J. Dairy Sci. 96:3108–3119
http://dx.doi.org/10.3168/jds.2012-6097

Regulation of bovine adipose tissue metabolism during lactation. 7. Metabolism and gene expression as a function of genetic merit and dietary energy intake[1]

S. M. Rocco and J. P. McNamara[2]
Department of Animal Sciences, President's Teaching Academy, 233 Clark Hall, PO Box 646351, Washington State University, Pullman 99164-6351

ABSTRACT

The regulation of adipose tissue metabolism is critical to the efficient establishment and support of lactation, through both energy supply and several endocrine and cytokine factors. We still lack detailed knowledge of the role of transcription and posttranslational regulation of metabolic flux. We need to quantitatively understand the genetic and environmental (primarily dietary) regulation of adipose tissue to help improve productive efficiency. Therefore, objectives of this project were to help define mechanisms of adipose tissue responses to lactation and energy deficit, including changes in gene expression and their relation to changes in metabolic flux and production. A total of 48 cows were selected for genetic merit based on sire predicted transmitting ability of milk. From 21 d prepartum to 60 d in milk (DIM), cows were fed to energy requirements or to 90% of energy requirements, with content of protein, vitamins, and minerals balanced to be the same for both treatments. Adipose tissue biopsies were taken at 21 and 7 d prepartum and 7, 28, and 56 DIM to determine rates of lipogenesis and lipolysis, and to measure gene expression of proteins controlling lipolysis. The cows on the restricted diet consumed 12% less feed prepartum and 16% less feed postpartum and dietary energy restriction decreased milk production. The slowest rates of lipogenesis occurred at 7 and 28 DIM; higher-merit cows had faster rates of lipogenesis at 7 DIM but slower rates than lower-merit cows at 28 DIM. Energy restriction decreased lipogenesis. Basal and isoproterenol lipolysis increased with higher milk production and was relatively unaffected by dietary energy intake. The expression of genes controlling lipolysis were not affected by lactation and were slightly increased by dietary restriction, but were not well related to rates of lipolysis. These data confirm and extend previous work that regulation of adipose tissue metabolism in lactation is a function of both diet and genetic merit and is controlled by multiple mechanisms including gene transcription and posttranslational protein modifications.
Key words: adipose tissue, gene expression, lactation

INTRODUCTION

Adipose tissue metabolism in pregnant and lactating dairy cattle is essential in the successful establishment and support of lactational efficiency (McNamara, 2012). We have known for quite some time that specific adaptations in enzymes controlling lipogenesis and lipolysis during lactation help to supply FA to the mammary gland and other organs (Shirley et al., 1973; Yang and Baldwin, 1973). Since this early work, much has been defined of the genetic and environmental effects on adipose metabolism, which, as part of the overall system of the cow, responds to the demand for milk synthesis and attenuates the environmental variation in nutrient availability and intake (McNamara, 2012). The adipose tissue of cows of greater genetic merit for milk production have faster lipolysis, an increased response to β-adrenergic stimulation, increased activity of hormone-sensitive lipase (**LIPE**), and decreased lipogenesis compared with average-genetic merit animals (McNamara, 1989; Smith and McNamara, 1990; Vernon, 2003).

The adaptations of decreased lipogenesis and increased lipolysis to lactation and genetic merit can be attenuated by dietary energy intake (McNamara, 1994; Parmley et al., 1996; Vernon, 2003). During early lactation, a decrease in expression of acetyl-CoA carboxylase (**ACACA**) and lipoprotein lipase (**LPL**), and a diminished response to insulin are common control adaptations for lipogenesis (Sumner-Thomson et al., 2011; McNamara, 2012). Recently, we demonstrated that the mRNA abundance for 5 genes that control lipolysis [3 β-adrenergic receptors: **B1AR**, **B2AR**, and **B3AR**;

Received August 28, 2012.
Accepted January 13, 2013.
[1]This project was supported by National Research Initiative Competitive Grant no. 2007-35206-17841 from the USDA Cooperative State Research, Education, and Extension Service and the Agricultural Research Center, Washington State University. This paper is published in conjunction with the NC-1040 CREES Regional Research Project "Metabolic Relationships in Lactating Dairy Cattle."
[2]Corresponding author: mcnamara@wsu.edu

LIPE; and perilipin (**PLIN**)] increased in expression in adipose tissue of dairy cattle during lactation, but not until after peak lactation (Sumner and McNamara, 2007). Gene transcription array work from the present trial has also demonstrated coordinated decreases in genes coding for anabolic pathways in early lactation, but not in genes controlling lipolysis (Sumner-Thomson et al., 2011; Khan et al., 2013). Other recent work has extended our knowledge to show that adipose tissue triacylglycerol lipase is a different enzyme than LIPE, and it appears that adipose tissue triacylglycerol lipase regulates chronic basal lipolysis, whereas hormone-sensitive lipase (**HSL**) is expressed in a mixed pattern of constitutive and responsive elements in which HSL can rapidly activate upon phosphorylation signals from the sympathetic nervous system and other hormones (Koltes and Spurlock, 2011).

The historical and recent data confirm the multifaceted regulation of adipose tissue metabolism and the importance of adipose tissue in the systems biology of the cow. Two main driving forces in metabolic control are the genetic merit of the cow to make milk and the dietary energy available for that production and supporting metabolism. To learn more about specific quantitative regulation of this system and eventually the mechanistic causes of differences in efficiency, the overall hypothesis tested was that animals that vary in genetic merit for milk production and in energy intake will have a different pattern of lipid metabolism in the adipose tissue, including expression of key regulatory genes. The expression of these genes will partially control the balance of lipogenesis and lipolysis, in turn altering the metabolic efficiency of the animals. Thus, the objective of this experiment was to investigate the role of changes in gene expression on the metabolic flux in adipose tissue as affected by the interaction of sire genetic merit for milk production and a mild energy deficit. Such data can be used to construct and update models of metabolic systems control in the cow that are more specific and precise.

MATERIALS AND METHODS

Animals and Treatment Protocol

Forty-eight Holstein cows from the Knott Dairy Herd (Pullman, WA) were selected, blocked by parity (first or second) and by sire genetic merit as predicted transmitting ability for milk (**PTAM**). There were 24 first-lactation and 24 second-lactation animals. Cows were selected for genetic merit (high merit, **HM**; low merit, **LM**) based on their sire PTAM. For the sires of the HM cows, PTAM was 1,913 lb (870 kg) and for the LM cows 832 lb [378 kg; SEM = 45 lb (20.5 kg)]. The 305-d ME for HM second-lactation animals was 30,582 lb (13,901 kg) and for LM it was 27,997 lb [12,726 kg; SEM = 562 lb (256 kg)]. The rational for using the sire PTAM was because our original and continuing studies since the 1980s (McNamara and Hillers, 1986a,b) were based on a national study at that time using that criterion and we have used it since. The authors recognize that many other potential genetic traits exist that could be used, but milk production continues to be a major genetic selection criterion. The experiment was approved by the Washington State University Institutional Animal Care and Use Committee (IACUC; project 3478) and was conducted from May 2008 through February 2009.

Dietary treatments were either (1) normal-energy (**NE**) cows fed a TMR to requirements (NRC, 2001) or (2) low-energy (**LE**) cows fed the same TMR (with adjustments to grain mix, see below) at 90% of the intake of the NE group based on intake as a percentage of BW (Table 1). Cows were fed from 21 d prepartum to 60 DIM through Calan gates (American Calan Inc., Northwood, NH); the full daily allotment was fed between 1000 and 1100 h and cows had access to feed at all times. The LE diet was fortified with 10% more protein as well as vitamin and mineral mixes in the grain mix so that these components were consistent across treatments. Dietary ingredients were sampled with each new batch; the TMR and orts were sampled weekly and composited monthly for analysis at Kuo Testing Labs Inc. (Othello, WA) using AOAC International methods for DM, ADF, NDF, CP, fat, Ca, and P (AOAC International, 2000). Some of the data gathered in this experiment have been published previously (McNamara, 2012; Khan et al., 2013); however, this is the first complete publication of the production and metabolism data.

Samples and Measurements

Cows were milked twice per day between 0800 and 1000 h, and between 2000 and 2200 h and yield was recorded daily. Milk composition was determined approximately monthly by DHIA sampling using infrared spectrophotometry at the regional DHIA laboratory in Burlington, Washington (AOAC International, 2000). Body weight and BCS (Waltner et al., 1994) were assessed weekly and these measures were used to calculate body fat (Waltner et al., 1994). Prior to the morning feeding, blood was collected weekly via venipuncture of the coccygeal vessel at 28, 21, 14, 11, 7, and 4 d prepartum and then postpartum at d 1, 3, and 7, and then weekly until wk 8.

Prior to the morning feeding, subcutaneous adipose tissue biopsies were collected at 21 and 7 d prepartum and at 7, 28, and 56 DIM, from the tail head region un-