FDA Report on 2019 Antimicrobial Sales and Distribution

The US Food and Drug Administration just (December 15, 2020) released their report on 2019 sales and distribution of antimicrobials for food animal use. Although there appeared to be an increase in sales overall (up 3 percent between 2018 and 2019), this report does not give the denominator of the number of head of food producing species that those sales were intended for. Most of the drugs sold were tetracyclines for cattle and swine. There was also an uptick in sales of penicillins. For more detailed information, see the report at the link above. The Veterinary Feed Directive Rule in 2017 was instrumental in reducing overall antimicrobial sales and distribution, reflected in the trends since its implementation.
Dairy: Cryptosporidium, Rotavirus, and Coronavirus Infections on Health and Performance of Male Dairy calves

By Dale A. Moore, WSU Extension Veterinarian

More than 30 years ago when I was in residency training for food animal medicine, herd health and reproduction, one of my senior clinicians (Dr. Brad Smith of Large Animal Internal Medicine fame) asked me if I wanted to edit and write for a set of papers for a veterinary journal called Veterinary Medicine. The food animal part of the issue was to be focused on calf diarrhea. He had been asked to be section editor because of his work with Salmonella in calves. But he was pretty good at delegating work to eager residents who needed to start their academic careers with publications. It was my first time writing and being published. The rest is, well, history, and I have been working on calf disease and management ever since. You have Dr. Smith to blame for that.

My first foray into writing and doing research was on Cryptosporidium and other causes of calf diarrhea. A lot has been discovered since then. However, a bit more is added to our knowledge from a very recent advance publication in the Journal of Dairy Science that examined health and growth in male dairy calves detected with the same pathogens we wrote about in 1986. What makes this article different was that testing for these disease agents was done multiple times across the first few weeks of life.

In this Canadian study, 198 veal calves were enrolled upon arrival to the rearing facility and were evaluated daily. They were tested 3 times - Day 1, Day 7, and Day 14 after arrival. Over the 3 sampling dates, 86 percent were PCR positive for Bovine Coronavirus, 94 percent were PCR positive for Bovine Rotavirus A, 1.5 percent were PCR positive for Bovine Rotavirus B, and 57 percent were positive for Cryptosporidium parvum. Factors on arrival that were associated with Bovine Coronavirus infection included the source of the calf and its Serum Total Protein (STP). For every 1 g increase in STP, the odds of infection decreased by 35 percent.

Eighty-four percent of the calves were treated for diarrhea, but treatment was not associated with infection status at any of the sampling times. The median days to treatment for diarrhea was about 7 days. However, based on daily fecal scoring, calves spent about 33 percent of the 28 days of fecal observation with diarrhea. The proportion of days with diarrhea was associated with bodyweight on arrival (BW); as BW increased by 1 kg, the proportion of days with diarrhea decreased by 3 percent. Calves that tested positive for C. parvum at 14 days after arrival had a 24 percent increase in the proportion of days with diarrhea compared to calves that did not test positive for C. parvum at 14 days.

The median days until treatment for respiratory disease was about 20. Body weight on arrival and source of calves was associated with respiratory disease. Calves that tested positive for C. parvum at any sampling point had a higher hazard of being treated for respiratory disease than calves that tested negative for C. parvum at all 3 time points. Fifteen percent of calves died during the study and the mean days to death was 30 days with 60 percent of those deaths due to respiratory disease and on necropsy, the respiratory signs were actually due to Salmonella Dublin infections.

Some of the most interesting findings were regards to calf growth and weight gain. Calves that spent less than 25 percent of the first 28 days with diarrhea had a higher body weight at 49, 56, and 77 days of age compared to calves that had more days with diarrhea. Calves with severe diarrhea gained even less weight. Calves that tested positive for Bovine Coronavirus or C. parvum also had poorer growth compared to those that tested negative.
To sum up this work and provide some take-homes, infection status does appear to matter. Many days with diarrhea early in life mean poorer growth. Cryptosporidiosis may predispose calves to other infections, such as those causing respiratory disease signs. Any way to reduce infections, particularly with Bovine Coronavirus and C. parvum would help reduce associated days with diarrhea, subsequent respiratory disease, treatment, and poorer growth. How do we accomplish this? There are cattle vaccines designed to protect calves from coronavirus infections. If these infections are causing problems in the herd, the veterinarian and farmer should develop a protocol for effective vaccination. Biosecurity is also important, since we know that source of calves can be an issue. Perhaps consider keeping calves in single-sourced groups would be helpful in reducing transmission.

Finally, identification of calves for treatment on the farm did not appear to be the same as clinical observations made by a trained observer and, in this study, was not associated with infection status. Training those responsible for treatments on what to look for would be key to more effective treatments and perhaps more judicious use of treatments.

References

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**Dairy: What Can Gene Expression Tell Us About Response to Disease?**

By Craig McConnel, WSU Extension Veterinarian

The [WSU Field Disease Investigation Unit](https://www.wsu.edu/ext/units/disease/) and collaborators have been investigating novel ways to describe the impacts of disease in dairy cows. Understanding how cows respond immunologically to diverse insults provides us with insight into an animal’s resilience based on balancing pathogen elimination (resistance) and tissue damage (tolerance). Ultimately, resistance and tolerance to infection are integrated through stress and damage responses that regulate how tissues respond to cytokines and other cues emanating from immune cells.

Given the variability in responses to diverse diseases, identifying common, conserved resistance and tolerance mechanisms should provide insight into resilience in the face of pathogenic microbes from different sites of infection. For example, altered expression profiles of peripheral leukocyte immune regulatory genes related to trafficking, migration, adhesion, energy metabolism, inflammatory mediators, cytokines, cell survival and apoptosis have been associated with both mastitis and uterine disease.

In an initial study ([Appl An Sci, 2020, Vol 36 (6), 784-798](https://doi.org/10.7745/18092-181118)), we examined the associations among circulating white blood cell gene expression and postpartum disease (clinical metritis, co-morbidities, and associated physiological changes). Cows were 14 days in milk or less and were categorized as having clinical metritis or being healthy. White blood cell RNA was obtained from the blood of each cow, and the RNA was analyzed for expression of genes related to health. Out of an initial set of 34,625 genes in the gene expression matrix, we identified 55 genes that were predictive of health status of which 15 genes were most represented in the diseased cows as compared with the healthy cows. These genes are primarily involved in immune cell and receptor function, tissue repair, and cell signaling.
The top-ranked gene in every rank or error test was *PGLYRP1*, which encodes for peptidoglycan recognition protein 1 (PGLYRP-1). This is an important protein in the innate immune system and has been shown to kill bacteria and have effects on gram-positive and gram-negative bacteria. Other genes that were identified are responsible for a variety of molecular and biological functions and encode for host-defense antimicrobial peptides and proteins that are key in modulating the immune response. These proteins provide insight into individual and population-level markers of disease resilience that may be used to help reduce disease incidence and antibiotic use in animal production, and guide improvements in host genetic selection.

We conducted a follow-up study to assess whether four circulating white blood cell genes expressed differentially in those dairy cattle with postpartum disease, also would be expressed differentially in circulating white blood cells from a diverse set of cows with clinical mastitis (*Front Vet Sci, 2020, Vol 7*). Specifically, we hypothesized that the top ranked gene (*PGLYRP1*) within our postpartum study would be expressed differentially in peripheral leukocytes from dairy cows of different breeds, parities, days in milk, production levels and pregnancy status with and without moderate to severe mastitis (grade 2 or 3) during the post-voluntary waiting period (>50 DIM).

Interestingly, three of the four genes investigated due to their association with postpartum disease also were upregulated in cows with mastitis. They included *PGLYRP1* as well as *CATHL6* and *LCN2*. Similar to peptidoglycan recognition protein, the cathelicidin-6 protein (*CATHL6* gene) is a member of a major group of host-defense antimicrobial peptides and has demonstrated potent antimicrobial activity against gram-negative and gram-positive bacteria. Lipocalin-2 (*LCN2* gene) is also a member of a highly diverse group of proteins that participate in modelling the immune response.

Overall, these genes encompass a range of antimicrobial and immunomodulatory activities, speaking to the importance of both disease resistance and tolerance in systemic resilience. Understanding this resilience is essential for managing the health of livestock and achieving a proper balance between pathogen elimination and excessive tissue damage. In fact, host defense (antimicrobial) peptides such as CATHL6, LCN2 and PGLYRP-1 are attractive candidates for therapeutic development and represent potential alternatives to antimicrobials for infection management. They impact disease resistance through direct antimicrobial activities, and they influence disease tolerance through multifaceted immunomodulatory activities, including profound anti-infective and selective anti-inflammatory properties.

The biological properties of these host defense peptides suggest that they and their synthetic derivatives likely possess wide-ranging clinical and diagnostic potential beyond antimicrobial replacement. Although further research is warranted to explain their functional mechanisms and bioactivity in cattle, our findings suggest that these conserved elements of innate immunity have the potential to bridge disease states and target tissues in diverse dairy populations.

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**Beef: BRD -- Are We Missing Something?**

By Dale Moore, WSU Extension Veterinarian

Bovine Respiratory Disease (BRD) is the most common and costliest disease of feedlot cattle but can occur in cattle of any age. Traditionally, pen riders in the feedlot are responsible for detecting cattle that need to be examined further. Staying back from the group, not going to the bunk, and other signs could indicate that the steer is ailing, likely from BRD. Observing these kinds of clinical signs is not unique to the feedlot but is also used for group pens of dairy heifers, and many farmers
have been using clinical scoring of nose, eye, ear, and other observations to identify calves that might need treatment. In fact, UC Davis investigators developed a phone application that aids in scoring calves for BRD.

But what might we be missing? A study some time ago found that many steers that went to harvest were found to have lung lesions but had never been pulled for treatment. In that study, Thompson and others (2006) reported clinical disease observed in 23 percent of the feedlot calves while 43 percent had lung lesions at harvest. A very recent study (November 2020) in the Journal of Animal Science looked at clinical scoring in addition to lung ultrasound and their association with some blood parameters and calf weight gain.

The collaborators from Ireland and the US Meat Animal Research Center in Nebraska studied 153, 200-day-old beef calves. They examined the mixed-lot calves at arrival to the feedlot and followed them for 65 days. Although no lung consolidation was detected by ultrasound in the calves on arrival, one-third of the calves developed lung consolidation of more than one cm-squared during the first 28 days after arrival.

On the day they detected BRD by ultrasound identification of lung consolidation, white blood cell numbers were much greater in BRD calves compared with healthy calves. The average daily gain (ADG) across the two months of follow-up did not differ between calves that had positive clinical scores and those that did not. However, calves with lung consolidation identified by ultrasound had lower ADG from arrival until day 28 compared to healthy calves without lung consolidation (0.22 lb per day versus 1.2 lbs per day). However, no differences in ADG were across the entire two-month period. This latter finding was likely because 81% of the cases of BRD were detected by 14 days after arrival and treated if they were classified with BRD based on clinical scores.

Traditional methods to diagnose BRD may not do a good job of detecting calves with lung lesions. Thoracic ultrasound, in combination with clinical signs may do a better job of detecting BRD early, give a better chance of treatment to work, before calves develop chronic pneumonia.
Melatonin - we think of it as a sleep aid or to help us with jet lag but in sheep it has some other uses, important to reproduction and maybe even lamb survival. Melatonin is produced by the pineal gland, a small endocrine (hormone producing) gland located in the middle of the brain. Melatonin is derived from serotonin and helps to modulate sleep cycles and seasonal cycles in animals. This hormone is sometimes used to induce another breeding cycle in seasonal breeding animals, like sheep. In people, there is some evidence that it might help protect the cardiovascular system, specifically the heart and blood pressure.

Thirty-percent of twin lambs may die before weaning in range sheep. About one-half of these deaths are likely due to prolonged lambing or difficult birth and the subsequent neonatal hypoxia that develops in the lambs. This hypoxia can lead to neurological damage and other consequences such as a taxed cardiovascular system of the newborns. In addition, small lambs suffer more from cold stress.

In an Australian study of range Merino sheep, investigators ran a clinical trial to determine if supplementing ewes that were 70 to 90 days pregnant with a slow-release implant with melatonin would influence lamb survival. Previous work in more controlled environments found that supplementing pregnant ewes with melatonin reduced the adverse effects of post-lambing hypoxia on the neonatal brain.

About 50 pregnant mixed age ewes were implanted with 1 and about 50 with 2 slow-release melatonin implants. About 50 control ewes received no supplementation. Investigators monitored the ewes twice daily throughout the lambing period. They evaluated lamb survival, body weight, and rectal temperature at birth. They evaluated serum immunoglobulin G (IgG) and looked at overall lamb survival and weight at 30 and 70 days of age.

Lamb survival was greater in those born to supplemented ewes compared to controls (about 95 to 98 percent compared to 83 percent) up to 3 days after birth. Up to 70 days of age, lamb survival was about 92 to 94 percent compared to 80 percent. Melatonin did not affect birthweight or growth. When investigating the specific reasons for lamb mortality, the rates of dystocia, stillbirth and birth injury were greater in the control lambs.

The authors’ conclusions were that “supplementing pregnant twin-bearing Merino ewes with melatonin may be a practical strategy to reduce neonatal mortality and improve weaning rates in
extensively managed sheep flocks”. They noted that replicating this study would be important since their sample size was small.

In a follow-up study, the same investigators studied the effects when providing ewes with fed melatonin capsules from day 80 of gestation to birth on both singleton and twin offspring. Although there were no treatment effects on singleton lambs, melatonin supplementation increased the survival of twin lambs from birth to weaning. In particular, the second-born lambs born to treated ewes survived better than those born to control ewes (82 vs. 57 percent survival). In addition, second-born twins of treated ewes involved in a long lambing (more than 90 min), survived better than lambs from control ewes (87 vs. 43 percent).

With more data in hand, there appears to be some significant effects on twin lamb survival in these populations of sheep. The economics of the use of these products needs to be considered first and repeat studies would help to confirm the effects in different populations of sheep.

Reference

Swine: FDA Approves Genetically Modified Pig for Food
By Dale Moore, WSU Extension Veterinarian

FDA has approved a genetically modified pig for food. The line of pigs are called GalSafe, and are missing the alpha-gal sugar on the surface of the pigs’ cells, to which some people are allergic. For details, see the [FDA Press Release](https://www.fda.gov/news-events/press-announcements/fda-approves-genetically-modified-pig-food).

WSU Ag Animal Faculty Research Updates


Modeling realistic human decision-making is an important feature of good policy design processes. The use of an agent-based modeling framework allows for quantitative human decision-models that assume fully rational agents. This research introduces a dynamic human decision-making submodel. The parameterisation of human memory and “rationality” in a decision-making model represents an important extension of decision-making in ABMs. A data driven model of herd movement within a dynamic natural environment is the context for evaluating the cognitive decision-making model. The natural and human environments are linked via memory and rationality that affect herdsmen decision-making to vaccinate cattle using a once-for-life vaccine (Rift Valley fever) and an annual booster vaccine (Contagious Bovine Pleuropneumonia). The simulation model uses environmental data from Samburu county, Kenya from 2004 to 2015. The cognitive parameters of memory and “rationality” are shown to successfully differentiate between vaccination decisions.
that are characterized by annual and once-for-life choices. The preliminary specifications and findings from the dynamic cognition-pastoralist agent-based model (PastoralScape) indicate that the model offers much to livestock vaccination modeling among small-scale herders.

https://doi.org/10.15232/aas.2020-02092

Objective: The aim of this study was to describe associations between peripheral leukocyte gene expression and early postpartum disease in dairy cows with clinical metritis. 

Methods: The study was conducted in a conventional dairy in Washington state. Diseased cows ≤ 14 DIM were enrolled (n = 11) based on evidence of clinical metritis with or without comorbidity or prior treatments. Healthy cows (n = 9) were selected based on comparative DIM and lactation numbers to diseased cows. Blood was collected for a complete blood count, serum biochemistry, leukocyte isolation, and RNA extraction at enrollment and twice more at 6- to 8-d intervals.

Results and Discussion: A total of 34,625 genes were considered and 55 were associated with health status by the Boruta all-relevant feature machine learning selection algorithm. These were filtered to the 15 most representative genes within the diseased cohort as compared with the healthy cohort. The top ranked gene during every rank or error test was PGLYRP1. Its associated protein, peptidoglycan recognition protein 1, and other immunomodulatory molecules associated with this study selectively enhance or alter host innate immune defense mechanisms and modulate pathogen-induced inflammatory responses.

Implications and Applications: Host-defense peptides such as those associated with this study provide insight into individual and population-level markers of disease resilience that may help improve therapeutics, guide genetic selection, and clarify the burden of disease on animal well-being. This is particularly relevant to the dairy cow transition period with its metabolic and physiologic changes and associated increase in disease susceptibility.


Specifically designed gene expression studies can be used to prioritize candidate genes and identify novel biomarkers affecting resilience against mastitis and other diseases in dairy cattle. The primary goal of this study was to assess whether specific peripheral leukocyte genes expressed differentially in a previous study of dairy cattle with postpartum disease, also would be expressed differentially in peripheral leukocytes from a diverse set of different dairy cattle with moderate to severe clinical mastitis. Four genes were selected for this study due to their differential expression in a previous transcriptomic analysis of circulating leukocytes from dairy cows with and without evidence of early postpartum disease. An additional 15 genes were included based on their cellular, immunologic, and inflammatory functions associated with resistance and tolerance to mastitis. This fixed cohort study was conducted on a conventional dairy in Washington state. Cows > 50 days in milk (DIM) with mastitis (n = 12) were enrolled along with healthy cows (n = 8) selected to match the DIM and lactation numbers of mastitic cows. Blood was collected for a complete blood count (CBC), serum biochemistry, leukocyte isolation, and RNA extraction on the day of enrollment and twice more at 6 to 8-days intervals. Latent class analysis was performed to discriminate healthy vs. mastitic cows and to describe disease resolution. RNA samples were processed by the Primate Diagnostic Services Laboratory (University of Washington, Seattle, WA). Gene expression analysis was performed using the Nanostring System (Nanostring Technologies, Seattle, Washington, USA). Of the four genes (C5AR1, CATHL6, LCN2, and PGLYRP1) with evidence of upregulation in cows with mastitis, three of those genes (CATHL6, LCN2, and PGLYRP1) were investigated due to their previously identified association with postpartum disease. These genes are responsible for
immunomodulatory molecules that selectively enhance or alter host innate immune defense mechanisms and modulate pathogen-induced inflammatory responses. Although further research is warranted to explain their functional mechanisms and bioactivity in cattle, our findings suggest that these conserved elements of innate immunity have the potential to bridge disease states and target tissues in diverse dairy populations.


The goal was to investigate the relationship among mRNA expressions of anti-Müllerian hormone (AMH), follicle-stimulating hormone receptor (FSHR) and responses to superovulation (SO) in embryo donor dairy cows. Holstein cows (n = 19) were submitted to a standard SO protocol, with twice daily FSH treatments, and artificially inseminated. Prior to SO (Day 0), relative mRNA expressions of AMH and FSHR in blood were determined for all cows. Day 7 embryos were collected and were graded to determine superovulatory response for each donor. Results showed that relative mRNA expressions of AMH and FSHR were positively correlated (R2 = 0.94). Relative mRNA expressions of both AMH and FSHR were positively correlated with total embryos (R2 = 0.68 and 0.69, respectively), total transferable embryos (R2 = 0.92 and 0.97, respectively) and total grade 1 embryos (R2 = 0.54 and 0.59, respectively). Further, transcript abundances of AMH and FSHR positively associated with milk production of donor cows, and meanwhile, they were negatively associated with days in milk (DIM) at submission of cows to SO (p < .05) protocol. The relative mRNA expression of AMH was higher (p < .05) in donor cows <5 years of age. However, age of donor at superovulation did not influence mRNA expression of FSHR. Collectively, we infer that the mRNA expressions of AMH and FSHR prior to superovulation can predict donor cows' positive response to superovulation.


The objective of this study was to compare effects of gastrointestinal parasite control over a long vs short term (PC-LT vs. PC-ST) on fecal parasite load, body condition and pregnancy in beef cows. On Day 0, fecal samples were collected from Angus cross cows (n = 1462) and they were assigned a body condition score (BCS: 1, emaciated; 9, Obese) and randomly divided into two groups (within location) to receive extended-release eprinomectin [PC-LT; n = 749; 50 mg/50 kg body weight (BW)] or pour-on ivermectin (PC-ST; n = 713; 25 mg/50 kg BW). All cows were synchronized with CO-Synch + CIDR [100 μg GnRH + progesterone vaginal insert (CIDR) application on Day 20, CIDR removal +25 mg PGF2a on Day 27, and artificial insemination +100 μg GnRH on Day 30 (66 h after CIDR removal)] protocol, artificially inseminated (AI; Day 30) and on Day 44, exposed to breeding bulls (1:40 bull to cow ratio) for the remainder of the 85 day breeding season. On Day 90, a second fecal sample was collected from all cows and the cows were examined to determine pregnancy/AI (P/AI). All cows were assigned a BCS on Day 180 and re-examined to determine pregnancy/breeding season (P/BS). Worm egg count per gram of feces (FEG) was determined by McMaster method. There were no differences (P > 0.1) between PC-LT and PC-ST groups on Day 0 for FEG (46.9 ± 13.1 vs 42.6 ± 15.2, respectively; mean ± SEM) or BCS (5.95 ± 0.12 vs 6.00 ± 0.20). The mean FEG (PC-LT, 12.3 ± 4.7 vs. PC-ST, 131.3 ± 10.9) on Day 90 and BCS (PC-LT, 6.04 ± 0.07 vs. PC-ST, 5.79 ± 0.13) on Day 180 differed (P < 0.05) between the two groups. Mean P/AI [PC-LT, 62.9 %; (471/749) vs PC-ST, 57.4 %; (409/713)] and P/BS [PC-LT, 92.9 % (696/749) vs PC-ST, 90.0 (642/713)] also differed (P < 0.05). Lower FEG at Day 90 resulted in moderate to good body condition at Day 180 and cows with moderate to good body condition at Day 180 had higher P/BS. In conclusion, lower worm burden with long-term parasite control reduced FEG and improved BCS, P/AI and P/BS.
Mean estrous response rate (%ERR) and pregnancy/AI percentages (%P/AI) were determined after imposing split-time AI (STAI) and fixed time AI (FTAI) following 14-d controlled internal drug release (CIDR)+PGF2α or 5-d Select Synch + CIDR regimens. In Experiment 1, 1152 heifers (five locations) were randomly assigned to 14- or 5-d and to 54 + 74- or 64 + 84-h STAI treatment combinations. Estrous detection patches were affixed at PGF2α administration (19 day after- and on day 5 at- CIDR removal for 14- and 5-d regimens, respectively), assessed at 54- or 64-h and again at 74- or 84-h after PGF2α. Heifers determined to be in estrus at respective times were inseminated and non-estrous heifers at 74- or 84-h were given GnRH and inseminated concomitantly. The %ERR between 54 + 74- and 64 + 84-h STAI combinations differed (73.2 % and 78.8 %, respectively; P < 0.05), but %P/AI did not. In Experiment 2, 2014 heifers (eight locations) were randomly assigned to 14- or 5-d regimens and were inseminated split-time (64+84-h combination, similar to Experiment 1) or at fixed time (72- or 56-h after PGF2α for 14- or 5-d regimens, respectively). There were differences (P < 0.01) between STAI and FTAI treatments for %ERR (81.3 % and 64.4 %) and %P/AI (61.2 % and 55.4 %). Estrous synchronization regimen by AI treatment interaction (P < 0.05) showed that the %ERR were 79.8 %, 82.6 %, 66.2 % and 62.8 % and the %P/AI were 58.9 %, 63.4 %, 56.5 % and 56.5 % (for 14-d/STAI, 5-d/STAI, 14-d/FTAI and 5-d/FTAI, respectively). In conclusion, the 5-d CIDR with 64+84-h STAI combination was the most effective because of the greater %P/AI when this regimen was imposed.

7) Kasimanickam RK, Kasimanickam VR. IFNT, ISGs, PPARs, RXRs and MUC1 in day 16 embryo and endometrium of repeat-breeder cows, with or without subclinical endometritis. Theriogenology. 2020 Sep 3;158:39-49.

Interferon-τ (IFNT), IFN stimulated genes (ISG15, CTSL1, RSAD2, SLC2A1, CXCL10, and SLC27A6), Peroxisome proliferator activated receptors (PPARA, D, and G), Retinoic acid receptors (RXRA, B, and G), and Mucin-1 (MUC1) play decisive roles in embryo elongation. The objective was to elucidate expressions of these genes in day 16 embryo [tubular (n = 4) vs. filamentous (n = 4)] and corresponding endometrium [without (n = 4) vs. with subclinical endometritis (SCE; n = 4)] of repeat breeder Holstein cows (2 × 2 factorial design). Results showed that the mRNA abundances (except PPARA and RXRB) were greater (P < 0.05) in filamentous embryo and endometrium without SCE compared with tubular embryo and endometrium with SCE, respectively. Overall, the mRNA abundances (except RSAD2, PPARA and RXRA) in filamentous embryo and corresponding endometrium of cows without SCE were greater (P < 0.05) than tubular embryo and corresponding endometrium of cows with SCE. Proteins IFNT, ISGs, PPARs and RXRs (except RXRB) were greater (P < 0.05) and protein MUC1 was lower (P < 0.01) in filamentous embryo and corresponding endometrium of cows without SCE compared to tubular embryo and corresponding endometrium of cows with SCE. On pairwise comparison, mRNA and protein abundances of MUC1 significantly differed between tubular embryo in uterus with or without SCE, and corresponding endometrium with or without SCE (P < 0.05). In conclusion, the mRNA and protein abundances of IFNT, ISG15, CXCL10, PPARG and MUC1 differed among filamentous and tubular conceptuses, and endometrium with or without SCE of repeat breeder cows on Day 16, indicating that these genes and their downstream signaling cascades play important roles in embryo elongation. Perhaps, interruptions in cross-talk between endometrium and conceptus impaired conceptus elongation in repeat breeder cows with SCE. In addition to disrupted signaling, the tubular conceptus (compared to filamentous conceptus) was unable to downregulate MUC1 (anti-adhesive glycocalyx) in repeat breeder cows with or without SCE, resulting in early embryonic demise.
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