Effects of ERK1/2/5 and PKA pathway inhibitors on GPR30-specific agonist suppression of LH secretion from bovine anterior pituitary

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Picomolar concentrations of estradiol produce the rapid suppression of GnRH-induced LH secretion from the bovine anterior pituitary (AP) via GPR30 as non-genomic manner. However, no research has investigated the cytoplasmic mechanism for rapid estradiol suppression of LH secretion from AP cells. ERK1/2/5 pathway and PKA pathway were reported as important pathways for genomic effect of estradiol in lactotroph. However, it is not clear whether PKA pathway and ERK1/2/5 pathway are the pathways in the downstream of GPR30 to suppress LH secretion in non-genomic mechanism. Therefore, this study was conducted to test the hypothesis that ERK1/2/5 or PKA pathways were the important pathway for estradiol mediated by GPR30 to suppress GnRH-induced LH release from bovine AP through rapid, non-genomic manner. The bovine AP cells (n = 8) were cultured for 3 days in steroid-free conditions. The AP cells were treated with either 1 μM of ERK1/2/5 inhibitor (U1026) or 5 μM of PKA inhibitor (H89) or both inhibitors for 30 min, then, also with 0.01 nM estradiol or GPR30-specific agonist, G1, for 5 min before GnRH stimulation. Pre-treatment with 0.01 nM estradiol or G1 in the absence of inhibitors treatment suppressed GnRH-stimulated LH secretion significantly (P<0.01). In contrast, pre-treatment with 0.01 nM estradiol in the presence of U0126 alone, H89 alone, or both inhibitors had no suppressive effect on GnRH-stimulated LH secretion. Therefore, both ERK1/2/5 pathway and PKA pathway are important for the rapid non-genomic suppression of estradiol on the GnRH-induced LH secretion from bovine AP cells.