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An examination of the molecular control of feed efficiency in beef cattle



Key external stakeholders:

Livestock industry, Animal nutrition and feed companies, Universities, Veterinarians, AI industry, Department of Agriculture, Food and the Marine, Irish Cattle Breeding Federation (ICBF).

Practical implications for stakeholders:

While discernible biochemical differences between feed efficient and inefficient beef cattle, measured in the current project in terms of ranking for residual feed intake (RFI) are evident, gene expression profiles across a number of metabolically important tissues (adipose, muscle and liver) are not consistent for breeds of contrasting beef merit or indeed varying dietary management regimens. Furthermore, it is clear that there is no consistent biological mechanism governing variation for RFI across breeds, diets or stages of development is evident for the key tissues studied here. This challenges the practicality of developing a robust set of functional biomarkers for RFI that would be of ubiquitous utility to the beef cattle industry. The future design of such resources must take cognisance of genomic differences amongst cattle both within and across breed as well as potential interactions with diet and stage of physiological maturity on gene expression profiles.

Main results:

1. Divergent phenotypic status for RFI in beef cattle was shown, for the first time, to have no effect on mitochondrial abundance in muscle or liver tissue. In addition, our studies provided no evidence for an effect of RFI status on the activity of the enzymatic complexes of the electron transport chain within skeletal muscle and liver. These findings suggest that variation in mitochondrial number and/or enzymatic capacity may not be major contributors to variation in RFI.
2. The expression of GLUT4 in adipose tissue is related to RFI. This finding would indicate that the decreased expression of GLUT4 in the high RFI animals represents less efficient glucose homeostasis and increased insulin resistance in these animals. GLUT4 is a strong target for further interrogation as a biomarker for this trait.
3. Transcriptomic analysis in liver tissue from bulls divergent for RFI, revealed evidence that efficient heifers had an enhanced capacity for mitochondrial function in muscle tissue, while oxidative response, protein mediation and cell signaling are likely to be processes that are influencing variation in feed efficiency in bull liver tissue. Cognisance must be taken, however, of the likely physiological age/stage of development differences between the bulls and heifers employed in the study despite the fact that chronologically, they were of similar age.
4. Efficient HF steers offered zero grazed grass subsequent to an extended period on a high concentrate diet, showed evidence of a lower immunocapacity than their less efficient counterparts as demonstrated by a dysregulation of immune system pathways. Given that the ability to mount an immune response is metabolically costly, and, animals consuming low dry matter, zero grazed grass after a period of being accustomed to an energy dense high concentrate diet could be considered to be under a form of metabolic/nutritional stress. It is possible that the more efficient animals employ a coping mechanism by damping their immune responsiveness.

Opportunity / Benefit:

The studies conducted for this project have led to the identification of differentially expressed genes in key metabolically important tissues (muscle, fat and liver) associated with improved feed efficiency across three different breeds of cattle viz. Simmental, Charolais and Holstein Friesian. These genes could be harnessed, following appropriate validation, to identify molecular biomarkers for the selection of cattle with greater

genetic potential for feed efficiency. Further investigation of these genes including their regulatory regions is warranted, in addition to the requirement to evaluate the DNA sequences of these genes in cattle varying in feed efficiency potential, which would aid in the discovery of genetic variants. The general lack of consistency, however, across either breed or diet in gene expression patterns between cattle of contrasting feed efficiency status, suggest that multi-breed molecular based genetic selection tools must reflect unique variants relevant to all beef breeds of economic importance.

Collaborating Institutions:

Trinity College Dublin (TCD)

Teagasc project team:

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External collaborators:

Dr. Richard Porter (TCD)

1. Project background:

Global agriculture is faced with the enormous challenge of feeding a rapidly growing population while being cognizant of the environmental footprint of such endeavours. A consequence of increased meat consumption worldwide is an increase in demand for animal feed. As feed provision is the single largest cost incurred by beef farmers, cattle with improved feed efficiency are central to profitable, sustainable and efficient beef production. A major constraint to genetic progress in feed efficiency is the difficulty and enormous expense of measuring it directly. Therefore, robust cost-effective molecular based biomarkers for feed efficiency are necessary. This multidisciplinary project aimed to: (i) establish and physiologically characterise two populations of cattle, genetically & phenotypically divergent for feed efficiency; (ii) examine the premise that efficiency of energy transduction in cattle is a function of mitochondrial abundance and mitochondrial functional efficiency; (iii) determine the expression of genes involved in fatty acid metabolism in adipose tissue from animals divergent for residual feed intake (RFI); and (iv) to examine the effect of RFI status, gender and diet (as well as their interactions) on targeted and global transcriptomic expression across three metabolically important tissues, namely liver, skeletal muscle and adipose tissue.

2. Questions addressed by the project:

- Is cellular mitochondrial abundance and functionality different between cattle of divergent feed efficiency status?
- Does gene expression profile for key metabolically important tissues differ between cattle of divergent feed efficiency status?
- Are these gene expression profiles consistent across gender
- Are differences in gene expression profiles between feed efficient and inefficient cattle consistent when animals are sequentially offered diets varying in nutrient composition or indeed the same diet, over time?

3. The experimental studies:

- Mitochondrial abundance and function in skeletal muscle and liver from beef cattle divergent for RFI
- Residual feed intake phenotype and gender affect the expression of key genes of the lipogenesis pathway in adipose tissue of beef cattle
- An examination of the transcriptional control of energetic efficiency in skeletal muscle and hepatic tissue from beef cattle divergent for residual feed intake
- The effect of breed and diet on the skeletal muscle transcriptome of beef cattle divergent for residual feed intake

4. Main results:

The observations from this work suggest that variation in mitochondrial number and/or enzymatic capacity may not be major contributors to variation in RFI. Secondly, the expression of GLUT4 in adipose tissue is negatively associated with RFI and has potential to be investigated further as a biomarker for RFI in cattle. Thirdly, transcriptomic analysis revealed evidence that efficient heifers had an enhanced capacity for mitochondrial function in muscle tissue, while oxidative response, protein regulation and cell signaling are likely to be processes that are influencing variation in feed efficiency in bull liver. Finally, effects of RFI on gene expression in muscle of beef cattle are not consistent across breed type or dietary phase. In

conclusion, while the results of this project provide a greater insight into the biological mechanisms governing RFI in cattle, they challenge the practicality of development a robust set of biomarkers for RFI that would be of ubiquitous utility to the beef cattle industry.

5. Opportunity/Benefit:

The studies conducted for this project have led to the identification of differentially expressed genes in key metabolically important tissues (muscle, fat and liver) associated with improved feed efficiency across three different breeds of cattle *viz.* Simmental, Charolais and Holstein Friesian. These genes could be harnessed, following appropriate validation, to identify molecular biomarkers for the selection of cattle with greater genetic potential for feed efficiency. Further investigation of these genes including their regulatory regions is warranted, in addition to the requirement to evaluate the DNA sequences of these genes in cattle varying in feed efficiency potential, which would aid in the discovery of genetic variants. The general lack of consistency, however, across either breed or diet in gene expression patterns between cattle of contrasting feed efficiency status, suggest that multi-breed molecular based genetic selection tools must reflect unique variants relevant to all beef breeds of economic importance.

6. Dissemination:

Main publications:

Savc M, Kenny DA and Beltman ME. 2016. The effect of parturition induction treatment on interval to calving, calving ease, post-partum uterine health and resumption of ovarian cyclicity in beef heifers. *Theriogenology*. 85:1415-1420.

McKenna, C., Waters, S., Keogh, K., Porter, R. and Kenny DA (2017). Expression of key genes of the lipogenesis pathway in adipose tissue of beef cattle phenotypically divergent for RFI. (Abstract) *Proc. of the International Society of Animal Genetics Conference* p160-161

McKenna C, Porter RK, Keogh KA, Waters SM, McGee M and Kenny DA. (2018). Residual feed intake phenotype and gender affect the expression of key genes of the lipogenesis pathway in adipose tissue of beef cattle. *Journal of Animal Science and Biotechnology*. 9:68.

Popular publications:

Waters, S., Creevey, C.J., McGee, M. and Kenny DA (2013). Improving feed efficiency. *Tresearch* 8, 2:24-25 ISSN 1649-8917.

7. Compiled by: David Kenny