

IMPACT OF FSH ON SMALL GROWING FOLLICLES IN VITRO: FOCUS ON THE ESTRADIOL (E2) AND ANTI MULLERIAN HORMONE (AMH) BALANCE

cadoret, veronique^{1,2}; Jarrier-Gaillard, Peggy¹; Frapsauce, Cynthia²; Locatelli, Yann¹; Monniaux, Danielle¹; Guerif, Fabrice^{2,1}; Dalbies-Tran, Rozenn¹

¹PRC, UMR85, INRA, CNRS, IFCE, Université de Tours, F-37380 Nouzilly, France, ²CHU Bretonneau, Médecine et Biologie de la Reproduction-CECOS, F-37044 Tours, France

A pivotal stage in early follicular development is the formation of an antral cavity, preceding the switch between anti-Müllerian hormone (AMH) and estradiol (E2) production, which reflects differentiation of granulosa cells. The role of FSH in regulating these changes and the interaction between these three hormones remains poorly understood. Using a recently validated sheep model of culture of individual follicles from the preantral stage (200µm) to the antral stage (up to 800µm) over a 20-day-long period, we have studied the effects of FSH onto follicle basal development. In vitro AMH expression was hardly affected throughout culture while AMH secretion per follicular cell decreased, in contrast with the strong activation that occurs in in vivo growing follicles. Culture of the follicles in control medium induced FSH receptor and CYP19A1 (aromatase) gene activation, coherent with E2 accumulation in the medium. In parallel, the ESR2/ESR1 ratio of estradiol receptors increased. Since ESR2 has been previously reported to repress AMH transcription, this could mediate an inhibiting effect of E2 on AMH expression. Supplementation with FSH promoted follicular growth and antrum formation, while it did not affect granulosa cell proliferation. It stimulated expression of FSH receptor in small antral follicles, but had no effect onto AMH expression or secretion. Finally, FSH strongly stimulated aromatase expression and secretion of E2. Overall, our results suggest that the culture of sheep preantral follicles induces early FSH sensitization and stimulation of the estradiol system, with a preferential expression the ESR2 receptor reported to downregulate AMH expression. Adding FSH does not lift in vitro induced blocking of AMH expression, while it stimulates antrum formation, FSH receptor expression and E2 production. Overall, FSH enhances culture induced precocious differentiation of the follicle.