

Dragos Ioan Inta

Dr. med.

Expression profile of 5-HT3-positive neurons in a transgenic mouse model

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Staatsexamen am 09.1999 an der Universität für Medizin und Pharmazie Targu-Mures
(Rumänien)

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Doktorvater: Frau Prof. Dr. med. H. Monyer

The family of serotonergic receptors comprises seven members of which the 5-HT₃ receptor is the only ligand-gated channel. The 5-HT₃ receptor is widely distributed in the central and peripheral nervous systems, with the 5-HT_{3A} subunit present in both systems and the 5-HT_{3B} subunit restricted to peripheral neurons. Although several studies suggested the involvement of 5-HT₃-mediated signals in various cortical and subcortical circuits, the morphological and functional characteristics of the neurons expressing this receptor are still incompletely deciphered. This is due to the sparse distribution of cortical interneurons expressing the 5-HT₃ receptors, thus hampering for electrophysiological investigations and also due to the limitations of the immunohistochemical tools used to identify this receptor.

To help in further characterization of 5-HT₃-positive neurons, we generated a transgenic mouse model, in which the *in vivo* marker green fluorescent protein (EGFP) was expressed under the

control of the 5-HT3A promoter. Using the BAC technology, the EGFP gene was inserted into the translational start of the 5-HT3A gene, in a 195 kb mouse BAC clone.

The analysis of two transgenic lines revealed a broad EGFP distribution in various brain regions, such as the cortex, amygdala, hippocampus and olfactory bulb. The specificity of the EGFP expression was suggested by immunohistochemical colocalization studies with other known markers (cholecystokinin, calretinin, calbindin) and electrophysiological data.

The 5-HT3-EGFP transgenic mouse model allowed the characterization of the developmental expression pattern of 5-HT3 receptors, revealing their expression in pioneering Cajal-Retzius cells both in the hippocampus and in the neocortex. The specific expression of EGFP in these mice in the subventricular zone and the subgranular layer of the dentate gyrus suggest that 5-HT3 receptors are important in modulating neurogenesis during adult life. Further functional studies are necessary to confirm this possible role of the 5-HT3 receptors.

The correct expression of the transgene and thus the faithful marking of 5-HT3 neurons in the developing and adult brain are a significant step forward to study this cell type at cellular and system level.