable to block CALHM1. Also, we have described a family of benzothiazepine derivatives that overcome the blocking effect of the best-known NCLX blocker CGP37178, the unique tool since the 1980s. Finally, we are developing the first family of ligands with demonstrated direct activity as PP2A activators. Many of these compounds present promising results in experiments assessing the neuroprotective effect, as they mitigate the neuronal death induced by toxic stimuli mimicking physiopathological events where the selected targets are implicated.

### Selection of publications

1. Lajarín-Cuesta R, Arribas RL, Nanclares C, García-Frutos EM, Gandía L, **de los Ríos 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.
309. 02. Gonzalez D, Arribas RL, Viejo L, Lajarín-Cuesta R, **De los Ríos C**. Substituent effect of *N*-benzylated gramine derivatives that prevent the PP2A inhibition and dissipate the neuronal Ca<sup>2+</sup> overload, as a multitarget strategy for the treatment of Alzheimer's disease. **Bioorg. Med. Chem.** 2018;26:2551-2560.
3. Arribas RL, Romero A, Egea J, **De los Ríos C**. Modulation of serine/threonine phosphatases by melatonin: therapeutic approaches in neurodegenerative diseases. **Brit. J. Pharmacol.** 2018;175:3220-3229.
4. Ramos E, Egea J, Romero A, Marco-Contelles J, Del Pino J, **De los Ríos C**. Analysis of Gene Expression Profiles of CR80, a Neuroprotective 1,8-Naphthyridine. **Future Med. Chem.** 2018;10:1289-1300.
5. Lajarín-Cuesta R, Nanclares C, Arranz-Tagarro JA, González-Lafuente L, Arribas RL, De Brito, Gandía L, **De los Ríos C**. Gramine Derivatives Targeting Ca<sup>2+</sup> Channels and Ser/Thr Phosphatases: A New Dual Strategy for the Treatment of Neurodegenerative Diseases. **J. Med. Chem.** 2016;59:6265-6280.
6. Martínez-Sanz FJ, Lajarín-Cuesta R, González-Lafuente L, Moreno-Ortega AJ, Punzón E, Cano-Abad MF, **De los Ríos C**. Neuroprotective Profile of Pyridothiazepines with Blocking Activity of the Mitochondrial Na<sup>+</sup>/Ca<sup>2+</sup> exchanger. **Eur. J. Med. Chem.** 2016;109:114-123.
7. Martínez-Sanz FJ, Lajarín-Cuesta R, Moreno-Ortega AJ, González-Lafuente L, Fernández-Morales JC, López-Arribas R, Cano-Abad MF, **De los Ríos C**. Benzothiazepine CGP37157 Analogues Exert Cytoprotection in Various in Vitro Models of Neurodegeneration. **ACS Chem. Neurosci.** 2015;5:1626-1636.
8. Romero A, Egea J, González-Muñoz GC, Martín De Saavedra MD, Del Barrio L, Rodríguez-Franco MI, Conde S, López MG, Villarroya M, **De los Ríos C**. ITH12410/SC058: A New Neuroprotective Compound with Potential in the Treatment of Alzheimer's Disease. **ACS Chem. Neurosci.** 2014;5:770-775.
9. Lorrio S, Romero A, Gonzalez-Lafuente L, Lajarín-Cuesta R, Martínez-Sanz FJ, Samadi A, Marco-Contelles J, García AG, Villarroya M, López MG, **De los Ríos C**. PP2A ligand ITH12246 protects against memory impairment and focal cerebral ischemia in mice. **ACS Chem. Neurosci.** 2013;4:1267-1277.
10. Gonzalez-Lafuente L, Egea E, León R, Martínez-Sanz FJ, Monjas L, Perez C, Merino C, Garcia-de-Diego AM, Rodríguez-Franco, Garcia AG, Villarroya M, Lopez MG, **De los Ríos C**. Benzothiazepine CGP37157 and Its Isosteric 2'-Methyl Analogue Provide Neuroprotection and Block Cell Calcium Entry. **ACS Chem. Neurosci.** 2012;3:519-529.