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Evaluation of the innate immune response of Angus heifers with genetic marker variation for intramuscular fat deposition following a lipopolysaccharide challenge ☆, ☆☆

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ABSTRACT

This study evaluated the effect of genetic selection for markers related to marbling deposition in Angus heifers on the immune response following a lipopolysaccharide (LPS) challenge. Fall-born heifers (n=19; ~7 months of age, 274±24 kg) with genetic variation for marbling were utilized including 10 heifers with no genetic markers (No-MVP) and 9 heifers with ≥1 markers (1+MVP). Genotypic variation for quantitative trait loci QG1 and QG2 heifers was determined. Twenty-four hour (h) prior to the LPS challenge, heifers were fitted with jugular catheters and vaginal temperature (VT) monitoring devices. Temperature monitoring devises were programed to record VT in 1 min intervals. On day (d) 0, 2 h prior to LPS challenge and 8 h post challenge, serum was collected in 0.5 h intervals (0800–1800 h). Serum was also collected at 12, 16, 20, and 24 h post LPS challenge. The LPS challenge was administered to the heifers at 1000 h via intravenous bolus (0.5 μg/kg BW). Serum was analyzed for cortisol, TNF-α, IL-6, IFN-γ, and haptoglobin (HAPT). A treatment × time interaction existed ($P \leq 0.001$) for VT; prior the LPS challenge, VT was similar. Vaginal temperature was elevated from 6 to 21 h post-LPS in 1+MVP compared to No-MVP. A treatment × time interaction ($P=0.02$) was observed for IFN-γ. Prior to the LPS challenge, IFN-γ concentrations were similar between the two groups. However, 3.5–7 h post-LPS concentrations of IFN-γ were greater ($P \leq 0.05$) for 1+MVP compared to No-MVP. There was no treatment effect ($P \geq 0.17$) for cortisol, TNF-α or IL-6. A treatment effect ($P=0.02$) was observed for HAPT; 1+MVP had decreased HAPT compared to No-MVP. Overall, results suggest that heifers selected based upon genetic markers for marbling may have an altered immune in response when challenged with LPS.

1. Introduction

With the mapping of the bovine genome, numerous quantitative trait loci for important production traits of cattle have been identified and as such, commercially available DNA marker assisted tests are available for cattle producers. A primary DNA marker assisted test available is the GeneSTAR® Molecular Value Predictions (GS-MVP; Zoetis, NJ) which is a 56-marker panel utilized to evaluate three core management traits of beef cattle; feed efficiency, marbling, and tenderness. For marbling, two markers have been identified to estimate marbling: QG1, which is *TG5*, a single-nucleotide polymorphism upstream from the start of the first exon of thyroglobulin, and QG2, which is an anonymous SNP (Van Eenennaam et al., 2007). The *TG5* favorable allele T has been associated with increases in marbling scores and accounts for 6.5%

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of the residual variance for the marbling phenotype (Barendse, 1999).

Intramuscular adipose tissue is directly related to beef quality (USDA quality grades), enhanced flavor, and an overall improvement in consumer satisfaction of beef. However, in the living system, intramuscular adipose tissue provides an important source of triacylglycerols during periods of increased energy demand (Shaw et al., 2010). Human kinesiology researchers have reported that a 2 h cycling event at 60% maximum oxygen uptake can result in a 60% reduction in intramuscular adipose tissue content (Shaw et al., 2010). While cattle may never experience maximum oxygen uptake, there are times when cattle have a need for increased energy such as during an immune insult. When challenged with an immune insult, metabolic priorities change in the host to support the activation and response of the immune system (Lochmiller and Deerenberg, 2000). Furthermore, as a result of the immune challenge, there may be suppression of feed intake, thus the body must rely on energy reserves to supply energy to support the immune response (Lochmiller and Deerenberg, 2000). Additionally, the febrile response during an immune insult has been estimated to increase metabolism rates by 10–13% for every degree Celsius increase in body temperature (Kluger and Rothenburg, 1979). While the exact physiological function of intramuscular adipose in beef cattle has not been fully elucidated, it is a source of stored energy, and as an energy source may provide additional energy in times of need.

Due to the important role of intramuscular adipose tissue, both within the living animal and the final product, the selection of sire and dam combinations for marbling QTL's may provide a dual benefit. The benefits marbling in the final product are well documented (Casas et al., 2007; Rincker et al., 2006; Van Eenennaam et al., 2007). However, to date, there has been no evaluation of the possible benefits for selection of marbling QTL's on the immune response of cattle. As an energy storage depot, intramuscular adipose tissue could potentially be an energy source when energy demands increase in order to initiate an immune response. Therefore, the objective of this study was to evaluate the innate immune response of cattle genetically selected to possess either one or more copies of the two QTL's associated with marbling deposition (QG1 and/or QG2).

2. Materials and methods

2.1. Experimental design

Use of animals and the procedures utilized in this study were approved by the Mississippi State University Animal Care and Use Committee prior to initiation of the experiments (approval #10-034). Fall-born heifers (n = 19; BW 274 ± 24 kg) were selected from the Angus GeneSTAR herd were utilized for this trial. The Angus GeneStar® herd is a pure-bred herd maintained for producing Angus cattle with genetic variation in the occurrence of QG 1 and QG 2. Determination of the presence or absence of QG 1 and QG 2 was determined via hair samples analyzed by Zoetis animal genetics (Florham Park, NJ). Based upon QTL determination, 10 heifers with no QTL markers (No-MVP) for marbling and 9 heifers with one or more QTL makers (1 + MVP) for marbling were identified for inclusion into the study.

Fourteen day (d) post-weaning, identified heifers were separated from the resident genetic herd and placed into a 1.62 ha paddock and allowed 21 d to acclimate to environment, diet, and human contact. The diet for the duration of the trial consisted of: 26.25% soybean hull pellets, 22.03% corn gluten feed, 27.66% of Bermudagrass (*Cynodon dactylon*) hay, 23.56% cracked corn, and 0.50% mineral premix (DM basis).

Twenty-four hour (h) prior to the immune challenge (D-1), heifers were fitted with indwelling jugular vein catheters for serial blood collection as well as indwelling vaginal temperature (VT) recording devices, programmed to record VT at 1 min intervals for the duration of the trial (Burdick et al., 2012). Between blood samples, all catheters were flushed with 5 mL of saline (0.9% wt/vol NaCl) followed by 3 mL of heparinized saline (1 mL of heparin 10,000 IU/mL in 500 mL of saline) to replace fluid volume and to maintain catheter patency.

After insertion of catheters and VT devices, heifers were placed into individual tie stalls and allowed ad libitum access to feed and water. On d 0 (day of the immune challenge), starting at 0800 h and continuing until 1600 h, blood samples were collect every 30 min (8 h time period) and again at 12, 16, 20, and 24 h post-lipopolysaccharide (LPS) challenge (2100, 0100, 0500, and 1000 h). Following the collection of blood at 1000 h, heifers received an i.v. bolus dose of LPS (0.5 μg/kg of BW LPS from *Escherichia coli* O111: B4; Sigma Aldrich, St. Louis, MO USA) via the jugular catheter. Whole blood was collected into 9 mL monovette tubes with no additive (Sarstedt Inc., Newton, NC, USA). After collection, blood samples were allowed to clot for 30 min at 21 °C, centrifuged at 2000 × *g* for 30 min (4 °C). Serum was collected and transferred into 1.5 mL microcentrifuge tubes and stored at −80 °C prior to analysis.

2.2. Cortisol, tumor necrosis factor – α, interferon – γ, interleukin – 6, and haptoglobin

All serum samples were analyzed in duplicate. Serum cortisol concentrations were determined using a commercially available enzyme immunoassay kit according to the manufacturer's directions (Arbor Assays, Ann Arbor, MI) by comparison of unknowns to standard curves generated with known concentrations of cortisol. The minimum detectable cortisol concentration was 45.4 pg/mL, and the intra- and inter-assay coefficients of variation were 5% and 20%, respectively. Data are presented as ng/mL.

Serum cytokine concentrations (TNF-α, IFN-γ, and IL-6) were determined by a custom bovine 3-plex sandwich-based chemiluminescence ELISA kit (Searchlight-Aushon BioSystems, Inc., Billerica, MA). The minimum detectable concentrations were 0.5, 0.1, and 3.3 pg/mL for TNF-α, IFN-γ, and IL-6, respectively. All intra-assay coefficients of variation were less than 5% and all inter-assay coefficients of variation were less than 20% for all assays. Data are presented as pg/mL. Serum haptoglobin concentrations were determined by measuring haptoglobin/hemoglobin complex by the estimation of difference in peroxidase activity (Hulbert et al., 2011). Results were expressed in arbitrary units resulting from the absorption reading at 450 nm × 100.

2.3. Statistical analysis

Summary statistics were calculated for each variable, and these summary statistics were averaged across each treatment. Response to the challenge over time was analyzed as repeated measures within the MIXED procedure of SAS as a block design (No-MVP vs. 1 + MVP) with individual animal serving as the experimental unit; and the model included sampling time, treatment, and sample time × treatment. Sample treatment × time was used as the error term to test whole plot effects. Vaginal temperature was initially recorded at 1 min intervals, but subsequently averaged over 30 min intervals to facilitate comparisons to other immune and physiological parameters. When results of *F*-test were significant ($P < 0.05$), group means were compared by use of least significant difference. Pair wise differences among least squares means at various sample times were evaluated with the PDIFF option of SAS.