CHARACTERIZATION OF PERFORMANCE AND PHYSIOLOGICAL DRIVERS CONTRIBUTING TO VARIATION IN FEED EFFICIENCY OF RED ANGUS-SIRED CATTLE

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AUTHORIZATION TO SUBMIT DISSERTATION

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ABSTRACT

There is considerable individual animal variation in feed intake, growth rates and maintenance requirements of beef cattle, but there is a lack of understanding regarding the impact of selection for feed efficiency (FE) and the physiological mechanisms that regulate this production efficiency trait. Therefore, the objectives of this study were to evaluate associations between residual feed intake (RFI; a measure of FE) and economically relevant traits of beef production and to identify physiological mechanisms driving variation in RFI.

Three cohorts of progeny (n = 222) from Red Angus (RA) sires divergent for maintenance energy (ME_M) EPD were evaluated for postweaning RFI and finishing phase FE. Progeny performance along with putative mechanistic indicators of FE were analyzed and reported across three categories: 1) relationships among performance traits, RFI, and product quality, 2) associations of serum IGF-I concentration, candidate genes, and fiber type composition with variation in RFI, and 3) relationships between progeny performance traits and sire ME_M and RFI EPD.

Results indicated that RFI measured during the postweaning growth phase is indicative of FE status in the finishing phase of beef production. In addition, neither postweaning RFI nor sire ME_M EPD negatively affected carcass or end-product quality, and no phenotypic association between postweaning RFI and sire ME_M EPD was observed.

Serum IGF-I concentration at weaning was not an indicator of the postweaning RFI phenotype in this study, although IGF-I was strongly and positively correlated with RFI EPD and strongly and negatively correlated with ME_M EPD. The identification of potential candidate genes that may be contributing to variation in RFI was inconclusive. The GH-IGF-I axis appeared to have some involvement with RFI at the molecular level; however, gene expression results were not consistent across cohorts. Additionally, results indicated that low RFI animals may have the ability to more efficiently maintain and accrete muscle mass due to their fiber type composition, specifically a greater proportion of type I fibers.

The heritability of RFI in this population of RA cattle is similar to that of other breeds evaluated for postweaning RFI. Sire ME_M EPD was found to be associated with measurements of growth and body size, while sire RFI EPD was more closely associated

with DMI. Also, sire ME_M EPD and sire RFI EPD were not associated, indicating that selection for reduced ME_M does not inadvertently select for improved RFI.

In conclusion, this scientific study has identified performance and mechanistic variables that may be contributing to the variation in RFI. Additionally, it has characterized ME_M EPD in the context of RFI. These findings will contribute to the growing body of knowledge regarding RFI as a measurement of FE and have potential to impact the use of ME_M EPD as an indicator of energy expenditure within the RA breed association and the beef industry.

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DEDICATION

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CHAPTER 1
Introduction and Literature Review

Introduction

There is a continued interest across the beef industry to improve feed efficiency (**FE**), especially given the recent volatility and rapid increase in feed costs (since 2006) associated with beef cattle production. Residual feed intake (**RFI**), a FE trait, measures the variation in feed intake beyond that needed to support maintenance, growth (Archer et al., 1999), and body composition (Basarab et al., 2003). Because RFI has been shown to be moderately heritable and independent of growth, it is considered valuable as a tool to improve FE (Herd and Bishop, 2000; Arthur et al., 2001b).

In 2004, the Red Angus Association of America (**RAAA**) was the first breed association to include a measure of efficiency in its international genetic evaluation program, attempting to reduce cow maintenance costs through the development of the maintenance energy (**ME_M**) EPD (Evans, 2001). Maintenance energy EPD is used as an indicator of energy expenditure required to sustain body tissues. Estimating the maintenance requirement of an animal is an innovative way to begin to partition energy required for maintenance away from other traits closely associated with energy consumption.

Various genetic, phenotypic, and physiological relationships have been identified within the context of RFI (Baker et al., 2006; Sherman et al., 2010; Kelly et al., 2011a). However, few studies have focused on energy expenditure associated with RFI. Due to the physiological importance of energy expenditure and industry motivation to produce feed-efficient cattle, it is important to identify the relationships between RFI and ME_M EPD and their interactions with other performance, end-product quality, and molecular variables.

The adoption of RFI has several advantages directly addressing the following goals: large savings in feed costs, enhancing economic opportunities and increasing profitability, and improving quality of life for beef producers. Furthermore, using less feed for similar production levels also means that this approach could result in reductions in waste products from beef cattle by using fewer animals to maintain desired production levels, and thus,

reduce the environmental impact of beef production. Therefore, investigation of RFI and its impact on beef production systems is of the utmost importance to the future profitability and sustainability of the United States (**US**) beef industry.

Feed Efficiency within the Beef Production Industry

Feed Costs and Profitability Associated with Beef Production

The genetic selection of beef cattle has traditionally revolved around economically relevant output traits, such as those pertaining to weight and carcass measurements, while little focus has been placed on cost-related input traits of feed intake (**FI**) and FE. The lack of interest associated with cost-related traits was due to the unavailability of genetic predictions for these traits, along with the relatively low feed costs of the past and the high costs associated with measuring individual FI in cattle (Ahola and Hill, 2012). However, in recent years (since 2006), feed input and market trends have become increasingly costly and unstable, forcing producers to explore various methods of cost minimization in an attempt to maintain profitability.

It has been estimated that feed-related costs are 55 to 75% of the total costs associated with beef cattle production (NRC, 2000). The primary feed inputs of the US beef industry are harvested feedstuffs, such as hay for the breeding cowherd and corn for feedlot cattle. In 2010 and 2011, the US average annual price for corn was approaching an unprecedented cost of $6.00/bushel. Additionally, much of the cost associated with hay has been influenced by the price of corn, where the cost of alfalfa and other types of hay had increased to an average of approximately $110/ton during the same time period (Ahola and Hill, 2012). In January 2014, the cost of corn had fallen to approximately $4.00/bushel (LMIC, 2014), providing a more profitable outlook compared to previous years. However, at this price, the cost of corn is still not approaching the low prices associated with increased profitability of the past (i.e., approximately $2.00/bushel in 2003). Therefore, it remains to be seen how a decrease in corn prices will impact production practices and affect profitability within various sectors of the beef industry. Other factors also affecting the price of feedstuffs include the demand of corn by the ethanol industry, variation in crop yields, and competition for corn and land against an increasing human population. Based on

this information, it is logical and opportunistic for the US beef industry to focus attention toward factors driving the increase of feed costs and emphasize the importance of FE improvement.

Historically, profitability of the cow-calf producer was determined by market forces such as high versus low supply rather than input cost. The cow-calf producer was more likely to be unprofitable when US cattle inventory was at a maximum (prior to 2006) due to an increase in market supply and a decrease in cattle prices, whereas profitability typically improved when US cattle inventory was at a minimum because of increased demand and a rise in cattle prices. However, this relationship between profitability and cattle inventory has been disrupted and current losses of the cow-calf producer are mostly associated with increased costs of production rather than factors determining revenue (Ahola and Hill, 2012). Dhuyvetter (2011) examined factors associated with high, medium, and low profit producers and determined that feed costs were the single largest cost difference ($87/cow) between high and low profitability operations. In this scenario, cost of production was more important in explaining profit differences among producers than revenue based factors, such as selling weight or calf prices. Other factors indicated as impacting profit and cost differences in this study were producer's management of non-feed costs, interest and labor, and herd size (Dhuyvetter, 2011). In addition, the US feedlot industry has evolved over a time period when energy and grain sources have been relatively inexpensive; however, these conditions have changed. With corn being the primary component of feedlot diets, it has influenced cost of gain and profitability, whereby feedlots have suffered financial losses due to the high-priced corn market since 2006 (Ahola and Hill, 2012). As previously mentioned, the demand for corn supply by the ethanol industry is a factor that is significantly impacting profitability of the beef industry. The US biofuels policy is in full support of corn-based ethanol production (Ahola and Hill, 2012), which has led to a competition for resources (i.e., corn and land) between the two industries and a concomitant rise in production expenses. Not only is beef production within the feedlot sector at risk, but also other US corn-dependent livestock production industries (i.e., poultry and swine) are at risk. Ultimately, the competition for corn and land resources could lead to a reduction in the amount of meat produced by these industries, resulting in decreased sustainability along with potential

negative affects upon efforts to feed the continually growing world population (Ahola and Hill, 2012).

Furthermore, due to increased cost of gain and lack of profitability, the efficiency of grain conversion to meat protein is of concern within the feedlot sector of the beef industry. Beef cattle are significantly less efficient at converting grain to meat protein when compared to monogastric species (e.g., poultry and swine), which results in a greater proportion of feed energy needed to produce a pound of beef protein. It has been estimated that only 5% (of all dietary energy required to produce beef) is used for protein accretion in progeny that are slaughtered (Dickerson, 1978). Compared to 14% and 22% of dietary energy devoted to protein accretion in swine and poultry slaughter progeny, respectively, the lack of efficiency within the beef industry is unfavorable (Ahola and Hill, 2012), reiterating the need for improved FE. Basarab et al. (2003) reported that a daily intake difference of 2.50 kg (assuming a cost of $0.101/kg) would equate to a feed cost savings of $37.87 per animal over a 150 day finishing period. Additionally, Fox et al. (2001) reported that a 10% improvement in FE would result in a profit increase of 43%, while a 10% improvement in gain would only result in a profit increase of 18%. Gibb and McAllister (1999) further substantiated this claim by estimating that a 5% increase in FE could potentially yield a fourfold greater result when compared to the same improvement in ADG.

Opportunities and Implications of Improved Feed Efficiency

Based on the fact that a considerable amount of individual animal variation exists regarding feed intake (Herd et al., 2003) and maintenance requirements (Johnson et al., 2003), there is opportunity within the beef industry to genetically select for feed efficient cattle, which has the potential to maximize profitability and sustainability within all sectors of the beef production system. When feed requirements of the US beef industry are evaluated, it is the breeding cowherd that requires more than half of the total feed requirements compared to feedlot cattle (Carstens and Tedeschi, 2006), indicating that these producers have an advantage to improve profitability through a reduction in feed costs (Ahola and Hill, 2012). Archer et al. (2002) reported that an improvement in postweaning efficiency would be reiterated in mature animal efficiency, based on estimates that a portion of the genetic variation resulting from biological processes regulating intake and efficiency

are similar during both life stages. Therefore, improvements in FE at different stages of production could positively impact total production system efficiency (Crews, 2005). Additionally, possibilities exist for improvement in beef production beyond the cost savings associated with reduced feed requirements. Okine et al. (2001) and Hegarty et al. (2007) reported reductions methane emissions (9-12%) and manure production (15-17%) from cattle with improved FE, indicating that selection for improve FE has the potential to reduce the carbon footprint associated with beef cattle production.

Ultimately, identifying and selecting beef cattle with reduced feed requirements and production attributes that equate to previously set standards of the industry will result in significant changes for the US beef industry. The implications of these changes are many and are likely to include, but are not limited to, improved profitability, increased net beef supply, reduced end-product cost, and environmental sustainability. Additionally, improvements in production efficiency of beef cattle will likely affect the competiveness of the beef industry with other US meat-producing industries (i.e., poultry and swine), resulting in an increase in overall revenue and long-term sustainability (Ahola and Hill, 2012).

Measures of Feed Efficiency

Many factors contribute to the efficiency of a beef production system, with feed inputs and production outputs being the primary determinants of efficiency. Since FI is generally correlated with production outputs, examination of these variables in isolation from each other provides limited insight or indications as to the complex relationships that are regulating efficiency. A number of indices exist for describing FE of livestock (Table 1.1), whereby each measure reflects different biological and mathematical aspects of efficiency (Archer et al., 1999). Since different indices are appropriate for different purposes, it is important that the index used to express efficiency be suitable for the comparison intended. In order to accurately measure FE, there are two essential pieces of data that must be collected: 1) FI and 2) liveweight gain (and ADG). The combination of basic growth traits and feed intake allow for the computation of different measures of FE that will be discussed.

Feed Conversion Ratio

One of the most common measures of efficiency is that of gross efficiency or its inverse, feed conversion ratio (FCR). This measure is a simple ratio of production outputs in relation to feed inputs over a certain period of time, where output is measured as the weight gain of growing animals and input is measured as feed intake (Archer et al., 1999). Measures of gross efficiency are highly associated with various aspects of production, whereby it has been suggested that selecting for production will produce a correlated response in gross efficiency (Archer et al., 1999). However, difficulties are encountered when using this trait to improve overall production efficiency. Feed conversion ratio of growing animals is largely a function of size and growth rates (Salmon et al., 1990) and, in facthas been shown to be negatively correlated with growth traits (Herd and Bishop, 2000). Thus, selection for improved FCR (i.e., high growth rates) would result in a reduction of feed needed for growth, which could be very beneficial to feedlot companies. However, this selection strategy would increase mature cow weights and maintenance requirements of the breeding herd, which is unfavorable (Archer et al., 1999). Due to its confounding relationship with mature size, FCR has not been utilized for genetic improvement of FE (Gunsett, 1984). Additionally, inherent complications associated with genetic evaluation of ratio traits (FCR, partial efficiency of growth, Kleiber ratio, and relative growth rate) occur because of the disproportionate manner in which selection pressure is exerted on the component traits (Arthur et al., 2001c). This uneven selection pressure will ultimately result in a prediction of change in the component traits that is uncertain for future generations. Therefore, the use of a ratio trait for selection purposes may not necessarily equate to improved efficiency.

Residual Feed Intake

A more recent measure of FE, RFI, is defined as a residual term resulting from the regression of actual intake on identifiable and measureable energy sinks such as body size, growth rate, and body composition (Crews and Carstens, 2012). Lower and more negative phenotypes of RFI are desirable, indicating that animals are consuming less feed than expected based on their daily weight gain. This concept was first introduced by Koch et al. (1963) and measures the variation in feed intake beyond that needed to support maintenance,

growth (Archer et al., 1999) and body composition (Basarab et al., 2003). Because RFI allows for the inclusion of more "energy sinks" besides that of growth and maintenance, this measure also allows for comparisons between animals across different segments of production and different stages of production, while still describing individual animal differences (Crews, 2005). Further, RFI has been shown to be moderately heritable (h^2 = 0.16 to 0.43) and independent of many other performance traits, such as growth, which characterize it is a valuable tool for improvement of FE (Herd and Bishop, 2000; Arthur et al., 2001b). In contrast to ratio traits, indices of efficiency that incorporate a linear index, such as RFI, will place a predetermined amount of pressure on the component traits, which results in a predictable amount of genetic change (Arthur et al., 2001c). The use of a linear index would potentially produce cattle that are efficient during different stages of production, which indicates that significant progress in FE improvement can be achieved through performance-based selection and breeding programs using RFI.

Residual Daily Gain

First introduced by Koch et al. (1963), the concept of residual daily gain (RDG) has recently received attention as an alternative efficiency measurement. Residual daily gain is considered to be more of a growth trait than a true efficiency trait, but its concept does parallel that of RFI. The RDG of a growing animal is defined as a residual term from the regression of ADG on intake. Higher and more positive phenotypes of RDG are desirable, indicating that animals are gaining more weight than expected based on their daily intake. More importantly, a characteristic of RDG is that it is has a high association with gain and thus is confounded by its relationship with many other performance traits (Crews and Carstens, 2012). Even though RDG is confounded through its association with gain, investigation regarding important phenotypic and genetic relationships between RDG and economically relevant production traits must be conducted in order to evaluate and quantify its value and purpose as an index for efficiency. Additionally, the implications of using this measure of efficiency as a basis for genetic selection have not been reviewed within the literature.

Residual Feed Intake as a Measure of Feed Efficiency

Relationship with Economically Relevant Traits

It is well documented within the literature that RFI is not associated with production traits such as ADG (Koch et al., 1963; Arthur et al., 2001b; Arthur et al., 2001c; Basarab et al., 2003) and thus, is not confounded by associations with growth rate and mature patterns. Data reported by Baker et al. (2006) illustrated the potential variation in RFI, with respect to ADG, in that two steers growing at similar rates (~1.46 kg/d) were consuming very different amounts of feed (8.6 kg/d and 11.5 kg/d). This study also indicated that animals with similar RFI values (-0.48 and -0.63) can display different growth rates (1.3 kg/d and 1.6 kg/d, respectively; Hill and Ahola, 2012). Additionally, it has been shown that RFI is positively associated with DMI (Herd and Bishop, 2000; Basarab et al., 2003), indicating that DMI has a greater effect on FE status than does ADG. The identification of these relationships and their implications for beef production practices has contributed to alleviation of long-term concerns regarding the selection and implementation of RFI and any correlated responses with growth and mature patterns that may occur.

Body composition is a major determinant of feed energy requirements and therefore, has been recognized as a partial driver of the variation in RFI. Studies within the literature indicate that differential RFI is partially associated with relatively greater lean tissue accretion (i.e., muscle) and a relative decrease in fat deposition (Richardson et al., 2001; Carstens et al., 2002; Basarab et al., 2003). Jensen et al. (1992) reported a positive genetic correlation of 0.17 ± 0.32 between RFI and carcass lean percentage; however, Herd and Bishop (2000) reported a contrasting negative genetic correlation of -0.47 ± 0.23 for the same relationship. Richardson et al. (2001) indicated that selection for reduced RFI resulted in a trend towards an increase in lean tissue content of carcasses, which is in agreement with results reported by Herd and Bishop (2000). Evaluating young Angus bulls and heifers, Arthur et al. (2001b) indicated that phenotypic and genetic correlations between RFI and rib fat depth (r_p = 0.14, r_g = 0.17), rump P8 fat depth (r_g = 0.11, r_g = 0.06), and LM area (r_p = 0.06, r_g = 0.09) were low. Schenkel et al. (2004) also reported positive phenotypic and genetic correlations (r_p = 0.17, r_g = 0.16) between phenotypic RFI and backfat thickness. When examining measurable differences contributing to variation in FE, Richardson and

Herd (2004) reported that approximately 5% of the variation in RFI was a result of variation in body composition, with less efficient (high RFI) animals being fatter than efficient (low RFI) animals (Figure 1.1). Due to indications of the relationship between RFI and body composition, a correction for body fatness (as ultrasound fat thickness) is included in the model to predict FI for the calculation of RFI, which protects against the potential negative consequences of selecting for RFI and simultaneously co-selecting for leaner animals (Ahola and Hill, 2012).

The relationship between RFI and product quality is of importance when considering market yields and return on investment, whereby it is crucial that selection strategies to improve FE do not inadvertently diminish established production quality traits. It has been suggested that improved RFI does not have antagonistic effects associated with carcass or product quality (Richardson et al., 1998; McDonagh et al., 2001; Nkrumah et al., 2004). Intramuscular fat (**IMF**) is an important component of the beef quality grading system, in that it represents the degree of carcass marbling and thus drives quality grade scores for beef cattle. Thus, it is linked to beef palatability and carcass value, both of which are key components determining market trends and return on investment. Previous studies (Carstens et al., 2002; Schenkel et al., 2004; Baker et al., 2006) reported no correlation between RFI and IMF. However, McGee et al. (2013) reported that RFI and ultrasound IMF tended to be negatively associated (r_p = -0.27; P = 0.11) when evaluating yearling Wagyu bulls. In addition, Basarab et al. (2003) reported that there was a tendency (P = 0.11 and 0.12, respectively) for RFI to be correlated with ultrasound marbling (r = 0.13 and 0.13, respectively) in crossbred cattle based on 2 consecutive years of study, but found no association between RFI and carcass marbling scores. Furthermore, McDonagh et al. (2001) reported that no differences between high and low RFI groups were observed when measuring Warner-Bratzler shear force (**WBSF**) of LM steaks aged for 1 or 14 d, whereby Ahola et al. (2011) indicated a similar relationship and also reported a lack of association between RFI and sensory traits. Baker et al. (2006) reported a tendency (P < 0.10) for lower juiciness and off-flavor scores of steaks from high RFI steers compared with steaks from low RFI steers, with all other taste scores reported as showing no differences between high and low RFI steers. Thus, there is a hint of suggestion that RFI may be associated with

important carcass measurements, such as IMF and marbling scores. However, this relationship appears to be disunited in some studies where RFI has been corrected for body fatness (Ahola and Hill, 2012). Because of the overall importance of IMF to the beef industry (as an indicator of product quality and palatability), any future studies evaluating improved FE (or RFI) should continue to investigate its relationship with IMF. Additionally, there appears to be little association between RFI and measurements of end-product quality, indicating that selection for RFI should not diminish taste or texture parameters associated with improved beef quality.

Production efficiency of cow-calf operations is largely influenced by reproductive performance, as cows must rebreed and wean a calf every 12 months. A variety of factors regulate reproductive performance, such as nutrient intake and body composition. Due to the influence of RFI on energy utilization and/or partitioning, the genetic selection of this trait requires investigation to determine if any detrimental effects upon reproductive performance will occur; however, very few studies have examined this relationship (Basarab et al., 2012). Small negative impacts of low RFI on fertility in Angus cows divergently selected for RFI have been reported (Arthur et al., 2001a; Arthur et al., 2005), where a trend was observed for low RFI cows to calve 5 days later in the year than high RFI cows (215 ± 2 vs. 210 ± 1 day from the beginning of the year, $P = 0.07$). Researchers indicated that the calving delay could have resulted from longer gestation length, longer anestrus period, and/or delayed pregnancy in low RFI cows. Basarab et al. (2007) also reported that cows producing low RFI progeny produced their next calf 5-6 days later ($P < 0.001$) in the year than cows producing high RFI progeny. Other studies (Johnston et al., 2009; Shaffer et al., 2011) have suggested that high RFI heifers experience the onset of puberty relatively quicker than low RFI heifers, due to their increased feed consumption and body condition (i.e., fat reserves). Additionally, negative impacts of RFI on pregnancy rate and calving and weaning rates have yet to be detected. Basarab et al. (2007) reported no differences in pregnancy rates of cows producing low and high RFI progeny (95.6% vs. 96.0%, $P = 0.90$), as well as Donoghue et al. (2011) who observed no differences in pregnancy rates of low and high RFI heifers. Arthur et al. (2005) reported that calving (89.2% vs. 88.3%, $P > 0.05$) and weaning (81.5% vs. 80.2%, $P > 0.10$) rates were similar between low and high RFI

cows, while Basarab et al. (2007) also indicated that cows producing low and high RFI progeny had similar calving rates. Further, bull fertility has not been observed as being negatively associated with RFI (Basarab et al., 2012). Arthur et al. (2001b) reported that RFI and scrotal circumference were not phenotypically or genetically associated in Angus bulls ($r_p = 0.10$; $r_g = -0.03 \pm 0.11$). Also, Wang et al. (2012) tested fertility of low and high RFI bulls in three breeding groups and reported similarities among the groups when exposed to cows (n = 288) for a 59 day breeding season. Thus, it appears that RFI does not negatively impact reproductive performance of beef cattle; however, the studies examining these relationships are few and results should be taken with caution.

Potential Physiological Mechanisms Contributing to Variation

Richardson and Herd (2004) analyzed results from several studies of cattle following divergent selection for RFI and determined that there were at least 5 major processes by which variation in efficiency can arise (Figure 1.1). They identified protein turnover, tissue metabolism, and stress as contributing approximately 37% to the variation in FE, while an undefined category of processes (i.e., ion transport, proton leakage, etc.) contributed 27%. Additionally, processes such as digestion, activity, and feeding behavior contributed less (approximately 36% combined) to variation when compared to contributions of underlying physiological mechanisms. Therefore, the investigation and identification of underlying physiological mechanisms responsible for the variation is a critical component to the understanding of RFI.

Tissue Metabolism: Substrate Utilization and Energetics

Metabolism is a highly coordinated process of cellular activity involving multiple enzymes, substrates, and metabolic pathways within the mammalian body. The process of metabolism serves to (1) obtain chemical energy via degradation of energy-rich nutrient molecules, (2) repartition substrates to meet the energy demands of tissues, and (3) synthesize and degrade biomolecules needed for specialized cellular functions (Nelson and Cox 2005). Depending on energy substrate profile within the blood stream, the mammalian body has the ability to selectively choose which nutrients are utilized by which tissues based on necessity and uptake efficiency of the tissue. This process is termed substrate partitioning and is dictated according to the metabolic state of the animal. There are three

distinct and identifiable mechanisms that regulate energy substrate partitioning. First, substrate mobilization includes processes in adipose tissue, liver, and muscle, resulting in reversal of the energy storage processes gluconeogenesis, lipolysis, and glycogenolysis (see Figure 1.2). These processes make the energy substrates glucose, free fatty acids, and ketone bodies available. Second, substrate uptake includes groups of mechanisms by which substrates enter each cell type. Third, substrate oxidation is a highly regulated process that determines which substrate will be utilized and their relative rates of utilization (Welch et al., 2012). It is this metabolic regulation that plays a critical role in the underlying variation of FE. Therefore, candidate tissues for the study of gene expression and metabolic function related to growth and energy expenditure, in the context of FE, are those that provide a large contribution to overall regulation of energy storage and energy expenditure. Thus, adipose tissue, skeletal muscle, and the digestive system (including the liver) have been proposed for study of FE.

Adipose Tissue

Deposition of adipose (fat) tissue is a highly energetic and costly investment within the beef industry. Cattle destined for harvest are fed high-energy grain diets in order to enhance the deposition of IMF or marbling, which is a major determinant of end-product quality and palatability. Nkrumah et al. (2004) indicated that improvements of lean to fat deposition ratio can ultimately reduce feed costs for producers via improvements in FE.

Each depot of adipose tissue varies in its metabolism, adipocyte size, and physiological dynamics, whereby variation in the proportion of adipose that is accumulated within each of the depots will affect the overall energetic metabolism of an animal. Also, adipose deposition is not uniform and varies greatly throughout animal development. For example, omental fat achieves its maximum growth rate first, followed by intermuscular and then subcutaneous fat, while IMF depots grow during the later stages of development and maturation (Welch et al., 2012).

A variety of regulatory factors influence the proliferation and differentiation of adipose tissue, such as glucocorticoids, insulin, IGFs, and GH, and differences in the metabolic pathways associated with these factors may be contributing to variations in basal metabolism and FE of beef cattle; however, these relationships have yet to be investigated.

Additionally, factors produced by adipose tissue, such as leptin, appear to have regulatory effects on metabolism and thus, may be an indicator of FE (Welch et al., 2012). Leptin has previously been implicated as a regulator of appetite, energy metabolism and partitioning, and body composition of beef cattle (Houseknecht et al., 1998). Circulating levels of leptin are increased at maturity, due to additional growth in the form of adipose deposition at this time (Geary et al., 2003). These authors reported positive associations between serum leptin concentration and carcass characteristics, including marbling, quality and yield grade, and backfat thickness, while a negative correlation was observed with LM area. Additionally, SNPs within exon 2 and the promoter regions of the bovine leptin gene have been reported (Buchanan et al., 2002; Crews et al., 2004), where a noted mutation of cytosine to thymine occurred in exon 2. This mutation, in turn, caused an amino acid change of arginine to cysteine, resulting in a partial loss of biological function associated with fatter carcasses and increased leptin mRNA expression (Buchanan et al., 2002). Further, Nkrumah et al. (2004) observed a positive relationship between the thymine allele of the leptin SNP and daily rate of gain in ultrasound backfat thickness, carcass grade fat, subcutaneous fat, and body cavity fat, indicating that animals carrying the thymine allele of the leptin SNP may have increased fat subcutaneous deposition and poorer yield grades with no increase in IMF.

Relationships among the various regulatory factors of adipose tissue and FE have not been completely defined in beef cattle studies. However, there are some indications as to the role of leptin in adipose deposition and its potential as a contributor to the variation in FE. Examination of the leptin gene and its receptor reveal polymorphisms that are associated with carcass fat measurements, which may be a partial underlying driver of variation in energy metabolism and FE of beef cattle (Welch et al., 2012).

Skeletal Muscle

Maintenance of skeletal muscle requires considerable energy on the part of the animal, depending on fiber type and composition of muscle mass (Challiss and Ferre, 1988). On average the mass of skeletal muscle accounts for approximately 40-45% of the total body mass of vertebrates, regardless of their body size (Blaxter, 1989). When considering the whole animal, skeletal muscle can contribute approximately 60% or more to systemic metabolism. In comparing metabolic activity of other bodily tissues, skeletal muscle is one

of the most energy-consuming tissues, even though the energetic cost required to deposit a unit of adipose tissue is much greater compared to that needed for synthesis and accretion of an equivalent unit of muscle mass (Herd and Arthur, 2009). Due to variation in protein turnover in lean muscle, muscle will ultimately consume more energy than will an equivalent unit of adipose over time. When active, muscle must be supplied with energy-rich substrates that can accommodate the needs of the resulting increased metabolism.

Protein turnover is an essential process for cellular function, growth, and repair of skeletal muscle tissue. When the rate of protein accretion exceeds the rate of protein degradation, the animal is in an anabolic phase. The rate at which protein turnover occurs is an important determinant of energy cost, with small reductions in this process having significant effects on the protein "economy" of an animal (Hill et al., 2003). Research discussed by Hill et al. (2003) suggested that improved FE through reduced protein degradation may be beneficial when cattle are exposed to conditions in which nutrient intake is limited. Further, in terms of growth efficiency, a reduction in protein degradation rate is energetically favorable, because it requires little or no energy input compared to an increase in protein accretion, which is an energy demanding process (Hill et al., 2003). Within the context of FE, animals classified as "efficient" may exhibit a reduced rate of protein degradation compared to their inefficient contemporaries. In doing so, these animals would be able to potentially synthesize and accrete an increased amount lean tissue mass without the additional energy costs associated with increased protein accretion. Since RFI is partially associated with relatively greater lean tissue accretion, this could result in substantial savings related to metabolic energy costs of synthesizing skeletal muscle, which could ultimately impact and improve overall systemic metabolism.

There are three main adaptations or changes that allow skeletal muscle to alter composition and function in response to different physiological conditions: (1) metabolic plasticity, (2) anabolic growth via the insulin-like growth factor (IGF) axis, and (3) muscle fiber plasticity. Due to the role of skeletal muscle in terms of FE and as a desired meat product, it is critical that we understand how each of these conditions affect not only skeletal muscle at the tissue level, but also how it contributes to the overall growth of an animal.

One of the most important alterations concerning metabolic plasticity is that of mitochondrial biogenesis. Mitochondrial biogenesis consists of two types of inclusive alterations within the muscle cell. First, there is an increase in mitochondrial content per gram of tissue, and/or, second, there is a change in the mitochondrial composition (Hood et al., 2006). These alterations are highly specific and occur in response to particular types of exercise (i.e., resistance vs. endurance), with changes exhibited most evidently in low-oxidative, white muscle (type IIb) fibers (Hoppeler, 1986). The consequences of mitochondrial biogenesis are metabolically beneficial for skeletal muscle at the cellular level. Since skeletal muscle is such an energy-demanding tissue, an increase in the number of mitochondria will allow for cellular metabolic preference to utilize high-energy lipid substrates instead of carbohydrates (i.e., glucose and glycogen). Ultimately, this preference will sustain glycogen stores within muscle, reduce the formation of lactic acid (due to an increase in aerobic capabilities), and reduce muscle fatigue. Skeletal muscles with a high capacity for lipid oxidation will ultimately exhibit greater efficiency for the mobilization of adipose (fat) storage and have an increased endurance rate. Thus, metabolic activity of muscle fibers and skeletal muscle tissue can serve another source of variation in the utilization of substrates, indicating underlying mechanisms that are potentially associated with the variation in energetic (feed) efficiency (Welch et al., 2012).

An important regulator of skeletal muscle growth is the somatotropic axis, where IGF-I plays a critical role in both prenatal and postnatal growth; additionally, IGF-II is also a major activator of prenatal growth, but its role in postnatal growth is not understood. The primary source of circulating (endocrine/systemic production) IGF-I is the liver (Salmon and Daughaday, 1957); however, IGF-I is produced both systemically and locally (at the tissue level), and it is now known that both endocrine and autocrine/paracrine effects of IGF are important for growth (Lund et al., 1986; Murphy et al., 1987).

Local IGF-I production occurs via autocrine and paracrine effects (Figure 1.2). In the context of skeletal muscle tissue, IGF-I production by an individual muscle cell can act upon itself to continue the cellular release of IGF-I or act upon other cells within a close proximity to produce IGF-I. Furthermore, IGFBPs are also produced locally within skeletal muscle tissue. Skeletal muscle expresses IGFBPs 2, 4, 5, and 6 (Florini et al., 1996a). The

major functions of these binding proteins are to assist in the transport of IGFs both locally and systemically, to prolong the half-life of IGFs and regulate plasma clearance, and to modulate the interactions of IGFs with their receptors. The binding proteins of IGFs can either potentiate or inhibit the actions of IGFs; however, IGFBP-4 is thought to be exclusively inhibitory (see review in Kokta et al., (2004)).

The effects of IGF-I on skeletal muscle are associated with anabolic growth, mainly that of hypertrophy. Both *in vivo* and *in vitro* studies have demonstrated that local and systemic production of IGF-I is involved in the generation of postnatal myofiber hypertrophy and muscle regeneration. In skeletal muscle, over-expression of the IGF-I gene promotes local muscle hypertrophy and can also delay atrophy of muscle fibers associated with ageing (Oksbjerg et al., 2004). In both instances, IGF-I improves muscle mass and strength. Furthermore, skeletal muscle has the unique ability to regenerate after damage, due to skeletal muscle satellite cells (Duan et al., 2010). Satellite cells have been defined as adult stem cells residing in a tissue-specific area, such as skeletal muscle (Kuang and Rudnicki, 2008). Due to the effects of IGF-I on skeletal muscle hypertrophy, it is now being investigated as to what effect IGF-mediated actions have on satellite cells regarding muscle regeneration (Philippou et al., 2007). It has been suggested that induced IGF-I skeletal muscle hypertrophy and regeneration is due to local production of IGF-I via autocrine and/or paracrine effects rather than circulating IGF-I (Bamman et al., 2001). Furthermore, IGF-I has been implicated as a stimulator of protein synthesis and an inhibitor of protein degradation, thus improving protein retention (Oddy and Owens, 1996).

Within the beef industry, indicators of growth and feed efficiency have become important topics of research, especially during trying times of high feed prices and elevated demand for product. The ability to measure serum IGF-I concentration on a large number of cattle prior to making important management decisions makes it a desirable genetic indicator. Serum IGF-I concentration has an estimated heritability of 32% and is positively correlated with important production traits, such as carcass and product quality (Davis and Simmen, 2000). Johnston et al. (2002) suggested that selection for reduced IGF-I concentration resulted in a correlated reduction in fatness, RFI, and FCR, while Lancaster et al., (2008) reported that genetic selection for postweaning IGF-I concentration had a

minimal effect on RFI in beef cattle. Thus far, correlations of serum IGF-I concentration with important beef production traits and increased feed efficiency are conflicting. Associations between systemic concentration of IGF-I and improved FE are not easily identifiable in beef cattle, typically requiring large numbers of cattle to yield informative results. Therefore, research is ongoing in this area to determine if serum IGF-I concentration is an appropriate indicator of FE (Welch et al., 2012).

Skeletal muscle is a dynamic tissue, responding to physiological stimuli and altering functional capacity in order to meet physical and biological demands of an animal. The IGF axis is considered to be a major contributor to the dynamic ability of skeletal muscle, being implicated in both muscle hypertrophy and regeneration. The role of IGF-I and its contribution to the variation in FE is still under investigation, remaining unclear at this point. Further research is needed to determine if IGF-I will become a reliable indicator for improved FE of beef cattle.

Digestive System and Liver

In order to gain insight into digestive processes driving variation in FE, a comprehensive understanding of nutrient digestion and absorption is needed, as well as information regarding conditions that alter the digestion process. Ferrell (1988) reviewed evidence from a variety of experimental approaches and indicated that the potential for variation in mass and energy expenditures of the GIT and liver has a major impact on total animal expenditures, with approximately 30 to 35% of total energy expenditures in growing-finishing animals being directed toward maintenance functions. It has been suggested that a reduction in the amount of energy required to perform vital functions of the GIT would have hypothetical benefits to FE status of the animal. The two most likely physiological factors contributing to differences in digestibility among animals are enzyme production and dilution rate from the rumen (Kerley, 2012). Simulated ruminal fermentation has indicated that animals with the ability to increase dilution rate would be expected to shift starch digestion from the rumen to the small intestine without reducing microbial protein flow (postruminally) due to an increase in microbial efficiency. This would potentially result in energetic gains by the animal because loss of energy from fermentation (methane) would be reduced (Kerley, 2012). After measuring differences in starch digestion from progeny lines

selected for negative or positive RFI, Channon et al. (2004) concluded that efficient cattle (low RFI) had greater fecal pH and dry matter content because they had greater capability for starch digestion. In addition, Montanholi et al. (2013) recently evaluated small intestine histomorphometry of beef feedlot steers divergent for FE and reported that efficient steers (low RFI) have a greater cellularity in the small intestinal crypts, both in the duodenum and ileum, than inefficient steers (high RFI). While average size of cells did not differ between the efficiency groups, a trend was observed for greater crypt area and crypt perimeter in the ileum of feed efficient steers.

The ruminant digestive system is advantageous in that pregastric fermentation allows for the derivation of both energy and protein from fermentation; however, it also suffers in that dietary inputs are altered in an unpredictable manner, resulting in a nutrient flow to the small intestine that is difficult to describe and predict based on diet formulation alone (Harmon and McLeod, 2001). Approximately 75% of substrate energy is recovered when carbohydrates are exposed to microbial fermentation, resulting in the production of VFAs that can be metabolized by the host (Merchen et al., 1997). This process results in significant losses as methane and heat of fermentation, with those losses estimated at 13-18% of gross energy (Harmon et al., 2004). Energetically, digestion in the small intestine is advantageous over ruminal fermentation of non-structural carbohydrates in that recovery of absorbed end-products (e.g., glucose) contains a greater proportion of substrate energy compared with the energy yield from fermentation of the substrate (Merchen et al., 1997). Using a theoretical evaluation of a carbohydrate-rich diet, Black (1971) estimated that approximately 33% more total net energy would be available from small intestine digestion compared to ruminal digestion. In addition, Owens et al. (1986) suggested that approximately 42% more energy was provided when starch was digested in the small intestine rather than the rumen. Ruminal starch digestion is typically 75-80% of starch intake, whereas 35 to 60% of starch leaving the rumen and entering the small intestine is digested there (Harmon et al., 2004). Approximately 35 to 50% of undigested starch escaping the small intestine is degraded in the large intestine (Harmon et al., 2004), indicating that additional starch is potentially available for digestion in the small intestine (Huntington et al., 2006).

There are three distinct phases or processes related to digestion and absorption of carbohydrates in the small intestine. The process begins with the initiation of carbohydrate digestion via pancreatic α-amylase, an endoglucosidase hydrolyzing internal α-1-4 glucosidic bonds to produce maltose and α-limit dextrins (Huntington et al., 2006). The role of pancreatic α-amylase has been questioned regarding the efficiency of small intestinal carbohydrate digestion. Due to the lack of an adaptive response of the ruminant pancreas to increased dietary starch (Kreikemeier et al., 1990), the biological control of pancreatic α-amylase is unclear, which has led most researchers to speculate that pancreatic α-amylase activity is the limiting process of carbohydrate assimilation (Huntington, 1997; Harmon and McLeod, 2001). In addition, the second phase of carbohydrate digestion occurs via action of carbohydrases that are located at the brush border membrane of intestinal microvilli. Ruminants possess a similar complement of enzyme activity as that of non-ruminants with the exception of sucrase (Kreikemeier et al., 1990), which is apparently not expressed. Therefore, ruminants depend primarily on maltase and isomaltase activity to produce glucose units for absorption (Harmon, 1992); however, neither sucrase-isolmaltase nor maltase-glucoamylase activity has been fully characterized in the ruminant (Harmon et al., 2004). Comparatively, few aspects concerning the process of glucose absorption have been described in detail for ruminants. The primary mode of glucose transport from the lumen into the bloodstream is that of the SGLT1 transporter, which couples glucose transport to an inwardly directed sodium gradient (Wright, 1993). Another important transporter, GLUT2, serves as the major route of glucose exit from the cells as well as entry of glucose from the blood into enterocytes (Thorens, 1993). Activity of glucose transporters and expression of SGLT1 and GLUT2 mRNA have been reported as being highly variable along the intestinal axis, exhibiting varied responses to luminal substrate availability and thus glucose absorption capabilities (Harmon and McLeod, 2001; NoziÃ¨re et al., 2010).

Ruminants derive 25% or less of their glucose supply from dietary glucose via carbohydrate digestion in the GIT, so gluconeogenesis is the primary source of glucose supply for ruminants (Huntington, 1997). The VFA, propionate, is quantitatively the most important source for glucose synthesis, whereas net propionate uptake by the liver accounts for approximately 70% of net liver glucose production (Huntington et al., 2006). A general

concept regarding gluconeogenesis and energy intake is that a positive relationship exists between these two variables, whereby a ruminant's glucose requirement increases along with potential dietary sources of glucose when they consume high-concentrate diets. Results of studies with multicatheterized ruminants indicate that the release of glucose by the liver may or may not change with increased supply of glucose or glucose precursors from the portal-drained viscera, but proportional use of precursors by the liver does reflect changes in the supply (Huntington, 1997). Synthesized glucose that is not immediately required for metabolism has several possible avenues of recycling, one of which includes glycogen production and glycogenolysis in the liver or muscle. During situations of enhanced glucose supply, activation of metabolic pathways to reduce energetic costs and increase substrate cycling may push the metabolic system in an energetically efficient manner.

Investigations of processes associated with the ruminal digestive system and liver are limited in the context of FE and as a driver of variation in RFI. Various studies have estimated that these tissues can account for approximately 30 to 50% of total energy expenditure, which is exceptionally high considering these organs only account for typically 10% of body mass (Ferrell, 1988; Archer et al., 1999; Caton et al., 2000). An examination of these tissues will provide insight into underlying physiological mechanisms that may be associated with improved FE.

Mitochondrial Function

Mitochondria are involved in the regulation of cellular homeostasis, being numerous in metabolically active cells (i.e., liver, muscle, brain cells) and producing approximately 90% of cellular energy as ATP via oxidative phosphorylation. Known as the "powerhouse" of the cell, mitochondria and their associated physiological processes impact overall growth and development of an animal, which as a result, may have implications upon FE as well. Studies investigating differences in mitochondrial function and biochemistry as they relate to growth performance and FE status of various livestock species have been published (Bottje et al., 2002; Kolath et al., 2006a; Bottje and Carstens, 2009).

To study mitochondrial function and FE (measured as G:F), isolated mitochondria from breast and leg muscles of broilers exhibiting a superior G:F phenotype were evaluated

(Bottje et al., 2002). This study indicated that RCR values (indicative of better respiratory chain coupling) were higher in broilers with superior G:F compared to broilers with inferior G:F when provided pyruvate and malate (NADH-linked substances), but no differences were observed with succinate. These results indicate that a site-specific defect may be present in Complex I of the electron transport chain in muscle mitochondria of inferior G:F broilers (Bottje and Carstens, 2012). Using liver mitochondria, Lancaster et al. (2007) also reported higher RCR values in steers with low RFI compared to high RFI steers. Additionally, Kolath et al. (2006a) examined the relationship between mitochondrial function and RFI in Angus steers via the LM muscle. This study indicated that low RFI steers exhibited a greater rate of state 2 and 3 respiration, respiratory control ratio, and hydrogen peroxide production than did high RFI steers when provided with glutamate or succinate. Both studies reported that mitochondrial function and the ability to perform oxidative phosphorylation was not different between high and low RFI animals, as was reported in broilers. Further, Kolath et al. (2006b) indicated that no differences were observed between high and low RFI animals in their expression of uncoupling protein 2 and 3 mRNA or protein, and that mitochondrial DNA sequence is not related to RFI status.

There are many aspects of mitochondrial physiology that can impact production efficiency of livestock, such as mitochondrial function, electron transport chain, and oxidative stress and protein oxidation. A great deal of research has been conducted to determine the manner in which these factors impact efficiency (Bottje et al., 2002; Ojano-Dirain et al., 2004; Iqbal et al., 2005; Ojano-Dirain et al., 2005; Bottje et al., 2009; Tinsley et al., 2010), especially in poultry. Studies have shown that inefficiencies of mitochondrial activity, such as proton leak and the production of reactive oxygen species, may contribute to a less-efficient phenotype (Bottje and Carstens, 2012). As research continues regarding mitochondrial function in the context of FE, the complex nature of these interactions will become clearer.

Developmental Programming and Epigenetics

Developmental programming is the concept that exposure to adverse events or positive affectors during specific periods of gestation and development can have lasting effects on offspring by “programming” gene expression and phenotype, while epigenetics is

a term that means “in addition to genetics”. Epigenetic modifications include gene silencing or activation that occurs independently of changes in the gene’s DNA sequence (Meyer et al., 2012), resulting in differences in gene expression that do not depend on mutations. An evolutionary advantage of developmental programming is that the genome can respond to the environment in the short term, rather than depending on long-term mechanisms such as gene mutation (Meyer et al., 2012).

Research investigating the effects of developmental programming and epigenetics in relation to FE of beef cattle is very limited, but suggests that FE during the growing phase may be programmed in utero. Price et al. (2009) reported that calves from dams (fed to meet NRC recommendations for gestation) had decreased FI and a lower RFI during the finishing phase compared with calves from dams (fed at 70% of NRC recommendations during early to mid-gestation), despite having similar ADG. Funston et al. (2010) indicated that growing heifers were more efficient (low RFI) if their dams were not supplemented with protein during the last third of gestation compared to those heifers born to protein-supplemented cows, while Martin et al. (2007) observed no differences in offspring RFI when cow nutritional management (meadow pasture vs. cool-season grass hay) was performed during early lactation.

The relationship between developmental programming, epigenetics, and FE is in the early stages of investigation. Although no specific associations have been identified, there is potential for this type of research to prove vital in the discovery factors that may impact offspring FE status while in utero. Further, organ systems have a clear role in whole animal FE, and contributions of developmental programming of these tissues may contribute significantly to FE of the animal (Meyer et al., 2012).

Physiological Indicators of Residual Feed Intake

Serum IGF-I Concentration

Systemic concentrations of various metabolic indicators have been evaluated at varying time-points within the production cycle in an attempt to identify their relationship with FE traits (Wood et al., 2004; Nkrumah et al., 2005; Lancaster et al., 2008; Kelly et al., 2011a) and their potential as indirect selection tools for RFI. Due to phenotypic and genotypic relationships with important bovine production traits (Davis et al., 1995;

Johnston, 2001) and its moderate heritability (Davis and Simmen, 2000), interest has been shown in using serum IGF-I concentration as an indirect selection tool for RFI.

Richardson et al. (1996) indicated that there were no phenotypic differences in circulating concentrations of IGF-I at the completion of a 120 d testing period for high and low RFI animals (276 ± 7 *v* 249 ± 17 μg/mL) fed a roughage-based diet. Lancaster et al. (2008) reported no associations between RFI of Angus bull and heifer progeny (from parents divergently selected for serum IGF-I concentration) and IGF-I concentrations (weaning and initial) in either study 1 (roughage-fed) or study 2 (grain-fed). However, Brown (2005) observed positive and negative relationships between RFI and IGF-I concentration when using roughage- and grain-based diets, respectively. Recently, Kelly et al. (2010) sampled systemic IGF-I concentration at d 1, 30, 60, and 84 during the experimental period and reported that IGF-I concentration was unrelated to any measure of FE when evaluating heifers that were consuming a grain-based diet and previously ranked as yearlings for phenotypic RFI. Furthermore, plasma IGF-I concentration at either the beginning or end of the performance test of bulls (10 mo of age) were not different between RFI groupings when they had consumed a primary concentrate diet (Kelly et al., 2011a). It is known that production and regulation of systemic IGF-I concentration within the mammalian endocrine system is influenced by plane of nutrition, and diet type (i.e., roughage-based vs. grain-based) has been implicated as a factor influencing the relationship between RFI and IGF-I concentration. However, it is not clear if diet type, growth stage or the interaction of diet type and growth stage may be drivers of variability in circulating concentrations of IGF-I and thus its relationship with RFI. Due to the inconsistencies reported among these studies, there doesn't appear to be a direct association between RFI performance and systemic IGF-I concentration at the phenotypic level.

In contrast, other studies have identified an association between these two variables at the genetic level, indicating that a relationship may exist. Johnston et al. (2002) reported positive genetic correlations (0.56 ± 0.35 and 0.39 ± 0.13) between RFI and serum IGF-I concentration, measured from 2 different data sets where temperate and tropically adapted breeds were evaluated for RFI and sampled for IGF-I concentration at various time points. In addition, Moore et al. (2005) reported a positive genetic correlation of 0.41 ± 0.21

between RFI evaluated at approximately 11 mo of age and IGF-I concentration measured either at, or prior to, weaning (average age 201 d) or postweaning (average age 310 d) in Australian Angus seedstock cattle. These analyses initially suggested that, due to the moderate to strong genetic correlations of RFI with IGF-I concentration, IGF-I concentration could serve as a potential indicator of RFI performance. However, Wolcott et al. (2006) sampled IGF-I concentration at postweaning, feedlot entry, and feedlot exit for Brahman and tropical composite yearling steers and reported a negative genetic correlation between feedlot-evaluated RFI and IGF-I concentration. When data were pooled and both breeds were analyzed together, the negative genetic correlation between RFI and IGF-I remained. Noticeably, stage of maturity can alter the observed relationship between RFI and IGF-I concentration. The physiological actions of IGF-I include stimulation of protein synthesis and inhibition of protein degradation, thereby improving protein retention and inducing muscular hypertrophy (Oddy and Owens, 1996). These complex interactions suggest that cattle evaluated for RFI at approximately 8 to 10 months of age would be expected to have proportionally greater lean tissue growth, and thus increased IGF-I concentration, compared to older cattle entering the finishing phase at approximately 12 to 14 months of age. This concept may have been a factor influencing the positive association between RFI and IGF-I concentration observed by Moore et al. (2005) while also contributing to the negative relationship observed by Wolcott et al. (2006). Johnston (2007) later reported IGF-I concentration to have a positive genetic correlation (0.17 ± 0.11) with postweaning RFI and a negative genetic correlation (-0.22 ± 0.16) with feedlot-evaluated RFI. Johnston (2007) further stated that the accuracy of using IGF-I concentration to predict breeding values for RFI was reduced and that the polygenic nature of RFI differed between the postweaning and feedlot test periods, indicating that the expression of genes responsible for IGF-I concentration differ as cattle become more physiologically mature.

Gene Expression

Very few studies have examined the contribution of key genes associated with metabolic processes such as muscle metabolism, oxidative phosphorylation, and cellular energetics. It is well documented that the somatotropic axis greatly influences growth and muscle metabolism (Florini et al., 1996b; Oksbjerg et al., 2004; Duan et al., 2010), which

indicates that this system could have substantial effects upon the overall energetic efficiency of feed efficient animals. In addition, the utilization of carbohydrates and lipids for energy deposition and mobilization within skeletal muscle is also of importance due to the differential metabolic costs of energy storage and partitioning associated with these substrates.

Growth hormone receptor (GHR) is a transmembrane-bound receptor found in many tissues throughout the body, and it is activated by the binding of GH. The release of GH and subsequent receptor binding is a main activator of the somatotropic axis and therefore an important regulator of postnatal growth. When considering tissue proportion in relation to body mass, skeletal muscle is quantitatively the major site of GH binding, initiating such cellular events as mitosis and differentiation, protein turnover, and lipid metabolism (Pell and Bates, 1990). Conducting a whole-genome association study, Barendse et al. (2007) reported that DNA variants in or near proteins contributing to cellular energetics were 10 times as common as those affecting appetite and body-mass homeostasis, while the largest group of variants consisted of those associated with gene regulation (i.e., control of the phenotype). Sherman et al. (2008) indicated that a SNP located in intron 4 of the GHR gene was associated with animal body weight (BW; dominance effect) and RFI (allele substitution effect). Chen et al. (2011) using global gene expression profiling revealed no statistical difference in the *GHR* expression of the liver using real-time PCR, although expression of *GHR* appeared to be higher in high RFI animals as suggested by microarray. In contrast, Kelly et al. (2013) reported that *GHR* expression was greater in the LM of low RFI animals compared with their high RFI contemporaries. In addition, Chen et al. (2011) observed that liver *IGFBP3* expression was higher in low RFI animals using both microarray and real-time PCR studies. Kelly et al. (2013) did not detect any differences between RFI groupings regarding the expression of *IGFBP3* or *IGFBP5* in skeletal muscle tissue. These studies suggest that the somatotropic axis may be involved in the regulation of RFI; however, the data are derived from too few animals precluding any deduction of the direction and magnitude of these relationships.

Various physiological aspects associated with energetic efficiency and homeostasis have been implicated as contributors to phenotypic differences in growth rate and FE of

livestock, and thus sources of variation resulting in the RFI phenotype (Herd and Arthur, 2009). A dominant regulator of mitochondrial biogenesis and lipid metabolism is *PGC1-α*, with its expression being specific in highly oxidative tissues such as brown adipose, muscle, and liver (Wu et al., 1999; Puigserver, 2005). Kelly et al. (2011b) found that *PGC1-α* expression was higher in the muscle of low RFI animals and detected a negative relationship between *PGC1-α* and DMI, RFI, and FCR. In adipose tissue, *PPAR-γ* is a dominant regulator of expression of genes that encode proteins essential for adipocyte differentiation and is also involved in the uptake and metabolism of fatty acids (Tontonoz et al., 1995; Rosen et al., 1999). In addition, a functional relationship exists between *PPAR-γ* and *C/EBP-α*, whereby the activation of *PPAR-γ* leads to the activation of *C/EBP-α* and both transcription factors work together to promote differentiation (Loftus and Lane, 1997). The existence of these genes and their metabolic function in adipose tissue has been well defined; however, even though these genes are thought to have a similar presence and function (activation of lipogenesis in muscle tissue), reports regarding their exact nature are sparse. Kelly et al. (2011b) indicated that RFI phenotypes were not different regarding muscle (*Longissimus dorsi*) *PPAR-γ* mRNA expression, although *PPAR-γ* was negatively associated with FCR (r = -0.53) and tended to be negatively associated with RFI and DMI. Data analyses from the aforementioned studies indicate that activation of lipogenic pathways in muscle tissue may be associated with RFI. From these observations, it can be inferred that more efficient animals (low RFI) may have the genetic potential to simultaneously regulate the uptake and metabolism of fatty acids, where inefficient (high RFI) animals may increase their production of fatty acids without concordantly increasing uptake and metabolism. These differences could be potential contributors to variation in metabolic efficiency and thus, variation in RFI.

Fiber Type Composition

Muscle fiber type is considered a contributor to variation in body composition and is influenced by several environmental and genetic factors, such as species, breed, gender, nutrition, and gene expression. Within the beef industry, fiber type composition is not only an important aspect of energy metabolism, but also of end-product quality. When thinking about the variation in FE, the goal is to select for and produce the most efficient cattle in

terms of energy usage and weight gain, whereby a difference in muscle fiber type composition may contribute to the variation in RFI. In relating this hypothesis to local availability of IGF-I in partitioning fiber type and muscle hypertrophy, there is literature to support enhanced paracrine responses to IGF-axis activity in promoting type I fiber composition (Musaro et al., 2001; Mavalli et al., 2010). This may suggest that higher, local concentration of IGF-I is available due to either increased tissue synthesis or from lower expression of inhibitory binding proteins. It has been suggested that IGF-I-induced skeletal muscle hypertrophy is due to local production of IGF-I via autocrine and/or paracrine effects rather than circulating IGF-I concentration (Bamman et al., 2001), which may be a potential contributor to the variability observed in studies looking exclusively at serum IGF-I concentration . Furthermore, IGF-I has been implicated as a stimulator of protein synthesis and an inhibitor of protein degradation, thus improving protein retention (Oddy and Owens, 1996; Hill et al., 1999), which is consistent with higher local IGF-I in muscle of feed efficient animals. In addition, type I fibers are associated with an increased number of mitochondria and a relatively greater capacity to perform oxidative phosphorylation. When thinking about substrate utilization in the context of FE, the ability to perform oxidative phosphorylation at an increased rate will result in a preference to utilize high-energy lipid substrates compared to carbohydrates, exhibiting greater efficiency for mobilization of adipose and an increased endurance rate. If feed efficient animals have a relatively greater proportion of type I fibers compared to type IIb fibers, then this may be a source of variation that is underlying differences in FE. Further, tenderness of LM muscle in beef cattle has been correlated with an increase in type I fibers (oxidative, red) (Ockerman et al., 1984; Maltin et al., 1998). To date, RFI has not been associated with an increase in tenderness of meat; however, there is still a vast amount of knowledge to uncover about the relationship between FE, fiber type composition, and meat quality.

Maintenance Energy

Development of the Maintenance Energy EPD

The RAAA, established in 1954 as the first performance registry for beef cattle, remains committed to the beef industry by maintaining an objective focus on genetic

selection with the most accurate genetic prediction method available. In 2004, the RAAA was the first breed association to include a measure of efficiency in its international genetic evaluation program in an attempt to lower cow maintenance costs through development of the ME_M EPD, which is an estimate of energy requirements needed to maintain an animal's BW and condition. The equation for calculation of ME_M is as follows: MEm_i = MEm (MW_i) + .10*MEp_i, where MEm_i = EBV of metabolizable energy requirements at maintenance for individual (i), MEm (MW_i) = EBV of metabolic body weight at 5 years of age and the population mean mature weight (**MW**) for individual (i) adjusted to a body condition score of 5, and MEp_i = lactation energy for individual (i) derived from the individual's genetic prediction for weaning weight (**WW**) maternal (Evans, 2001). The prediction is divided by 2 to be reported as a progeny difference or EPD and is expressed in Mega-calories per month (Enns et al., 2003). Because these components are known to affect maintenance requirements (Montano-Bermudez et al., 1990; MacNeil et al., 1991), estimating an animal's energy requirement using this approach is an innovative way to begin to partition energy required for maintenance away from other traits closely associated with energy consumption, such as growth and fertility. However, these components are also highly associated with growth and mature size, which implies that there is a confounding relationship between ME_M EPD these traits.

In 2009, Williams and others discussed potential bias associated with MW and the ME_M EPD, because the calculation does not account for selection on animals that is occurring at weaning or 1 yr of age (Williams et al., 2009). The authors stated that cattle producers are presumably selecting for animals with a heavier immature BW, whereby the resulting consequence is a heavier MW in the cow herd that is not properly accounted for prior to selection. Ultimately, this method of ME_M EPD calculation is failing to reward sires that produce offspring with heavy WW and low maintenance requirements. Williams et al. (2009) suggested that the MW analysis should include these younger observations, in order to account for selection of animals with heavier immature BW and remove bias of that selection.

Value as an Indicator of Feed Efficiency

It is very challenging to accurately estimate ME_M EPD due to many factors, including the lack of reliable ways to directly measure and partition energy required for maintenance and productivity measures. Thus, less reliable, surrogate measurements have provided the basis of data used in its estimation. Unfortunately, the science underlying the partitioning of energy for maintenance and production in mature cows in extensive environments is very limited. In addition, biological mechanisms contributing to underlying variation in maintenance and production (and thus, efficiency) are poorly understood.

Energy devoted to maintenance is among one of the most important concepts regarding FE and overall animal efficiency. The maintenance requirement of an animal can be summarized as the amount of feed energy required to produce a zero BW change (or a zero body energy change) after allowing for the various energy densities of body components (Ferrell and Jenkins, 1985). More specifically, these requirements represent the amount of energy necessary to maintain processes such as basal metabolism (i.e., protein synthesis and degradation, ion transport, cellular signaling, etc.), vital organ function, voluntary movements, and thermoregulation (Thompson et al., 1983). Energy expenditures for maintenance functions vary in beef cattle, according to genetic potential, production status, and physiological state. It has been estimated that maintenance functions account for 70 to 75 % of total energy expenditure in the producing female and anywhere from 35 to 50 % in growing and finishing animals (Ferrell, 1988). Studies have indicated that variation in maintenance requirements can be partially explained by the variation in body composition (i.e., lean and fat tissue) and associated metabolic processes (Ferrell et al., 1979; Cleveland et al., 1983). Other contributors to an animal's maintenance requirement are body tissues (i.e., visceral organs) with increased metabolic activity (Ferrell, 1988; Caton et al., 2000) and cellular processes (Whittam, 1961; Gregg and Milligan, 1982). Therefore, maintenance requirements of an animal are driven by both the cellular activity of highly metabolic tissues and overall body composition, which further justifies the physiological importance of maintenance requirements and the need to understand its impact on RFI.

It is hypothesized that animals exhibiting an improvement in RFI will have decreased maintenance requirements (Richardson et al., 2004). However, very few studies

have evaluated the relationship between maintenance requirements and RFI. Castro Bulle et al. (2007) suggested that RFI may be negatively correlated with ME for maintenance via protein metabolism measurements of steers tested for RFI, but these results must be viewed with caution due to the small number of replicates in the study. Due to the limited knowledge regarding the relationship between maintenance requirements and RFI, it is unknown as to the validity of ME_M EPD as an indicator of FE and, more specifically, RFI.

Awareness and Perceptions of Feed Efficiency

Adoption of Feed Efficiency and Residual Feed Intake

Selection for RFI has been successfully implemented for the genetic improvement of beef cattle in other countries, such as Australia and Canada; however, adoption of RFI as a selection practice is relatively new in the US, where the willingness to accept this concept, as a measure of FE and incorporation into production practices, is lagging. Within the context of agriculture, there are documented factors which affect the rate of adoption for new practices or technologies, including social status, economic constraints, and lack of information and awareness (Wulfhorst et al., 2012). Therefore, there may be several possibilities as to why selection for RFI has not been fully adopted in the US.

Even though beef producers are continually experiencing consumer demand for their product, they are often faced with a variety of social and economic factors affecting production practices, which can influence and complicate the decision-making process. When discussing selection for RFI and implementation as a measure of FE, the long-term benefits of selecting for RFI are significantly greater than the short-term benefits. However, if producers are not fully informed about the potential savings in feed costs over the lifespan of their animals and production operation, they may decide that the long-term benefits do not outweigh the present costs associated with improving FE of cattle in their operation (Wulfhorst et al., 2010). Additionally, the assessment of willingness for or barriers against adoption of selection for FE technologies is limited, where studies that include the use of a social survey to evaluate beef producer selection practices in the US beef industry are unavailable, except for that of Wulfhorst et al. (2010).

Wulfhorst et al. (2010) conducted a national survey oriented toward producers within the beef industry, in order to assess the current level of understanding of FE within the industry. In addition, a follow-up survey was conducted to determine perceptions related to the economic impacts of evaluating bulls using RFI as a measure of bull quality. The study was conducted over a 3 year period and collected a variety of information to characterize respondents and cattle operations. Nearly two-thirds of all respondents (63.6%) had not heard of RFI prior to the survey. The other 36.4% of respondents, who had indicated they had heard of RFI, received their information via breed association magazines (53%), weekly livestock newspapers (30%), and University Extension programs (27%), as well as other less commonly noted sources. For producers who indicated they had heard of RFI, well over three-quarters of them responded that they had limited (60.8%) to no knowledge (23.6%) of the use of RFI as a measure of genetic value. Furthermore, when considering the economic value of RFI, three-quarters of respondents (75.9%) indicated they perceived bulls were worth more if evaluated for RFI, while 80% of respondents indicated that there was a demand for RFI evaluated bulls by bull-buying customers. This type of response indicates that RFI-evaluated bulls are broadly recognized as having added value due to the FE measurement, even though knowledge about RFI is lacking.

Overall, RFI is a complex FE trait that is not readily understood by many within the beef industry. It appears that important factors influencing the adoption of selection practices including RFI as a FE measure for genetic improvement are awareness and education. Therefore, it is likely that more education about RFI will motivate those within the beef industry that set the precedent for acceptance of new technologies to incorporate this trait for improvement of profitability (Wulfhorst et al., 2012).

Development of a Feed Efficiency EPD

Over the last few decades, the beef industry has utilized data-driven methods to improve the genetic merit of beef cattle, which has been characterized by a strong emphasis on productive traits, mainly BW at various ages, with little regard for economically important traits, such as feed requirements (Garrick and Golden, 2009). Some within the industry have now recognized that feed requirements are a significant component of both cow-calf and feedlot operations and have expressed a desire for an EPD to reflect FE in

breeding programs. However, there are limitations as to the inclusion of a FE EPD as part of the national cattle evaluation (**NCE**), which was discussed in detail by Crews (2005).

Originally, individual FI was not measured and intake was determined at the pen level, which is inappropriate for an evaluation system that is characterizing individual animal differences. However, advances in technologies related to the measurement of individual FI of cattle fed in groups have occurred recently, although the cost associated with this type of monitoring equipment is high. In addition to the cost of measuring individual FI, the suitability of data is another concern, especially regarding the lack of parentage and pedigree for the majority of harvest cattle. Further, some predictions exist for an efficiency EPD that do not require the measurement of individual FI, where accuracy depends on genetic correlations between traits for which phenotypes are available and traits of interest. However, few phenotypes or indicator traits have been identified for RFI, which is partially due to the independence of RFI and other production traits (Crews, 2005).

Implementation of an efficiency measure in the NCE has the potential to significantly impact beef production systems, but the US beef industry does not have a national system to collect and manage FI measurements or an agreed upon approach as how to process that type of information (Garrick, 2005). Currently, there is ongoing research and discussion within the beef industry as to which measure of FE is appropriate for production selection practices and the validity of producing an EPD for this measure. An alternative approach that has been suggested is creating an EPD for FI (Garrick, 2005). In any case, if the beef industry is to move forward with the development of a FE EPD, an approved method of measurement of genetic value must be agreed upon.

Research Objectives and Hypotheses

Focus of research

The purpose of this research was to gain a more in-depth understanding of the relationships between FE (specifically RFI) and economically relevant production traits and to identify potential physiological mechanisms that may contribute to the variation in RFI. Selecting animals with improved FE has great potential impact upon the beef industry; therefore, this trait must be fully understood in order to avoid any unwanted production

affects. This research will further contribute to the growing body of knowledge regarding improvements and implications of improved FE in beef cattle.

Development of hypothesis I (relevant to Chapter 2)

Identifying and understanding FE relationships between various stages of growth and production is of great interest to the beef industry, whereby implementation of a FE measure that is applicable and beneficial to both the cow-calf and feedlot sectors is desirable. If selection for improved FE is implemented, it should not negatively impact well-established production traits associated with carcass and product quality of beef cattle. Additionally, the relationship between maintenance requirements and FE is unknown, but highly speculative. The evaluation of this relationship will provide insight into a possible alternative selection trait relating to FE in RA cattle. Therefore, it was hypothesized that 1) RFI measured during the postweaning growth phase is indicative of FE status in the finishing phase, 2) postweaning RFI is not associated with carcass or end-product quality traits, and 3) ME_M EPD is an indicator of postweaning RFI.

Development of hypothesis II (relevant to Chapter 3)

A considerable amount of variation exists in FI, growth rates and maintenance requirements of individual animals during various stages of the beef production cycle. The investigation and identification of underlying physiological mechanisms responsible for the variation is a critical component to the understanding of FE; however, it is currently unknown as to the specific metabolic pathways and/or genes that are regulating FE. Additionally, the identification of a metabolic indicator that will be indicative of FE status early in the production cycle is desirable, but little progress has been made in this endeavor. Candidate tissues for the study of gene expression related to growth and energy expenditure are those that provide a large contribution to overall regulation of energy storage and energy expenditure. Thus, muscle, adipose tissue, and gut (including the liver) have been proposed for study of FE. In the present study, muscle was chosen, and candidate genes involved in regulation of muscle growth and energy expenditure provided a focus for these processes. Thus, it was hypothesized that 1) specific genes related to regulation of muscle growth, lipogenesis, and lipolysis are involved in the regulation of RFI at the molecular level, 2) low

RFI animals exhibit differences in fiber type composition compared to high RFI animals, and 3) serum IGF-I (at weaning) is an indicator of RFI.

Development of hypothesis III (relevant to Chapter 4)

The importance of including a measure of FE into profitable selection programs has become a recent topic of interest within the beef industry. Currently, information is limited as to whether it is more beneficial to develop an EPD of FE or feed intake as a trait for implementation into a selection index. Additionally, selection programs that include traits related to FE may be able to ultimately reduce maintenance requirements of beef cattle, which is a major contributor to the observed animal variation that exists in feed utilization. Therefore, it was hypothesized that sire ME_M EPD is an indicator of sire RFI EPD.

Summary of dissertation hypotheses

The remaining chapters will provide information regarding the experimental design, testing, and conclusions associated with the following hypotheses:

1) RFI measured during the postweaning growth phase is indicative of FE status in the finishing phase
2) Postweaning RFI is not associated with carcass or end-product quality traits
3) ME_M EPD is an indicator of postweaning RFI
4) Specific genes related to growth, lipogenesis, and lipolysis are involved in the regulation of RFI at the molecular level
5) Low RFI animals exhibit differences in fiber type composition compared to high RFI animals
6) Serum IGF-I (at weaning) is an indicator of postweaning RFI
7) ME_M EPD is an indicator of RFI EPD

Figure 1.1. Contributions of biological mechanisms to variation in residual feed intake (RFI)

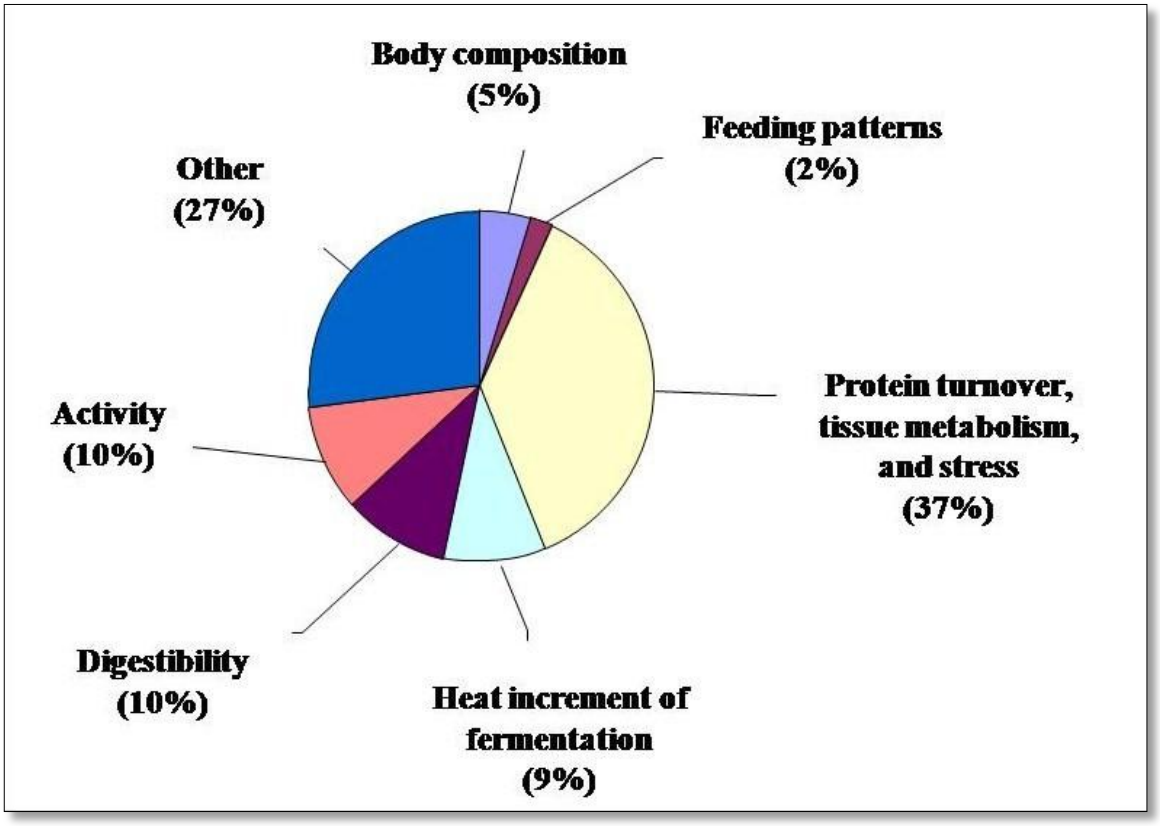

Fig 1.1. Contributions of biological mechanisms to variation in RFI as determined from experiments on divergently selected cattle (Richardson and Herd, 2004). Permission to reprint figure was obtained from CSIRO Publishing on January 6, 2014.

Figure 1.2. Overview of pathways and processes that link muscle and adipose tissue as potential contributors to variation in energy metabolism and feed efficiency (FE)

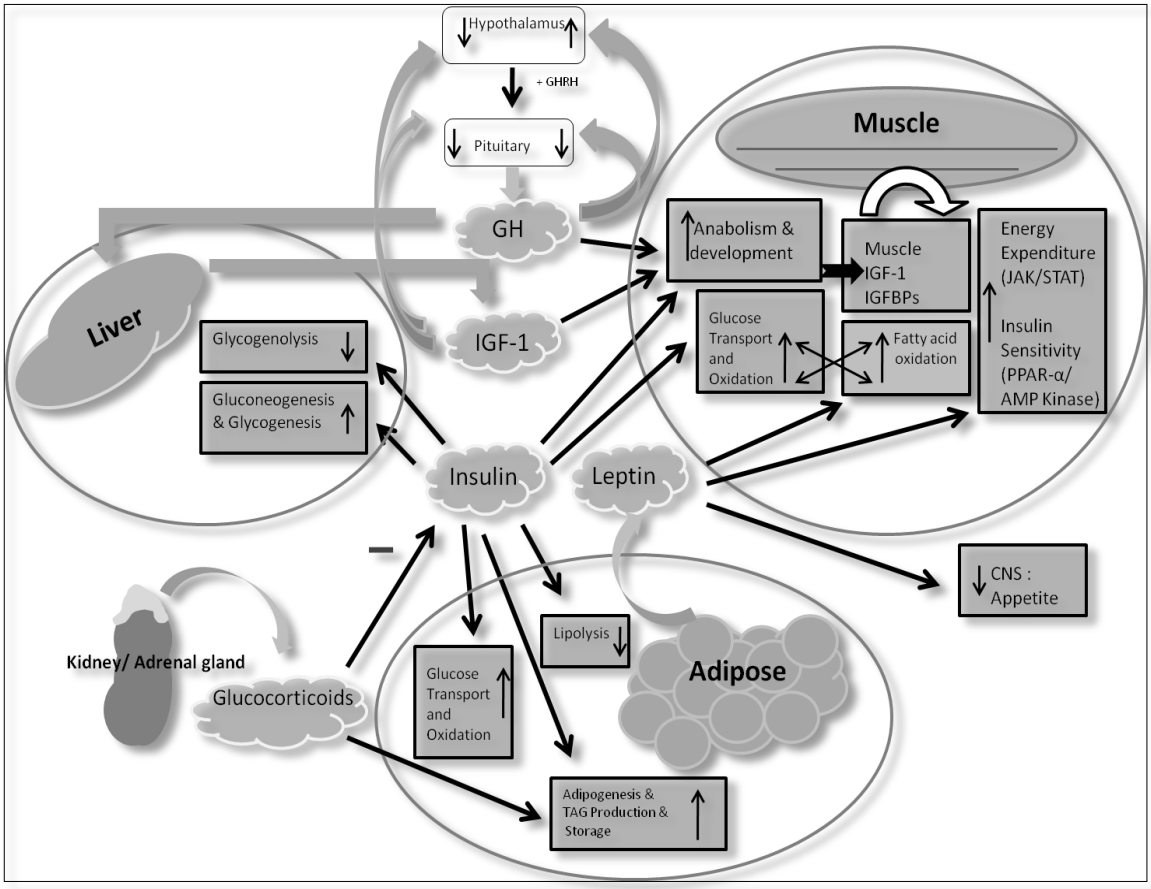

Fig 1.2. A brief overview of the pathways and processes that link muscle and adipose tissues with potential to contribute to variation in energy metabolism and thus FE. Note: The pathways depicted are shown in the case of positive energy balance. The factors involved include GH, IGF-I, insulin, leptin and glucocorticoids. Figure Key: the main tissues of focus are shown along with tissue-specific processes (grey boxes). Broad, grey arrows link tissues to endocrine factors and endocrine feed-back loops. Heavy, black arrows link endocrine signals to tissue-specific processes. Black arrows within process boxes indicate either up-regulation or down-regulation responses. Within muscle, some additional processes are depicted. The crossed arrows indicate the competing interactions of insulin and leptin that stimulate glucose oxidation and fatty acid oxidation, respectively. Interactions of these pathways can repartition oxidation between these two substrates. Each pathway also may inhibit the action of the other. The broad white arrow indicates that stimulation of locally produced IGF-I and IGFBPs results in autocrine/paracrine signaling that also regulates anabolic processes in muscle (Welch et al., 2012b). Permission to reprint figure was obtained from Wiley-Blackwell Publishing on December 12, 2013.

Table 1.1. Different measures of feed efficiency and formulas for calculation[1]

Trait	Abbreviation	Definition	Formula
Liveweight	LWT	Weight (wt) at a specified age	
Average daily gain	ADG	Wt gain per day	Regression coefficient from the regression of wt on time (days)
Feed intake	FI	FI per day	
Feed conversion ratio	FCR	FI per unit wt gain	FI ÷ ADG
Partial efficiency of growth	PEG	Efficiency of wt gain net of maintenance feed (F_m) requirements	ADG ÷ (FI-F_m)
Residual feed intake	RFI	FI net of the expected feed requirements for maintenance and growth, with expected (exp) FI obtained by regression	FI-expFI, where expFI was obtained by the regression of FI on average test period $LWT^{0.75}$ and ADG
Relative growth rate	RGR	Growth relative to instantaneous size, expressed as percentage of change in LWT per day	100 x (log end wt – log start wt) ÷ days on test
Kleiber ratio	KR	Wt gain per unit metabolic body wt	ADG ÷ average test period $LWT^{0.75}$

[1]Table adapted from Arthur et al. (2001c).

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CHAPTER 2

Relationships among performance, residual feed intake, and product quality of progeny from Red Angus sires divergent for maintenance energy EPD

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Abstract

Energy expenditure is a physiological process that may be closely associated with residual feed intake (**RFI**). The maintenance energy (**ME_M**) EPD was developed by the Red Angus Association of America (**RAAA**) and is used as an indicator of energy expenditure. The objectives of this study were to evaluate and quantify the following relationships using progeny of Red Angus (**RA**) sires divergent for ME_M EPD: 1) postweaning RFI and finishing phase feed efficiency (**FE**), 2) postweaning RFI and end product quality, and 3) postweaning RFI and sire ME_M EPD. A total of 12 RA sires divergent for ME_M EPD were chosen using the RAAA-generated ME_M EPD values and were partitioned into 2 groups: high ME_M EPD (≥ 4 Mcal/mo) and low ME_M EPD (< 4 Mcal/mo), based on the breed average of 4 Mcal/mo. Commercial crossbred cows were inseminated to produce 3 cohorts of progeny, which were tested for postweaning RFI (cohorts 1, 2, and 3) and finishing phase FE (cohorts 1 and 3). Results indicate that postweaning RFI and finishing phase FE of steer progeny tended to be positively correlated (r = 0.38; $P = 0.06$) in cohort 1 and were positively correlated (r = 0.50; $P = 0.001$) in cohort 3. In addition, postweaning RFI was not phenotypically correlated ($P > 0.05$) with any carcass traits or end-product quality

measurements. Sire ME_M EPD was phenotypically correlated ($P < 0.05$) with carcass traits in cohort 1 (HCW, LM area, KPH, fat thickness, and yield grade) and cohort 2 (KPH and fat thickness). However, variation in measured LM area was not explained by the genetic potential of ribeye area EPD, and therefore, the observed correlation between sire ME_M EPD and measured LM area may suggest an association between ME_M EPD and LM area. A correlation ($r = 0.24$; $P = 0.02$) was observed between postweaning RFI and ultrasound intramuscular fat (**UIMF**) percentage in cohort 2, but was not detected in cohorts 1 or 3. In addition, no phenotypic relationship was observed ($P > 0.05$) between progeny postweaning RFI and sire ME_M EPD. Therefore, results suggest the following: 1) RFI measured during the postweaning growth phase is indicative of FE status in the finishing phase, 2) neither RFI nor sire ME_M EPD negatively affected carcass or end-product quality, and 3) RFI and sire ME_M EPD are not phenotypically associated.

Introduction

In order to decrease costs, there is a renewed interest across the beef industry to improve FE, especially since the recent and rapid increase in feed costs (since 2006). Residual feed intake, a FE trait, measures the variation in feed intake beyond that needed to support maintenance, growth (Archer et al., 1999a), and body composition (Basarab et al., 2003). Because RFI has been shown to be moderately heritable and independent of growth, it is considered valuable as a tool to improve FE (Herd and Bishop, 2000; Arthur et al., 2001a).

In 2004, the RAAA was the first breed association to include a measure of efficiency in its international genetic evaluation program, attempting to lower cow maintenance costs through the development of the ME_M EPD (Evans, 2001). Maintenance Energy EPD is used as an indicator of energy expenditure required to sustain body tissues. Estimating an animal's ME_M requirement is an innovative way to begin to partition energy required for maintenance away from other traits closely associated with energy consumption.

Various genetic, phenotypic, and physiological relationships have been identified within the context of RFI (Baker et al., 2006; Sherman et al., 2010; Kelly et al., 2011). However, few studies have focused on energy expenditure associated with RFI. Due to the

physiological importance of energy expenditure and industry motivation to produce feed efficient cattle, it is important to identify the relationships between RFI and ME_M EPD and their interactions with other performance and end-product quality variables. Therefore, the objectives of this study were to evaluate and quantify the following relationships using progeny of RA sires divergent for ME_M EPD: 1) postweaning RFI and finishing phase FE, 2) both postweaning RFI and sire ME_M EPD with end-product quality, and 3) postweaning RFI and sire ME_M EPD.

Materials and Methods

All animal procedures were reviewed and approved by the Institutional Animal Care and Use Committee (2011-3) as required by federal law and University of Idaho (**UI**) policy.

Selection and Use of Sires

A total of 12 RA sires divergent for ME_M EPD were chosen using the RAAA-generated ME_M EPDs. Criteria for recruiting sires to the study were as follows: (1) ME_M EPD accuracy ≥ 0.50, (2) balance of other production traits across sires for which EPDs were available, and (3) availability of adequate semen supplies. Developed by Evans (2001), the equation for calculation of ME_M is as follows: $MEm_i = MEm\ (MW_i) + .10*MEp_i$, where MEm_i = EBV of metabolizable energy requirements at maintenance for individual (i), MEm (MW_i) = EBV of metabolic body weight at 5 years of age and the population mean mature weight for individual (i) adjusted to a body condition score of 5, and MEp_i = lactation energy for individual (i) derived from the individual's genetic prediction for weaning weight maternal. The prediction is divided by 2 to be reported as a progeny difference or EPD and is expressed in Mega-calories per month (Enns et al., 2004).

The active sire breed average for RA ME_M EPD was 4 Mcal/mo in 2011 (RAAA, 2011). Based on this information, the sires were partitioned into 2 groups: high ME_M EPD ($\geq$ 4 Mcal/mo) and low ME_M EPD (< 4 Mcal/mo), with the groups being different ($P < 0.001$) for ME_M EPD. In order to obtain a balance of other traits across the high and low ME_M EPD groups, mean EPD values were calculated for both groups, and no differences ($P > 0.05$) were found between the high and low ME_M EPD groups for the following RAAA quantitative traits: milk, total maternal, calving ease maternal, stayability, ribeye area, yield

grade, 12th rib fat thickness, and marbling. It was not possible to balance for other EPDs: calving ease direct ($P = 0.04$), birth weight ($P = 0.04$), heifer pregnancy ($P = 0.03$), weaning weight ($P = 0.03$), and carcass weight ($P = 0.04$). Yearling weight ($P = 0.15$) was not different between the high and low ME_M EPD groups. Table 1 summarizes important trait EPDs for sires represented within their respective ME_M EPD group in each cohort. Each sire was represented across 2-3 cohorts. Cross-bred cows were estrus synchronized and bred by artificial insemination over three years. All cows and calves were managed under routine industry management practices. Progeny were genotyped for sire validation (Pfizer Animal Genetics, Kalamazoo MI) prior to RFI evaluation. Upon completion of the 3 annual breeding cycles, 11 out of 12 sires produced 15 or more F_1 progeny.

Postweaning Residual Feed Intake Evaluation

In 2008, crossbred calves (steers, n = 25; heifers, n = 17) were transported from the Nancy M. Cummings Research, Extension and Education Center (**NMCREEC**, Carmen, ID), to the UI campus (Moscow, ID) for cohort 1 RFI evaluation, using Calan gates (American Calan, Northwood, NH) to measure individual feed intake. In 2009, cohort 2 crossbred calves (steers, n = 8; heifers, n = 11) from Wood Cattle Company (Ardmore, SD) were simultaneously evaluated for RFI with NMCREEC crossbred calves (steers, n = 38; heifers, n = 34), and, in 2010, cohort 3 crossbred calves (steers, n = 38; heifers, n = 50) from NMCREEC were evaluated, using electronic, individual feed intake recording equipment (GrowSafe Systems Ltd., Airdrie, Alberta, Canada) located at NMCREEC.

Testing protocols were conducted in a similar manner for all cohorts, with stability of feed intake being the primary indicator for initiation of testing period. Prior to postweaning RFI evaluation, steers and heifers were allowed approximately 2 wk to adjust to the diet and feeding system environment (Calan gates and GrowSafe). Animals not adapting to the feeding system within the 2 wk adjustment period were removed from the test. Before the morning feeding, animals were weighed on 2 consecutive days at the beginning (d 0 and 1) and end (d 84 and 85) of the test period and every 2 wk during the test period. Animals were fed an industry-standard growing ration (Table 2) and were allowed *ad libitum* access to fresh water and feed, in which feed was provided twice daily at the same time each day. When using the Calan gate feeding system, feed was delivered

manually twice daily and orts were removed and weighed daily. Mechanical feeding equipment was used to deliver feed when using the GrowSafe feeding system. Daily orts removal was not necessary; however, bunks were cleaned weekly to prevent feed accumulation and spoilage. Bunk attendance and feed disappearance were recorded using GrowSafe Data Acquisition software (GrowSafe Systems Ltd.). Individual feed intake data were excluded from analysis during circumstances such as equipment failure or poor animal health. A certified UGC technician collected ultrasound measurements for fat thickness (**UFT**), UIMF, and LM area (**ULMA**) on d 84. Hair was removed, vegetable oil was applied between the 12th and 13th ribs, and measurements were taken using an Aloka 500V (Aloka America, Wallingford, CT). Images were processed using the UICS software for interpretation by a certified lab technician. In addition, the images were not standardized or adjusted for age or BW by the software or interpreter.

Finishing Phase Feed Efficiency Evaluation

Following postweaning RFI evaluation, the growing ration was modified in 4 stages to a finishing ration (Table 3). Individual feed intake and growth were recorded for steers only (not heifers) in cohorts 1 and 3 to evaluate finishing phase FE. Cohort 2 steers were commercially finished at Snake River Farms (AgriBeef Inc., American Falls, ID) due to an occupancy conflict within the testing system. Testing protocols used for postweaning RFI evaluation were also implemented for finishing phase FE evaluation. Steers were finished to a target BW of 591 kg (group average) before shipment for harvest, which resulted in a recorded feed intake period of approximately 110 d (including all modifications of the finishing ration).

Harvest and Carcass Data Collection

All steers were harvested at Washington Beef (Toppenish, WA), where carcass data were collected for cohorts 1, 2, and 3 via the VBG2000 Vision Camera (Vision For You LLC, Dakota Dunes, SD) and a trained carcass evaluator. In addition, the LM (i.e., strip loin) and *biceps femoris* (Thornton et al., 2012) were collected from the left side of each carcass (cohorts 1 and 2 only) during the fabrication process for various measurements of product quality.

Product Quality Measurements

Following harvest of cattle in cohorts 1 (May, 2009) and 2 (July, 2010), the vacuum packaged strip loins (IMPS 180) were purchased and transported to the UI campus meat science laboratory (Moscow, ID) for aging and post-harvest processing. On day 9 (cohort 1) and on day 10 (cohort 2) postmortem, wholesale cuts were removed from the vacuum packages. The anterior end of the strip loin was prepared by removing a slice approximately 2 cm-thick, perpendicular to the long axis of the LM. Subsequently, a total of 5 steaks were cut from the LM muscle, with each steak being 2.54 cm-thick. Steaks were allowed to age for an additional 4 d at 4°C before testing procedures were conducted. Individual steaks were used for the following analyses: proximate analysis, pH and color measurement, percent cook loss, Warner-Bratzler shear force (**WBSF**), glycogen content (Thornton et al., 2012), and sensory panel evaluation.

For proximate analysis, steaks were sent to SDK Laboratories (Hutchinson, KS). Moisture and DM were determined separately from CP and lipid content. On d 14 postmortem, ultimate pH of steaks was determined with a portable pH meter (model 1140, Mettler-Toledo, Woburn, MA) equipped with a puncture-type electrode, measured from the anterior end of the strip loin. The pH meter was calibrated using standard pH 4.0 and 7.0 buffers chilled to 4 ºC. Two objective color measurements were taken per steak using a Hunter MiniScan XE (Restin, VA). This instrument is equipped with a 25 mm-diameter measuring area and a 10° standard observer. The instrument was set to D_{65} illuminant and Commission International de l'Eclairage L*, a* and b* duplicate values taken from 2 locations on the steak were recorded. The scale for L* is from 0 (black) to 100 (white). Positive a* and b* values are red and yellow, respectively. Negative a* and b* values are green and blue, respectively. Calibration of the machine was carried out each day by measuring against the black and white calibration tiles, as suggested by the manufacturer. Hue angle was calculated as tan-1 a*/b* (Wheeler et al., 1996). Steaks were weighed and cooked to a final internal temperature of 71ºC. Steaks were re-weighed to determine cooking loss and allowed to cool to room temperature. Six cores (1.27 cm diam.) from each steak were mechanically removed parallel with the muscle fiber orientation using a drill press-mounted coring device. Shear force was determined by shearing each core

perpendicular to the muscle fiber using a WBSF instrument (GR Manufacturing, Manhattan, KS).

A consumer panel evaluated steaks for overall acceptance, tenderness, juiciness, flavor, and off-flavor. Overall acceptance, tenderness, juiciness, and flavor were rated from 1 = extreme dislike to 9 = extreme like, while off-flavor was rated as 1 = yes or 2 = no. A random number list was generated for each steak to prevent bias or steak identification by the panelist. Each steak was cut into 8 cubes (1.3 x 1.3 cm x steak thickness) after cooking and placed into a numbered container. Each panelist evaluated 5 samples per session, none of which were from the same steak. Demographic characteristics of consumer panelists were similar for both taste panels, with 62% of panelists being 21 to 29 yr old and > 42% of panelists consuming beef more than 2 times/wk, most commonly as ground beef and steak.

Computations and Statistical Analyses

Statistical analyses were conducted using the SAS system (Version 9.2, SAS Inst. Inc., Cary, NC). Residual feed intake was calculated as the difference between actual and predicted feed intake by regressing (SAS:REG) DMI on mid-test $BW^{0.75}$, ADG (Koch et al., 1963), and UFT (Basarab et al., 2003). For postweaning RFI evaluation, RFI was computed within each contemporary group (i.e., year, origin, and sex). All other statistical analyses, including measures of growth efficiency and performance, were calculated across cohort. Analysis of finishing phase FE was conducted using the same statistical methods as that for postweaning RFI; however, due to the evaluation of only steers from cohorts 1 and 3 in the finishing phase, origin and gender were not included when defining the contemporary group for analysis of FE.

After RFI computation within contemporary group, steers and heifers were grouped into either inefficient (> 0.5 SD above the mean), marginal (± 0.5 from the mean), or efficient (< 0.5 SD below the mean) categories to define RFI status. Analysis of variance (SAS:GLM) was employed to test RFI grouping (inefficient, marginal, or efficient), sire grouping (low or high ME_M EPD), animal sex, and cohort effects with respect to performance variables, carcass data, and objective product quality measurements (pH, color values, cooking loss and WBSF). When a significant effect was noted ($P \leq 0.05$), least square means were partitioned using pair-wise comparisons. In addition, Spearman rank

correlations were used to quantify relationships of progeny RFI and sire ME_M EPD with the parameters previously mentioned. Contingency tables and Chi Square tests were used to analyze subjective product quality measurements (consumer taste panel) to determine if a difference of association existed among RFI and sire groups within testing traits.

Results

Postweaning Residual Feed Intake

Performance traits of RA progeny evaluated for postweaning RFI are summarized in Table 4. Means for performance variables ADG and DMI were different ($P < 0.0001$) among all cohorts with cohort 2 (1.5 and 11.5 kg/d) having a greater ADG and DMI than either cohorts 1 (1.1 and 8.4 kg/d) or 3 (1.4 and 11.0 kg/d). There was no difference ($P > 0.05$) in mean RFI values among the cohorts. In addition, feed to gain ratio (**F:G**) and G:F of cohorts 1 and 2 were different ($P < 0.0001$) from cohort 3. Initial BW was different ($P < 0.0001$) in that cohort 1 was less than cohorts 2 and 3, whereas final (d 84) BW was different ($P < 0.0001$) among all cohorts with cohort 1 being the smallest, cohort 2 being the largest, and cohort 3 being intermediate. The differences in final (d 84) BW were reflected in the UFT measurement but not in the ULMA or UIMF measurements. Ultrasound fat thickness was greater ($P < 0.0001$) in cohorts 2 and 3 (1.24 and 1.05 cm, respectively) than in cohort 1 (0.51 cm), but ULMA was similar ($P > 0.05$) for all cohorts. Furthermore, UIMF was greater ($P < 0.0001$) in cohorts 1 and 2 (5.1 and 4.8 %, respectively) when compared to cohort 3 (3.9 %).

Residual feed intake was not correlated ($P > 0.05$) with ADG, was positively correlated ($P < 0.05$) with DMI and F:G, and was negatively correlated ($P < 0.05$) with G:F in all cohorts (data not shown). In addition, there were no interactions ($P > 0.05$) in any cohort between RFI group and sex of animal when evaluating performance measures, such as ADG, DMI, UFT, ULMA, or UIMF.

Postweaning and Finishing Phase Performance

Residual feed intake tended to be positively correlated ($P = 0.06$) with finishing phase FE for cohort 1, and the 2 measures were positively correlated ($P < 0.01$) in cohort 3 (Table 5). When evaluating other performance measures in the same manner, postweaning

DMI was positively correlated ($P < 0.001$) with finishing phase DMI, while there appeared to be no association ($P > 0.05$) between postweaning and finishing phase ADG in either cohort.

Carcass Traits and Product Quality Parameters

Postweaning RFI was not correlated ($P > 0.05$) with important carcass traits in any of the cohorts (Table 6). In addition, progeny RFI and sire ME_M EPD were not correlated ($P > 0.05$) in any of the cohorts. Maintenance energy EPD was correlated ($P < 0.05$) with 5 carcass traits in cohort 1 (HCW, LM area, KPH, fat thickness, and yield grade), while it was only correlated with 2 carcass traits in cohort 2 (KPH and fat thickness) and not correlated ($P > 0.05$) with any carcass traits in cohort 3. Neither progeny RFI nor sire ME_M EPD were correlated ($P > 0.05$) with marbling scores or quality grade in any of the cohorts.

Both objective measurements (i.e., pH, cooking loss, WBSF, and proximate analysis) and subjective measurements (i.e., consumer taste panel) of product quality were not different ($P > 0.05$) among RFI groups or sire ME_M EPD groups in either cohort 1 or 2 (data not shown). Consistently, panelists evaluated steaks from different RFI groups with a "like" or "marginal" response in the categories of overall acceptance, juiciness, tenderness, and flavor, with < 10% of the response preference being "dislike" in those categories. Neither RFI group nor sire ME_M EPD group was identified ($P > 0.05$) as having an off-flavor associated with taste.

Residual Feed Intake Relationships: UIMF and ME_M EPD

There was no correlation ($P > 0.05$) between progeny postweaning RFI values and UIMF percentages at the end of the RFI test for cohorts 1 or 3 (Figure 1A, C), although there was a positive correlation ($r = 0.240$; $P = 0.022$) between RFI and UIMF for cohort 2. Note that the model predicting RFI included UFT, thus variation in UIMF was independent of UFT. For all cohorts, the relationship pattern between RFI and UIMF was similar. Clustering of data points for RFI was between values -1 and 1, while UIMF values were between approximately 3 and 7%.

Progeny postweaning RFI and sire ME_M EPD was not correlated ($P > 0.05$) in any of the cohorts (Figure 2). Data revealed similar patterns of progeny RFI value distribution in

both low and high sire ME_M EPD groups, reflecting the non-significant correlation between these 2 variables.

Discussion

Evaluating relationships between RFI and phenotypic performance traits is imperative to the understanding of this particular FE trait. Selection pressures have been placed upon performance traits (i.e., ADG, DMI, fat thickness, ribeye area, etc.) in order to improve growth and product quality potential, resulting in a greater return on investment. Therefore, it is necessary to determine whether RFI negatively impacts performance traits of RA crossbred cattle for which industry standards have been defined.

Previous reports in the literature (Koch et al., 1963; Arthur et al., 2001a; Arthur et al., 2001b; Basarab et al., 2003) state the mean value of RFI within a test group is close to zero and that RFI is not correlated with growth traits such as ADG. Data from the current study are consistent with these reports, and implies that RFI is independent of ADG in growing RA crossbred progeny. In addition, results indicated that RFI is positively correlated with DMI and F:G, which is also in agreement with other studies (Herd and Bishop, 2000; Basarab et al., 2003). In the current study, both steers and heifers were evaluated for RFI. Inherent physiological differences between sexes warranted investigation to determine if there was a sex x RFI group interaction for several measures of performance. These data indicate that both steers and heifers respond similarly within RFI groups and combining the sexes for evaluation of performance measures (after calculation of RFI within contemporary group) has no adverse effects on the analysis.

Understanding the drivers of feed intake of growing and mature animals is of importance within all sectors of the beef industry. The ideal approach is to measure feed intake throughout an animal's life in order to obtain an accurate FE measurement and to determine how FE status can alter during different stages of the production cycle. However, measuring feed intake of mature animals is both difficult and impractical. Therefore, measuring feed intake of growing animals is a more realistic approach, because it is manageable within current livestock production systems (Archer et al., 1999b). Archer et al. (1998) suggested that the RFI value of a growing animal is correlated with that animal's RFI

value as a mature breeding animal, thus providing a selection tool for improved FE. In addition, Richardson et al. (1998) reported that steer progeny of parents previously ranked for postweaning net feed efficiency (**NFE**, which is a term with full identity with RFI) were more efficient in the feedlot than low NFE progeny, consuming less feed per unit of gain. In the current study, phenotypic correlation measurements were evaluated for steers tested during both postweaning growing and finishing phases. Results suggest that feed efficient (or low RFI) steers during postweaning RFI testing were also efficient during finishing phase FE testing. Current data support that RFI status detected during postweaning growth could be a potential indicator of RFI status during later stages of the production cycle. Furthermore, it is the combination of several traits, including feed intake, growth, carcass and meat quality, reproduction, etc., that determine the overall efficiency of a beef production system (Archer et al., 1999b). When considering performance traits associated with improved FE, analysis of the current study suggests that DMI (which was highly correlated between growing and finishing phases, cohort 1, r = 0.69, $P = 0.001$ and cohort 3, r = 0.56, $P = 0.0003$) has a greater effect on FE status (also highly correlated between growing and finishing phases, cohort 1, r = 0.38, $P = 0.06$ and cohort 3, r = 0.50, $P = 0.001$) than ADG (not correlated, cohort 1, $P = 0.12$, and cohort 3, $P = 0.56$). The associations between postweaning and finishing phase DMI and ADG are expected, as the literature consistently shows that RFI (growing phase) and finishing phase FE are positively correlated with feed intake and independent of growth traits. This observation also suggests that the moderate prediction power of identifying feed efficient animals in the growing phase, may partially abrogate the need to test for feed efficiency in the finishing phase, at least in the research context. However with no relationship between ADG between the two phases, there is no potential to use growing phase ADG to predict time to target finish weight for individual animals irrespective of their feed efficiency status.

The relationship between postweaning RFI and product quality is of importance when considering market yields and return on investment. When considering economic improvement along with industry standards for beef quality, any improvement in FE must be achieved while at least maintaining and if possible, improving product quality. Therefore, it is crucial that selection strategies to improve FE do not inadvertently diminish other

important production or quality traits. In the current study, there was no phenotypic correlation between postweaning RFI and any measured carcass trait at harvest, suggesting that improving RFI does not have antagonistic effects associated with carcass or product quality. These data are consistent with other studies (Richardson et al., 1998; McDonagh et al., 2001; Nkrumah et al., 2004; Baker et al., 2006) reporting similar findings. In contrast, sire ME_M EPD was correlated with several measured carcass traits at harvest. Due to the nature of this study, it is important to discern whether these phenotypic associations are truly an influence of sire ME_M EPD or if the correlations detected were due to the genetic potential of other sire traits that were inherent within the breeding design (refer to Table 1). To determine whether correlations were driven by sire divergence in ME_M or if other sire traits might be drivers of the observed relationships, data were evaluated using the average values of each high and low ME_M EPD group (within each cohort) for ME_M EPD, HCW, LM area, fat thickness, and yield grade. Average trait values for high and low ME_M EPD groups suggest that correlations between ME_M EPD and HCW (cohort 1), KPH (cohorts 1 and 2), fat thickness (cohorts 1 and 2), and yield grade (cohort 1) are reflective of sire genetic potential for these traits rather than a ME_M effect. The average carcass weight EPD for high and low ME_M EPD groups in cohort 1, 47.5 and 18.5, respectively was the most divergent of the three cohorts. Due to the large difference between averages, it may be predicted that a correlation would be detected between ME_M EPD group and HCW, whereas the averages for cohort 2 (35.3 and 24.5, respectively) and cohort 3 (34.0 and 34.0, respectively) were more similar and no correlations were identified. Note that ME_M EPD is also strongly associated with growth EPDs for the sires used in this study. From this information, it is also expected that yield grade would be correlated with ME_M EPD in cohort 1, as yield grade is primarily driven by the ratio of ribeye area to HCW in the carcass grading system. A moderate, positive correlation was observed between ME_M EPD and LM area in cohort 1, but not in cohorts 2 or 3. There is not a clear association between the correlation and average ribeye EPD for high and low ME_M EPD groups (-0.01 and -0.21, respectively); therefore, this relationship may be reflective of a ME_M effect. Due to limited research regarding the relationship between ME_M and product quality, it remains to be demonstrated if these 2 variables are associated. In addition, using objective and subjective

testing procedures, results indicated that there were no negative associations of either RFI or ME_M EPD with product quality. McDonagh et al. (2001) reported similar results in that no differences between high and low RFI groups were observed when measuring WBSF of LM steaks aged for 1 or 14 d. Additionally, Baker et al. (2006) reported a tendency ($P = 0.10$) for lower juiciness scores in steaks from high RFI steers compared with steaks from low RFI steers, with all other flavor scores reported as showing no differences between high and low RFI steers.

Reports in the literature concerning the relationship between RFI and UIMF are not conclusive. Intramuscular fat is an important component of the beef quality grading system, in that it represents the degree of carcass marbling and thus drives quality grade scores for beef cattle. Thus, it is linked to beef palatability and carcass value, both of which are key components determining market trends and return on investment. Previous studies (McDonagh et al., 2001; Carstens et al., 2002; Baker et al., 2006) reported no correlation between RFI and intramuscular fat. However, results from the current study suggest that a slight phenotypic correlation existed between postweaning RFI and UIMF in cohort 2, while no relationship was later observed between RFI and carcass marbling score. Also, there were no such relationships detected for cohorts 1 or 3. In agreement with the current study, Basarab et al. (2003) (based on 2 consecutive years of study) reported that there was a tendency ($P = 0.11$ and 0.12, respectively) for RFI to be correlated with ultrasound marbling ($r = 0.13$ and 0.13, respectively) in crossbred cattle, but the study found no association between RFI and carcass marbling scores. Even this hint of a suggestion that RFI and IMF percentage may be related in some cattle populations provides a strong motivation to be vigilant in simultaneously monitoring efficiency, production and quality parameters.

There are several different performance aspects to consider when evaluating FE measures. Energy devoted to maintenance is among one of the most important concepts regarding FE and overall animal efficiency. The ME_M requirement of an animal can be summarized as the amount of feed energy required to produce a zero BW change (or a zero body energy change) after allowing for the various energy densities of body components (Ferrell and Jenkins, 1985). More specifically, these requirements represent the amount of energy necessary to maintain processes such as basal metabolism (i.e., protein synthesis and

degradation, ion transport, cellular signaling, etc.), vital organ function, voluntary movements, and thermoregulation (Thompson et al., 1983). Energy expenditures for maintenance functions vary in beef cattle, according to genetic potential, production status, and physiological state. It has been estimated that maintenance functions account for 70 to 75 % of total energy expenditure in the producing female and anywhere from 35 to 50 % in growing and finishing animals (Ferrell, 1988). Studies have indicated that variation in ME_M requirements can be partially explained by the variation in body composition (i.e., lean and fat tissue) and associated metabolic processes (Ferrell et al., 1979; Cleveland et al., 1983). Other contributors to an animal's ME_M requirement are body tissues (i.e., visceral organs) with high metabolic activity, particularly the liver and digestive tract. Studies have estimated that the combination of these tissues can account for approximately 40 to 50 % of total animal energy expenditure, which is a proportionally large amount of energy considering the liver and digestive tract account for typically 10 % of body mass (see reviews in Ferrell et al (1988), Archer et al. (1999b) and Caton et al. (2000)). At the cellular level, activity of the plasma membrane Na^+, K^+-ATPase has been estimated to account for 20 to 45 % of the oxygen uptake in resting cells (Whittam, 1961). Gregg and Milligan (1982) reported similar findings in that the activity of the Na^+, K^+-ATPase accounted for a minimum of 40 % of muscle O_2 consumption. Therefore, ME_M requirements of an animal are driven by both the cellular activity of highly metabolic tissues and overall body composition, which further justifies the physiological importance of ME_M and the need to understand its impact on RFI.

It is hypothesized that animals exhibiting an improvement in RFI will have decreased ME_M requirements (Richardson et al., 2004), possibly due to genetic potential of efficient feed conversion into lean tissue (i.e., muscle) via protein deposition. A small change in the rate of synthesis or degradation could have large impacts on the amount of energy needed to support ME_M requirements. For example, a reduction in protein degradation is beneficial in that it requires little to no energy input when compared to protein accretion (Hill et al., 2003). Therefore, animals classified as RFI efficient may have the ability to convert feed nutrients into muscle mass at a more efficient rate than their inefficient contemporaries. Previous studies within the literature support this hypothesis,

indicating that improvement in RFI is associated with an increase in lean tissue (i.e., muscle) and a decrease in fat (Arthur et al., 2001a; Richardson et al., 2001; Carstens et al., 2002; Basarab et al., 2003). However, very few studies have evaluated the relationship between ME_M and RFI. Castro Bulle et al. (2007) suggested that RFI may be negatively correlated with ME for maintenance via protein metabolism measurements of steers tested for RFI, but these results must be viewed with caution due to the small number of replicates in the study. In the present study, the relationship between sire ME_M EPD and progeny RFI was evaluated to determine whether the use of sires with a low ME_M EPD would result in progeny with improved RFI. However, results indicate that sire ME_M EPD and progeny RFI are not correlated on a phenotypic basis, and does not support the initial hypothesis of this study that sire ME_M EPD is positively correlated with progeny RFI. The author's are not aware of any other studies examining this relationship, warranting the need for further scientific investigation in this area.

Implications

This study demonstrates that RFI does not negatively affect carcass quality or product quality in RA crossbred cattle. In addition, no relationship was identified between sire ME_M EPD and progeny postweaning RFI. These findings provide a basis for further research to better characterize RFI relationships with production performance variables and sire ME_M EPD. Further characterization of the relationship between ME_M EPD and RFI will be helpful to determine if sire ME_M EPD can be implemented into breeding strategies as a possible indicator trait of RFI potential. Also, further study of associations of RFI with other production and quality traits will continue to advance the beef industry toward the selection of more feed efficient cattle to reduce inputs while maintaining or improving production outputs.

Figure 2.1. Distribution of progeny residual feed intake (RFI) values and ultrasound intramuscular fat (UIMF) percentages

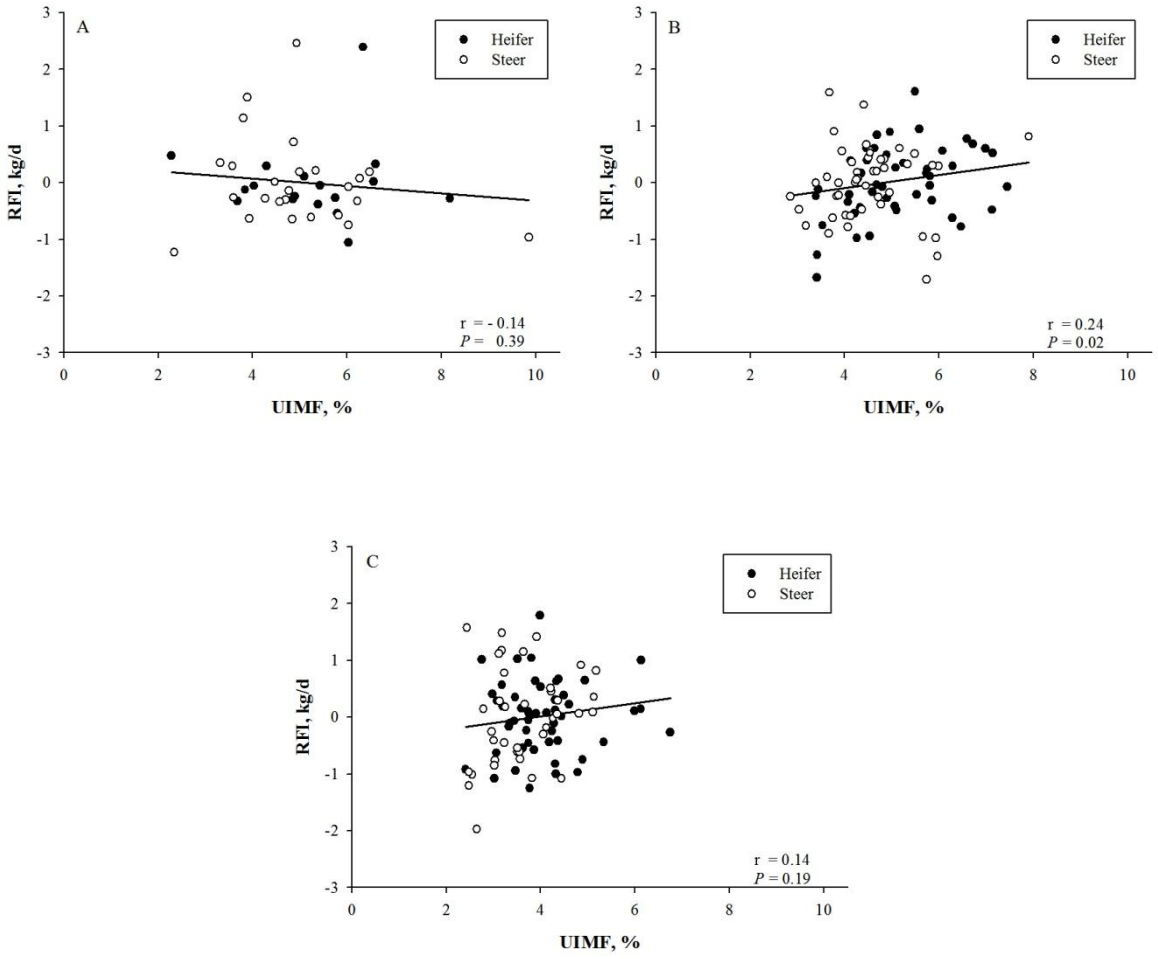

Fig 2.1. Distribution of progeny postweaning RFI values and UIMF percentages at the end of the RFI test for (A) Cohort 1 (df = 41), (B) Cohort 2 (df = 90), and (C) Cohort 3 (df = 87).

Figure 2.2. Distribution of progeny residual feed intake (RFI) values and sire maintenance energy (ME_M) EPD

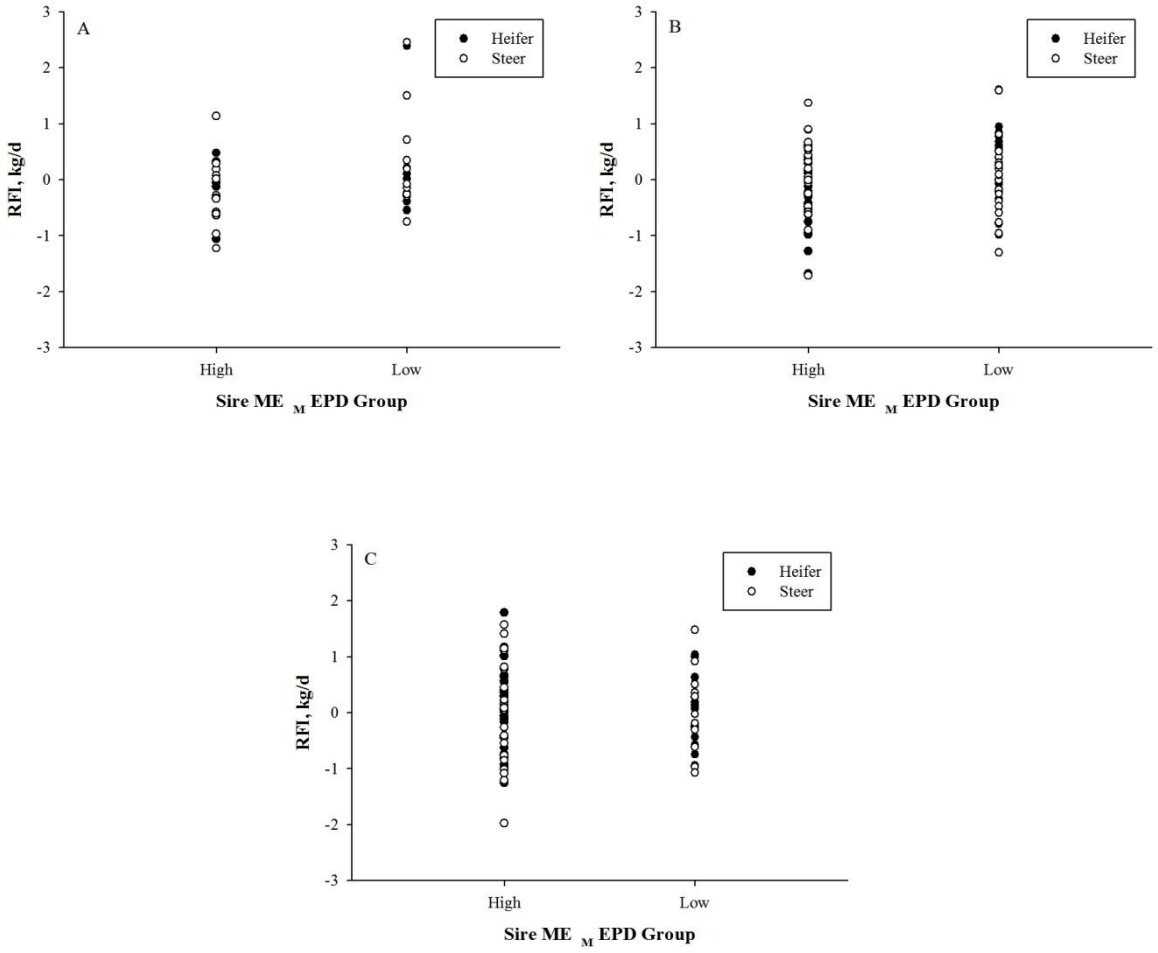

Fig 2.2. Distribution of progeny postweaning RFI values and sire ME_M EPD for (A) Cohort 1 (df = 41), (B) Cohort 2 (df = 90), and (C) Cohort 3 (df = 87). Sires were categorized into high or low groups based on their individual ME_M EPD value. Note: the Red Angus Association of America national breed average for ME_M EPD is 4. Sires with a ME_M EPD $\geq$ 4 were classified as high ME_M EPD, and sires with a ME_M EPD < 4 were classified as low ME_M EPD.

Table 2.1. Mean, SD, maximum and minimum EPD values of Red Angus sires

Grouping[1]			Sire Traits (EPD)[2]						
			ME_M	YW	MARB	YG	CW	REA	FAT
Cohort 1	Low (n = 2)	Avg	**-9.0**	45.0	0.23	0.11	18.5	-0.21	0.05
		SD	1.4	19.8	0.06	0.08	10.6	0.10	0.01
		Max	-8.0	59.0	0.27	0.16	26.0	-0.14	0.05
		Min	-10.0	31.0	0.19	0.05	11.0	-0.28	0.04
	High (n = 2)	Avg	**7.5**	79.5	0.35	0.06	47.5	-0.01	0.01
		SD	5.0	21.9	0.25	0.18	13.4	0.01	0.05
		Max	11.0	95.0	0.53	0.18	57.0	0.00	0.04
		Min	4.0	64.0	0.17	-0.07	38.0	-0.02	-0.03
Cohort 2	Low (n = 4)	Avg	**-7.8**	47.5	0.16	-0.04	24.5	0.11	0.02
		SD	5.6	18.2	0.12	0.19	13.2	0.48	0.03
		Max	0.0	67.0	0.27	0.16	42.0	0.80	0.05
		Min	-13.0	31.0	-0.02	-0.29	11.0	-0.28	-0.02
	High (n = 4)	Avg	**13.8**	57.8	-0.01	-0.01	35.3	-0.12	-0.02
		SD	4.5	11.9	0.23	0.10	6.2	0.15	0.02
		Max	20.0	68.0	0.18	0.10	39.0	0.00	0.01
		Min	10.0	41.0	-0.30	-0.11	26.0	-0.33	-0.04
Cohort 3	Low (n = 2)	Avg	**-2.5**	62.0	0.17	-0.12	34.0	0.29	-0.01
		SD	3.5	7.1	0.03	0.23	11.3	0.72	0.02
		Max	0.0	67.0	0.19	0.04	42.0	0.80	0.01
		Min	-5.0	57.0	0.15	-0.29	26.0	-0.22	-0.02
	High (n = 4)	Avg	**12.8**	56.0	-0.10	0.03	34.0	-0.23	-0.01
		SD	5.0	11.2	0.21	0.10	5.9	0.09	0.02
		Max	20.0	68.0	0.18	0.10	39.0	-0.12	0.01
		Min	9.0	41.0	-0.30	-0.11	26.0	-0.33	-0.04
ALL Sires	Low (n = 5)	Avg	**-7.2**	49.4	0.16	-0.02	24.8	0.04	0.02
		SD	5.0	16.3	0.11	0.17	11.4	0.44	0.03
		Max	0.0	67.0	0.27	0.16	42.0	0.80	0.05
		Min	-13.0	31.0	-0.02	-0.29	11.0	-0.28	-0.02
	High (n = 7)	Avg	**11.4**	64.4	0.03	0.04	38.6	-0.14	0.00
		SD	4.9	16.4	0.28	0.10	9.4	0.14	0.03
		Max	20.0	95.0	0.53	0.18	57.0	0.00	0.04
		Min	4.0	41.0	-0.30	-0.11	26.0	-0.33	-0.04
		P	< 0.0001	0.15	0.37	0.47	0.04	0.33	0.20

[1]Max = maximum; Min = minimum.

[2]ME_M = maintenance energy; YW = yearling weight; MARB = marbling; YG = yield grade; CW = carcass weight; REA = ribeye area; FAT = fat thickness.

Table 2.2. Ingredient composition and chemical analysis (DM basis) of the postweaning diet fed to steers and heifers (Cohorts 1, 2, and 3) for evaluation of residual feed intake (RFI)

Item	Cohort 1	Cohort 2	Cohort 3
Ingredient, %			
Alfalfa hay mid-bloom	34.8	60.0	60.0
Timothy hay full-bloom	25.2	—	—
Barley grain heavy	17.5	—	—
Corn grain cracked	9.8	30.0	30.0
Distillers grain soluble	8.1	—	—
Grower supplement	4.6	—	—
Molasses (VTM)[1]	—	10.0	10.0
Chemical analysis			
DM, % as fed	69.4	82.6	80.9
CP, %	15.9	15.4	16.4
ADF, %	21.3	20.6	20.7
Fat, %	3.9	3.5	2.3
Ash, %	7.5	8.6	8.1
NE_m, Mcal/kg	1.9	1.7	1.6
NE_g, Mcal/kg	1.2	0.9	0.9
TDN, %	76.4	68.4	65.8

[1]VTM = vitamin/trace minerals.

Table 2.3. Ingredient composition and chemical analysis (DM basis) of the finishing diet fed to steers (Cohorts 1 and 3) for evaluation of finishing phase feed efficiency (FE)

Item	Cohort 1	Cohort 3
Ingredient, %		
Alfalfa hay mid-bloom	9.0	31.0
Barley grain heavy	65.3	—
Corn grain cracked	—	46.0
Distillers grain soluble	20.7	10.0
Finishing supplement	5.0	—
Molasses (VTM)[1]	—	13.0
Chemical analysis		
DM, % as fed	71.9	81.1
CP, %	15.8	15.2
ADF, %	9.6	15.1
Fat, %	4.3	3.9
Ash, %	5.5	6.8
NE_m, Mcal/kg	2.0	1.9
NE_g, Mcal/kg	1.2	1.1
TDN, %	77.2	74.3

[1]VTM = vitamin/trace minerals.

Table 2.4. Summary statistics and ANOVA results for performance traits of Red Angus progeny tested for postweaning residual feed intake (RFI)

	Cohort[2]						
	1		2		3		
Trait[1]	Mean	SEM	Mean	SEM	Mean	SEM	*P*-value
ADG, kg/d	1.1[a]	0.04	1.5[c]	0.02	1.4[b]	0.02	< 0.0001
DMI, kg/d	8.4[a]	0.18	11.5[c]	0.12	11.0[b]	0.13	< 0.0001
RFI, kg/d	0.0	0.11	0.0	0.07	0.0	0.08	1.000
F:G	7.5[a]	0.16	7.6[a]	0.11	8.3[b]	0.11	< 0.0001
G:F	0.14[b]	0.003	0.13[b]	0.002	0.12[a]	0.002	< 0.0001
Initial BW, kg	291.4[a]	5.40	318.8[b]	3.67	317.4[b]	3.73	< 0.0001
d 84 BW, kg	384.6[a]	6.87	445.2[c]	4.67	429.9[b]	4.74	< 0.0001
d 84 UFT, cm	0.51[a]	0.04	1.24[c]	0.03	1.05[b]	0.03	< 0.0001
d 84 ULMA, cm^2	65.1	1.24	65.7	0.84	65.5	0.86	0.928
d 84 UIMF, %	5.1[b]	0.16	4.8[b]	0.11	3.9[a]	0.11	< 0.0001

[1]F:G = feed:gain; UFT = ultrasound fat thickness; ULMA = ultrasound LM area; UIMF = ultrasound intramuscular fat.

[2] Cohort 1 – n = 42, avg on test age = 263 d, avg off test age = 348 d;
Cohort 2 – n = 91, avg on test age = 320 d, avg off test age = 405 d;
Cohort 3 – n = 88, avg on test age = 271 d, avg off test age = 358 d.

[a,b,c]Means within a row lacking a common superscript letter differ at $P \leq 0.05$.

Table 2.5. Comparison of performance traits (Spearman rank correlations) between Red Angus sired steers (Cohorts 1 (df = 24) and 3 (df = 38) tested for postweaning residual feed intake (RFI) and finishing phase feed efficiency (FE)

	Cohort 1		Cohort 3	
Trait	r	*P*-value	r	*P*-value
ADG	0.32	0.12	0.10	0.56
DMI	0.69	0.0001	0.56	0.0003
FE	0.38	0.06	0.50	0.001

Table 2.6. Spearman rank correlations of progeny residual feed intake (RFI) and sire maintenance energy (ME_M) EPD with carcass measurements for Red Angus sired steers in Cohort 1 (df = 24), Cohort 2 (df = 40), and Cohort 3 (df = 38)

	Cohort 1		Cohort 2		Cohort 3	
Trait	RFI	ME_M EPD	RFI	ME_M EPD	RFI	ME_M EPD
HCW	-0.23	0.48*	0.01	-0.16	0.10	0.23
LM area	-0.22	0.46*	0.07	-0.04	0.06	0.06
KPH	0.14	-0.55*	0.18	-0.32*	-0.09	-0.17
Fat thickness	0.35†	-0.78*	0.06	-0.33*	-0.03	0.02
Yield grade	0.24	-0.79*	-0.03	-0.19	0.16	-0.05
Marbling score	0.00	-0.05	0.14	-0.22	0.27	-0.05
Quality grade	0.10	-0.08	0.12	-0.24†	0.31†	-0.21
RFI	—	-0.33	—	-0.01	—	0.03
ME_M EPD	-0.33	—	-0.01	—	0.03	—

*Correlations are significant at $P \leq 0.05$.
†Correlations are marginal at $P \leq 0.10$.

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CHAPTER 3

An examination of the association of serum IGF-I concentration, potential candidate genes, and fiber type composition with variation in residual feed intake in progeny of Red Angus sires divergent for maintenance energy EPD

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Abstract

Investigating the genetic and physiological drivers of postweaning residual feed intake (**RFI**) and finishing phase feed efficiency (**FE**) may identify underlying mechanisms that are responsible for the variation in these complex FE traits. The objectives were 1) to evaluate the relationship of serum IGF-I concentration and muscle gene expression with postweaning RFI and sire maintenance energy (**ME_M**) EPD and 2) to determine fiber type composition as it relates to postweaning RFI and finishing phase FE. Results indicate that RFI and serum IGF-I concentration were not associated ($P > 0.05$); however, negative correlations ($P < 0.05$) between sire ME_M EPD and serum IGF-I concentration were observed. Gene expression differences between high and low RFI animals were observed in cohort 1, where *IGFBP5* expression was greater ($P < 0.05$) in high RFI animals. When animals were grouped according to sire ME_M EPD, the low ME_M EPD group of cohort 1 showed greater muscle mRNA expression ($P < 0.01$) of *fatty acid synthase* (***FASN***) and marginally ($P < 0.10$) greater expression of *IGFBP5* and *C/EBP alpha* (***C/EBPα***), whereas the high ME_M EPD group of cohort 2 had greater muscle mRNA expression of *IGFBP2* ($P < 0.05$) and *C/EBPα* ($P \leq 0.01$) and marginally ($P < 0.10$) greater expression of *IGFBP3*.

Biopsy tissue samples collected at harvest revealed that the percentage of type IIa fibers was lower ($P \leq 0.05$) in high RFI steers, with a similar trend ($P < 0.10$) being observed in high finishing phase FE steers. The percentage of type IIb fibers was higher ($P < 0.05$) in high RFI (and finishing phase FE) steers than in low RFI (and finishing phase FE) steers. There was a marginal, negative correlation between RFI and type I (r = -0.36; $P = 0.08$) and IIa (r = -0.37; $P = 0.07$) fiber percentages and a positive correlation (r = 0.48; $P = 0.01$) between RFI and type IIb fiber percentage, while finishing phase FE was negatively correlated (r = -0.43; $P = 0.03$) with type I fiber percentage and positively correlated (r = 0.44; $P = 0.03$) with type IIb fiber percentage. Therefore, our data indicate that 1) serum IGF-I (collected at weaning) is not an indicator of postweaning RFI, 2) the GH-IGF axis appears to have some involvement with RFI at the molecular level; however, muscle gene expression results were not consistent across cohorts, and 3) low RFI animals may have the ability to more efficiently maintain and accrete muscle mass due to their fiber type composition, specifically a greater proportion of type I fibers.

Introduction

Feed efficiency is a critical component of beef production systems that can have a substantial impact on the overall efficiency of the beef industry. Residual feed intake is an FE trait that is moderately heritable (Herd and Bishop, 2000; Arthur et al., 2001) and phenotypically independent of the traits used to measure it (Archer et al., 1999; Basarab et al., 2003); however, measurement is costly and labor intensive. Therefore, genetic and physiological drivers are being investigated in order to identify mechanisms underlying variation in RFI and to detect predictive molecular markers of this trait.

Due to the relationship between serum IGF-I and linear growth, IGF-I has been suggested as a potential indicator of RFI, but results have been inconsistent (Johnston et al., 2002; Lancaster et al., 2008). Recent studies, such as whole-genome association (Barendse et al., 2007) and identification of whole genome SNPs (Sherman et al., 2010), have attempted to identify genetic markers associated with RFI, while gene expression profiling of differentially expressed genes between animals divergent for RFI has attempted to

identify potential candidate genes associated with RFI (Chen et al., 2011). However, it has been difficult to replicate findings and confirm genetic associations in different populations.

In addition, studies that have evaluated the relationship between RFI and end-product quality suggest that selection for RFI has no negative effects on end-product quality (McDonagh et al., 2001; Baker et al., 2006); however, the relationship between RFI and fiber type proportion has yet to be examined and may provide additional insight into the relationship between RFI and end-product quality. Therefore, the objectives of this study were 1) to evaluate the relationship of serum IGF-I concentration and muscle gene expression with postweaning RFI and sire ME_M EPD and 2) to determine fiber type composition as it relates to postweaning RFI and finishing phase FE.

Materials and Methods

All animal procedures were reviewed and approved by the Institutional Animal Care and Use Committee (2011-3) as required by federal law and University of Idaho policy. For a more detailed description of sire selection, postweaning RFI evaluation, and finishing phase FE evaluation, refer to Welch et al. (2012). In brief, a total of 12 Red Angus sires divergent for ME_M EPD were chosen using the Red Angus Association of America-generated ME_M EPD. Crossbred cows were estrus synchronized and bred by artificial insemination over 3 yr, with each sire being represented across 2 to 3 cohorts and 11 out of 12 sires producing 15 or more F_1 progeny. Testing protocols were conducted in a similar manner for evaluation periods within and among cohorts. Within each cohort, steers and heifers were evaluated for postweaning RFI, whereby animals were fed an industry-standard growing ration and BW was recorded every 2 wk during the testing period. After postweaning RFI evaluation, the growing ration was modified in 4 stages to a finishing ration, and steers in cohorts 1 and 3 were evaluated for finishing phase FE. Steers were finished to a target BW of 591 kg (group average) prior to shipment for harvest at Washington Beef (Toppenish, WA). Due to an occupancy conflict within the testing system, cohort 2 steers were finished at Snake River Farms (AgriBeef Inc., American Falls, ID), and finishing phase FE was not evaluated. Upon completion of both postweaning RFI

and finishing phase FE evaluation, ultrasound measurements were recorded to determine fat thickness, intramuscular fat, and longissimus muscle area.

IGF-I Measurements

To determine serum IGF-I concentration at weaning, blood samples were collected via jugular venipuncture, using vacutainer (red-top, 10 mL) venous blood collection tubes (Fisher Scientific, Houston, TX), and allowed to clot overnight at 4°C. Serum was collected by centrifugation (3000 × *g* at 4°C for 20 min) and stored at -20°C until IGF-I concentration analysis. Samples were analyzed in duplicate using the Human IGF-I Quantikine ELISA Kit (SG100: R & D Systems, Inc., Minneapolis, MN) with 100% cross-reactivity with bovine IGF-I and previously validated (Moriel et al., 2012). The mean concentration values of duplicate samples were used for analysis. The mean CV for inter-assay analysis was 2.9%, and a CV standard of 8% was applied to ensure accuracy between sample duplicates. Sensitivity for minimum detection was 0.04 ng/mL.

Tissue Sampling

Surgical procedures for muscle biopsy were exactly as described (Schneider et al., 2010). For cohort 1, muscle biopsy samples of the *biceps femoris* were taken from all steers (n=25) and heifers (n=17) following postweaning RFI evaluation (February 2009) at approximately 12 mo of age. Following finishing phase FE evaluation, muscle tissue samples were taken again from steers (n=25) after harvest (May 2009) at approximately 15 mo of age. Due to a greater number of animals in cohort 2, an estimate of postweaning RFI was calculated prior to completion of the evaluation period. Based on this information, the most RFI-divergent steers (n=20) and heifers (n=17) were chosen for biopsy following postweaning RFI evaluation (April 2010) at approximately 14 mo of age. At completion of the postweaning RFI evaluation period, final RFI was calculated, and 87% of the animals previously selected for muscle biopsy retained their estimated RFI status. Biopsy samples were not collected from steers of cohort 2 at harvest or from any animals in cohort 3. Each biopsy sample was divided into two portions. One portion of the sample was snap frozen in liquid nitrogen and stored at -80°C for RNA extraction, while the other portion was mounted on cork (perpendicular to the fibers) and frozen in super-cooled isopentane for histochemical fiber type analysis (Pette et al., 1997).

RNA Isolation, Quantification, and cDNA Synthesis

Total RNA was extracted from *biceps femoris* samples using TRIzol reagent (Invitrogen, Carlsbad, CA) according to the manufacturer's protocol. Isolated RNA was quantified using a Nanodrop® ND-1000 UV-Vis Spectrophotometer (Nanodrop Technologies, Wilmington, DE), and total RNA integrity was assessed via 1.5% denaturing formaldehyde agarose gel electrophoresis. All samples were adjusted to a concentration of 2 μg/μL and DNase treated (Ambion, Foster City, CA) prior to cDNA synthesis, which was completed using a high-capacity cDNA reverse transcription kit (Applied Biosystems, Foster City, CA).

Quantitative real-time PCR (qRT-PCR)

Real-time PCR quantification of mRNA was determined using the Taqman MGB® primer/probe system. Primer express 3.0 software (Applied Biosystems, Foster City, CA) was used to design primer/probe sets for each gene (Table 1). An ABI 7500 fast real-time PCR system (Applied Biosystems, Foster City, CA) was used to determine relative mRNA expression (Chapalamadugu et al., 2009) of genes categorized as GH-IGF axis members, lipogenic, or lipolytic genes. Specific genes were chosen based on their known physiological functions and potential association with variation in RFI. Muscle biopsy samples taken following postweaning RFI evaluation (cohorts 1 and 2) were used to determine relative mRNA expression of the following genes. The GH-IGF axis gene category included *Type I-IGF receptor* (***IGF-IR***), *IGFBP2*, *IGFBP3*, *IGFBP5*, and *GH receptor* (***GHR***). The lipogenic genes included *PPAR gamma* (***PPARγ***), *PPARγ coactivator 1 alpha* (***PGC1α***), *C/EBPα*, *FASN*, and *acetyl CoA carboxylase alpha* (***ACACα***), while the lipolytic gene category included *carnitine palmitoyltransferase 1 beta* (***CPT-1β***). To normalize for cell number and loading error, *18S rRNA* was chosen as a reference gene due to its low variability in expression levels across all samples. Samples were analyzed in duplicate, and the differential Ct (ΔCt) values of each candidate gene with that of the matched *18S rRNA* value were used for analysis.

Fiber Type Composition

Cork-mounted *biceps femoris* samples were serial cryosectioned (10μm thick) for histochemical fiber type analysis. Serially sectioned samples were stained using a succinate

dehydrogenase (**SDH**) stain and a myosin ATPase stain at three different pH values (4.3, 4.6, and 9.4). Staining protocols were adapted from those previously described (Pearse, 1968; Brooke and Kaiser, 1970; Picard et al., 1998). Images were captured using a Nikon 80i microscope with NIS-BR elements software (Nikon, Melville, NY). For every sample, an image was captured for each stain, printed in color, and utilized for fiber type counting. A minimum of 250 fibers were counted per image, and the number of fibers (type I, type IIa, and type IIb) was reported as a percentage of the total fiber count for analysis. Representative serial images of fiber type staining are reported in Thornton et al. (2012).

Computations and Statistical Analyses

One-way ANOVA (SAS:GLM) was employed to test postweaning RFI quartile (high and low RFI), finishing phase FE quartile (high and low finishing phase FE), and sire grouping (high and low ME_M EPD) effects with respect to serum IGF-I concentration, gene expression, and fiber type proportions. Due to variation among cohorts, all statistical analyses were calculated within cohort. Gender was initially tested as a fixed effect; however, if no differences were noted, subsequent analyses were pooled over gender when appropriate. When a significant effect was noted ($P \leq 0.05$), least square means were partitioned using pair-wise comparisons. Spearman rank correlations were used to quantify relationships of RFI, finishing phase FE, and sire ME_M EPD with the parameters previously mentioned. For further gene expression analysis, $\Delta\Delta$Ct values were calculated using the mean ΔCt value for each gene of interest, comparing high to low groups with respect to RFI and sire ME_M EPD groups. Using $\Delta\Delta$Ct values, one-way ANOVA (SAS:GLM) was employed to obtain *P*-values. Fold change was calculated as $2^{-\Delta\Delta Ct}$ (Pfaffl, 2001). Prior to analyses, all responses were assessed for normality and homogeneity to meet the assumptions of ANOVA and correlation analyses. Statistical analyses were conducted using the SAS system (Version 9.2, SAS Inst. Inc., Cary, NC).

Results

Serum IGF-I Concentration

No association ($P > 0.05$) was observed between RFI and serum IGF-I concentration at weaning in any of the cohorts (Table 2). However, negative correlations between sire

ME_M EPD and serum IGF-I concentration were observed in all cohorts. In cohort 1, there was a marginal (r = -0.30; *P* = 0.06) correlation between sire ME_M EPD and serum IGF-I concentration of progeny (steers, heifers, and combined), and that same relationship was highly significant in cohorts 2 (r = -0.31; *P* = 0.003) and 3 (r = -0.36; *P* = 0.0006). Both highly significant and marginal correlations were observed between sire ME_M EPD and serum IGF-I concentration of steer progeny in cohorts 2 (r = -0.36; *P* = 0.01) and 3 (r = -0.27; *P* = 0.10), respectively. In addition, a highly significant (r = -0.50; *P* = 0.0002) correlation between sire ME_M EPD and serum IGF-I concentration of heifers was observed in cohort 3.

Gene Expression (*Biceps femoris*)

In cohort 1, muscle expression of *IGFBP5* in high RFI animals was 1.7 fold greater (*P* < 0.05) when compared to that of low RFI animals (Table 3). No other associations were detected between other genes of interest and RFI. When analyzing gene expression in terms of sire ME_M EPD, *IGFBP5* and *C/EBPα* expression were both marginally different (*P* ≤ 0.10) between the high and low ME_M EPD groups, with animals in the low ME_M EPD group showing marginally higher expression levels (approximately 1.7 fold) when compared to levels in the high ME_M EPD group. In addition, a significant difference (*P* < 0.01) and similar pattern of expression was observed for *FASN*. Muscle *FASN* was expressed at a greater level (1.5 fold) in animals from the low ME_M EPD group when compared to animals from the high ME_M EPD group. No other associations (*P* > 0.05) were detected between other genes of interest and sire ME_M EPD group. Furthermore, Spearman rank correlation analysis determined that expression of *C/EBPα* was marginally correlated (*r* = 0.26, *P* = 0.10) with RFI and not correlated (*P* > 0.05) with ME_M EPD, while expression of *FASN* was marginally correlated (*r* = 0.30, *P* = 0.06) with RFI and highly correlated (*r* = -0.38, *P* = 0.01) with ME_M EPD (data not shown).

No differences (*P* > 0.05) were detected in muscle expression between high and low RFI quartiles (Table 3) in cohort 2. Expression of *IGFBP3* was marginally different (*P* < 0.10) between the high and low ME_M EPD groups, with muscle expression levels in the high ME_M EPD group showing marginally greater *IGFBP3* expression (1.5 fold) when compared to its expression levels in the low ME_M EPD group. Significant differences and similar

magnitudes of *IGFBP2* ($P < 0.05$) and *C/EBPα* ($P \leq 0.01$) expression were detected between ME_M EPD groups, with muscle expression levels in the high ME_M EPD group being greater (approximately 1.8 fold) when compared to expression levels in the low ME_M EPD group. In addition, Spearman rank correlation analysis showed that no other associations ($P > 0.05$) were detected between other genes of interest and RFI. However, muscle *IGFBP2* expression was marginally correlated ($r = 0.32$, $P = 0.09$) with ME_M EPD, while C/EBPα was correlated ($r = 0.34$, $P = 0.04$) with ME_M EPD (data not shown).

Fiber Type

No relationships were detected between fiber type composition and RFI when analyzing muscle biopsy samples collected immediately after the postweaning RFI evaluation period for cohorts 1 and 2 (data not shown). Using muscle tissue samples collected at harvest, no differences were observed in the percentage of type I fibers when evaluating high and low quartiles of both RFI and finishing phase FE values of cohort 1 steers; however, percentage differences of type IIa and IIb fibers were detected (Table 4). The percentage of type IIa fibers was lower ($P \leq 0.05$) in high RFI steers when compared to low RFI steers, with a similar trend ($P < 0.10$) being observed between high and low quartiles of finishing phase FE steers. In addition, the percentage of type IIb fibers was higher ($P < 0.05$) in high RFI (and finishing phase FE) steers than in low RFI (and finishing phase FE) steers. Furthermore, there was a marginal, negative correlation between RFI and type I (r = -0.36; $P = 0.08$) and IIa (r = -0.37; $P = 0.07$) fiber percentages, while a highly significant, positive correlation (r = 0.48; $P = 0.01$) was observed between RFI and type IIb fiber percentage (Table 5). Finishing phase FE was negatively correlated (r = -0.43; $P = 0.03$) with type I fiber percentages and positively correlated (r = 0.44; $P = 0.03$) with type IIb fiber percentages. No relationship (r = -0.31; $P = 0.13$) was detected between finishing phase FE and type IIa fiber percentages.

Discussion

Systemic concentrations of various metabolic indicators, such as IGF-I (Wood et al., 2004; Lancaster et al., 2008) have been evaluated at varying time-points within the production cycle in an attempt to identify their relationship with FE traits. Physiological

differences in metabolic pathways associated with the functioning of the IGF axis-may be important factors influencing the variation in RFI. The somatotropic axis is highly conserved across mammalian species, and its functions include molecular signaling involving the IGF ligands (IGF-I and IGF-II), IGF receptors (IGF-IR and IGF-IIR), and multiple binding proteins (IGFBP 1-6). Insulin-like growth factor signaling has been noted as a critical factor in the regulation of skeletal muscle growth, differentiation, and maintenance of muscle tissue homeostasis (Duan et al., 2010). Due to phenotypic and genotypic relationships with important bovine production traits (Davis et al., 1995; Johnston, 2001) and its moderate heritability (Davis and Simmen, 2000), interest has been shown in using serum IGF-I concentration as an indirect selection tool for RFI; however, current reports in the literature are conflicting as to the exact nature of this relationship.

Richardson et al. (1996) indicated that there were no phenotypic differences in circulating concentrations of IGF-I at the completion of a 120 d testing period for high and low RFI animals (276 ± 7 *v* 249 ± 17 µg/mL) fed a roughage-based diet. Lancaster et al. (2008) also reported no associations between RFI of Angus bull and heifer progeny (from parents divergently selected for serum IGF-I concentration) and IGF-I concentrations (weaning and initial) in either study 1 (roughage-fed) or study 2 (grain-fed). However, Brown (2005) observed positive and negative relationships between RFI and IGF-I concentration when using roughage- and grain-based diets, respectively. Recently, Kelly et al. (2010) sampled systemic IGF-I concentration at d 1, 30, 60, and 84 during the experimental period and reported that IGF-I was unrelated to any measure of FE when evaluating heifers that were consuming a grain-based diet and previously ranked as yearlings for phenotypic RFI. Furthermore, plasma IGF-I concentration at either the beginning or end of the performance test of bulls (10 mo of age) were not different between RFI groupings when they had consumed a primary concentrate diet (Kelly et al., 2011a). In the current study, all cohorts were fed a roughage-based diet during the experimental period, and no relationship was observed between RFI and IGF-I concentration (at weaning) in any of the cohorts. It is known that production and regulation of systemic IGF-I within the mammalian endocrine system is influenced by plane of nutrition, and diet type (i.e., roughage-based vs. grain-based) has been implicated as a factor influencing the relationship

between RFI and IGF-I concentration. However, it is still not clear if diet type, growth stage or the confounding of diet type and growth stage may be drivers of variability in circulating (systemic) concentrations of IGF-I and thus its relationship with RFI. Due to the inconsistencies reported among these studies, there doesn't appear to be a direct association between RFI performance and systemic IGF-I concentration at the phenotypic level.

In contrast, other studies have identified an association between these two variables at the genetic level, indicating that a relationship may exist. Johnston et al. (2002) reported positive genetic correlations (0.56 ± 0.35 and 0.39 ± 0.13) between RFI and serum IGF-I concentration, measured from 2 different data sets where temperate and tropically adapted breeds were evaluated for RFI and sampled for IGF-I at various time points. In addition, Moore et al. (2005) reported a positive genetic correlation of 0.41 ± 0.21 between RFI evaluated at approximately 11 mo of age and IGF-I concentration measured either at, or prior to, weaning (average age 201 d) or postweaning (average age 310 d) in Australian Angus seedstock cattle. This correlation later increased to 0.57 ± 0.25 when statistical analysis included only RFI and IGF records from contemporary groups containing common sires, indicating that genes responsible for greater IGF-I concentration were also associated with increased RFI. Data analyses from Johnston et al. (2002) and Moore et al. (2005) initially suggested that, due to the moderate to strong genetic correlations of RFI with IGF-I concentration, IGF-I could serve as a potential indicator of RFI performance. However, Wolcott et al. (2006) sampled IGF-I concentration at postweaning, feedlot entry, and feedlot exit for Brahman and tropical composite yearling steers and reported a negative genetic correlation between feedlot-evaluated RFI and IGF-I concentration. When data were pooled and both breeds were analyzed together, the negative genetic correlation between RFI and IGF-I remained. Noticeably, stage of maturity can alter the observed relationship between RFI and IGF-I concentration. The physiological actions of IGF-I include stimulation of protein synthesis and inhibition of protein degradation, thereby improving protein retention and inducing muscular hypertrophy (Oddy and Owens, 1996). These complex interactions suggest that cattle evaluated for RFI at approximately 8 to 10 months of age would be expected to have proportionally greater lean tissue growth, and thus increased IGF-I concentration, compared to older cattle entering the finishing phase at approximately 12 to

14 months of age. This concept may have been a factor influencing the positive association between RFI and IGF-I concentration observed by Moore et al. (2005) while also contributing to the negative relationship observed by Wolcott et al. (2006). Johnston (2007) later reported IGF-I concentration to have a positive genetic correlation (0.17 ± 0.11) with postweaning RFI and a negative genetic correlation (-0.22 ± 0.16) with feedlot-evaluated RFI. Johnston (2007) further stated that the accuracy of using IGF-I concentration to predict breeding values for RFI was reduced and that the polygenic nature of RFI differed between the postweaning and feedlot test periods, indicating that the expression of genes responsible for IGF-I concentration differ as cattle become more physiologically mature.

Recent studies have examined the bovine genome in reference to RFI, identifying potential QTL and SNPs associated with the trait. However, very few studies have examined the contribution of key genes associated with metabolic processes such as muscle metabolism, oxidative phosphorylation, and cellular energetics. Since skeletal muscle accounts for a large proportion of body mass and has high metabolic demands, investigating the regulation of important metabolic pathways within this tissue may provide insight into the physiological mechanisms associated with RFI and the variation that exists within this trait. It is well documented that the somatotropic axis greatly influences growth and muscle metabolism (Florini et al., 1996; Oksbjerg et al., 2004; Duan et al., 2010), which indicates that this system could have substantial effects upon the overall energetic efficiency of feed efficient animals. In addition, the utilization of carbohydrates and lipids for energy deposition and mobilization within skeletal muscle is also of importance due to the differential metabolic costs of energy storage and partitioning associated with these substrates.

Growth hormone receptor is a transmembrane-bound receptor found in many tissues throughout the body, and it is activated by the binding of GH. The release of GH and subsequent receptor binding is a main activator of the somatotropic axis and therefore an important regulator of postnatal growth. When considering tissue proportion in relation to body mass, skeletal muscle is quantitatively the major site of GH binding, initiating such cellular events as mitosis and differentiation, protein turnover, and lipid metabolism (Pell and Bates, 1990). Conducting a whole-genome association study, Barendse et al. (2007)

reported that DNA variants in or near proteins contributing to cellular energetics were 10 times as common as those affecting appetite and body-mass homeostasis, while the largest group of variants consisted of those associated with gene regulation (i.e., control of the phenotype). Sherman et al. (2008) indicated that a SNP located in intron 4 of the GHR gene was associated with animal BW (dominance effect) and RFI (allele substitution effect). Chen et al. (2011) using global gene expression profiling revealed no statistical difference in the *GHR* expression of the liver using real-time PCR, although expression of *GHR* appeared to be higher in high-RFI animals as suggested by microarray. In contrast, Kelly et al. (2013) reported that *GHR* expression was greater in the LM of low-RFI animals compared with their high-RFI contemporaries. In the current study, no associations were found between *GHR* expression and RFI, but an association was observed between *IGFBP5* expression and RFI, with *IGFBP5* expression being greater in high-RFI animals. In addition, Chen et al. (2011) observed that liver *IGFBP3* expression was higher in low-RFI animals using both microarray and real-time PCR studies. Kelly et al. (2013) did not detect any differences between RFI groupings regarding the expression of *IGFBP3* or *IGFBP5* in skeletal muscle tissue. These studies suggest that the somatotropic axis may be involved in the regulation of RFI; however, the data are derived from too few animals precluding any deduction of the direction and magnitude of these relationships.

Various physiological aspects associated with energetic efficiency and homeostasis have been implicated as contributors to phenotypic differences in growth rate and FE of livestock, and thus sources of variation resulting in the RFI phenotype (Herd and Arthur, 2009). Mitochondria are involved in the regulation of cellular homeostasis, being numerous in metabolically active cells (i.e., liver, muscle, brain cells) and producing approximately 90% of cellular energy as ATP. Studies investigating differences in mitochondrial function and biochemistry as they relate to growth performance and FE status of various livestock species have been published (Bottje et al., 2002; Kolath et al., 2006; Bottje and Carstens, 2009). A dominant regulator of mitochondrial biogenesis and lipid metabolism is *PGC1-α*, with its expression being specific in highly oxidative tissues such as brown adipose, muscle, and liver (Wu et al., 1999; Puigserver, 2005). Kelly et al. (2011b) found that *PGC1-α* expression was higher in the muscle of low-RFI animals and detected a negative relationship

between *PGC1-α* and DMI, RFI, and FCR. Expression of *PGC1-α* was not associated with RFI in the current study. In adipose tissue, *PPAR-γ* is a dominant regulator of expression of genes that encode proteins essential for adipocyte differentiation and is also involved in the uptake and metabolism of fatty acids (Tontonoz et al., 1995; Rosen et al., 1999). In addition, a functional relationship exists between *PPAR-γ* and *C/EBP-α*, whereby the activation of *PPAR-γ* leads to the activation of *C/EBP-α* and both transcription factors work together to promote differentiation (Loftus and Lane, 1997). The existence of these genes and their metabolic function in adipose tissue has been well defined; however, even though these genes are thought to have a similar presence and function (activation of lipogenesis in muscle tissue), reports regarding their exact nature are sparse. Kelly et al. (2011b) indicated that RFI phenotypes were not different regarding muscle (*Longissimus dorsi*) *PPAR-γ* mRNA expression, although *PPAR-γ* was negatively associated with FCR (r = -0.53) and tended to be negatively associated with RFI and DMI. There were no differences detected in *PPAR-γ* mRNA expression between high and low RFI groups in the current study. Even though no relationship was observed between RFI and *PPAR-γ* expression in this study, *C/EBP-α* expression tended to be positively correlated with RFI. In addition, expression of *FASN*, an important regulator of fatty acid synthesis, was also higher in high-RFI animals. Data analyses from the aforementioned studies indicate that activation of lipogenic pathways in muscle tissue may be associated with RFI. From these observations, it can be inferred that more efficient animals (low-RFI) may have the genetic potential to simultaneously regulate the uptake and metabolism of fatty acids, where inefficient (high-RFI) animals may increase their production of fatty acids without concordantly increasing uptake and metabolism. These differences could be potential contributors to variation in metabolic efficiency, and thus, variation in RFI.

Fiber type composition is an important aspect of energy metabolism as well as end-product quality. However, to the authors' knowledge, there are no studies to date that examine the relationship between fiber type and RFI. It has been previously shown that the effects of IGF-I on skeletal muscle are associated with anabolic growth and modulation of muscle catabolism in both heifers (Hill et al., 1999) and rodents (Smith et al., 2008). Furthermore, changes in fiber type have the potential to contribute to variation in FE as

outlined below. Our data analyses suggest that type IIb fibers are more abundant in high-RFI (inefficient) steers, whereas type I fibers may tend to be more abundant in low-RFI (efficient) steers. According to Harrison et al. (1996), energy expenditure per unit of tension developed is lower in type I fibers (oxidative) than in type IIb fibers (glycolytic). When thinking about the variation in FE, the goal is to select for and produce the most efficient cattle in terms of energy usage and weight gain. In the context of fiber type, it is important to think about FE in relation to muscle energy utilization. In this proposed scenario, feed efficient (low-RFI) animals, having similar gain and muscle mass and having a greater proportion of type I fibers, are able to produce similar weight gain with a relatively lower feed intake compared to their contemporaries. For individual animals whose muscles contain a relatively greater proportion of type I fibers compared to type IIb fibers, it is this difference in muscle fiber type that may contribute to the variation in FE. In relating this hypothesis to local availability of IGF-I in partitioning fiber type and muscle hypertrophy, there is literature to support enhanced paracrine responses to IGF-axis activity in promoting type I fiber composition (Musaro et al., 2001; Mavalli et al., 2010). This may suggest that higher, local levels of IGF-I are available due to either increased tissue synthesis or from lower expression of inhibitory binding proteins. It has been suggested that IGF-I-induced skeletal muscle hypertrophy is due to local production of IGF-I via autocrine and/or paracrine effects rather than circulating IGF-I (Bamman et al., 2001), which may be a potential contributor to the variability observed in studies looking exclusively at serum IGF-I levels. Furthermore, as noted above, IGF-I has been implicated as a stimulator of protein synthesis and an inhibitor of protein degradation, thus improving protein retention (Oddy and Owens, 1996; Hill et al., 1999) consistent with higher local IGF-I in muscle of feed efficient animals.

Energetic efficiency is an intricate process associated with and dependent upon various factors, as noted above. Welch et al. (2012) discussed sire ME_M EPD in context of the relationship that may exist between maintenance energy and RFI, which also alluded to the importance of overall energetic efficiency. Based on this concept, measurements that could provide substantial input regarding variation in RFI were also analyzed in terms of sire ME_M EPD. In the present study, a negative relationship was observed between sire

ME_M EPD and progeny IGF-I concentration (weaning). Data analyses indicate that disconnects may exist between the heritability of ME_M EPD and the concentration of IGF-I (measured at a specific time), whereas a higher serum IGF-I concentration is associated with lower sire ME_M EPD. There is increased variability associated with measurement of serum or circulating IGF-I due to the intricate relationship that exists between IGF-I and GH, whereby the release of GH, which is regulated in a pulsatile and diurnal manner, stimulates the release of IGF-I from other systemic tissues into circulation. When thinking about this relationship in biological terms, an increased concentration of IGF-I would be related to an increase in maintenance of lean muscle tissue and thereby an increase in the ME_M; however, the negative relationship observed in this study suggests otherwise. Since progeny ME_M was not determined, it is difficult to conclude if ME_M is in fact negatively associated with IGF-I concentration. In addition, results of GH-IGF axis and lipogenic gene expression were opposite in direction and magnitude between cohorts, indicating that different sires across the cohorts may have imposed a genetic influence upon energetic efficiency independently of sire ME_M EPD. For a complete discussion regarding the influences of sire ME_M EPD on fiber type composition and end-product quality, the reader is referred to Thornton et al. (2012).

Implications

This study evaluated physiological mechanisms/pathways that may at least partially, account for the variation in RFI, and thereby demonstrate the complexity of the RFI trait. Although no phenotypic relationship was observed between serum IGF-I concentration and RFI in this study, context from other published findings suggests that a relationship may exist between IGF-I concentration and RFI at the genetic level, indicating that the IGF-axis may be a factor driving variation in RFI. In addition, various metabolic pathways were investigated within the context of RFI to determine potential candidate genes that may influence its variation. At this time, current reports are inconclusive as to the exact underlying physiological mechanisms controlling RFI, but findings from this study provide a basis for further research. Since previous findings have suggested that RFI does not negatively impact end-product quality, observed differences in fiber type composition

between RFI groups suggest that fiber type composition may be a component contributing to the variation in RFI, but will require further investigation to determine if this is in fact a source of variation.

Table 3.1. Primer and probe sequences used in real-time PCR[1]

Gene name	Accession number	Primers and TaqMan probe sequences, 5'- 3'
18S	AF243428	FP: CCACGCGAGATTGAGCAAT RP: GCAGCCCCGGACATCTAA TP: ACAGGTCTGTGATGCC
Type I- IGF receptor (*IGF-IR*)	XM_606794.3	FP: TTCGCACCAACGCATCAG RP: GTTTGAGGCCGAGAGGACATC TP: TCCTTCCATCCCCC
IGFBP2	NM_174555.1	FP: CTGTGACAAGCATGGCCTGTA RP: CGCTGCCCGTTCAGAGA TP: AACCTCAAACAGTGCAAG
IGFBP3	NM_174556.1	FP: CGCCTGCGCCCTTACC RP: TTCTTCCGACTCACTGCCATT TP: CTACCGTCCGCGTCAG
IGFBP5	NM_001105327.1	FP: CCGTGTACCTGCCCAACTG RP: AGGTTTGCACTGCTTTCTCTTGT TP: ACCGCAAAGGGTTC
GH receptor (*GHR*)	NM_176608.1	FP: TGGACCCCCTACTGCATCAA RP: CAACAGAGAAACACTTATGATCCACAA TP: CTAACTAGCAATGGCG
PPAR gamma (*PPARγ*)	NM_181024.2	FP: AGACCGCCCAGGTTTGC RP: GCTTGCAGCAGATTGTCTTGTATG TP: AACGTGAAGCCCATTGA
PPARγ coactivator 1 alpha (*PGC1α*)	NM_177945.3	FP: CCAGCACGAAAGGCTCAAG RP: TTTCGGATTCCCGCTTCTC TP: AAGAATACCGCAGAGAGT
C/EBP alpha (*C/EBPα*)	NM_176784.2	FP: GTGCTGGAGCTGACCAGTGA RP: AGTTCGCGGCTCAGTTGTTC

		TP: AATGACCGCCTGCGCA
Fatty acid synthase (*FASN*)	NM_001012669.1	FP: GCAGAAGGTGCTCCAGAGTGA RP: CCCCAGGCCCCATCA TP: CTGGTGATGAATGTCT
Acetyl CoA carboxylase alpha (*ACACα*)	NM_174224.2	FP: TGTCCGAAACGTCGATTTTTG RP: ACGACCTGGTTGCTGTGATAGA TP: TGTCCTACCAAACTTC
Carnitine palmitoyltransferase 1 beta (*CPT-1β*)	NM_001034349.2	FP: TACGGCAAGGCCCTGTTG RP: GTGTGAAGGACTTGTCGAACCA TP: CGGCAACTGCTACAAC

[1]Forward primer (FP), reverse primer (RP), and Taqman probe (TP) sequences were indices along with GenBank accession number for the genes analyzed using the Taqman ® primer/probe system of real-time PCR.

Table 3.2. Spearman rank correlations of postweaning residual feed intake (RFI) and sire maintenance energy (ME_M) EPD with serum IGF-I levels of Red Angus sired steers and heifers measured at weaning in Cohorts 1, 2, and 3

	Cohort[1]					
	1		2		3	
Grouping	RFI	ME_M EPD	RFI	ME_M EPD	RFI	ME_M EPD
Steers	-0.12	-0.32	0.19	-0.36[*]	0.01	-0.27[†]
Heifers	0.08	-0.38	0.19	-0.22	-0.06	-0.50[*]
Steers & Heifers	-0.07	-0.30[‡]	0.17	-0.31[**]	-0.04	-0.36[**]

[1] Cohort 1 – n = 42; steers = 23, heifers = 17.
Cohort 2 – n = 90; steers = 46, heifers = 44.
Cohort 3 – n = 88; steers = 38, heifers = 50.
[*]Correlations are significant at $P \leq 0.01$.
[†]Correlations are marginal at $P \leq 0.10$.
[**]Correlations are significant at $P \leq 0.01$.
[‡]Correlations are marginal at $P \leq 0.10$.

Table 3.3. Muscle gene expression (*Biceps femoris*) in Red Angus sired steers and heifers tested for postweaning residual feed intake (RFI) in Cohorts 1 and 2[1]

Cohort[2]	Grouping[3]	Gene name[4]	ΔΔCt	*P*-value	$2^{-\Delta\Delta Ct}$
1	RFI Quartile	*IGFBP5*	-0.77	0.035	1.71
	ME_M EPD	*IGFBP5*	0.51	0.086	0.70
		C/EBP alpha (*C/EBPα*)	0.47	0.108	0.72
		Fatty acid synthase (*FASN*)	0.97	0.005	0.51
2	RFI Quartile	—	—	—	—
	ME_M EPD	*IGFBP2*	-0.91	0.023	1.88
		IGFBP3	-0.56	0.073	1.47
		C/EBPα	-0.77	0.016	1.70

[1]Biopsies were taken immediately following postweaning RFI evaluation. Mean ΔCt values for each gene was used to calculate ΔΔCt values for comparison of high and low RFI quartiles and sire ME_M EPD groups (i.e., high ΔCt – low ΔCt = ΔΔCt). Using ΔΔCt values, a one-way ANOVA was employed to obtain *P*-value. Fold change is represented by $2^{-\Delta\Delta Ct}$ values.

[2]Cohort 1 – n = 42; steers = 25, heifers = 17.
Cohort 2 – n = 37; steers = 20, heifers = 17.

[3]Grouping into high (n = 11, 10) and low (n = 11, 10) quartiles was based on the most divergent progeny postweaning RFI values for cohorts 1 and 2, respectively; grouping into high (n = 22, 21) and low (n = 20, 16) ME_M EPD groups was based on the most divergent sire ME_M EPD values of each progeny for cohorts 1 and 2, respectively.

[4]Gene expression was evaluated in both cohorts 1 and 2 using the same genes. However, only those genes with differences in expression between high and low RFI quartiles and sire ME_M EPD groups are reported.

Table 3.4. *Biceps femoris* fiber type percentages for Red Angus sired steers tested for both postweaning residual feed intake (RFI) and finishing phase feed efficiency (FE) in Cohort 1[1]

Fiber Type	Quartile[2]	RFI			FE		
		Mean, %	SEM	*P*-value	Mean, %	SEM	*P*-value
I	High	19.9	2.55	0.170	20.8	2.12	0.105
	Low	25.2			26.0		
IIa	High	20.0[a]	2.03	0.053	21.0	1.93	0.066
	Low	26.2[b]			26.5		
IIb	High	60.0[b]	3.66	0.048	58.3[b]	3.50	0.050
	Low	48.6[a]			47.5[a]		

[1]Biopsies were taken at the time of harvest (avg age of 15 mo).
[2]Steers were grouped into high (n = 7) and low (n = 7) quartiles based on RFI and FE values.
[a,b]Means lacking a common superscript letter differ at $P \leq 0.05$.

Table 3.5. Spearman rank correlations of postweaning residual feed intake (RFI) and finishing phase feed efficiency (FE) values with *Biceps femoris* fiber type composition for Red Angus sired steers in Cohort 1[1]

	Fiber Type		
Trait	Type I	Type IIa	Type IIb
RFI	-0.36[‡]	-0.37[‡]	0.48[†]
FE	-0.43[*]	-0.31	0.44[*]

[1]Biopsies (n = 25) were taken at the time of harvest (avg age of 15 mo).
*Correlations are significant at $P \leq 0.05$.
[†]Correlations are significant at $P \leq 0.01$.
[‡]Correlations are marginal at $P \leq 0.10$.

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CHAPTER 4

Development of a residual feed intake EPD and relationships among phenotypic measurements of progeny from Red Angus sires divergent for maintenance energy EPD

Abstract

Feed efficiency is well established as a component of genetic improvement programs in beef cattle. The objectives of this study were to 1) determine heritability and phenotypic variance for feed intake, growth, and residual feed intake (**RFI**) using the progeny of Red Angus (**RA**) sires divergent for maintenance energy ($\mathbf{ME_M}$) EPD, 2) develop a RFI EPD for each sire, and 3) evaluate relationships between various phenotypic performance measurements and EPDs of progeny and sires. The phenotypic variance for RFI (0.465) appears lower than other literature values, whereas heritability estimates for ADG (0.32), DMI (0.38), metabolic BW (**MBW**; 0.39), and RFI (0.38) are in agreement with values reported in studies of other breeds of beef cattle. Positive correlations ($P < 0.02$) were observed between sire ME_M EPD and phenotypic progeny ADG (r = 0.32), DMI (r = 0.21), and MBW (r = 0.22), while sire ME_M EPD was negatively correlated with phenotypic progeny FCR (r = -0.21, $P = 0.019$) and serum IGF-I concentration (r = -0.34, $P < 0.0001$). Sire RFI EPD was positively correlated ($P < 0.001$) with phenotypic progeny DMI (r = 0.31), FCR (r = 0.50), and serum IGF-I concentration (r = 0.31). However, no relationships ($P > 0.05$) were observed between sire RFI EPD and either phenotypic progeny ADG or MBW. Sire ME_M EPD was positively correlated (P < 0.001) with both progeny ADG EPD (r = 0.43) and MBW EPD (r = 0.24). No relationship ($P > 0.05$) was observed between sire ME_M EPD and progeny RFI EPD calculated in two ways 1) without ultrasound backfat included in the model to predict DMI (RFI_0) or 2) with ultrasound backfat included in the model to predict DMI (RFI_1). There were highly significant ($P < 0.0001$) correlations between sire RFI EPD and progeny DMI EPD (r = 0.40), RFI_0 EPD (r = 0.65), and RFI_1 EPD (r = 0.61) EPD. Sire RFI EPD and progeny ADG EPD were also correlated (r = -0.17, $P = 0.012$), but there was no correlation ($P > 0.05$) between sire RFI EPD and progeny MBW EPD. In addition, sire ME_M EPD and RFI EPDs were not correlated ($P > 0.05$).

Thus the heritability of RFI in this population of RA cattle is similar to that of other breeds evaluated for postweaning RFI. Sire ME_M EPD is highly associated with measurements of growth and body size, while sire RFI EPD is more closely associated with DMI. Sire ME_M EPD is inversely related to FCR and serum IGF-I concentration, while sire RFI EPD exhibits a parallel relationship with these performance measurements.

Introduction

Within all sectors of the beef production system there is a common goal to improve or at least maintain profitability in the context of rising costs and unstable market trends. Traditionally, beef programs have focused on the collection of phenotypic data for the improvement of output-based characteristics. Even though feed-related costs are estimated to be 55 to 75% of the total costs associated with beef cattle production, there has been little selection pressure to develop animals that are metabolically and energetically more efficient. Therefore, there is considerable scope to improve the efficiency of feed use and to reduce input costs associated with beef cattle production, substantially impacting profitability.

Earlier attempts at improving the genetics of feed utilization were based on feed conversion ratio (**FCR**). Because it is highly associated with growth and mature size, FCR is considered less favorable for genetic selection when considering overall production efficiency (Kennedy et al., 1993; Archer et al., 1999). However, residual feed intake (**RFI**), a measure of feed efficiency (**FE**), has been shown to be moderately heritable and independent of growth (Herd and Bishop, 2000; Arthur et al., 2001), suggesting that genetic improvement in feed utilization may be achieved through selection using RFI. The importance of FE as a component in beef genetic improvement programs was discussed in detail by Crews (2005). Furthermore, selection programs, that include traits related to FE, may reduce maintenance energy (**ME_M**) requirements of beef cattle, a major contributor to the variation that exists in feed utilization.

Therefore, the objectives of this study were to 1) determine heritability and phenotypic variance for feed intake, growth, and RFI using the progeny of Red Angus (**RA**) sires divergent for ME_M EPD, 2) develop a RFI EPD for each sire, and 3) evaluate

relationships between various phenotypic performance measurements and EPDs of progeny and sires.

Materials and Methods

All animal procedures were reviewed and approved by the Institutional Animal Care and Use Committee (2011-3) as required by federal law and University of Idaho policy.

For a more detailed description of sire selection, postweaning RFI evaluation, and finishing phase FE evaluation, refer to (Welch et al., 2012). In brief, a total of 12 ME_M EPD-divergent RA sires were chosen using the Red Angus Association of America (**RAAA**)-generated ME_M EPD database. Three cohorts of crossbred progeny were generated, with each sire being represented across 2 to 3 cohorts and producing 15 or more progeny. For each cohort, steers and heifers were evaluated for postweaning RFI. Testing procedures were conducted in a similar manner for evaluation periods among cohorts.

Breeding Value Prediction

Beginning with animals with at least daily DMI, a minimum of a four generation ancestral pedigree (n = 597) and the inverse numerator relationship ($\mathbf{A^{-1}}$) was constructed using the RAAA pedigree database. Breeding values for DMI, ADG, metabolic body weight (**MBW**), and RFI, calculated in two ways: 1) without ultrasound backfat included in the model to predict DMI, (RFI_0), and 2) with ultrasound backfat included in the model to predict DMI (RFI_1), were predicted using a standard mixed linear animal model that can be represented in matrix notation as $\mathbf{y} = \mathbf{X\beta} + \mathbf{Zu} + \mathbf{e}$, where fixed contemporary group (year of birth × cohort × pen of feeding × sex, n = 13) effects in $\boldsymbol{\beta}$ were related to observations in $\mathbf{y}$ with the known incidence matrix $\mathbf{X}$, random animal genetic effects in $\mathbf{u}$ were related to observations with the known incidence matrix $\mathbf{Z}$, and $\mathbf{e}$ was a vector of random residuals, specific to animals with data. First and second moments for $\mathbf{u}$ and e were assumed to be $E(\mathbf{u}) = E(\mathbf{e}) = 0$ leading to $E(\mathbf{y}) = \mathbf{X\beta}$; $var(\mathbf{u}) = \mathbf{A^{-1}}\lambda$ [$\lambda = (1 - h^2)/h^2$ and h^2 = heritability] and $var(e) = \mathbf{I}\sigma^2_e$ (i.e., an identity matrix of appropriate order dispersed with estimated residual variance). Extension to the multivariate case followed in a straightforward manner as has been outlined elsewhere (e.g., Beef Improvement Federation, (BIF, 2010)). Attempts to use REML with an average information algorithm (ASReml, version 3.0, VSN International,

Hemel Hempstead, UK) to estimate animal genetic and residual variances for a full animal model failed to converge, most likely due to low numbers of observations and a non-positive-definite estimate of the genetic covariance matrix. Therefore, genetic and residual (co)variances among the four traits were obtained from an adaptation of the meta-analysis results reported by Pendley (2010). The animal model equation system and inverse relationship matrix was constructed, breeding value solutions for all animals predicted, and the system coefficient matrix directly inverted using tools in the Animal Breeder's Tool Kit (version 4.0, Colorado State University Center for Genetic Evaluation of Livestock). The inverse coefficient matrix was then used to obtain estimates of prediction error variances for individual animal effects, which were subsequently used for computation of accuracy values as per BIF guidelines (BIF, 2010).

Computations and Statistical Analyses

Statistical analyses were conducted using the SAS system (Version 9.3, SAS Inst. Inc., Cary, NC). Spearman rank correlations were used to quantify relationships of phenotypic progeny performance measurements and serum IGF-I concentration (at weaning) with Red Angus sire ME_M EPD and RFI EPDs. Sire RFI_1 EPD (with ultrasound backfat included in the model to predict DMI) was utilized in the following analyses and will be defined only as sire RFI EPD for the remainder of the text. Spearman rank correlations were also used to quantify relationships between calculated EPDs of progeny performance traits and Red Angus sire ME_M EPD and RFI EPDs. Furthermore, in order to gain insight regarding potential underlying sire effects, progeny serum IGF-I concentration and performance EPDs were studied along with sire ME_M EPD and RFI EPDs using a cluster analysis approach (CLUSTER, SAS). To form the clusters, an Average Linkage method was chosen, where the distance between two clusters is defined as an average multivariate distance metric computed between all possible pairs of observations. Each observation was the collection of all responses for each animal. Data points were assigned to clusters based on similarity of their respective distance metrics. Following cluster analysis, simple statistics and frequencies (MEANS and FREQ, respectively, SAS) were used to describe and identify similarities among and within clusters.

Results

Phenotypic variances for ADG, DMI, MBW, and RFI were 0.031 $kg.d^{-1}$, 1.341 $kg.d^{-1}$, 25.378 kg, and 0.465 $kg.d^{-1}$, respectively, while corresponding heritability estimates were 0.32, 0.38, 0.39, and 0.38, respectively, for those performance variables (Table 1). Calculated RFI EPDs for each sire are presented in Table 2, with values ranging from -0.085 $kg.d^{-1}$ to 0.287 $kg.d^{-1}$ and -0.297 $kg.d^{-1}$ to 0.210 $kg.d^{-1}$ for RFI_0 and RFI_1, respectively. In addition, accuracies for these EPDs (RFI_0 and RFI_1) were similar in value.

Relationships between sire ME_M EPD and RFI EPD with phenotypic progeny performance measurements are presented in Table 3. Positive correlations ($P < 0.02$) were observed between sire ME_M EPD and phenotypic progeny ADG (r = 0.32), DMI (r = 0.21), and MBW (r = 0.22), while a negative correlation was observed between sire ME_M EPD and phenotypic progeny FCR (r = -0.21, $P = 0.019$). In addition, a highly significant, negative correlation was observed between sire ME_M EPD and progeny serum IGF-I concentration (r = -0.34, $P < 0.0001$). Sire RFI EPD was positively correlated ($P < 0.001$) with phenotypic progeny DMI (r = 0.31), FCR (r = 0.50), and serum IGF-I concentration (r = 0.31). However, no significant relationships ($P > 0.05$) were observed between sire RFI EPD and phenotypic progeny ADG or MBW.

Furthermore, positive correlations ($P < 0.001$; Table 4) were observed between sire ME_M EPD and progeny ADG EPD (r = 0.43) and MBW EPD (r = 0.24). No relationships ($P > 0.05$) were observed between sire ME_M EPD and progeny DMI, RFI_0, or RFI_1 EPD. The relationships between sire RFI EPD and progeny DMI (r = 0.40), RFI_0 (r = 0.65), or RFI_1 (r = 0.61) EPD were highly significant and positively correlated ($P < 0.0001$). A negative correlation was observed between sire RFI EPD and progeny ADG EPD (r = -0.17, $P = 0.012$). No relationship was observed between RFI EPD and MBW EPD ($P > 0.05$). In addition, results indicate that sire ME_M EPD and RFI EPDs were not associated ($P > 0.05$; data not shown).

When evaluating the tree diagram derived from cluster analysis (Supplemental Figure 1), it was possible to identify 8 main clusters for further investigation. Each cluster was then summarized by determining the number of progeny within known groups, such as cohorts, genders, sire classifications, and sire ME_M EPD or RFI EPDs (Table 5). All

clusters, except cluster 8, were composed primarily of animals from cohorts 2 and 3, which is not surprising given that cohorts 2 and 3 were much larger in animal numbers when compared to cohort 1. In addition, cluster 1, 2, and 5 were mainly composed of steers, whereas clusters 3, 4, 6, and 7 were mainly composed of heifers. Sires with a high ME_M EPD appeared to be more strongly represented in clusters 3, 4, 6, and 7, while sires classified with a low RFI EPD appeared to be more strongly represented in clusters 3, 4, 7, and 8. In addition, means and SD for sire ME_M EPD and RFI EPDs, progeny performance trait EPDs, and phenotypic progeny IGF-I concentration are summarized in Table 6. It appears that a parallel relationship exists between phenotypic progeny IGF-I concentration and progeny RFI_1 EPD and sire RFI EPD, with lower IGF-I concentration clustering with lower RFI_1 EPD and RFI EPD in clusters 3, 4, 7, and 8. Progeny IGF-I concentration seems to also be inversely related to sire ME_M EPD within the clusters, as high IGF-I concentration clustered with lower ME_M EPDs in clusters 1, 2, 5, and 8. Sire ME_M EPD appears to be inversely related to sire RFI EPD, whereby higher sire ME_M EPD clustered with lower sire RFI EPD in clusters 3, 4, and 7. Furthermore, clusters 1 and 2 were formed at a different branching point and were more similar to each other and distinctly different from clusters 3 through 8.

Discussion

Evaluating relationships among feed intake, growth, and energy requirements of beef cattle is necessary to identify physiological drivers and resulting performance attributes associated with FE. Results from the current study highlight important associations between sire ME_M EPD and RFI EPD and various performance measurements, which may serve as potential indicators for improved FE. Furthermore, this study addresses the need for an EPD that reflects FE and discusses its incorporation into profitable breeding selection programs, as a means to genetically improve FE within the beef production system.

Heritability estimates for growth traits of beef cattle are well documented within the literature, whereby Koots (1994a) reviewed these estimates and indicated that they are all moderately heritable. In recent years, heritability estimates for FE traits in beef cattle have become more available, with the majority of these estimates focusing on feed intake, FCR,

and RFI. Previous studies (Herd and Bishop, 2000; Schenkel et al., 2004), regarding the genetic variation in RFI and its use as a tool for the improvement of feed utilization, are supported by the current study. Using Angus bulls and heifers, Arthur et al. (2001) reported heritability estimates for ADG, DMI, MBW, and RFI as 0.28, 0.39, 0.40, and 0.39, respectively. Crowley et al. (2010) evaluated different breeds of Irish beef bulls and reported ADG, concentrate intake, MBW, and RFI estimates as 0.30, 0.49, 0.69, and 0.45, respectively. In addition, Rolfe et al. (2011) reported ADG (0.26), DMI (0.40), MBW (0.35), and RFI (0.52) heritability estimates for mixed-breed steers. In the current study, heritability estimates are in general agreement with those reported in the literature, while the phenotypic variance of RFI in the current study (0.465) is less than that reported by Arthur et al. (2001) and Nkrumah et al. (2007) at values of 0.58 and 0.774, respectively. Differences in the method of calculating RFI among studies and genetic potential of animals being evaluated may be contributing to the variation in heritability estimates and variances of performance measurements that are associated with FE.

The process of genetic evaluation includes statistical procedures that accurately predict breeding values in the form of an EPD for traits that are of economic relevance to beef production. Over the past few decades, the generation of EPDs has been based upon output characteristics, such as weaning and yearling weight, carcass and meat quality, and fertility, rather than input-related characteristics (Archer et al., 1999). The RAAA published the first mature cow ME_M EPD in 2004, which is predicted from mature weight of the cow adjusted for BCS and milk production (Evans, 2001). For a more in-depth discussion regarding the prediction of ME_M EPD, please refer to Williams et al. (2009). Because these component traits have been shown to affect maintenance requirements (Montano-Bermudez et al., 1990; Enns et al., 2003), it is logical that a relationship between ME_M EPD and RFI may exist. In addition to the ongoing research associated with improved FE of beef cattle, many producers have expressed a need for an EPD that reflects FE to be incorporated into breeding selection programs. Therefore, a RFI EPD was developed for each of the sires in the present study.

The authors are unaware of any previous literature that reports the relationship between sire ME_M EPD, RFI EPD, and progeny performance traits associated with FE.

Nevertheless, relationships among various performance measurements reported in the literature provide a context in which to discuss the data from the current study and support the findings. Rolfe et al. (2011) reported positive genetic and phenotypic correlations between ADG and MBW ($r_g = 0.86$; $r_p = 0.51$), DMI and ADG ($r_g = 0.56$; $r_p = 0.64$), and DMI and MBW ($r_g = 0.71$; $r_p = 0.72$). Although animal numbers available in the current study limited the calculation of genetic correlations, phenotypic measurements of progeny growth (ADG), body size (MBW), and intake (DMI) were moderately and positively correlated with sire ME_M EPD. Mature size is a component in the calculation of ME_M EPD, and our observation of a consistent, positive relationship between these closely inter-related production measures and ME_M EPD was expected. Furthermore, Nkrumah et al. (2007) stated that high genetic correlations of DMI with ADG and MBW imply that a considerable proportion (76%) of the genetic variation in intake is associated with genetic differences in maintenance and growth. This supports the need to further explore the relationship between these variables, as maintenance requirements are likely an underlying source of the variation that is observed in RFI among beef cattle. In addition, Crowley et al. (2010) reported negative genetic and phenotypic correlations between ADG and FCR ($r_g = -0.53$; $r_p = -0.71$), while Robinson and Oddy (2004) reported a genetic correlation between MBW and FCR as -0.62 ± 0.18. In the current study, both ADG and MBW were positively associated with sire ME_M EPD, while FCR was negatively associated with ME_M EPD on a phenotypic basis. A negative phenotypic correlation was also observed between progeny serum IGF-I concentration and sire ME_M EPD. Cluster analysis of this study also supports this negative correlation in that high IGF-I concentration clustered with low ME_M EPD values. Our previously published results (Welch et al., 2013) also reported negative correlations between progeny serum IGF-I concentration and sire ME_M EPD, when evaluated within each individual cohort of the study.

There are several reports in the literature concerning the relationship between various performance measurements and RFI, and they are in agreement with the results of the current study. Arthur et al. (2001) reported that ADG and MBW were genetically and phenotypically independent of RFI. Rolfe et al. (2011) also reported no association between ADG and RFI or MBW and RFI, but did report positive genetic and phenotypic correlations

between DMI and RFI (r_g = 0.66; r_p = 0.61). We have also shown that RFI was not phenotypically correlated with ADG, but was positively correlated with DMI and FCR (Welch et al., 2012). In addition, Arthur et al. (2001) reported that feed intake was more strongly correlated with RFI (r_g = 0.69) than with FCR (r_g = 0.31), while Herd and Bishop (2000) reported strong phenotypic correlations between RFI and feed intake (r_p = 0.64) and RFI and FCR (r_p = 0.70) in British Hereford cattle. Crowley et al. (2010) also reported a genetic correlation of 0.48 and a phenotypic correlation of 0.41 between FCR and RFI. In the current study, no association was detected between sire RFI EPD and progeny ADG and MBW on a phenotypic basis; however, a positive phenotypic correlation was observed between sire RFI EPD and progeny DMI and FCR measurements, indicating that RFI is independent of growth traits and that DMI has a greater effect on FE status. Furthermore, in previously published results (Welch et al., 2013), we reported that there was no association between RFI and progeny serum IGF-I concentration (at weaning) when evaluated within each individual cohort of the study. However, a positive association was observed between sire RFI EPD and progeny serum IGF-I concentration, indicating that serum IGF-I may in fact be an underlying driver of FE. To further substantiate this claim, the cluster analysis of this study revealed that a parallel relationship may exist between RFI EPD and serum IGF-I, whereby low IGF-I concentration clustered with low RFI EPD values. Serum IGF-I concentration as an indicator of RFI status in growing animals has been explored for some time; however, reports in the literature are conflicting as to the exact nature of this relationship. For a more in-depth discussion regarding the relationship between RFI and serum IGF-I concentration, the reader is referred to Welch et al. (2013).

When evaluating the relationships of sire ME_M EPD and RFI EPD with calculated EPDs of progeny performance traits, the results were similar to those of phenotypic progeny performance measurements. Sire ME_M EPD was positively correlated with progeny ADG and MBW EPDs, whereby these relationships support the previous discussion and provide further indications that maintenance requirements are highly associated with growth and size. Additionally, sire ME_M EPD was not associated with either progeny DMI, RFI_0, or RFI_1 EPDs. The lack of a relationship between sire ME_M EPD and progeny RFI_0 and RFI_1 EPDs continues to question the relationship between maintenance requirements and FE,

suggesting a need for further research on this topic. Furthermore, sire RFI EPD was positively correlated with progeny DMI, which further substantiates the notion that feed intake is a major driver of the variation in FE. Also, a negative correlation was observed between RFI EPD and ADG EPD. Moreover, sire RFI EPD was highly and positively associated with progeny RFI_0 and RFI_1 EPDs, indicating that RFI was heritable in this study.

An objective of this study was to evaluate the relationship between sire ME_M EPD and sire RFI EPD. No relationship was observed between these two variables. However, cluster analysis of the EPD data revealed that high sire ME_M EPD values clustered with low sire RFI EPD values, indicating a possible inverse relationship. Factors that may be contributing to these discrepancies are likely related to the number of sires used in the study and the extent of divergence and range of RFI EPD values. The 12 sires used in this study were divergent for ME_M EPD, with an accuracy greater than 0.50. When a RFI EPD was developed for each sire, the divergence and range of values were much smaller compared to the values of ME_M EPD. Therefore, in order to gain insight as to the relationship that exists between these two EPD variables, a greater number of sires with complete divergence in both EPDs may be needed.

We conclude that the heritability of RFI in this population of RA cattle is similar to that of other breeds evaluated for postweaning RFI. Sire ME_M EPD is highly associated with measurements of growth and body size, while sire RFI EPD is more closely associated with DMI. Sire ME_M EPD is inversely related to FCR and serum IGF-I concentration, while sire RFI EPD exhibits a parallel relationship with these performance measurements.

Table 4.1. Summary of phenotypic variance, heritability, genetic correlation and residual (co)variance estimates used in the multivariate genetic evaluation[†]

Trait[1]	ADG	DMI	MBW	RFI
Phenotypic Variance	0.031	1.341	25.378	0.465
ADG	**0.32**	0.831	0.259	0.000
DMI	0.38	**0.38**	15.480	0.186
MBW	0.45	0.40	**0.39**	0.000
RFI	0.00	0.38	0.00	**0.38**

[†]Heritability values are shown on the diagonal (in bold), genetic correlations are below the diagonal, and residual (co)variances above the diagonal.
[1]MBW = metabolic body weight; RFI = residual feed intake.

Table 4.2. Calculated EPD and accuracy for performance traits of 12 Red Angus sires whose progeny were tested for residual feed intake (RFI)

	Trait[2]											
	ME_M		ADG		DMI		MBW		RFI_0		RFI_1	
Sire[1]	EPD	Accuracy	EPD	Accuracy	EPD	Accuracy	EPD	Accuracy	EPD	Accuracy	EPD	Accuracy
A	20	52	0.055	0.749	0.434	0.773	1.417	0.776	0.208	0.773	0.172	0.773
B	15	61	0.010	0.738	-0.280	0.762	-1.138	0.765	-0.321	0.762	-0.297	0.762
C	11	57	-0.021	0.712	-0.125	0.737	-0.280	0.741	-0.025	0.737	0.002	0.737
D	11	55	0.020	0.693	0.000	0.720	1.238	0.724	-0.162	0.720	-0.108	0.720
E	10	55	0.066	0.713	0.302	0.740	1.256	0.743	0.084	0.740	0.092	0.740
F	11	58	-0.062	0.748	-0.140	0.772	-1.485	0.775	0.098	0.772	0.125	0.772
G	4	62	0.013	0.585	-0.089	0.615	0.695	0.620	-0.083	0.616	-0.078	0.615
H	-5	60	-0.042	0.735	0.122	0.758	-1.241	0.761	0.287	0.758	0.210	0.758
I	-1	60	-0.030	0.722	-0.054	0.749	1.302	0.752	-0.061	0.749	-0.022	0.749
J	-10	56	0.011	0.729	0.331	0.755	0.525	0.758	0.095	0.755	0.003	0.754
K	-11	56	-0.035	0.719	-0.092	0.744	-1.690	0.748	0.131	0.744	0.044	0.744
L	-14	54	-0.062	0.726	-0.318	0.752	-1.639	0.756	-0.085	0.752	-0.046	0.752

[1]Individual sire code assigned to each of the 12 sires.

[2]ME_M = maintenance energy; MBW = metabolic body weight; RFI_0 = excludes ultrasound fat thickness in the model predicting DMI; RFI_1 = includes ultrasound fat thickness in the model predicting DMI.

Table 4.3. Spearman correlations (*P*-values) of phenotypic progeny performance measurements and serum IGF-I concentration (at weaning) with Red Angus sire maintenance energy (ME_M) EPD and residual feed intake (RFI) EPD[†]

	Trait[1]				
	ADG	DMI	MBW	FCR	IGF-I
ME_M EPD	0.32 (0.0002)	0.21 (0.019)	0.22 (0.013)	-0.21 (0.019)	-0.34 (< 0.0001)
RFI EPD	-0.09 (0.325)	0.31 (0.0005)	0.09 (0.291)	0.50 (< 0.0001)	0.31 (0.0004)

[†]Performance measurements – n = 128; serum IGF-I concentration – n = 127.
[1]MBW = metabolic body weight; FCR = feed conversion ratio.

Table 4.4. Spearman correlations (*P*-values) of calculated EPDs of progeny performance traits with Red Angus sire maintenance energy (ME_M) EPD and residual feed intake (RFI) EPD[†]

	Trait[1]				
	ADG	DMI	MBW	RFI_0	RFI_1
ME_M	0.43 (< 0.0001)	0.09 (0.175)	0.24 (0.0004)	0.10 (0.145)	-0.04 (0.538)
RFI	-0.17 (0.012)	0.40 (< 0.0001)	0.00 (0.971)	0.65 (< 0.0001)	0.61 (< 0.0001)

[†]n = 221.

[1]MBW = metabolic body weight; RFI_0 = excludes ultrasound fat thickness in the model predicting DMI; RFI_1 = includes ultrasound fat thickness in the model predicting DMI.

Table 4.5. Categorical information of 8 clusters identified using the Average Linkage method of cluster analysis[†]

Grouping[1]		Cluster[2]							
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
n		19	27	22	41	28	32	27	21
Cohort	1	1	3	3	8	5	7	6	7
	2	4	10	18	18	10	8	16	6
	3	14	14	1	15	13	17	5	8
Gender	Heifer	2	9	14	26	8	24	19	9
	Steer	17	18	8	15	20	8	8	12
Sire	A	0	2	3	7	3	1	3	2
	B	0	1	5	6	0	2	3	3
	C	5	1	2	3	1	3	2	1
	D	0	1	0	7	5	1	2	0
	E	1	4	2	0	3	6	2	1
	F	2	3	1	5	1	6	2	1
	G	0	0	2	1	0	3	4	2
	H	6	2	1	1	5	1	0	2
	I	2	2	2	4	1	2	2	2
	J	0	2	0	4	3	4	3	5
	K	1	4	3	2	3	2	1	1
	L	2	5	1	1	3	1	3	1
Sire ME_M EPD	High	8	12	15	29	13	22	18	10
	Low	11	15	7	12	15	10	9	11
Sire RFI EPD	High	9	11	7	13	12	14	7	6
	Low	10	16	15	28	16	18	20	15

[†] n = 217.

[1]Each grouping variable is associated with a data point, where a data point is equivalent to a single progeny of the data set. ME_M = maintenance energy; RFI = residual feed intake.

[2]The number of observations that represent each variable are identified within the 8 clusters.

Table 4.6. Means (SD) of sire maintenance energy (ME_M) and residual feed intake (RFI) EPD, progeny performance trait EPDs, and phenotypic progeny IGF-I concentration within 8 clusters identified using the Average Linkage method of cluster analysis[†]

Trait[1]		Cluster							
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
n		19	27	22	41	28	32	27	21
Sire	ME_M EPD	0.842 (9.42)	0.148 (12.00)	6.455 (11.10)	7.658 (10.54)	1.288 (11.67)	4.656 (9.64)	4.519 (11.31)	1.810 (11.51)
	RFI EPD	0.080 (0.103)	0.038 (0.109)	-0.025 (0.171)	-0.015 (0.154)	0.050 (0.114)	0.024 (0.116)	-0.022 (0.131)	-0.004 (0.151)
Progeny	ADG EPD	-0.029 (0.032)	-0.012 (0.032)	0.015 (0.039)	0.003 (0.036)	-0.003 (0.030)	0.007 (0.037)	0.005 (0.038)	0.021 (0.052)
	DMI EPD	-0.008 (0.243)	-0.035 (0.161)	0.005 (0.205)	-0.026 (0.247)	0.013 (0.175)	0.067 (0.255)	-0.009 (0.216)	0.084 (0.257)
	MBW EPD	-0.213 (1.060)	-0.284 (0.986)	-0.037 (1.241)	-0.075 (1.004)	0.010 (1.025)	-0.123 (1.055)	0.079 (1.193)	0.165 (1.122)
	RFI0 EPD	0.067 (0.162)	0.012 (0.123)	-0.005 (0.121)	-0.027 (0.177)	0.017 (0.120)	0.051 (0.154)	-0.018 (0.100)	0.015 (0.149)
	RFI1 EPD	0.054 (0.137)	0.002 (0.107)	-0.009 (0.104)	-0.030 (0.162)	0.018 (0.114)	0.047 (0.125)	-0.011 (0.099)	0.001 (0.110)
	IGF-I	252.66 (11.21)	203.02 (11.11)	46.70 (12.44)	93.86 (16.21)	177.70 (5.74)	154.04 (9.50)	123.19 (4.34)	137.74 (4.18)

[†]n = 217.

[1] MBW = metabolic body weight; RFI0 = excludes ultrasound fat thickness in the model predicting DMI; RFI1 = includes ultrasound fat thickness in the model predicting DMI.

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CHAPTER 5

Conclusions

Summary

An improved understanding of the physiological mechanisms that contribute to variation in RFI is of the utmost importance to the beef production industry. Current financial conditions associated with beef production systems warrant the need for this research, as a reduction in costs associated with production would be beneficial not only to the industry, but to the consumer as well. In addition, improved FE will result in a reduction in the environmental impact of beef production, through reduced methane and nitrogenous compound excretion for a similar level of production. The research presented in this dissertation investigates ME_M EPD as a potential indicator of RFI and examines performance and physiological factors that may be driving the variation that is seen in this FE trait. Therefore, the following hypotheses were tested:

RFI measured during the postweaning growth phase is indicative of FE status in the finishing phase

Outcome: It was observed that steers classified as feed efficient (or low RFI) during postweaning RFI evaluation were also classified as feed efficient (or low finishing phase FE) during finishing phase evaluation. This outcome is desirable because the implementation of a FE measure that is applicable and beneficial to both the cow-calf and feedlot sectors of the industry is highly advantageous. This observation also suggests that the moderate prediction power of identifying feed efficient animals in the growing phase may partially abrogate the need to test for FE in the finishing phase, at least in the research context.

Postweaning RFI is not associated with carcass or end-product quality traits

Outcome: No phenotypic association was observed between postweaning RFI and any carcass trait (at harvest) or product quality (post-harvest) measurement, suggesting that improving RFI does not have antagonistic effects associated with carcass or product quality. This relationship is desirable and of importance when considering market yields and return

on investment. Any improvement in FE must be achieved while at least maintaining and if possible, improving product quality that is defined by industry standards. Therefore, it is crucial that selection strategies to improve FE do not inadvertently diminish other important production or quality traits. In addition, these observations suggest that it is possible to simultaneously improve FE and product quality in beef cattle.

ME_M EPD is an indicator of postweaning RFI

Outcome: No phenotypic association was observed between sire ME_M EPD and progeny postweaning RFI, which does not support the initial hypothesis of this study that sire ME_M EPD is a possible indicator of progeny postweaning RFI. Energy devoted to maintenance is among one of the most important concepts regarding FE and overall animal efficiency. Furthermore, these observations provide support that ME_M EPD is essentially a trait that is closely related to growth rate. The more complex notion of an RFI EPD that simultaneously incorporates improved FE across a range of animal growth rates is a highly desirable alternative, especially due to its independence of the great majority of other production and product quality traits.

Specific genes related to growth, lipogenesis, and lipolysis are involved in the regulation of RFI at the molecular level

Outcome: The GH-IGF axis was observed as having some involvement with RFI at the molecular level; however, muscle gene expression results were not consistent across cohorts. Identifying underlying physiological mechanisms that contribute to variation in RFI is necessary to full understand this FE trait. However, due to the obstacles associated with this type of investigation, very little progress has been made toward the discovery of key genes and metabolic pathways controlling this trait.

Low RFI animals exhibit differences in fiber type composition compared to high RFI animals

Outcome: It was observed that feed efficient (or low RFI) animals may have the ability to more efficiently maintain and accrete muscle mass due to their fiber type composition, specifically a greater proportion of type I fibers, when compared to their inefficient (or high RFI) contemporaries. Feed efficient (low RFI) animals, having similar gain and muscle mass and having a greater proportion of type I fibers, are able to produce similar weight gain

with a relatively lower feed intake compared to their contemporaries. For individual animals whose muscles contain a relatively greater proportion of type I fibers compared to type IIb fibers, it is this difference in muscle fiber type that may be a contributor to the variation in FE.

Serum IGF-I (at weaning) is an indicator of postweaning RFI

Outcome: No phenotypic association was observed between postweaning RFI and serum IGF-I concentration at weaning, although IGF-I was strongly and positively correlated with RFI EPD and strongly and negatively correlated with ME_M EPD. The use of a metabolic variable as an indirect selection tool for RFI and the ability to identify feed efficient animals early in the production cycle has invaluable potential within the beef production industry. The present study has made a small contribution to understanding the complex relationships between the genes of the GH-IGF axis, serum IGF-I, growth and FE. Thus, there is much more to discover about the potential of serum IGF-I as an indicator of postweaning RFI status.

ME_M EPD is an indicator of RFI EPD

Outcome: No phenotypic association was observed between sire ME_M EPD and RFI EPD. This outcome does not support the initial hypothesis regarding the relationship between these two measures of genetic value. Originally, it was thought that ME_M EPD could potentially serve as an indirect selection tool for FE. However, it was concluded that selection for reduced ME_M does not inadvertently select for improved RFI.

Future directions

The findings of this scientific study and resulting dissertation have contributed to the current body of knowledge regarding the use of RFI as a FE measure and its potential impact on beef production systems. Even though a wealth of information has been discovered during this study, the complexities of the biological process that underpin the regulation of growth, feed intake and FE, and the selection and management decisions that are based on this supporting knowledge require that much greater efforts are expended in further building our knowledge base. Overall, there are three hypotheses from this study

that could significantly contribute to the physiological understanding of RFI with further investigation.

The first hypothesis is **ME_M EPD is an indicator of postweaning RFI**. Because ME_M is closely associated with many biological functions and thus production traits, it has been hypothesized that ME_M is a driver of the variation that is seen in RFI of beef cattle. The ability to genetically select for improved RFI of progeny via the selection of sires with a lower ME_M EPD was not only insightful, but also potentially profitable. However, this study was unable to identify any association between sire ME_M EPD and progeny postweaning RFI. Continued investigation into the relationship between ME_M and RFI is essential to understanding the complex nature of FE and the eventual implementation of this trait into breeding programs.

The second hypothesis is **specific genes expressed in muscle, related to growth, lipogenesis, and lipolysis are involved in the regulation of RFI at the molecular level.** Identifying the underlying physiological mechanisms associated with variation in RFI is of upmost importance. The identification of key genes and metabolic pathways associated with this trait could offer advanced genetic selection via screening tools for efficiency and provide underpinning information for more targeted management practices. However, the complexities associated with understanding the contributions of these physiological mechanisms to variation in FE means that more sophisticated tools are needed to improve our mechanistic insights. New technologies such as transcriptome analysis using RNA-Seq applied at specific, critical time-points in the animal's life and through study of specific tissues at those time-points provide exciting possibilities for discovery. Thus, there remains huge potential for significant discoveries to further the knowledge of RFI.

The third hypothesis is **low RFI animals exhibit differences in fiber type composition compared to high RFI animals.** Fiber type composition is of great importance when considering market yields and return on investment, and the goal is to select for and produce the most efficient cattle in terms of energy usage and weight gain. In the context of fiber type, it is important to think about FE in relation to muscle energy utilization. This study suggested that feed efficient (low RFI) animals, having similar gain and muscle mass and having a greater proportion of type I fibers, are able to produce similar

weight gain with a relatively lower feed intake compared to their contemporaries. This observation provides great insight as to a potential physiological source of variation in RFI. Further investigation into the dynamics of muscle energy utilization could improve the overall understanding of energy utilization in feed efficient cattle.

In conclusion, this scientific study and resulting dissertation has relayed important information to the scientific community, regarding potential physiological sources of variation in RFI. However, further investigation of the scientific ideas presented here will continue to increase the knowledge and understanding of FE and RFI.

Benefits of the research presented in this dissertation

The work of this dissertation has presented several important findings related to the implementation of RFI as a measure of FE. This study has reiterated previous findings within the literature, which suggest that the implementation of RFI is not associated with negative impacts upon previously established production traits. This is an important finding because selection strategies to improve FE should not inadvertently diminish already established production or quality traits. This study has also identified potential underlying physiological mechanisms that may be a source of the variation that is exhibited in beef cattle evaluated for RFI. Furthermore, this research has left many questions unanswered, which has provided a foundation for further characterization of relationships investigated in this study. Overall, this study has contributed to advancing the beef production industry toward the selection of more feed efficient cattle, in order to reduce inputs while maintaining or improving production outputs.

Appendix A

Animal Care and Use Committee Approval from the University of Idaho

Date: Friday, March 26, 2010

To: Rod Hill

From: University of Idaho

Re: Protocol 2007-66
Residual Feed Intake Research and Outreach

Your requested amendment to the animal care and use protocol shown above was reviewed by the University of Idaho on Friday, March 26, 2010.

This protocol was originally submitted for review on: Friday, June 15, 2007
The original approval date for this protocol is: Monday, July 23, 2007
This approval will remain in affect until: Friday, July 23, 2010
The protocol may be continued by annual updates until: Friday, July 23, 2010

Federal laws and guidelines require that institutional animal care and use committees review ongoing projects annually. For the first two years after initial approval of the protocol you will be asked to submit an annual update form describing any changes in procedures or personnel. The committee may, at its discretion, extend approval for the project in yearly increments until the third anniversary of the original approval of the project. At that time, the protocol must be replaced by an entirely new submission.

Brad Williams, DVM
Campus Veterinarian
University of Idaho
208-885-8958

Appendix B

Institutional Review Board Approval from the University of Idaho

To: Dr. Rod Hill
Animal & Veterinary Science
University of Idaho
Moscow, ID 83844-2230

From: Traci Craig, PhD
Chair, University of Idaho Institutional Review Board
University Research Office
Moscow Idaho 83844-3010

IRB No.: IRB00000843

FWA: FWA00005639

Date: December 11, 2009

Project: Approval of "Residual Feed Intake – Research and Outreach" Project 09-079

On behalf of the Institutional Review Board at the University of Idaho, I am pleased to inform you that the above-named project is approved as exempt from review by the Committee. Please note, however, that you should make every effort to ensure that your project is conducted in a manner consistent with the three fundamental principles identified in the Belmont Report: respect for persons; beneficence; and justice.

Should there be significant changes in the protocol for this project, it will be necessary for you to resubmit the protocol for review by the Committee.

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Journal: Australian Journal of Experimental Agriculture 44(5) 431 - 440
Published: 04 June 2004

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