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## Developmental and adult expression of the GPR88: Establishment of its interaction with nuclear partner proteins in the cerebral cortex

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GPR88 is a neuronal orphan G-protein-coupled receptor preferentially concentrated in synaptic sites of the GABAergic MSNs, highlighting a neurotransmission role for GPR88 in MSNs which play a central role in a wide array of psychomotor functions subserved by the basal ganglia. However, no extensive description of its developmental expression has been provided so far. We reported that GPR88 protein is initially detected at embryonic day 16 (E16) in the rat striatal primordium. From E16-E20 to adulthood, the highest expression levels of both protein and mRNA are observed in striatum, olfactory tubercle, nucleus accumbens, amygdala, and neocortex. We also observed an intracellular redistribution of GPR88 during cortical lamination. In the cortical plate, GPR88 presents a classical GPCR plasma membrane/cytoplasmic localization that shift, on the day of rat birth, to nuclei of neurons progressively settling in layers V to II. This intranuclear localization remains throughout adulthood and was also detected in mouse, monkey and human cortex. Transfections of GPR88 fluorescent chimeras into the rat cortical neurons demonstrated that nuclear localization depends on the I3 and C-terminus domains. GPR88 protein has no known NLS motifs, suggesting that GPR88 is driven into the cell nucleus by partner proteins. A yeast two-hybrid screen on a mouse brain cDNA library enabled to identify nuclear proteins including ATRX, TOP2B and BAZ2B as potential partners of GPR88. The results of proximity ligation assay experiments on neuronal cultures of cortex from WT and KO-GPR88 mice have validated the interaction of GPR88 with these nuclear proteins which are involved in the chromatin remodeling. The current description of the GPR88 subcellular expression may provide precious functional insights into this novel receptor. Furthermore, the GPR88 nuclear localization suggests nonclassical GPCR modes of action of the protein that could be relevant for cortical development and psychiatric disorders.

### Biography

Rebeillard F is a Doctor in Pharmacy and a first year PhD student. With his Medical and Scientific training his area of expertise includes pharmacology and health while integrating both fundamental science/research and patients care. This distinctive project about the unusual working principle of a nuclear GPCR is motivated by the need of supporting fundamental/academic research, and hopefully providing new openings for psychiatric treatments to improve patients' lives.

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