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Endometrial Mucin-1 Expression Increases In Mid-Diestrus Following PG-600 Administration in sheep

Hayder M.H. Habeeb[1,*], Ann Ramsey[2] & Michelle A. Kutzler [3]

[1]Department of Animal Production, College of Agriculture, Al-Qasim Green University, Babylon, Iraq 51001

[2]Carlson College of Veterinary Medicine, Oregon State University, Corvallis, Oregon, USA 97331

[3]Department of Animal and Rangeland Sciences, Oregon State University, Corvallis, Oregon, USA 97331

***Corresponding author email: H.M.H.H.**: Hayder.Habeeb@agre.uoqasim.edu.iq; **A.R.**: annramsey101@gmail.com; **M.A.K.**: Mihchelle.Kutzler@oregonstate.edu

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Abstract: Mucin-1 (MUC-1) is an anti-adhesion glycoprotein expressed on the apical surface of the endometrial luminal and glandular epithelium which prevents interactions between the trophectoderm and endometrial epithelium. The aim of this study was to investigate the outcome of PG-600 on ovine endometrial MUC-1 immunoexpression during early and mid-diestrus. Twenty-four cycling ewes (Polypay) were administered progesterone for 9 days. Two days before progesterone withdrawal, ewes were treated with cloprostenol. At progesterone withdrawal (d0), ewes were treated with either PG-600 (5 mL) or saline (5 mL) group. Endometrial tissues were collected surgically on days 4 and 7 after PG-600 or saline (n=6/group/timepoint) and were subjected to immunohistochemistry followed by image acquisition. Stained area for MUC-1 was quantified using Image J. The diestrous intercaruncular endometrium of both treated and control ewes expressed MUC-1. However, the percent area expressing MUC-1 varied between endometrial area (luminal and superficial glandular epithelium), time (day four, day 7), and treatment group. PG-600 treatment increased MUC-1 expression in the luminal epithelium on day 7 and in the superficial glandular epithelium expression on day 4. The results of this study show that administration of PG-600 to ewes increases endometrial MUC-1 expression in mid diestrus, which provides a possible mechanism for lower fertility found following treatment by PG-600 in sheep.

Keywords: Endometrium,Iimmunohistochemistry, luminal epithelium, Pregnancy loss, Sheep .

Introduction

Ewes are seasonal short-daylight breeders, which means they have estrous cycles and ovulate at times of reduced daylight but do not come into estrus and ovulate at times of longer daylight (Bartlewski *et al*., 1999). The reproductive efficiency of the ewes can improve throughout the year using hormonal methods to induce estrous cyclicity and ovulation in the non-breeding season (Umberger *et al*., 1994; D'Souza *et al*., 2014; Habeeb *et al*., 2020). PG-600® is a commercially available drug that contains 40 IU/mL human chorionic gonadotropin and 80 IU/mL equine chorionic gonadotropin. PG-600 is marketed for inducing estrus in pigs but used off label in sheep as well (Cross *et*

al., 2019; Habeeb *et al*., 2020). Equine chorionic gonadotropin, similar to follicle stimulating hormone (FSH), interacts with its receptor on ovarian granulosa cells to induce follicle development and growth (Tisdall *et al*., 1995). A previous report concluded that PG-600 delivered to ewes to induce estrous cyclicity decreased fertility rates (Habeeb *et al*., 2019). The cause of the reduced pregnancy rates was not examined in that report, but it may be due to changes in the early maternal-embryo interaction.

Mucins are glycosylated proteins produced by specialized epithelial cells throughout the body including the respiratory tract, gastrointestinal tract, and reproductive tract (Tabak, 2010; Jonckheere et al., 2021). Throughout various periods of the reproductive cycle, mucin-1 (MUC-1), an anti-adhesion glycoprotein, is expressed on the luminal and glandular epithelium of the endometrium (Margarit et al., 2010; Song *et al*., 2012). This has been reported in baboons (Hild-Petito *et al*., 1996; Ren *et al*., 2010), swine (Bowen *et al.,* 1996), rodents (Carson *et al*., 2000), human (Carson *et al*., 2000), and sheep (Johnson *et al*., 2001). Prior to embryo attachment, MUC-1 plays an essential role in forming a protective barrier on the endometrial epithelium to prevent pathogen entry (Brayman *et al*., 2004). However, MUC-1 can also impede embryo attachment by preventing connections between the endometrial tissue and embryonic trophectoderm (Aplin, 1997).

Embryonic attachment is a carefully orchestrated event occurring between embryo and endometrium in the first stage of pregnancy (Guillomot *et al*., 1981). MUC-1 expression normally declines in the uterine luminal epithelium in ewes around day seven from estrus, which would allow embryonic attachment if pregnancy occurs (Dharmaraj *et al*., 2009). However, dysregulation in hormone production or receptor expression at this stage of gestation can result in a reduced pregnancy rate or failure it (Johnson *et al*., 2001). For example, estradiol treatment increased MUC-1 expression in cultured sheep endometrial epithelial cells and resulted in decreased blastocyst adhesion rate (Wang *et al*., 2018). There have been no studies investigating the impact of PG-600 administration on endometrial expression of MUC-1 in any species. The aim of this study is to investigate the outcome of PG-600 on ovine endometrial MUC-1 immunoexpression during early and mid-diestrus. We hypothesized that PG-600 would increase endometrial MUC-1 expression compared to control group.

Materials & Methods

Animals and tissue sampling

The oversight for the ethical use of animals for research was approved by Oregon State University (#5036). Twenty-four Polypay ewes during the breeding season were treated with progesterone (Eazi-Breed® , Zoetis, Kalamazoo, MI, USA) for 9 days. Two days prior to progesterone removal (d-2), ewes were intramuscularly injected with cloprostenol to remove any corpora lutea might be present (125 µg, Estrumate®, Intervet/Merck Animal Health, Madison, NJ, USA). At the time of progesterone removal (d0), ewes were randomized into treatment (3.3±1.6 years) and control groups (3.0±1.4 years) to receive PG-600 (5 mL; Intervet/Merck Animal Health) or an equal volume of saline, respectively. Endometrial tissues were collected on days 4 (d4) and 7 (d7) after PG-600 or saline treatment (six ewes per group per day). Endometrial tissue samples were surgically obtained from all ewes. The details of this procedure have been previously reported (Habeeb *et al*., 2023). Briefly, ewes were anesthetized by diazepam

and ketamine intravenous injection, and isoflurane was used to maintain anesthesia. After clipping, ewes were sterilely prepared for a laparotomy. For each animal and each ovary, the number of corpora lutea were counted. The uterine horn was opened on the same side as the ovary with the largest quantity of corpora lutea and intercaruncular endometrial tissue was collected. Samples were kept in formalin (10%) until processed for immunohistochemistry.

Immunohistochemistry

Formalin-fixed paraffin-embedded endometrial tissues were cut (5 μm) onto charged slides. A series of xylene and graded ethanol baths were used on all sections for deparaffinization and rehydration stages, respectively. Washing steps were performed by using wash buffer (#S3006). Heat-induced antigen retrieval with sodium citrate buffer (#S1699, Dako) was used to expose epitopes. After that, deionized water was used for washing the sections and then hydrogen peroxide (3%) was used to block endogenous peroxidase. A serum-free protein block was applied for 20 minutes at 37°C (#X0909, Dako). Anti-rabbit MUC-1 antibody (Polyclonal #ab104978, Abcam, Cambridge, MA, USA) was added (1:50) for 2 hours at 37°C. Negative controls were treated in a comparable manner using the Universal Negative Control Rabbit IgG (#NC495H, Biocare Medical, Pacheco, CA, USA). The ovine endometrium itself served as a positive control for MUC-1 as previously documented by Raheem *et al*., (2016). Following washing, a secondary antibody was incubated with all tissue sections for 30 minutes at 37°C (#IH-8064 ImmunoBiosCience, Mukilteo, WA, USA). All sections were then incubated with NovaRED (Vector Laboratories, Burlingame, CA, USA) for 4 minutes at 37°C. Sections were finally washed in wash buffer, counterstained with hematoxylin, washed in tap water, dehydrated in ethanol, passed through three consecutive xylene baths, and cover slipped.

Image acquisition and quantitative analysis

Sections were examined by using bright field microscopy (Leica DM4000B) at 400X magnification. Images of the endometrial luminal and superficial glandular epithelium from each tissue section (3-5 images per animal) were taken by a digital camera (QICAM 12-bit, #QIC-F-M-12-C, QImaging, Surrey, BC) and analyzed (QCapturePro, QImaging). The percent area stained for MUC-1 was quantitatively determined by a single observer blinded to treatment group using Image J software. Images were transformed to greyscale using the RGB stack function and staining was isolated using manual thresholding kept consistent at 175/193. For each animal, five measurements were collected from each area of interest (endometrial luminal and superficial glandular epithelium) using rotated rectangles of uniform dimensions (150X142 pixels) and orientation. Rectangles were placed in areas of interest to achieve measurements representative of staining in the overall area. Fraction of threshold area (FTA) was then recorded.

Data analysis

Endometrial MUC-1 immunoexpression was described as mean ± standard error of the means. The effect of PG-600 treatment, day, and PG-600 treatment X day on MUC-1 expression was determined using a two-way ANOVA followed by a post hoc Tukey's test. MUC-1 expression was compared between endometrial epithelial area (luminal vs. superficial glandular) using a paired Students t test. $P<0.05$ was defined as a significant difference.

Results

The luminal (L) and superficial (S) glandular endometrial epithelium of both treated and control ewes expressed MUC-1 (Figure 1; Table 1). There was no change in MUC-1 immunoexpression within the control group between day four and day seven in the luminal and superficial glandular endometrial epithelium. However, MUC-1 immunoexpression within the treated group between day 4 and day 7 increased in the luminal epithelium (47 ± 3 FTA and 56 ± 4 FTA, respectively) and decreased in the superficial glandular endometrial epithelium (45 ± 2 FTA and 35 ± 3 FTA, respectively).

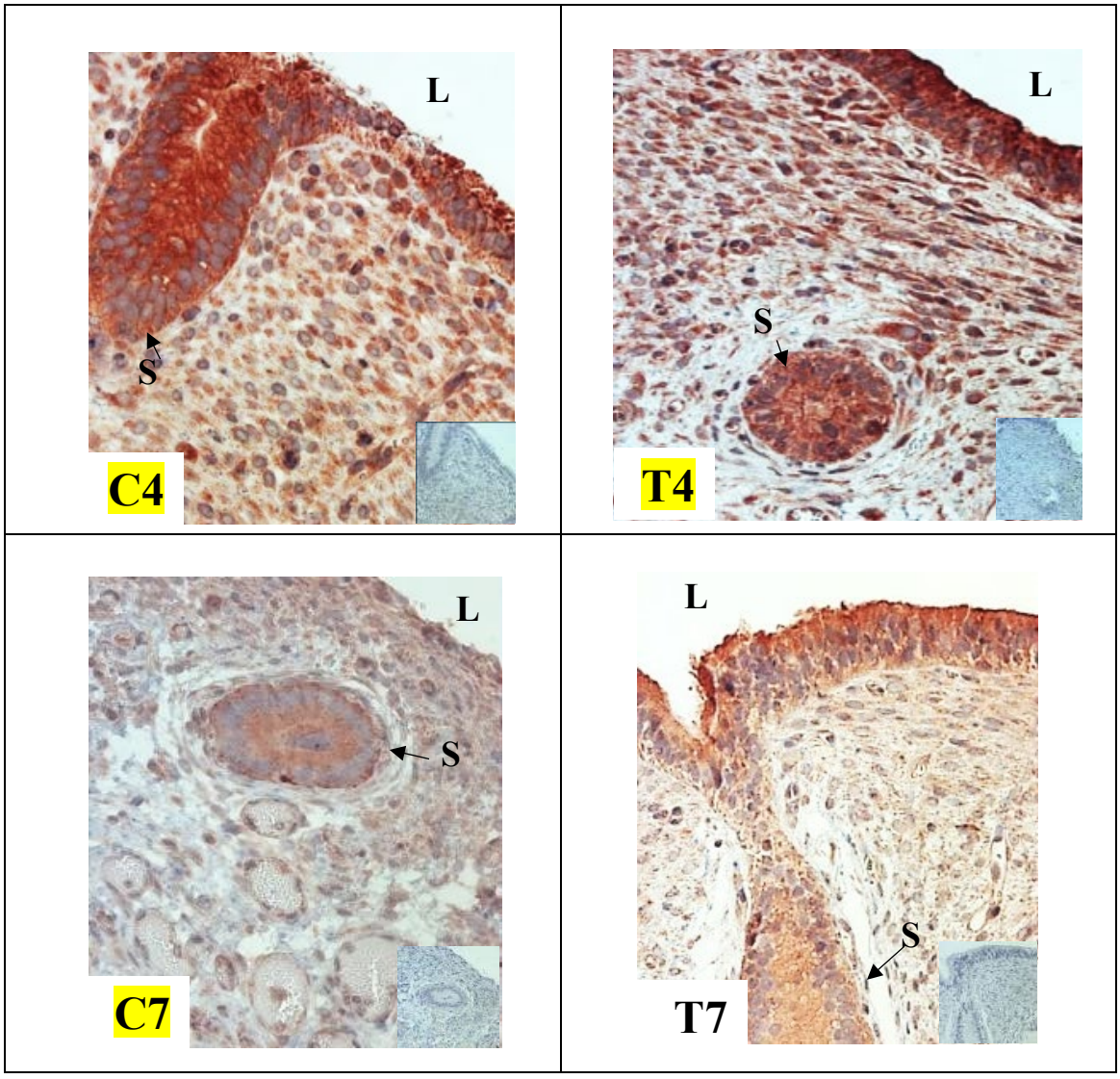

Fig. (1): Representative images of mucin-1 expression in the luminal (L) and superficial (S) glandular epithelium of the ovine intercaruncular endometrium on 4 days or 7 days following treatment with saline (control, C4 or C7, respectively) or PG-600 (treatment, T4 or T7, respectively). Red-brown (NovaRED) stain reflects mucin-1 immunoexpression. Hematoxylin was used as a counterstain. Negative IgG control section (insets).

There was also an effect between the control and treated group such that MUC-1 immunoexpression in the superficial glandular epithelium was increased on day 4 (35 ± 3 FTA and 45 ± 2 FTA, respectively) and was increased in the luminal epithelium on day 7 (32 ± 4 FTA and 56 ± 4 FTA, respectively).

Table (1): Mean ± SEM of the fraction of threshold area (FTA) immunoexpressing mucin-1 within the ovine endometrium on 4 days or 7 days following treatment with saline (C4 or C7, respectively) or PG-600 (T4 or T7, respectively).

Characters	Mucin-1 immunoexpression, FTA, Mean±SEM	Mucin-1 immunoexpression, FTA, Mean±SEM	Mucin-1 immunoexpression, FTA, Mean±SEM
Endometrial compartment	C4	T4	C7
Luminal epithelium (L)	40 ± 5 ax	47 ± 3 ax	32 ± 4 ax
Superficial glandular epithelium (S)	35 ± 3 ax	45 ± 2 ay	34 ± 4 ax

[ab]Different superscript indicates significant difference between day 4 and day 7 ($p<0.05$).
[xy]Indicates a significant difference between treated and control groups ($p<0.05$)

Discussion

Previous work with this group of sheep investigated the effects of PG-600 treatment on hormone concentrations (Habeeb *et al*., 2023). The estradiol-17 β concentration did not differ between treatment, day, or an interaction between treatment X Day (all $p>0.05$). In addition, progesterone concentration did not differ between treatment groups on d4 ($p>0.05$) but was higher irrespective of treatment on d7 ($p<0.05$). However, progesterone concentration in treated ewes was higher compared to controls on d7 ($p<0.05$). Endometrial MUC-1 is influenced by circulating progesterone concentrations (Johnson *et al*., 2001). In swine and rodents treated with exogenous progesterone, endometrial MUC-1 expression was down-regulated (Surveyor *et al*., 1995; Bowen *et al*., 1996). In the current research, circulating progesterone was significantly higher in both groups on day 7 (timing of initial embryo attachment in sheep) but instead of a down-regulation in MUC-1 expression as shown in the control group, the treated group had a rise in MUC-1 expression in the endometrial luminal epithelium.

Dysregulation of endometrial MUC-1 contributes to reduced fertility in women as well (Wu *et al*., 2018). Infertile women with polycystic ovary have higher MUC-1 expression compared to fertile women (Margarit *et al*., 2010). The higher MUC-1 expression in the PG-600 treated ewes on day seven in the current study may explain why pregnancy rates were reduced in ewes treated with PG-600 (Habeeb *et al*., 2019). This finding is also supported by work of Wang *et al*., (2018) who reported altered MUC-1 expression and a reduction in pregnancy rate following estrus induction in sheep (Wang *et al*., 2018).

Conclusion

In conclusion, PG-600 administration at the time of estrus in sheep increases MUC-1 expression in the luminal endometrial tissue at the timing of embryo attachment compared to controls. This research provides a mechanism for reduced fertility following estrus induction with PG-600 treatment in ewes.

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Contributions of authors

H.MH.H.: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

A.R.: Methodology, investigation, Writing – review & editing.

M.A.K.: Conceptualization, Formal analysis, Funding acquisition, Methodology, Resources, Supervision, Validation, Writing – original draft, Writing – review & editing.

ORCID

H.MH.H.: https://orcid.org/0000-0002-0229-9523

A.R.: https://orcid.org/0009-0005-5959-3415

M.A.K.: https://orcid.org/0000-0001-7262-8137

Conflicts of interest

The authors disclose that they have no actual or potential conflicts of interest that may affect their ability to objectively present or review research or data.

Ethical approval

The oversight for the ethical use of animals for research was approved by Oregon State University (#5036) ethical guidelines.

References

Aplin, J. D. (1997). Adhesion molecules in implantation. *Reviews of Reproduction*, *2*(2), 84–93. https://doi.org/10.1530/ROR.0.0020084

Bartlewski, P. M., Beard, A. P., & Rawlings, N. C. (1999). Ovarian function in ewes at the onset of the breeding season. *Animal Reproduction Science*, *57*(1–2), 67–88. https://doi.org/10.1016/S0378-4320(99)00060-3

Bowen, J. A., Bazer, F. W., & Burghardt, R. C. (1996). Spatial and temporal analyses of integrin and Muc-1 expression in porcine uterine epithelium and trophectoderm in vivo. *Biology of Reproduction*, *55*(5), 1098–1106. https://doi.org/10.1095/biolreprod55.5.1098

Brayman, M., Thathiah, A., & Carson, D. D. (2004). MUC1: a multifunctional cell surface component of reproductive tissue epithelia. *Reproductive Biology and Endocrinology*, *2*(4), 1-9. https://doi.org/10.1186/1477-7827-2-4

Carson, D. D., Bagchi, I., Dey, S. K., Enders, A. C., Fazleabas, A. T., Lessey, B. A., & Yoshinaga, K. (2000). Embryo implantation. *Developmental Biology*, 223(2), 217-237. https://doi.org/10.1006/dbio.2000.9767

Cross, L. J., Cross, R. M., & Stormshak, F. (2019). Optimal dose of PG600 when given to progestogen-synchronized ewes during anestrus as affected by day of the year and temperature1. *Translational Animal Science*, *3*(1), 433-442. https://doi.org/10.1093/tas/txy092

D'Souza, K. N., Rastle-Simpson, S. L., Redhead, A. K., Baptiste, Q. S., Smith, B., & Knights, M. (2014). Gonadotropin stimulation using P.G. 600?? on reproductive success of non-lactating anestrous ewes. *Animal Reproduction Science*, *148*(3–4), 115–120. https://doi.org/10.1016/j.anireprosci.2014.05.001

Dharmaraj, N., Gendler, S. J., & Carson, D. D. (2009). Expression of Human MUC1 During Early Pregnancy in the Human MUC1 Transgenic Mouse Model1. *Biology of Reproduction*, *81*(6), 1182–1188. https://doi.org/10.1095/biolreprod.109.079418

Guillomot, M., Fléchon, J. E., & Wintenberger-Torres S. (1981). Conceptus attachment in the ewe: an ultrastructural study. *Placenta*. *2*(2):169-82. https://doi.org/10.1016/s0143-4004(81)80021-5

Habeeb, H., Hazzard, T., Stormshak, F., & Kutzler, M. (2020). Ovulation, pregnancy, and lambing rates during nonbreeding season with or without exogenous gonadotropin stimulation. *Clinical Theriogenology*, *12*(1), 23–28.

Habeeb, H. M. H., Hazzard, T. M., Stormshak, F., & Kutzler, M. A. (2019). Effect of different dosages of PG-600 on ovulation and pregnancy rates in ewes during the breeding season.

Translational Animal Science, *3*(1), 429–432. https://doi.org/10.1093/tas/txy112

Habeeb, H. M. H., Kleditz, L., Hazzard, T., Bishop, C., Stormshak, F., & Kutzler, M. A. (2023). Ovine endometrial estrogen receptor expression is altered following PG-600 administration. *Veterinary Medicine and Science*, *9*(3), 1379–1384. https://doi.org/10.1002/vms3.1119

Hild-Petito, S., Fazleabas, A. T., Julian, J., & Carson, D. D. (1996). Mucin (Muc-1) expression is differentially regulated in uterine luminal and glandular epithelia of the baboon (Papio anubis). *Biology of Reproduction*, *54*(5), 939–947. https://doi.org/10.1095/BIOLREPROD54.5.939

Johnson, G. A., Bazer, F. W., Jaeger, L. A., Ka, H., Garlow, J. E., Pfarrer, C., Spencer, T. C., & Burghardt, R. C. (2001). Muc-1, integrin, and osteopontin expression during the implantation cascade in sheep. *Biology of Reproduction*, *65*(3), 820–828. https://doi.org/10.1095/biolreprod65.3.820

Jonckheere, N., Vincent, A., Neve, B., Van Seuningen, I. (2021). Mucin expression, epigenetic regulation and patient survival: A toolkit of prognostic biomarkers in epithelial cancers, *Biochimica et Biophysica Acta - Reviews on Cancer, 1876*, (1),188538, https://doi.org/10.1016/j.bbcan.2021.188538.

Margarit, L., Taylor, A., Roberts, M. H., Hopkins, L., Davies, C., Brenton, A. G., Conlan, R. S., Bunkheila, A., Joels, L., White, J. O., & Gonzalez, D. (2010). MUC1 as a discriminator between endometrium from fertile and infertile patients with PCOS and endometriosis. *The Journal of Clinical Endocrinology and Metabolism*, *95*(12), 5320–5329. https://doi.org/10.1210/JC.2010-0603

Raheem, K. A., Marei, W. F. A., Campbell, B. K., & Fouladi-Nashta, A. A. (2016). In vivo and in vitro studies of MUC1 regulation in sheep endometrium. *Theriogenology*, *85*(9), 1635-1643.https://doi.org/10.1016/j.theriogenology.2016.01.018

Ren, Q., Guan, S., Fu, J., & Wang, A. (2010). Temporal and spatial expression of Muc1 during implantation in sows. *International Journal of Molicular Sciences*, *27*(6):2322-2335. https://www.mdpi.com/1422-0067/11/6/2322

Song, G., Kim, J., Dunlap, K. A., Satterfield, M. C., Johnson, G. A., Burghardt, R. C., & Wu, G. (2012). Uterine biology in pigs and sheep. *Journal of Animal Science and Biotechnology*, *3*(23), 1-21 https://doi.org/10.1186/2049-1891-3-23

Surveyor, G. A., Gendler, S. J., Pemberton, L., Das, S. K., Chakraborty, I., Julian, J., Pimental, R. A., Wegner, C. C., Dey, S. K., & Carson, D. D. (1995). Expression and steroid hormonal control of Muc-1 in the mouse uterus. *Endocrinology*, *136*(8), 3639–3647. https://doi.org/10.1210/EN.136.8.3639

Tabak, L. A. (2010). The role of mucin-type O-glycans in eukaryotic development. *Seminars in Cell & Developmental Biology*, *21*(6), 616–621. https://doi.org/10.1016/J.SEMCDB.2010.02.001

Tisdall, D. J., Watanabe, K., Hudson, N. L., Smith, P., & McNatty, K. P. (1995). FSH receptor gene expression during ovarian follicle development in sheep. *Journal of Molecular Endocrinology*, *15*(3), 273–281. https://doi.org/10.1677/jme.0.0150273

Umberger, S. H., Jabbar, G., & Lewis, G. S. (1994). Seasonally anovulatory ewes fail to respond to progestogen treatment in the absence of gonadotropin stimulation. *Theriogenology, 42*(8), 1329–1336. https://doi.org/10.1016/0093-691X(94)90253-F

Wang, X., Zhu, B., Xiong, S., Sheng, X., Qi, X., Huang, Q., Chen, C., Guo, Y., & Ni, H. (2018). Expression and function of MUC1 in uterine tissues during early pregnancy in sheep after natural oestrous or artificially-induced oestrous. *Theriogenology*, *108*, 339–347. https://doi.org/10.1016/j.theriogenology.2017.12.030

Wu, F., Chen, X., Liu, Y., Liang, B., Xu, H., Li, T. C., & Wang, C. C. (2018). Decreased MUC1 in endometrium is an independent receptivity marker in recurrent implantation failure during implantation window. *Reproductive Biology and Endocrinology*, *16*(1), 1–7. https://doi.org/10.1186/s12958-018-0379-1

ارتفاع تعبير ال MUC-1 في بطانة الرحم الأغنام في وسط فترة انتهاء الشبق بعد المعاملة ب PG-600

حيدر محمد حسن حبيب[1]، ان رمزي[2]، ميشيل كتزلر[3]

[1] قسم الإنتاج الحيواني، جامعة القاسم الخضراء، بابل، العراق 51001

[2] كلية كارلسون للطب البيطري، جامعة ولاية اوريغون، كورفالس، اوريغون، الولايات المتحدة الامريكية 97331

[3] قسم علوم الحيوان والمراعي، جامعة ولاية اوريغون، كورفالس، اوريغون، الولايات المتحدة الامريكية97331

المستخلص: ان MUC−1 هو بروتين سكري مضاد للالتصاق يعبر عنه على الخلايا اللمعية والغدية السطحية لظهارة الرحم مما يمنع الارتباط بين الجنين وبطانة الرحم. ان الهدف من الدراسة الحالية هو لدراسة تأثير المعاملة ب PG−600 على التعبير المناعي النسيجي ل MUC−1 في بداية ووسط دورة الشبق. تم معاملة اربع وعشرين نعجة نوع Polypay بالبروجستيرون لمدة 9 أيام, وقبل يومين من سحب البروجسترون، عولجت النعاج بالكلوبروستينول. عند سحب البروجسترون (d0)، عولجت النعاج إما بمجموعة PG−600 (5 مل) أو محلول ملحي (5 مل). تم جمع أنسجة بطانة الرحم جراحيًا في اليومين الرابع والسابع بعد إعطاء PG−600أو محلول ملحي (ن = 6 / مجموعة / وقت) وخضعت للمناعة الكيميائية تليها عملية التقاط الصور. تم استخدام طريقة الكيمياء المناعية النسيجية لتقدير المنطقة الملونة لـ MUC−1 باستخدام برنامج J image. أظهرت النتائج ان التعبير لل MUC−1 قد ظهر في كل من الخلايا الغديه السطحية واللمعية لظهارة الرحم للنعاج. ومع ذلك، فإن النسبة المئوية للمساحة التي أظهرت تعبير ال MUC−1 قد اختلفت معنويا بين منطقة بطانة الرحم (الظهارة الغدية اللمعية والسطحية) والوقت (اليوم الرابع، اليوم السابع)، ومجموعة العلاج. زاد علاج PG−600 من تعبير MUC−1 في الظهارة اللمعية في اليوم السابع وفي تعبير الظهارة الغدية السطحية في اليوم الرابع. تظهر نتائج هذه الدراسة أن معاملة النعاج ب PG−600 يزيد من تعبير MUC−1 لبطانة الرحم في وسط دورة الشبق، مما قد يساهم في انخفاض الخصوبة بعد المعاملة ب PG−600 في الاغنام

الكلمات المفتاحية: بطانة الرحم, الكيمياء النسيجية المناعية, الظهارة الغدية السطحية, الظهارة اللمعية, فقدان الحمل, الأغنام.