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Plasma metabolites associated with residual feed intake and other productivity performance traits in beef cattle

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ABSTRACT

The objective of this study was to identify blood metabolites associated with variation primarily in residual feed intake (RFI) in two populations of beef steers at the University of Guelph and University of Alberta, Canada, representing the discovery and validation populations, respectively. Other productivity performance traits including average body weight (ABW), average feed intake (AFI), dry matter intake (DMI) and average daily gain (ADG) were also investigated. In the discovery population, blood plasma samples were obtained from 32 steers (16 high- and 16 low-RFI, from a population of 112 steers and maximizing the divergence between groups for RFI) at three periods 1, 2 and 3, corresponding to weeks 2, 6 and 10 respectively of the 140 d feeding and performance test. In the validation population, blood samples were obtained from 20 (10 high and 10 low RFI) steers from periods 1 and 2 corresponding to weeks 2 and 6 of a 90 d feeding test period. Metabolite concentrations in plasma were determined using nuclear magnetic resonance (NMR) and multiple regression analysis was performed in SAS 9.1. Creatine and glycine were associated ($P<0.05$) with RFI in period 1 accounting for 36.3% of the phenotypic variation in RFI. At period 2, threonine, carnitine, acetate, creatine, phenylalanine, lysine, citrate, betaine, glutamate and hippurate were significant ($P<0.05$) and accounted for 74.2% of the variation in RFI. At period 3, hydroxyisobutyrate, tyrosine and formate were significant ($P<0.05$) and accounted for 52.1% of the variation in RFI. In the validation population, three metabolites (creatine, carnitine and hippurate) were significant ($P<0.05$) in both discovery and validation populations and these three metabolites accounted for 32% of the phenotypic variation in RFI in the validation population. Some of the metabolites associated with RFI were also associated with other performance traits discussed in subsequent sections. Metabolic networks for RFI in each period were reconstructed using IPA and suggested that the biological processes associated with RFI were involved in energy and protein metabolism as well as metabolism of urea and methane. The analysis of metabolites and evaluation of

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biological processes create a better understanding of the metabolic processes that affect RFI. Upon further validation, these indicators may have potential to be utilized as biomarkers to enhance the selection of beef cattle.

1. Introduction

Residual feed intake is a measure of feed efficiency defined as the difference between an individual's actual feed intake and the predicted feed intake (Koch et al., 1963). In beef cattle, the predicted feed intake is estimated based on the individual's requirements for maintenance of body weight (BW) and growth (average daily gain-ADG). Therefore RFI is phenotypically independent of both BW and ADG but correlated with feed intake.

Phenotypic selection for RFI poses challenges because it requires measurement of each individual's feed intake for a minimum of 70 days, which is expensive, time and labor intensive and limited to the capacity of the recording equipment (Williams, 2010). As a result, there is need to develop alternative approaches for selection of beef cattle for RFI.

One of the alternative approaches is marker assisted selection (MAS) using genetic markers or other types of predictive markers. RFI is especially a good candidate for genetic MAS because it is moderately heritable (Arthur et al., 2001). However, although variations in several genes have been reported to influence RFI variation, the frequency of the alleles, the associations and the direction of the effects are either breed or population specific and are not always reproducible in genetically diverse populations (Sherman et al., 2010).

The identification of metabolites, associated with economically important traits in livestock such as blood plasma levels of carnitine and body weight in cattle (Weikard et al., 2010), indicates a potential for using metabolites as biomarkers to predict RFI. Metabolite MAS may be optimized and used as an alternative or complementary approach to genetic MAS. The significant metabolites may also be used to discover novel biological pathways influencing the variation in feed efficiency. Metabolite based techniques have the potential to be refined making them accurate and relatively easy and fast to use.

In addition, combining metabolite association studies with genetic association studies will develop a triple association analysis between genotypes, metabolic phenotypes and productive performance traits. This approach was utilized by Weikard et al. (2010) to identify genotypes and metabolites associated with growth and lipid metabolism in cattle, and to identify metabolites associated with specific genotypes in humans (Kettunen et al., 2012). As a selection tool, metabolite profiles have also been used to predict levels of phenotypes such as body mass in birds (Jenni-Eiermann and Jenni, 1994), bird growth rates (Albano et al., 2011), growth and body composition in sheep (Hegarty et al., 2006) and diagnosis of diseases such as diabetes (Kulkarni, 2012).

In this study, we used the NMR technique to assess the levels of metabolites in plasma followed by regression analysis to identify the metabolites associated with RFI, ABW, ADG, AFI and DMI in beef cattle. The metabolites associated with RFI were then used to analyze metabolic interactions by reconstructing metabolic networks using IPA (Ingenuity® Systems, www.ingenuity.com) and to suggest biological pathways associated with these interactions.

2. Materials and methods

2.1. The animal resources and RFI estimation

A detailed description of the animals, management and the experimental design utilized in collecting the phenotypic data in the discovery population can be obtained from Montanholi et al. (2013). In summary, the steers were managed according to the Canadian Council on Animal Care guidelines (1993) and this component of the experiment was approved by the University of Guelph animal care committee. A total of 112 crossbred beef steers were fed for 168 d at the Elora Beef Research Centre, University of Guelph, Canada. The average age of the steers at the start of the experiment was $275 \pm \pm 25$ d (mean $\pm$ standard deviation) and the initial and final body weights were 338 ± 44 and 519 ± 51 kg, respectively. The overall breed composition of the steers was 58.3% Angus, 30.6% Simmental and 11.1% other European breeds (i.e. Hereford, Gelbvieh and Piedmontese).

Steers were allowed to adjust to the feeding facilities for a minimum of 15 d before the start of the trial. Individual feed intake was used to calculate individual dry matter intake which was used to calculate feed efficiency measures as reported by Montanholi et al. (2013).

Blood samples were collected through jugular venipuncture between 8:00 and 12:00 h every 14 d during the feeding test period, into 10 ml blood collection tubes (Vacuntainers; BD Inc., Franklin Lakes, USA) containing sodium heparin mounted on a 2.5 cm 20 GA needle. Blood samples were stored in ice until centrifugation (3000*g* for 20 min) to separate the blood plasma, which was stored at -80 °C until further analysis.

When the RFI values for each steer were available, the plasma samples were sorted into 2 batches according to the corresponding RFI values so that one group consisted of steers with high RFI and the other group consisted of steers with low RFI. The plasma samples were then sorted to establish 3 sets of samples from each batch (making a total of 6 sets) according to the period when the blood samples were collected. The three time periods considered in this study included periods 1, 2 and 3, which corresponded to weeks 2, 6 and 10 into the feeding trial respectively.

A subset of plasma samples was selected in each period from 16 steers with the highest RFI and 16 steers with the lowest RFI.

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