Subcellular Localization of Histamine H3 Receptor in Human Mammary Cells

Vanina A Medina[(1)], Maximo Croci[(2)], Nora A Mohamad[(1)], Ernesto JV Crescenti[(2)], Rosa M Bergoc[(1)], Elena S Rivera[(1)].

[(1)]Radioisotopes Laboratory, School of Pharmacy and Biochemistry, University of Buenos Aires. Buenos Aires, 1113, ARGENTINA.
[(2)] Immunooncology Institute, 3200 Córdoba Av., Buenos Aires, 1187, ARGENTINA.

We have reported the expression of histamine (HA) H3 and H4 receptors (H3R, H4R) in non-tumorigenic (HBL-100) and tumorigenic (MDA-MB-231) breast cell lines and also in benign and malignant lesions from human mammary gland. In MDA-MB-231 cells HA modulates proliferation in a concentration dependent manner through H3R and H4R. In this work we evaluated the modulation of the H3R expression and its cellular localization after treatment with HA, H3R ligands or starvation in MDA-MB-231 cells. The cellular localization of H3R was determined by immunocytochemistry using two antibodies (Alpha Diagnostic and Sigma) against the human H3R and FITC-conjugated secondary antibody. On intact and permeabilized cells, nuclei were stained with ethidium bromide and fluorescence was observed under confocal microscopy. The semiquantification was performed by flow cytometry. Results demonstrate a very low H3R detection in intact cells while, permeabilization allows detection. Only a few untreated permeabilized cells showed H3R immunoreactivity especially with cytoplasmic localization. Serum deprivation and 10 μM HA treatment considerable increased the H3R expression in all cells, within the intracellular compartment with nuclear and perinuclear localization. 10 μM Imetit and Clobenpropit addition increased the H3R expression. The former with H3R immunoreactivity localized in nucleus and preferentially in plasma membrane while the later augmented the H3R expression with nuclear and perinuclear localization. These intracellular localizations of the H3R were confirmed in permeabilized HBL-100 cells and in benign and malignant breast lesions determined by immunohistochemistry. To our knowledge, this is the first report that describes the modulation of the H3R expression and cellular localization of the human H3R under different proliferative stimuli. The precise mechanism involved in these effects remains unknown and may represent a novel way for the regulation of H3R signaling.