

## Pharmacological characterization of zinc interaction with 5-HT<sub>1A</sub>

Grzegorz Satała, Beata Duszyńska, Tomasz Lenda, Krystyna Nęcza, Andrzej J. Bojarski

Department of Medicinal Chemistry, Institute of Pharmacology Polish Academy of Sciences, 12 Smętna Street, 31-343 Kraków, Poland

Zinc, as an essential trace element in living organisms, plays an important role in the number of biological processes, especially within the central nervous system [1]. There is an evidence for the involvement of Zn ions in depression and so constitutes potential angle of therapy, as emphasized by numerous preclinical and clinical trials. However, its exact molecular mechanism of action is still not fully understood [2]. Our interests are focused on its effects mediated by serotonin receptors, which are key players in the etiology of anxiety and mood disorders [3].

Here we present radioligand binding assays used to characterization of the pharmacological profile of Zn<sup>2+</sup> at serotonin 5-HT<sub>1A</sub> receptor (5-HT<sub>1A</sub>R). The direct influence of Zn<sup>2+</sup> on agonist binding to human 5-HT<sub>1A</sub>R, stably expressed in HEK293 cells, was investigated by a set of *in vitro* radioligand binding methods (saturation, competition and both association and dissociation kinetic studies) using [<sup>3</sup>H]8-OH-DPAT, as a selective agonist tool compound. It has been demonstrated that in addition to previously reported negative allosteric modulation [4], for both antagonist and agonist binding, Zn<sup>2+</sup> at low concentration may also potentiate binding of endogenous serotonin to 5-HT<sub>1A</sub>R.

[1] Chasapis C.T., Loutsidou A.C., Spiliopoulou C.A. et al. *Arch. Toxicol.* 86 (2012) 521.

[2] Dickerman B., Liu J. *Topics in Clinical Nutrition.* 26 (2011) 257.

[3] Nichols D.E., Nichols C.D. *Chem Rev.* 108 (2008) 1614.

[4] Barrondo S. Salles J. *Neuropharmacology.* 56 (2009) 455.

### Acknowledgements

The study was partially supported by a grant PRELUDIUM DEC-2012/05/N/NZ7/02110 financed by the National Science Centre.