

Pharmacoperone IN3 enhances the apoptotic effect of leuprolide in prostate cancer cells by increasing the gonadotropin-releasing hormone receptor in the cell membrane

Sánchez, Catherine A.

Mercado, Alejandro J.

Contreras, Héctor R.

Cabezas, Juan C.

Huidobro, Christian C.

Castellón, Enrique A.

Gonadotropin-releasing hormone (GnRH) agonists are widely used for the treatment of advanced prostate cancer (PCa). Agonists activate the GnRH receptor (GnRH-R), triggering apoptosis in PCa cells. In gonadotropes, the amount of GnRH-R in the plasma membrane is regulated by protein folding and endoplasmic reticulum retention, mechanisms that can be overcome by the pharmacoperone IN3. Our aim was to describe the intracellular distribution of GnRH-R in PCa cells and its relation to response to GnRH analog treatments. The expressions of GnRH-R in PCa biopsies were evaluated by immunohistochemistry and the intracellular distribution was determined by immunofluorescence in primary cell cultures from human PCa samples. Cultured cells were pretreated with IN3 and then with leuprolide. Cell survival was evaluated by 1-(4,5-dimethylthiazol-2-yl)-3,5-diphenylformazan (MTT) thiazolyl blue formazan and cell cycle and apoptosis by flow cytometry. We observed that the expression of GnRH-R decreased