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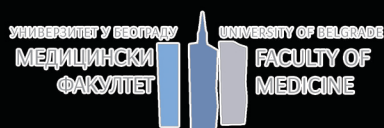


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**Editors**

Selma Kanazir and Danijela Savić

**Assistant editors:**

Anica Živković  
Željko Pavković

**Technical editor:**

Anđela Vukojević

**Graphic design:**

Olga Dubljević, Irina Veselinović

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## GnRHR signaling in neuronal cells: *in vitro* and *in vivo* data

Ana Milosevic<sup>1</sup>, Katarina Milosevic<sup>1</sup>, Ljiljana Nikolic<sup>1</sup>, Jelena Bogdanovic Pristov<sup>2</sup>, Iva Bozic<sup>1</sup>, Anica Zivkovic<sup>1</sup>, Irena Lavrnja<sup>1</sup>, Danijela Savic<sup>1</sup>, Marija Janjic<sup>1</sup>, Ivana Bjelobaba<sup>1</sup>

<sup>1</sup>*Institute for Biological Research “Siniša Stanković”, National Institute of the Republic of Serbia, University of Belgrade, Belgrade, Serbia*

<sup>2</sup>*Institute for Multidisciplinary Research, University of Belgrade, Belgrade, Serbia*

\*[ana.milosevic@ibiss.bg.ac.rs](mailto:ana.milosevic@ibiss.bg.ac.rs)

Gonadotropin-releasing hormone (GnRH) is a hypothalamic decapeptide that controls mammalian reproduction by acting on its receptor (GnRHR) expressed on pituitary gonadotrope cells. While GnRHR signaling in gonadotropes is well described, knowledge of GnRHR activation-related events at extrapituitary sites including neurons is limited. It was proposed that GnRH analogs (GnRH<sub>a</sub>) induce distinct changes in hippocampal gene expression, emotional processes, and cognitive functions.

To explore neuronal GnRHR signaling we used the human neuroblastoma cell line SH-SY5Y. Further, we explored the regional expression of *Gnrhr* in rat brain and investigated the expression of several relevant genes in the hippocampus and preoptic area of peripubertal male rats treated with GnRH<sub>a</sub>.

GnRHR is expressed in SH-SY5Y cell line, but its expression does not change after adding GnRH<sub>a</sub> in the incubation media. Electrophysiological recordings confirmed that GnRH<sub>a</sub> induced membrane depolarization but could not evoke action potentials. In the rat brain, *Gnrhr* expression could be detected in the hippocampus, amygdala, and hypothalamus, including the preoptic area. Prolonged treatment of peripubertal rats with GnRH<sub>a</sub> had no effect on the expression of genes in the hippocampus previously shown to be affected in the sheep model of delayed puberty.

These results imply that neuronal GnRHR is either differently coupled (not coupled with G<sub>q/11</sub> protein), or that its membrane density is too low to induce transcriptional events. More investigation is needed to elucidate the role(s) of GnRH-GnRHR signaling in the brain.

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