Abstract

To elucidate the impact of glucocorticoids on ovarian steroidogenesis and its molecular mechanism by focusing on bone morphogenetic proteins (BMPs), we examined the effect of dexamethasone (Dex) on estradiol and progesterone synthesis by using primary culture of rat granulosa cells. It was revealed that Dex treatment dose-dependently decreased estradiol production but increased progesterone production induced by follicle-stimulating hormone (FSH) by granulosa cells. In accordance with the effects of Dex on estradiol synthesis, Dex suppressed P450arom mRNA expression and cAMP synthesis induced by FSH. Dex treatment in turn enhanced basal as well as FSH-induced levels of mRNAs encoding the enzymes for progesterone synthesis including P450scc and 3βHSD but not StAR and 20αHSD. Of note, Dex treatment significantly upregulated transcription of the BMP target gene Id-1 and Smad1/5/9 phosphorylation in the presence of BMP-15 among the key ovarian BMP ligands. It was also found that Dex treatment increased the expression level of BMP type-I receptor ALK-6 among the type-I and -II receptors for BMP-15. Inhibitory Smad6/7 expression was not affected by Dex treatment. On the other hand, BMP-15 treatment upregulated glucocorticoid receptor (GR) expression in

1 granulosa cells. Collectively, it was revealed that glucocorticoids elicit
2 differential effects on ovarian steroidogenesis, in which GR and BMP-15 actions
3 are mutually enhanced in granulosa cells.