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GPR40 as a target to modulate hypothalamic adult newborn cells

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Abstract

Statement of the Problem: There is extensive experimental evidence that high fat diet-induced obesity is accompanied by functional and structural alterations in the hypothalamus, the central structure involved in the control of caloric intake and energy homeostasis. Depending on time and magnitude of hypothalamic damage, key neurons involved in the regulation of food intake and energy expenditure can undergo apoptosis. Studies have shown that under physiological conditions, postnatal neurogenesis contributes to the maintenance of the number of neurons in the adult hypothalamus, influencing the energy homeostasis control. Previous studies have shown that polyunsaturated fatty acids induce an increase in the number of proliferating cells and mature neurons in the hypothalamus which seems to be mediated by activation of the GPR40 receptor (a free fatty acid receptor). Therefore, we hypothesized that GPR40 might play an important role in regulating the adult hypothalamic neuroplasticity involved in energy homeostasis control. Methodology & Theoretical Orientation: We used agonists and antagonist of the GPR40 in in vivo and in vitro models to study cell proliferation and differentiation of hypothalamic neural progenitor cells (NPC). Findings: GPR40 receptor agonist increased NPC proliferation in the hypothalamus of adult mice, as well as cell differentiation. In vitro, the agonist increased the number of neurospheres in isolated adult hypothalamic NPC, while the antagonist decreased the number of formed neurospheres. Additionally, embryonic hypothalamic mouse NPC treated with GPR40 agonist, during 18 days of differentiation, generated a higher number of mature neurons. Conclusion & Significance: Our results indicate that the GPR40 may be an interesting target to modulate hypothalamic structural plasticity improving energy homeostasis control in obesity.

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Biography

Daiane has been dedicated to evaluate the effect of metabolism disruption over the central nervous system. Particularly, her research focus has been in the adult neural precursor cells and their therapeutical potential in neurodegenerative conditions. Daiane graduated in Pharmacy and Biochemistry, had a MsC degree in Neuroscience and PhD in Biochemistry. Her recent projects evaluate the effect of cholesterol metabolism and obesity over hippocampal and hypothalamic adult neural precursor cells.

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