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Effect of pharmacological inhibition of Progesterone receptors PGRMC1 and nPR on bovine oocyte meiosis

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Abstract

Folliculogenesis is the process which leads to the acquisition of the oocyte developmental competence and to its maturation. Both aspects are the result of oocyte and follicular cells interplay (Luciano *et al.*, 2004).

Recent studies in cattle describe Progesterone (P4) as a key molecule acting during follicle development through different signaling pathways involving different receptors (Aparicio *et al.*, 2011, Nilsson *et al.*, 2009). The aim of this study is to evaluate the effect on oocyte meiotic maturation of inhibiting two P4 receptors: Progesterone Receptor Membrane Component 1 (PGRMC1) and the classic nuclear Progesterone Receptor (nPR) respectively using the specific inhibitors AG205 and Aglepristone. Bovine cumulus cell-oocyte complexes (COCs) and denuded oocytes (DOs) were in vitro matured with different concentrations of AG205. Our results showed a decrease both in first polar body (PBI) extrusion and in the percentage of oocytes reaching MII stage in treated oocytes compared to controls (one way ANOVA, $P<0.05$); these effects were more marked in DOs, confirming PGRMC1 specific role in the oocyte. In AG205 treated oocytes aberrant meiotic figures were observed, including double metaphase plates or DNA scattered in the ooplasm. In addition, aberrant meiotic plates showed irregular co-localization of PGRMC1 and AURKB; the proteins didn't localize at the centromeric region of each chromosomes as previously described (Luciano *et al.*, 2013). This results suggests a P4 role in meiotic division mediated by PGRMC1 receptor.

By contrast, Aglepristone inhibition of nPR didn't affect dramatically the percentage of oocytes reaching MII stage of maturation. However, MII plates morphology analysis showed a significantly greater tubulin spindle length. This feature could account for the previously described reduced in vitro embryo development consequent to nPR inhibition (Aparicio *et al.*, 2011). Thus, P4 driven nuclear maturation could act on different oocyte development stages. Further studies are in progress to elucidate P4 complex action in mammalian oocyte function.

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