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The Group:
Working at the Medicinal Chemistry Institute (IQM-CSIC, Madrid, Spain), is currently formed by three Staff people (Dr. Rosario González-Muñiz, Dr. Mercedes Martín-Martínez and Dr. María Jesús Pérez de Vega), together with several postdocs and PhD students, and is integrated within the Peptidomimetic's group (6 Staff scientists).

Main expertise:
Within the experience in **organic synthesis**, the group is familiar with the chemistry of peptides, peptidomimetics, secondary structure mimetics, conformationally restricted amino acid derivatives, chiral heterocycles and different types of organic small-molecules. Solid-phase and solution approaches, as well as combinatorial chemistry methodologies are commonly applied for the preparation of new chemical entities.

Our main results in **medicinal chemistry** are related to the discovery of antagonists for relevant bioactive peptides (CCK, NT, PACAP27, BDNF, etc), inhibitors of enzymes (aminopeptidases, HCMV protease), and modulators of therapeutically relevant protein-protein interactions (VEGF-VEGFR). In recent years, we have focused our efforts on the modulation of different ion channels and interrelated proteins. On one hand, on TRP channels implicated in inflammatory and neuropathic pain, among other disorders, and on the nicotinic receptor (α7) linked to pain perception, but apparently implicated also in neurodegenerative processes. On the other hand, we have started collaborative works on the mineralocorticoid receptor (MR), and on the orphan receptor GPR37, either directly or indirectly interconnected with ion channels.
Computer-assisted drug design and optimization are applied whenever possible. The generation of molecular diversity for HTS campaigns is the alternative strategy when the target structure is unknown.
Regarding **MR**, we have started collaboration with Dr. Diego Alvarez de la Rosa aimed at developing non-steroid ligands for the mineralocorticoid receptor. To this end, we have performed studies on the binding pocket with known MR antagonists, and a virtual screening search (VS) to discover new ligands. We have already identified initial hits, able to block aldosterone-induced MR-dependent gene transactivation. The first promising results prompted us to start a hit-to-lead optimization to find MR ligands with high affinity, ideally selective for MR vs other steroid receptors, and with appropriate ADME properties. To this aim, we are

exploring additional pockets near the active site that could be occupied to improve the first hits. The group of Prof. Ming-Ming Zhou of the Mount Sinai School of Medicine is collaborating with us in the VS program.

Contribution/Benefit of our participation in ADMIRE:
We are pleased and excited to be involved in WG2 in the COST action ADMIRE. We consider that the antagonists that might evolve from the optimization process we have initiated could constitute useful pharmacological tools for some of you to get further biochemical/pharmacological insights into the receptor, thus contributing to the innovation in this field. Additionally, our ultimate goal will be to have candidates improved enough to further progress them towards the development of new drugs (after translation). Our chemical expertise could also complement other groups within the consortium, being useful for the generation of different chemical probes for biological studies and/or diagnosis. We think that this is an excellent opportunity for us to consolidate our research work on MR, and to interact with other groups pursuing common goals in Europe. We firmly believe that the joint efforts will result in benefits to the scientific community and in last term to the society.