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Cooperative Properties of Zinc Binding to 5-HT7 Receptor – Pilot Studies.

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The main objective is to investigate cooperative properties of zinc ions at 5-HT7 serotonin receptor, to determine whether allosteric regulation of these ions reported at 5-HT1AR [1] is subtype selective, or it can also be detected at other representatives of serotonergic receptor family. It was shown that zinc ions are natural allosteric modulator for several different groups of G-protein coupled receptors (GPCR), such as dopamine D1 and D2, alpha1 and beta2-aderenergic [2], which suggests a more universal character of this mode of zinc ions interaction. Results of our pilot studies seem to support this hypothesis, as a cooperative properties of zinc binding to 5-HT7 receptor has been detected.
Binding of allosteric modulator promotes changes in receptor conformation, which influences the affinity of the endogenous (or other orthosteric) ligand and the formation of ligand-receptor complex. In order to study the mechanism of this interaction, changes in affinity and dissociation rate of orthosteric ligands, radioligand binding methods were used with HEK293 cell lines stably transfected with cDNA vector encoding the human serotonin 5-HT7b receptor and [3H] 5-CT as a radioligand. To the analysis of allosteric reaction results, so-called “allosteric ternary complex model” was adopted.
Both serotonin receptors and zinc ions play important functions in the central nervous system (CNS) but many aspects of their action remains unclear. In recent years, various aspects of GPCR allosterism were intensively studied, because the interaction with the receptor according to other than classical, competitive model of orthosteric ligand binding, creates new possibilities for its regulation. It is even believed, that in a longer research term, it could be an area for the search of the next generation of drugs acting on the CNS.

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[2] Gregory K.J., Sexton P.M., Christopoulos A.: *Curr. Protoc. Pharmacol*. 2010 Dec; Chapter 1: Unit 1.21.