B4GALNT2, A NEW MAJOR FECUNDITY GENE IN THE LACAUNE OVINE BREED

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In the Lacaune sheep breed, the large variation in ovulation rate and then litter size (between 1 and 7 lambs) is explained by the segregation of the FecLmutation. This mutation was recently shown to induce the ovarian ectopic expression of the B4GALNT2 gene encoding for a glycosylation enzyme with GalNac transferase activity. The specific glycosylation activity of B4GALNT2 checked by the Dolichos Biflorus Agglutinin (DBA) lectin was observed only in FecLmutated ovaries. B4GALNT2 target glycoproteins were purified from follicular fluids by lectin DBA affinity and identified by mass spectrometry. Among them were the inhibin alpha (INHA) and beta A (INHBA) subunits, generating inhibin A and activin A hormones. We thus considered these two proteins as strong physiological candidates to explain the increased prolificacy of FecLewes. While granulosa cell INHA and INHBA expression at the mRNA or protein levels was not drastically affected by FecL, Inhibin A accumulation was higher in FecL follicular fluids. Intriguingly, circulating Inhibin A concentration was 3 fold-lower in FecL plasma without incidence on gonadotropin hormone levels. These observations suggest a direct consequence of the glycosylation on the paracrine activity of inhibin/activin A mainly at the ovarian level. To conclude, we propose that the atypical glycosylation of inhibin A by B4GALNT2 in the ovary is a new mechanism of ovulation rate regulation in sheep, and could contribute to open new fields of investigation to understand women infertility pathogenesis.