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Author(s)	BELLO, Taiwo Kamar-deen
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Abstract of the dissertation

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氏名：BELLO Taiwo Kamar-deen
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学位論文題名

Effects of osteopontin therapy at the first insemination after calving to improve fertility in dairy cows
and the underlying changes in epidermal growth factor and leptin receptors in the endometrium
(分娩後初回授精時の乳牛に対するオステオポンチン投与による受胎性改善効果とその背景と
なる子宮内膜での上皮成長因子およびレプチン受容体の変化)

Delayed recovery of cyclic changes in endometrial epidermal growth factor (EGF) concentration is associated with low conception rates after the first insemination following parturition. An intravaginal infusion of OPN normalizes the EGF profile and improves fertility in repeat breeder (RB) cows. Therefore, the present study determined whether this treatment can restore normal EGF profile in postpartum cows and improve fertility. First, the effects of recombinant osteopontin (rOPN) and OPN peptide were examined. In cows with abnormal EGF profiles, treatment with both rOPN and OPN peptides increased the normalization rate of EGF profile (78.3% and 53.1%, respectively) and conception rates (47.8% and 61.2%, respectively), with the rates being higher than those of the control group (25.0% and 20.0%, respectively). Second, the effects of combined OPN and hormonal therapy, an established treatment for this abnormality in RB cows, were investigated. Cows were treated with OPN peptide (320 nmol or 1,600 nmol) alone and in combination with hormonal therapy. The combined treatment significantly increased EGF normalization and conception rates compared to the peptide alone (40.5% vs. 21.9% and 35.1% vs. 19.0%, respectively). However, the EGF normalization and conception rates were lower than previously reported and may be attributed to heat stress, as this study was conducted

during the summer period. The combined treatment achieved the highest conception rate among all groups, including those that received 1,600 nmol OPN peptide with or without hormonal therapy. Additionally, the results showed that the beneficial effects of OPN on EGF normalization and fertility restoration were reduced during the summer, suggesting the involvement of heat-stress-related mechanisms. It has been known that RB cows' resistance to treatment to normalize endometrial EGF concentrations is associated with increased leptin receptor (Ob-R) expression, which is part of the leptin system linking metabolism and reproduction. Therefore, I hypothesized that a similar mechanism underlies the reduced therapeutic effect of OPN during the hot season in high-yielding cows at first postpartum insemination. This study investigated the relationship between Ob-R expression and EGF concentration in the endometrium. In this study, endometrial biopsies (winter, n=5; summer, n=7) for EGF assay and Ob-R expression were collected on day 3 of the estrous cycle. In the winter period, a positive linear association was observed between the EGF concentration and Ob-R, as indicated by the regression equation ($y = 46604x + 4.3275$). The correlation analysis showed a positive correlation ($r = 0.73$), which was statistically significant ($P < 0.05$). In contrast, no significant association was detected between EGF concentration and Ob-R in the summer period. These results suggest that the association between EGF and Ob-R is present during winter but disrupted during the summer in postpartum cows. In conclusion, these results indicate that although the OPN peptide alone improves fertility, combining it with hormonal therapy may be a better option for cows at the first insemination following parturition. Additionally, while the OPN-based therapies improve endometrial function and fertility in postpartum cows, heat stress may impair the leptin-EGF axis, thereby limiting therapeutic efficacy during the hot season.