

droxysteroid dehydrogenase, also inhibited hCG-induced PACAP gene expression. Similarly, in preovulatory follicles cultured in serum-free medium, treatment with both RU486 and epostane inhibited LH-induced PACAP gene expression in a dose-dependent manner. We further evaluated the role of PR in the control of PACAP promoter activity by transfections of preovulatory granulosa cells with PACAP promoter gene using *luciferase* gene reporter system. Treatment with LH resulted in a marked increase (10-fold) in PACAP promoter activity. Addition of RU486 or epostane dose-dependently inhibited LH action on the stimulation of PACAP promoter activity. The present results indicate that LH exerts its action on the induction of PACAP gene expression through the endogenous activation of PR in rat preovulatory follicles.

P-46 **Role of MAP Kinase Activation in Gonadotropin-induced
Expression of Pituitary Adenylate Cyclase-Activating
Polypeptide Gene in Preovulatory Follicles
of Rat Ovary**

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Pituitary adenylate cyclase-activating polypeptide (PACAP) is a novel neuropeptide with considerable homology to vasoactive intestinal peptide and growth hormone-releasing hormone. Because we have shown previously that gonadotropins induce a transient induction of PACAP in preovulatory follicles (*Endocrinology* 1999 140:818), the present studies evaluated the role of MAP kinase activation in gonadotropin action on the induction of PACAP gene expression in cultured rat preovulatory follicles obtained from ovaries treated with PMSG for 2 days. Treatment of cultured follicles with PD98059, an inhibitor of ERK, suppressed the LH-stimulated PACAP gene expression in a dose-dependent manner. Similarly, treatment with SB203580, an inhibitor of p38 kinase, also suppressed the LH-stimulated PACAP gene expression. Western analysis using phospho-specific antibodies revealed that activation of ERK occurred between 3-6 h after LH treatment. In contrast, the basal levels of the activated forms of p38 kinase and JNK was high at the time of incubation (0 h) and remained constant until 3 h after LH treatment. Assay of MAP kinase activity demonstrated an increase within 10 min. and at 3 h after LH treatment. The present results indicate that the activation of MAP kinase, possibly ERK, is necessary for LH action in the induction PACAP gene in preovulatory follicles.