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Differences in the expression of genes involved in the somatotropic axis in divergent strains of Holstein-Friesian dairy cows during early and mid lactation

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ABSTRACT

Differences in genetic selection criteria for dairy cows internationally have led to divergence in the Holstein-Friesian breed. The objective of this study was to compare hepatic expression of genes of the somatotropic axis in the North American Holstein-Friesian and the New Zealand Holstein-Friesian strains of dairy cow at early and mid lactation. Mature cows of both the North American Holstein-Friesian (n = 10) and New Zealand Holstein-Friesian (n = 10) strains were selected. Liver tissue was collected by percutaneous punch biopsy from all cows at 35 and 140 d postpartum, representing early and mid lactation, respectively. Total RNA was extracted and the hepatic expression of genes involved in the control of the somatotropic axis was examined. Abundance of insulin-like growth factor (IGF)-1 mRNA was greater in the New Zealand strain, concomitant with a tendency for increased expression of acid-labile subunit mRNA. Across strains, mRNA abundance of IGF-binding protein-1, IGF-binding protein-2, and growth hormone receptor 1A decreased from d 35 to 140 postpartum, whereas expression of IGF-1 and acid-labile subunit tended to increase. Abundance of suppressor of cytokine signaling-3 mRNA was increased at d 140 postpartum. Both the strain of Holstein-Friesian cow and the stage of lactation influenced expression of genes controlling the somatotropic axis in hepatic tissue.

Key words: Holstein-Friesian, liver, gene expression, somatotropic axis

INTRODUCTION

Strain comparison studies in New Zealand and Ireland have reported lesser milk volume, greater BCS throughout lactation, and superior reproductive performance for the New Zealand (**NZ**) Holstein-Friesian (**NZHF**) compared with the North American (**NA**) Holstein-Friesian (**NAHF**; Horan et al., 2005b). The NAHF strain has been selected for increased milk yield, body size, and angularity in a production system based on year-round calving and greater levels of concentrate supplementation, with little emphasis on traits such as fertility (Hoekstra et al., 1994; Pryce and Veerkamp, 2001; Macdonald et al., 2007). The NZHF strain, on the other hand, has been selected for increased concentrations of milk fat and protein, reduced maintenance energy costs, and improved fertility and survival traits under pasture-based systems of production.

The occurrence of negative energy balance (**NEB**) during early lactation is a widely reported phenomenon (Bauman and Currie, 1980). During NEB, mobilization of body reserves is necessary to meet the energy requirements of lactogenesis. It is generally accepted that the growth hormone (**GH**)-IGF (or somatotropic) axis in the liver becomes uncoupled, whereby elevated plasma GH concentrations fail to stimulate an increase in hepatic IGF-1 synthesis (Thissen et al., 1994; Fenwick et al., 2008; Lucy, 2008). Insulin-like growth factor-1 plays a critical role in stimulating the anabolic and mitogenic activity of GH in various tissues (Laron, 2001). The liver is the major source of circulating IGF (Miller et al., 1981; Schwander et al., 1983; Thissen et al., 1994); therefore, this organ plays a central role in the metabolism of the cow.

Numerous reports have suggested that nutritionally compromised cows have reduced systemic concentrations of insulin and IGF-1 (Patton et al., 2006; Lucy, 2008), and Lucy et al. (2009) reported that NAHF cows experience an uncoupling of the somatotropic axis in conjunction with reduced BCS. It has been reported that irreversible glucose loss leads to some degree of uncoupling of the somatotropic axis as plasma concentrations of IGF-1 decline concomitantly with a reduction

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in hepatic mRNA abundance of IGF-1 and GH receptor (**GHR**; Meier et al., 2008). Furthermore, insulin is hypothesized to be a key metabolic signal regulating the coupling of the somatotropic axis (Butler et al., 2003).

Current knowledge indicates that the IGF system is composed of 2 ligands (IGF-1 and IGF-2); 2 receptors (**IGF-1R** and **IGF-2R**); 6 binding proteins [IGF binding protein (**IGFBP**)-1 to IGFBP-6] and the IGFBP acid-labile subunit (**ALS**). The somatotropic axis also includes the GHR, which is expressed as multiple mRNA variants in different tissues. In liver, the GHR1A variant is the principal GHR mRNA transcript, and its expression plays a key role in the coupling of the somatotropic axis. The effects of GH on the IGF system are primarily mediated by the Janus kinase 2 (**JAK2**) protein and 2 members of a family of DNA-binding proteins called signal transducers and activators of transcription (**STAT**), namely, STAT5a and STAT5b (Udy et al., 1997; Teglund et al., 1998).

Previous studies have demonstrated that systemic concentrations of the metabolic hormone IGF-1 in early lactation are positively associated with the subsequent calving-to-service interval and ultimately the pregnancy outcome in dairy cattle (Taylor et al., 2004; Patton et al., 2007; Wathes et al., 2007). Therefore, a greater understanding of the molecular regulation of hepatic expression of IGF-1 and its associated molecules is of critical importance in elucidating how this system may influence cow fertility. Recently, it was reported that although the NAHF and NZHF strains had similar postpartum energy balance (**EB**) profiles, plasma concentrations of IGF-1 were greater in NZHF cows during the posttransition period (30 to 90 d postcalving; Patton et al., 2008). Thus, the objective of this study was to determine the effect of strain of Holstein-Friesian cow on the transcriptional regulation of key hepatic genes controlling the somatotropic axis during early and mid lactation.

MATERIALS AND METHODS

Animals, Experimental Design, and Tissue Collection

All experimental procedures involving animals were licensed by the Department of Health and Children, Ireland, in accordance with the Cruelty to Animals Act (Ireland 1876) and European Community Directive 86/609/EEC. The animal model used in this study was described previously (Horan et al., 2005a). Briefly, the NA strain was developed by breeding the top 50% of cows in the Moorepark herd (based on the pedigree index for milk production) with 5 NAHF sires, selected as the highest available in Ireland for pedigree index for milk production. The animals in the NZ strain were imported from NZ as embryos and implanted into Holstein heifers. These embryos were generated by mating high-genetic-merit NZHF cows with 5 high-genetic-merit NZHF sires (based on breeding worth; the NZ genetic evaluation system). For the purposes of the current study, 10 mature NAHF cows and 10 mature NZHF cows were selected from their respective strains within the Moorepark strain comparison study (Horan et al., 2005a). Milk production, DMI, EB, and blood hormone and metabolite profiles of these animals have been reported previously (Patton et al., 2008). Briefly, NA cows had greater peak milk yields and total lactation milk yields (7,387 vs. 6,208 kg; SE of the difference = 359), lower milk fat, and similar protein concentrations compared with NZ cows. Body condition scores tended to be lower for NA cows, and this strain tended to have greater DMI (17.2 vs. 15.7 kg/d; $P = 0.07$) for wk 1 to 20 of lactation. Similar magnitudes of EB nadir were recorded for the NA and NZ strains [−6.88 vs. −7.31 Unité Fourragère Lait (**UFL**)/d; $P = 0.72$]. One UFL is the NE_L equivalent of 1 kg of air-dry standard barley as described by Jarrige (1989). All cows were managed in a similar manner as a single group throughout the lactation period. The prepartum diet was composed of ad libitum grass silage, with 2 kg/d of the lactating concentrate introduced from 2 wk before the expected calving date. The early postpartum diet consisted of ad libitum grass silage and 8 kg of concentrate. From March 20, all lactating cows were offered ad libitum zero-grazed grass (*Lolium perenne* spp.) supplemented with 4 kg of concentrate. Grass was harvested and fed each morning. The diet offered was designed to simulate normal feeding practices in seasonal-calving systems of milk production in Ireland. All cows were fed ad libitum grass silage and 8 kg of concentrate at the time of the first biopsy, and ad libitum zero-grazed grass supplemented with 4 kg of concentrate at the time of the second biopsy. The concentrate ingredients and the chemical composition of the concentrate and forages were reported previously (Patton et al., 2008).

Liver tissue was collected from all cows at 35 (±0.5) and 140 (±2.4) d postpartum by percutaneous punch biopsy as described by Smith et al. (2003). Briefly, a biopsy site between the 11th and 12th ribs was shaved, sanitized with 7.5% povidone-iodine and 70% ethanol, and anesthetized (lidocaine hydrochloride: 2%). An incision of approximately 1 cm was made through the skin, and the biopsy instrument was used to pierce the intercostal muscles and peritoneum. Approximately 1 to 1.5 g of liver tissue was collected, washed with sterile PBS, snap-frozen in liquid nitrogen, and stored at −80°C until further analysis.