

## RAPID IDENTIFICATION OF A 5-HT<sub>2c</sub> ANTAGONIST: A SYNERGIC APPROACH BASED ON MEDICINAL AND COMPUTATIONAL CHEMISTRY

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Anxiety disorders are among the most common psychiatric illnesses affecting both adults and children causing a remarkable social impact.

Serotonin (5-hydroxytryptamine, 5-HT) is known to play an important role in anxiety (1) through actions mediated by a wide family of receptors, including the 5-HT<sub>2</sub> receptors (2). Evidence supporting a role for 5-HT<sub>2</sub> receptors in anxiety arises mainly from studies showing that drugs acting as agonists at the 5-HT<sub>2c</sub> receptor present anxiogenic effects in clinical and experimental forms of anxiety.

In particular, the observation that m-chlorophenylpiperazine (mCPP), a functionally selective agonist at the 5-HT<sub>2c</sub> receptor, induces anxiety states in patients and in animal models (3), has prompted different research lines aimed at developing 5-HT<sub>2c</sub> receptor antagonists for the treatment of anxiety disorders.

Our approach to potent and selective 5-HT<sub>2c</sub> antagonist compounds based on a synergic Medicinal and Computational chemistry strategy will be reported.

### References:

1. Graeff FG *Psychopharmacology* 2002, **163**:467–476.
2. Martin JR et al. *J Pharmacol Exp Ther* 1998, **286**:913–924.
3. Kahn RS et al. *Biol Psychiatry* 1988, **23**:189–208; Jones N et al. *Psychopharmacology* 2002, **164**:214–220.