STUDIES OF THE ACTIVIN PATHWAY IN DOMINANT AND SUBORDINATE BOVINE FOLLICLES BEFORE, DURING AND AFTER SELECTION

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In monovulatory species such as cattle, one of a cohort of developing follicles assumes dominancy and continues to grow in each follicular wave. After dominant follicle selection, pituitary-derived FSH levels decrease through a negative feedback loop mediated by oestradiol and inhibin A produced by the dominant follicle. The dominant follicle itself only requires very low basal levels of FSH, thus escaping atresia which is the fate of the subordinate follicles. The mechanisms involved in dominant follicle (DF) selection remain unclear. Most studies have focused on the stages following selection. To investigate what roles activin and inhibin play in DF selection we looked at the quantitative changes in the expression of the genes coding for the activin/inhibin subunits (*Inhibin α, βA* and *βB*) as well as other genes in the activin pathway (*SMAD2, ActRIIA/B, follistatin (FST), FSHR*). We examined mRNA levels in follicular granulosa cells (GCs) before (d1.5), during (d2.5) and after (d3.5 and 7) DF selection using real-time RT-PCR. Prior to DF selection, highest levels of *inhibin βA, FST and SMAD2* transcripts converged on the largest follicles. *Inhibin α*, *ActRIIA/B* and *FSHR* levels did not correlate with follicular size at this stage. At Day 2.5, highest levels of *inhibin βA, inhibin α, FST and SMAD2* transcripts were seen in a single putative DF. *ActRIIA/B* and *FSHR* did not show any difference between follicles. By Days 3.5 and 7, a dramatic difference in expression levels of *inhibin βA, inhibin α and FST* were seen in DF compared to SF. Yet in absolute terms *inhibin βA* levels decreased after selection, whereas *inhibin α* levels increased. *Inhibin βB* expression was only detected in Day 7 GCs and was significantly higher in the DF. These results suggest a shift from an activin environment during the pre and peri-DF selection period, to an inhibin environment following DF selection. Inhibin/activin protein levels in the follicular fluid using western ligand blotting confirmed this. We postulate that the higher activin activity within DF influences the selection mechanism as activin and inhibin have been shown to play a role in gonadotropin regulation in the ovary around the time of selection.

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