



## A novel paradigm for effective and safer treatment of schizophrenia: biased (ANT) agonists with a characterized polypharmacological profile (PSYBIAS)

**Project Coordinator:** Dr. Jana Selent, Research Programme on Biomedical Informatics (GRIB), Hospital del Mar Research Institute (IMIM), Barcelona, Spain

**Project Partners:**

Prof. Peter Kolb, Department of Pharmaceutical Chemistry, Philipps-Universität Marburg (UM), Marburg, Germany

Prof. Michel Bouvier, Department of Biochemistry and Molecular Medicine, University of Montreal (UdeM), Montreal, Canada

**Project aim:** The treatment of schizophrenia remains an utmost challenge: Up to 30% of patients are resistant and up to an additional 30% respond only partially to antipsychotic treatment. Most of the patients that receive treatment suffer diverse side effects. The aim of this project is to elaborate a framework for improved medication. We will use a multidisciplinary approach grounded in novel concepts such as signaling bias and polypharmacology applied to antipsychotic drug targets. Specifically, we will tackle two main objectives: On one hand, we will interrogate the implication of specific signaling pathways in distinct symptoms of SZ. Ultimately, we will translate obtained insights into lead- and drug-like candidates with an improved therapeutic profile.

**Work plan & exploitation of results:** First research efforts will be dedicated to the detection of signaling probes that are specific to individual signaling pathways applying newest computer technology, simulation/screening algorithms and validation in living cells with BRET-based biosensors. Obtained signaling probes will be used to study in vivo the association of specific pathways to symptoms of SZ (positive, negative and cognitive deficits). From here, we will develop molecular candidates which act only on SZ-implicated pathways with a characterized polypharmacological profile. This will be the starting point for the development of antipsychotic drugs superior to current treatments in terms of efficacy and safety.