

Impact of eCG/anti-eCG antibodies complexes on the signalling pathways induced by FSHR

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Introduction: In dairy of goats, treatments associating a progestogen and the equine Chorionic Gonadotropin (eCG) are the easiest way to induce and synchronize estrus and ovulation. The injection of eCG induces, in some females, the production of anti-eCG antibodies (Abs). In most cases, antibodies negatively modulate the LH and FSH bioactivities of the eCG, leading to poor fertility of the treated females. Nevertheless, we have shown that some antibodies, when complexed to eCG, positively modulated the LH and FSH bioactivities and improved fertility after treatment (Hervé *et al.*, 2004). This potentiating effect is observed only with eCG/anti-eCG Abs complexes. The aim of our study is to analyse the impact of these complexes on the intracellular signalling pathways induced by the FSHR; namely cAMP/PKA and β -arrestins pathways.

Methodology: First, we have investigated the effect of various eCG/Abs complexes on the phosphorylation of ERK (Extracellular-signal Regulated Kinases), a pathway which is stimulated by both pathways. Second, we studied the effect of the eCG/Abs complexes on cAMP production. Third, we utilized pharmacological tools and siRNA, to specifically inhibit cAMP/PKA or β -arrestins pathways, allowing us to understand their respective contributions to the potentiating effects of the complexes.

Results and Discussion: The results showed that, in all cases, the potentiating effects were observed on ERK phosphorylation whereas it was not systematically linked to an increase in cAMP production. We suggest that some eCG/Abs complexes can selectively modulate cAMP/PKA and β -arrestin pathways, depending on antibodies properties. We hypothesised that the binding of Abs on eCG probably changes the hormone's conformation.

Conclusion: Such modifications induced by the complexes on the signalling pathways could explain the biological effects observed *in vivo*.