

Relationship between bone morphogenetic protein-15 (BMP-15) and formation of the hyaluronan-rich cumulus-oophorus extracellular matrix (ECM).

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It is well known that bidirectional communication between cumulus cells and oocyte is necessary for oocyte cytoplasmic maturation and subsequent developmental competence. Factors secreted by the oocyte, including BMP-15, have been shown to be implicated in the regulation of follicular cell functions. However, the complex role of BMP15 within the oocyte-cumulus complexes (OCCs) is not fully understood. To elucidate the molecular mechanisms of BMP-15 action on the regulation of the FSH/LH signaling pathway in porcine OCCs cultured *in vitro*, we investigated the effect of BMP-15 on FSH/LH -induced 1/ cumulus expansion by stereomicroscopy; 2/ hyaluronan (HA) synthesis by OCCs by radioimmunoassay (RIA); 3/ expression of oocyte maturation-related transcripts (*AREG*, *CCND2*, *CD44*, *CYP11A1*, *HAS2*, *PCNA*, *PTGS2*, *STAR* and *TNFAIP6*) at different time points of the cultivation by real-time RT-PCR; and 4/ progesterone (P4) production either by OCCs or granulosa cells (GCs) by RIA. **Results:** We found that gonadotropin-stimulated OCCs in the presence of BMP-15 were 1/ full-expanded and formed elastic cumulus extracellular matrix (ECM); 2/ amount of HA retained within the ECM was significantly increased compared to FSH/LH alone (65% versus 35%, respectively). 3/ Moreover, BMP-15 enhanced FSH/LH-induced expression of the cumulus-related transcripts such as *TNFAIP6* and *AREG* (both after 16 h) and *CYP11A1* (after 24 h). 4/ Surprisingly, BMP-15 markedly increased (~69%) FSH/LH-stimulated P4 secretion by OCCs compared to FSH/LH alone, while BMP-15 caused a significant decrease (about 35%) in FSH/LH-induced P4 release by GCs. **Conclusions:** We have shown that addition of BMP-15 as well as differences in culture conditions, such as the absence or presence of serum, strongly affect the structural organization of oocyte-cumulus ECM and consequently the functionality of cumulus cells surrounding the oocyte. To our knowledge, this is the first study demonstrating the relationship between BMP-15 and formation of the HA-rich cumulus-oophorus ECM.