UNIVERSITÀ DEGLI STUDI DI PADOVA

PROJECT

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1) Project title
In vitro pharmacological characterization of novel GPCR ligands
2)Abstract (max 500 words)
Pharmacological studies will be performed in vitro with the aim of characterizing innovative ligands for GPCR for their pharmacological activity (full and partial agonism, antagonism, inverse agonism), potency, selectivity of action, and signaling properties. The following techniques will be used: calcium mobilization, BRET assay for measuring receptor interaction with G proteins and beta arrestins, and label-free assays i.e. dynamic mass redistribution (DMR). The advantages of the DMR assay, namely comprehensive view of all the intracellular events that follow receptor activation, no need for artificial labels, high sensitivity, makes this approach of paramount importance to improve the translationability between the in vitro pharmacology and the in vivo outcomes. In addition, we intend to deeper the transducerome analysis of GPCRs with the TRUPATH biosensor platform that has been recently made available to the scientific community by the BL Roth laboratory. TRUPATH represents the most robust, complete, and thoroughly documented suite of G protein-based GPCR signaling biosensors available to date. TRUPATH will be used in the frame of this project to compare at single pathway resolution the signaling preferences of the innovative ligands investigated. These in vitro pharmacological approaches will be applied to i) the NOP and classical opioid receptors for which a long-standing and fruitful collaboration is ongoing with medicinal chemists (Guerrini, Trapella, Preti) of the University of Ferrara, ii) ectopic olfactory receptors (including Olfr78 and Olfr544) for which a novel collaboration has been established with medicinal chemists (Moro, Sturlese, Mattarei) of our department. Translational studies in the field of NOP and opioid receptors will be performed in collaboration with a large panel of experts at national, European, and international levels (see GC list of publications). Translational studies in the field of ectopic olfactory receptors will be performed in collaboration with colleagues of our Ph.D. program (Alimonti and De Martin).