Autocrini/paracrine effects of inhibin and activin in chicken ovary

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ABSTRACT

Bone morphogenetic proteins (BMPs) and their receptors (BMPRs) are now known to have important roles in mammalian ovarian folliculogenesis. This study determined the expression of the mRNA encoding for BMPs and their receptors in the chicken ovary and explored possible roles for them. The expression of the mRNA for BMP-2, -4, -6, -7, and BMPR-IA, -IB, and -II was determined and quantified by a semiquantitative RT-PCR. The mRNAs for all the BMPs and receptors determined were present in both the granulosa (G) and theca (T) cells of the F1, F2, and F3 follicles. All BMP mRNAs increased in G cells with follicular development, whereas only BMP-7 mRNA had this trend in the T cells. BMP-2, -4, and -6 mRNAs in T were similar between follicles. BMPR-IA mRNA was similar in F2G and F3G but lower in F1G. BMPR-IB mRNA was similar in G of all follicles, and BMPR-II mRNA increased with development. In the T, each receptor subtype showed equal distribution between follicles. mRNA levels for BMPR-IB and -II were higher in G than in T, suggesting that the G is a major target for BMPs. BMP-4 and -7 stimulated basal, IGF-I-, and gonadotropin-stimulated progesterone production by cultured G cells, with differential responses between cells from the F1 and F3/4. This suggests involvement in follicular differentiation. BMP-4 and -7 reversed the inhibitory effects of transforming growth factor (TGF)- on basal and gonadotropin-stimulated G cell progesterone production, with greater effect in the F1 than in the F3/4. This effect suggests an important role for BMPs interacting with TGF- in modulating the effects of gonadotropins and IGF-I on follicular differentiation. Finally, BMP-7 stimulated G cell proliferation, but BMP-4 inhibited TGF- + IGF-I- and/or FSH-stimulated G cell proliferation, suggesting a role in the control of follicular growth during development. These effects of BMP-4 and -7 on the G cell function showed relationships with the expression levels of the BMPs and the BMPR-II.
chicken; bone morphogenetic proteins; bone morphogenetic protein receptors; theca; steroidogenesis

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THE BONE MORPHOGENETIC PROTEINS (BMP) are a group of growth and differentiating factors belonging to the transforming growth factor- superfamily. By molecular cloning, at least 15 members of the group have been identified and are called BMP-2 through BMP-15. The BMPs signal via complexes of serine/threonine kinase types I and II receptors that have been designated BMPR-IA, BMPR-IB, and BMPR-II. In vertebrates, the BMPs have been implicated in several functions during both embryonic and postembryonic life. These functions include formation of bones, cartilage (25), neurons (1), teeth (7), eyes, kidney (8), and feathers (2). They are also involved in the delivery of positional information, including organogenesis, tissue patterning, and remodeling (14, 32). However, a virtually unexplored role in the reproductive tissues is emerging. Recently, it was shown that the BMPs and their receptors are involved in the autocrine/paracrine regulation of ovarian folliculogenesis in some mammals. BMP-2,

-4, -6, -7, and -15, and their receptors have been specifically implicated in rat, sheep, and cattle ovarian function. In rat, the mRNA encoding BMP-4 and -7 are expressed in the theca, whereas those encoding the BMP-6 and BMP-15 are confined to the oocytes of the follicles. All BMPRs are expressed in the granulosa, theca, and oocyte (4, 11, 28). In this species, BMP-4, -7, and -15 regulate granulosa cell steroidogenesis, whereas BMP-6 and -15 induce cell proliferation (10, 21, 22, 28). In sheep, a crucial role for the BMPs in the regulation of ovarian folliculogenesis has been established since the discovery that the presence of heterozygous mutation in the BMP-15 gene results in improved prolificacy in Inverdale, known as FecX, ewes (5). On the other hand, carrying Q249R mutations in the BMPR-IB also confers improved prolificacy on Booroola, or FecB, ewes (15, 31). Except for BMP-15, there is a dearth of information on the types of BMPs that are expressed in the sheep ovary and their functional significance. Souza et al. (30) reported the localization of BMPR-IA, -IB, and -II in the granulosa (G) and to a lesser extent in the theca (T) of the sheep ovary. These authors and Wilson et al. (37) have demonstrated that BMP-2 and -4 regulated G cell steroidogenesis in sheep.

In the avian species, the gene expression or a role for the BMPs in the ovary is still unexplored. Previous studies have shown that other growth factors, such as IGF-I, EGF, TGF- , TNF- , and FGF, are expressed in the chicken ovary and perform important roles alone or in their interaction with LH, FSH, or GH in the regulation of follicle growth and differentiation (17–19, 24, 39). The aim of the current study was to determine the expression of mRNA encoding BMP-2, -4, -6, and -7 and of their receptors BMPR-IA, -IB, and -II in the chicken ovary. Having found the transcripts of the BMPs and BMPRs, we further determined the effects of two of the highly expressed BMPs, BMP-4 and -7, on G cell progesterone production and proliferation in culture. The effects of their interaction with LH, FSH, and other growth factors (IGF-I, IGF-II, and TGF-) on these functions were also determined.