RESEARCH ARTICLE

Single nucleotide polymorphisms for feed efficiency and performance in crossbred beef cattle

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Abstract

Background: This study was conducted to: (1) identify new SNPs for residual feed intake (RFI) and performance traits within candidate genes identified in a genome wide association study (GWAS); (2) estimate the proportion of variation in RFI explained by the detected SNPs; (3) estimate the effects of detected SNPs on carcass traits to avoid undesirable correlated effects on these economically important traits when selecting for feed efficiency; and (4) map the genes to biological mechanisms and pathways. A total number of 339 SNPs corresponding to 180 genes were tested for association with phenotypes using a single locus regression (SLRM) and genotypic model on 726 and 990 crossbred animals for feed efficiency and carcass traits, respectively.

Results: Strong evidence of associations for RFI were located on chromosomes 8, 15, 16, 18, 19, 21, and 28. The strongest association with RFI (P = 0.0017) was found with a newly discovered SNP located on BTA 8 within the ELP3 gene. SNPs rs41820824 and rs41821600 on BTA 16 within the gene HMCN1 were strongly associated with RFI (P = 0.0064 and P = 0.0033, respectively). A SNP located on BTA 18 within the ZNF423 gene provided strong evidence for association with RFI (P = 0.0028). Genomic estimated breeding values (GEBV) from 98 significant SNPs were moderately correlated (0.47) to the estimated breeding values (EBVs) from a mixed animal model. The significant (P < 0.05) SNPs (98) explained 26% of the genetic variance for RFI. In silico functional analysis for the genes suggested 35 and 39 biological processes and pathways, respectively for feed efficiency traits.

Conclusions: This study identified several positional and functional candidate genes involved in important biological mechanisms associated with feed efficiency and performance. Significant SNPs should be validated in other populations to establish their potential utilization in genetic improvement programs.

Keywords: Candidate genes, Single nucleotide polymorphism, Feed efficiency, Carcass traits

Background

As feed costs are a major factor influencing the profitability of beef cattle production, there are many endeavors to reduce these costs. Improving feed efficiency can be achieved by novel feeding strategies and genetic improvement technologies. Although residual feed intake (RFI) has emerged as one of the important feed efficiency traits for beef cattle [1], there are limitations with RFI for direct selection to improve feed efficiency industry-wide. These limitations are the expense and difficulty of recording an animal’s daily feed intake. Genomic approaches offer opportunities to select cattle that are more efficient, as once the relationships between genetic markers and feed efficiency are determined, this prediction can be applied to animals that are genotyped, but are not phenotyped with costly feed intake measurements [2].

Since 2000, advances in high-throughput genotyping and sequencing techniques have resulted in high density SNP chips, such as the Illumina BovineSNP50 BeadChip [3] being available. The use of the Bovine SNP50 in dairy cattle has increased the accuracy for predicting the
genetic value of animals [4]. In beef cattle, the use of such developments will benefit most traits such as feed efficiency and carcass traits which are difficult to measure or require the animals to be slaughtered for recording their phenotypes [5]. Several genome-wide association studies (GWAS) indicated that many genes affect feed efficiency traits and that the majority of these effects are small [6–11]. These studies reported many SNPs conferring genetic variation in feed efficiency. Nonetheless, although many SNPs were studied, the genetic architecture of feed efficiency was not completely explained.

Results from fine-mapping by Abo-Ismail et al. ([12]) suggested a list of candidate genes for further investigation to identify the causal mutations for feed efficiency within these genes [12]. Discovery of the causal mutations within these genes could help explain the genetic architecture of feed efficiency. Furthermore, this approach could provide a panel of the most informative SNPs that could be used to predict feed efficiency accurately and affordably for producers. Therefore, the objectives of this study were to: (1) identify new SNPs for RFI and performance traits within candidate genes identified in previous GWAS studies; (2) estimate the proportion of variation in feed efficiency traits explained by the detected SNPs; (3) estimate the effect of detected SNPs on carcass traits to avoid undesirable correlated effects when selecting for feed efficiency; and (4) map the corresponding genes to a biological process and pathway to understand the biological meaning behind the detected associations. In this way it was hoped to identify causal mutations or to identify markers in strong linkage disequilibrium with such mutations.

**Methods**

**Animals and phenotypic data**

The study was approved from The University of Guelph Animal Care Committee based on the recommendations outlined in the Canadian Council on Animal Care (1993) guidelines.

**Feed efficiency traits**

Average daily dry matter intake (DMI), average daily gain (ADG), midpoint metabolic weight (MMWT), RFI and feed conversion ratio (FCR) phenotypes were measured on 726 crossbred beef cattle, heifers (38), steers (387), and bulls (301) at the University of Guelph’s Elora Beef Research Center (EBRC). Average breed compositions were formed by Angus (45.9%), Simmental (20.7%), Piedmontese (5%), Gelbvieh (4.2%), Charolais (2%) and Limousin (1.4%). Animals primarily originated from one of two University of Guelph herds (EBRC and NLARS), the Agriculture and Agri-Food Canada Kapuskasing Research Centre (KAP) or were purchased from producers in Ontario, Canada. Calves were weaned at approximately 200 days of age, and were involved in various post-weaning trials at the EBRC with different nutrition treatments. The body weights of the animals were recorded a number of times over the trials with most trials recording weights at least every four weeks.

The ADG for individual animals was calculated as a linear regression coefficient of their live weights on the actual days of measurement using the nlme package from R software [13]. The MMBW was calculated as the midpoint body weight (kg) to the power 0.75. The DMI was calculated for each animal as total DMI divided by number of days for the test period. The RFI was calculated from the difference between the average of the animal’s actual daily DMI and its expected daily DMI [14]. Expected DMI was determined through the regression coefficients estimated from the data through a multiple phenotypic regression model as follows:

\[
y_{ijk} = \mu + \beta_1(ADG_k) + \beta_2(MWT_k) + Sex_i + TTY_j + e_{ijk}
\]

Where, \(y_{ijk}\) is the total DMI for animal \(k\) during the feeding period, \(\mu\) is the overall mean, \(\beta_1\) is the regression coefficient of the linear regression on ADG as determined through a linear regression of weights on days on trial as described, \(\beta_2\) is the regression coefficient of the linear regression on MMWT, \(Sex_i\) is the effect of \(i^{th}\) sex, \(TTY_j\) is the effect of \(j^{th}\) treatment \(\times\) trial \(\times\) year (42 levels) and \(e_{ijk}\) is the residual random effect associated with the animal \(k\) and is the resulting RFI used in further analyses.

**Carcass and meat quality traits**

The association analysis of carcass and meat quality traits was carried out on 693–990 (depending on the trait) crossbred animals, including heifers (\(n = 33\)), steers (\(n = 705\)), and bulls (\(n = 252\)). In total 698 of these animals have RFI measures. All cattle were slaughtered at the University of Guelph Meat Science Laboratory Abattoir. Hot carcass weight (HCW) was measured just before the carcass was placed in the cooler. Meat Laboratory staff assessed the \(longissimus\) muscle interface (i.e. muscle surface) between the 12th and 13th ribs to obtain the following carcass measurements: subcutaneous fat depths between the 1st and 2nd, 2nd and 3rd, and 3rd and 4th quadrants of \(longissimus\) muscle (recorded as F1, F2 and F3, respectively), the grade fat (GRF), the minimum measurement of subcutaneous fat depth within the 4th quadrants of \(longissimus\) muscle and \(longissimus\) muscle area, measured using an electronic planimeter (MOP-3; Carl Zeiss Inc., Thornwood, NY) after acetate tracing (Bergen et al. [15]). Canadian Beef Grading Agency formulae (www.beefgradingagency.ca/) were used to determine lean yield (LY), an estimate of the percentage
of the carcass that is red meat. Marbling was assessed to determine the average amount, size and distribution of fat particles or deposits within longissimus muscle and was scored as ≤3.0 = devoid; 3.1 to 4.0 = traces; 4.1 to 5.9 = slight; 6.0 to 7.0 = small to moderate; and ≥7.0 = slightly abundant to abundant. Rib dissection traits were also measured using a 4-6 rib section depending on the trial and year (physical separation of ribs 8-12 or 6-12, respectively). This procedure determines the amount of lean meat and bone, and a quantitative and qualitative assessment of fat depots (body, subcutaneous and intermuscular) within the rib to evaluate carcass composition. A complete description of carcass measurements was discussed by [15].

SNP discovery, DNA isolation and genotyping
Messenger RNA from seven tissue types (adipose, muscle, hypothalamus, duodenum, liver, lung and kidney) was extracted using TRIzol (Invitrogen). The tissue samples were collected from beef cattle at the Lacombe Research Centre in Alberta (Canada). RNA from 7 to 14 animals was pooled for each tissue before sequencing. Sequencing libraries were constructed from each RNA pool according to a standard protocol (mRNA Sequencing Sample Preparation Guide, Illumina, USA). Sequencing was performed on the Illumina Genome Analyzer II following the manufacturer’s recommendations. The resulting reads (more than 140 M) were mapped to transcript sequences from the reference bovine genome assembly (Btau4.0) [16] using maq 0.6.6 [17]. More than 1.2 million SNPs were detected by comparing the aligned reads to the reference transcripts. From this list a subset of 300 SNPs from 215 candidate genes was selected based on SNP functional consequences assigned by NGS-SNP [18]. An additional 158 coding SNPs were chosen from publicly available SNPs within the same candidate genes (Additional file 1). These genes were selected based on their proximity (on average distance 116,963 base pair) to significant SNPs identified in a previous study [12].

Tissue or blood samples were prepared and sent to Laboratory Services, University of Guelph, for genomic DNA extraction. Then, prepared DNA samples were sent to GeneSeek, Inc. for genotyping using a commercial platform for high-throughput SNP genotyping. In total, 1,032 animals, as assessed by the numerator relationship matrix using CFC, born subsequent to the animals used in the GWAS population [12] were genotyped for 458 SNP. The 300 SNPs identified through this work that were verified through genotyping have been submitted to dbSNP under the handle name “UALG”.

Quality control (QC) was done using the GenABEL package [19] in R software. Animals (n = 14) and individual SNPs (n = 5) with a low call-rate (<90%) were excluded from the analysis. Mean Identical By State (IBS) was 0.783 ± 0.0327. Animals (n = 1) with high estimation of IBS (≥0.95) were excluded. SNPs (n = 114) with a minor allele frequency (MAF) (< 1%) were excluded from the analysis of feed efficiency traits. Mean autosomal heterozygosity (HET) was 0.27 ± 0.036; animals (n = 6) with high HET (≥0.446) were excluded. Three hundred thirty nine SNPs and 727 animals passed all QC criteria where these SNPs were mapped to 180 corresponding genes (83,58, 24, 9, 4, and 2 genes including only 1, 2, 3, 4, 5 and 6 SNPs, respectively). The distribution of genotyped SNPs (339) across 29 chromosomes of the bovine genome is presented in Figure 1.
Association analysis

**Single locus regression model (SLRM)**

Genotypic data were coded as 0, 1, 2 corresponding to the number of minor alleles using GenABEL. In this model, phenotypes were regressed on the number of copies of a minor allele (0, 1, or 2) for estimating the allele substitution effect using ASReml 3 software [20]. For feed efficiency traits, the univariate animal model was fitted as follows:

\[
Y_{ijkl} = \mu + \text{Sex}_i + \text{HY}_j + \text{TTY}_k + \beta_1 \text{SNP}_l + \beta_2 \text{AET}_1 + \sum_{\text{breed}=1}^{i} \beta_i \text{breed} + \beta_9 \text{HET}_1 + a_l + e_{ijkl}
\]

in which \( Y_{ijkl} \) is the trait measured in the \( l \)th animal of the \( j \)th herd-year of birth and the \( k \)th treatment-trial-year group; \( \mu \) is the overall mean for the trait; \( \text{Sex}_i \) is the fixed effect of the \( i \)th sex of \( l \)th animal; \( \text{HY}_j \) is the fixed effect of the \( j \)th (17 level) herd-year of birth; \( \text{TTY}_k \) is the fixed effect of the \( k \)th (42 level) treatment-trial-year of the test group; \( \beta_1 \) is the regression coefficient of the linear regression on the number of copies of a minor allele; \( \beta_2 \) is the regression coefficient of the linear regression on age at the end of the test period (AET) of the \( l \)th animal; \( \beta_9 \) is the regression coefficient of the linear regressions on proportion of AN, CH, LM, SM, PI, and GV breeds in the \( l \)th animal; \( a_l \) is the random additive genetic (polygenic) effect of the \( l \)th animal; and \( e_{ijkl} \) is the residual random effect associated with the \( l \)th animal. The TTY level that had less than three animals was excluded from the analysis. Phenotypes that were not within the mean ± 3 standard deviations for the respective trait were excluded from the analysis.

For carcass traits, the previous model (2) was modified to include the effect of the treatment trial-year-sex group instead of TTY and to include the fixed effect of the herd-year slaughter season instead of HY. Also, the effect of age at the end of the test period (day) was substituted by the age at slaughter (day).

The significance of associations was determined by an overall value of \( P < 0.05 \). To allow for multiple hypothesis-testing, chromosome wise false discovery rate (FDR) was used [21]. A threshold of 5 and 20% FDR were used for strong and suggestive associations, respectively.

**Genotypic model**

This model was fitted only for feed efficiency traits to consider genetic effects other than the additive effect. The model included the same effects in the SLRM, except that the allele substitution effect was replaced with the genotype effect. This model was not fitted for carcass traits to reduce the volume of results as the trait of primary interest was feed efficiency for this study.

**Estimation of genetic variance explained by identified SNPs**

The proportion of phenotypic variance in RFI explained by the full set of SNPs (339) that passed QC was estimated using the BayesC algorithm implemented in GenSel 3.13 software [22]. Also, the proportion of the genetic variance of RFI explained by the set of significant SNPs for at least one of the feed efficiency traits using SLRM and/or the genotypic model was estimated. Missing genotypes were inferred using fastPHASE [23]. Estimated breeding value (EBV) was determined with the SLRM without the regression on SNPs by ASReml. BayesC was then used to run the analysis with the two sets of SNPs (the full set [339 SNPs] and significant SNPs from the two models [98 SNPs]). Posterior residual and genetic variances were estimated after 41,000 iterations including 1,000 burn-in cycles. The proportion of genetic variance explained by the set of SNPs was estimated as the posterior genetic variance divided by phenotypic variance (posterior residual plus posterior genetic variance). In addition, the correlations between genomic breeding values predicted by estimated solutions and EBVs were estimated.

**Enrichment analysis**

The significant (\( P < 0.05 \)) SNPs (98) from the SLRM and genotype models for at least one feed efficiency trait from the association analysis were mapped to 74 genes. The list of the genes was submitted to DAVID 6.7 Beta software [24] for an *in silico* functional analysis. In DAVID, Gene ontology (GO) was used to identify functionally related genes. The genes were also mapped to biological pathways using web software in the Kyoto Encyclopedia of Genes and Genomes (KEGG) [25].

**Results and discussion**

**Heritability estimates**

Our goal in the current study was to identify informative or causal mutations for feed efficiency traits for use in Marker Assisted Selection (MAS). This would accelerate genetic improvement in beef cattle by improving the accuracy of selection and shortening intervals between generations [26]. Genetic Improvement of feed efficiency could subsequently minimize methane production [27] while optimizing beef production. In this study, a cross-bred population was used to evaluate the relationship between potential genes identified from fine mapping and RFI. The descriptive statistics of feed efficiency, performance and carcass traits are given in Table 1. Using the single trait animal model in ASReml, the estimates
of heritabilities are given in Table 2. Heritability estimates for feed efficiency traits are in the range reported in the literature. The estimated heritability for RFI (0.19) is within the reported range from 0.16 to 0.45 [28,29], whereas heritability (0.35) for ADG is in agreement with [30]. Estimated heritability for DMI (0.42) is within the reported range, from 0.31 to 0.44 [30,31]. FCR (0.25) is also within the reported range (0.17 to 0.37) [28,30] as is MMWT (0.48) from 0.36 to 0.69 [28,29]. The genetic variation and moderate heritabilities in feed efficiency traits indicate effective selection would be possible, where the trait is measured. However, the detected genetic variation also indicates that MAS could be effective where the genetic markers are closely linked to or is the causative mutation and that have repeatable effects across independent populations.

### Association analysis

In the current study, SNP effects were estimated using an allele substitution effect model or the genotypic model. To avoid population stratification effects from influencing the estimated SNP effect, the phenotypes were adjusted for breed proportion, and the polygenic effect was fitted using the animal model to account for possible family effects [32]. The population used in the GWAS using the Illumina BovineSNP50 was different animals to those used in the current study. However, the two populations are not independent as the animals in the current study were born subsequent to the animals used in the GWAS population from the same primary herds. The average relatedness among individuals between the two populations was estimated to be low at 0.0005 on average using the numerator relationship matrix calculated using CFC [33]. There was zero pedigree-based in-breeding among the animals used in the current study. There was no separate dataset for feed efficiency traits on the same 339 SNP chip that could be used for validation. Thus, these significant associations require validation in other independent populations.

Results indicated 15 SNPs were significantly (at less 5% FDR) associated with at least one feed efficiency trait phenotype using the allele substitution effect model (Table 3). These findings reveal several candidate genes that provide highly significant evidence of association with RFI (Table 3). These promising candidate genes are located on *Bos taurus* autosome (BTA) 8, 15, 16, 18, 19, 21, and 28. The strongest evidence of association with RFI and DMI was in SNP (8: 10674426) in the three prime untranslated region (3’ UTR) of gene elongation protein 3 homolog (*ELP3*). Gene *ELP3* modulates transcription by

### Table 1 Descriptive statistics (mean, SD, min and max) in feedlot beef cattle for feed efficiency, performance and carcass traits

| Table 1 | | | | |
|---|---|---|---|---|
| Trait | No | Mean | SD | Min | Max |
| Feed efficiency traits: | | | | | |
| Average daily gain (ADG), kg d⁻¹ | 726 | 1.70 | 0.385 | 0.71 | 3.30 |
| Mid-test metabolic weight (MMWT), kg | 726 | 92.4 | 11.70 | 53.3 | 128.1 |
| Daily dry matter intake (DMI), kg d⁻¹ | 726 | 9.81 | 1.76 | 4.18 | 15.54 |
| Residual feed intake (RFI), kg d⁻¹ | 726 | –0.066 | 1.126 | –3.70 | 3.35 |
| Feed conversion ratio (FCR), kg gain kg⁻¹ DM | 726 | 6.09 | 1.87 | 3.11 | 16.76 |
| Carcass traits: | | | | | |
| Hot carcass weight (HCW), kg | 959 | 353.7 | 52.47 | 208 | 503 |
| Longissimus muscle area (LMA), cm² | 848 | 94.3 | 14.61 | 59.4 | 138.4 |
| Lean meat within the rib section (LR), % | 664 | 54.6 | 6.79 | 25.0 | 75.2 |
| Lean yield grade (LY), % | 846 | 60.1 | 2.78 | 51.0 | 65.0 |
| Fat 1 (F1), mm | 850 | 13.4 | 5.62 | 1.0 | 30.0 |
| Fat 2 (F2), mm | 850 | 15.7 | 6.49 | 1.0 | 36.0 |
| Fat 3 (F3), mm | 847 | 9.6 | 3.66 | 1.0 | 22.0 |
| Grade fat (GRF), mm | 846 | 8.8 | 3.25 | 1.0 | 19.0 |
| Proportion of intramuscular fat (IFR) within the rib section, % | 687 | 10.09 | 3.22 | 1.2 | 20.5 |
| Proportion of body cavity fat within the rib section (BFR), % | 684 | 3.48 | 1.244 | 0.96 | 7.30 |
| Proportion of subcutaneous fat from the rib section (SQFR), % | 685 | 10.30 | 2.60 | 2.44 | 18.53 |
| Marbling score<sup>b</sup> | 851 | 4.90 | 0.734 | 3.0 | 6.0 |

<sup>1</sup>F, subcutaneous fat depth between the 1<sup>st</sup> and 2<sup>nd</sup> quarter of the longissimus; F2, subcutaneous fat depth between 2<sup>nd</sup> and 3<sup>rd</sup> quarter of the longissimus; F3, subcutaneous fat depth between the 3<sup>rd</sup> and 4<sup>th</sup> quarter of the longissimus.<br>
<sup>2</sup>No. = Number of animals’ phenotypes and genotypes for testing the association.<br>
<sup>b</sup>Marbling was scored as ≤ 3.0 = devoid; 3.1 to 4.0 = traces; 4.1 to 5.9 = slight; 6.0 to 7.0 = small to moderate; and ≥ 7.0 = slightly abundant to abundant.
Table 2 The heritability estimates ($h^2$) ± standard error (SE) for growth and feed efficiency related traits estimated in crossbred beef cattle

| Trait                                           | $h^2$ ± SE  |
|-------------------------------------------------|-------------|
| Average daily gain, kg d$^{-1}$                  | 0.35 ± 0.12 |
| Mid-test metabolic weight, kg                    | 0.48 ± 0.13 |
| Daily dry matter intake, kg d$^{-1}$              | 0.42 ± 0.17 |
| Residual feed intake, kg d$^{-1}$                 | 0.19 ± 0.11 |
| Feed conversion ratio, kg gain kg$^{-1}$ DM      | 0.25 ± 0.13 |
| Hot carcass weight (HCW), kg                      | 0.29 ± 0.10 |
| Longissimus muscle area (LMA), cm$^2$             | 0.50 ± 0.11 |
| Lean meat within the rib section (LR), %          | 0.48 ± 0.13 |
| Lean yield grade (LY), %                         | 0.31 ± 0.10 |
| Fat1 (F1), mm                                     | 0.10 ± 0.08 |
| Fat2 (F2), mm                                     | 0.24 ± 0.10 |
| Fat3 (F3), mm                                     | 0.22 ± 0.10 |
| Grade fat (GRF), mm                              | 0.24 ± 0.10 |
| Proportion of intermuscular fat (IFR) within rib section, % | 0.54 ± 0.14 |
| Proportion of body cavity fat within rib section (BFR), % | 0.23 ± 0.12 |
| Proportion of subcutaneous fat from rib section (SQFR), % | 0.20 ± 0.12 |
| Marbling score,$^{b}$                            | 0.41 ± 0.10 |

$^a$F1, subcutaneous fat depth between the 1st and 2nd quarter of the longissimus; F2, subcutaneous fat depth between 2nd and 3rd quarter of the longissimus; F3, subcutaneous fat depth between the 3rd and 4th quarter of the longissimus.

$^{b}$Marbling was scored as ≤ 3.0 = devoid; 3.1 to 4.0 = traces; 4.1 to 5.9 = slight; 6.0 to 7.0 = small to moderate; and ≥ 7.0 = slightly abundant to abundant.

working as a catalytic histone acetyltransferase subunit of the RNA polymerase II elongator complex involved in transcriptional elongation [34,35]. In Drosophila, reduction in ELP3 expression during the development of the nervous system increases activity and decreases sleep [36] and the growth of adult flies (or could be lethal for the pupa) [37].

In the current study on BTA 16, the splice site intronic mutation (rs41820824) and the missense mutation (rs41821600) within gene hemicentin 1 (HMCNI) were associated with RFI, where the substitution with the minor allele was associated with increased RFI and decreased F1. In addition, the minor allele of SNP rs41824268, within gene HMCNI, was associated with decreasing HCW, whereas in SNP rs41820800, it was associated with decreasing F2. Gene HMCNI is known to be involved in age-related, macular degeneration [38], and polymorphisms within gene HMCNI were associated with diabetes in man [39].

Synonymous coding SNP (18: 17150858), within the gene encoding zinc finger protein 423 (ZNF423), was associated with RFI, DMI and MMWT and located near a reported QTL (ID: 4449) for DMI [6]. In addition, the minor allele of SNP (18: 17152044) was associated with decreasing GRF, F3, and F2, and increased LY, and was located near a reported QTL (ID: 11062) for LMA and body weight (ID: 11061) [40]. Gene ZNF423 is a transcription factor involved in metal ion-binding. Down regulation of ZNF423 expression increases cell growth and retards differentiation as a consequence of its important role with the Vitamin A metabolite, retinoic acid [41].

On BTA 6, the SNP (6: 37288379) at 3’ UTR, within gene protein phosphatase, Mg$^{2+}$/Mn$^{2+}$ dependent, 1 K (PPM1K), was associated with increased MMWT and HCW and decreased RFI, FCR, marbling, and IFR and was located near a reported QTL (ID: 10761) for fat thickness at the 12th rib and a QTL (ID: 10758) for marbling score (EBV) [40] and a QTL (ID: 1753) for milk fat percentage [42]. Gene PPM1K is involved in the phosphorous metabolic process or in amino acid dephosphorylation. In addition, PPM1K plays a key role in cellular survival and development by regulating mitochondrial permeability transition pore function [43]. However, different genes are involved in mitochondrial adenosine triphosphate (ATP) synthesis efficiency and associated with differences in RFI [44-46], therefore, the effect of gene PPM1K on mitochondrial ATP synthesis is not clear [43].

For ADG, the most significant (at less than 5% FDR; P = 0.0009) SNP (rs41574929) was located on BTA 6, at 5’ UTR, within gene family with sequence similarity 190, member (A FAM190A; ID: 616908) (Table 3). The SNP rs41574929 was also associated significantly at less than 5% FDR with HCW (P = 0.006). This result is in agreement with the function described for FAM190A where it is a necessary regulator for normal mitosis [47]. A deletion mutation in FAM190A causes a cell division defect [47].

Allele substitution effect estimates of SNPs influencing (P ≤ 0.05) growth and efficiency traits, but which did not pass chromosome wise false discovery rate (FDR) threshold q = 0.2 were listed in Additional file 2. Also, all the SNPs associated at P-value < 0.05 using the genotypic model for growth and feed efficiency traits were listed in Additional file 3.

The association analysis using SLRM indicated that 59 SNPs were strongly (Table 4) or suggestively (Additional file 4) associated at 5% or 20% FDR test, respectively, for at least one carcass trait phenotype. Results indicated that the majority of the strong or suggestive associations were for intermuscular fat % (IFR) (14 indications). Thirteen SNPs were strongly associated with marbling, whereas 12 SNPs were associated with longissimus muscle area (LMA), and as follows HCW (9), F3 (8), GRF (8), F2 (6), LY (6), body cavity fat within the rib section (BFR) (5), % lean meat within the rib section (LR)
Significant effects (at less 5% FDR) were found in 27 genes where gene ERCC5 (ID: 509602) had the highest proportion of the effects, revealing 8 of the significant associations with carcass traits (Table 4). The newly discovered SNP on BTA 12 (76889667 bp), within gene ERCC5 (ID: 509602), provided evidence of association with 5 of the studied carcass traits where the substitution of the minor allele was associated with increases of

Table 3 Significant and suggestive SNP based on false discovery rate (FDR) q threshold of 0.05 and 0.2 for feed efficiency traits using single locus regression model (SLRM) on 339 SNPs

| Trait | Gene ID | BTA | Ref. SNP | Pos. (bp) | MAF | Alleles | n | Estimate ± SE | P-value |
|-------|---------|-----|----------|----------|-----|---------|---|--------------|---------|
| ADG   | 523789  | 3   | rs42417924 | 75523597 | 0.102 | C/G     | 726 | −0.062 ± 0.02 | 0.0104* |
| DMI   | 616055  | 5   | ss914082855 | 11951668 | 0.37 | A/G     | 726 | −0.234 ± 0.08 | 0.0025* |
| DMI   | 616055  | 5   | ss914082856 | 11957146 | 0.37 | T/C     | 720 | −0.237 ± 0.08 | 0.0023* |
| MMWT  | 616908  | 6   | rs41574929 | 36099801 | 0.388 | T/G     | 716 | 0.992 ± 0.40  | 0.0132& |
| ADG   | 616908  | 6   | rs41574929 | 36099801 | 0.388 | T/G     | 716 | 0.049 ± 0.01  | 0.0009* |
| MMWT  | 540329  | 6   | ss914082878 | 37288379 | 0.152 | T/C     | 726 | 1.342 ± 0.54  | 0.0128& |
| MMWT  | 536203  | 6   | ss914082880 | 37386084 | 0.16  | A/G     | 725 | 1.293 ± 0.53  | 0.0148& |
| DMI   | 784720  | 8   | ss914082889 | 10674426 | 0.483 | A/G     | 726 | 0.483 ± 0.15  | 0.0017* |
| MMWT  | 614507  | 7   | ss914082689 | 79315960 | 0.364 | T/C     | 718 | 0.933 ± 0.39  | 0.0176& |
| RFI   | 533166  | 15  | rs41755948 | 30710940 | 0.207 | T/C     | 726 | −0.201 ± 0.07 | 0.0078& |
| RFI   | 533166  | 15  | ss9140828737 | 30717928 | 0.207 | T/C     | 726 | −0.201 ± 0.07 | 0.0078& |
| RFI   | 521326  | 16  | rs41821600 | 64875340 | 0.462 | A/G     | 726 | 0.462 ± 0.14  | 0.0008* |
| RFI   | 521326  | 16  | rs41820824 | 64950387 | 0.012 | A/G     | 726 | 0.785 ± 0.29  | 0.0064* |
| RFI   | 508025  | 18  | ss914082689 | 17150858 | 0.365 | T/C     | 723 | 0.191 ± 0.06  | 0.0028* |
| FCR   | 282411  | 19  | rs41914675 | 37278418 | 0.072 | T/C     | 726 | 0.278 ± 0.10  | 0.0048& |
| RFI   | 282411  | 19  | rs41914675 | 37278418 | 0.072 | T/C     | 726 | 0.342 ± 0.12  | 0.0048& |
| DMI   | 282411  | 19  | rs41914675 | 37278418 | 0.072 | A/G     | 726 | 0.462 ± 0.14  | 0.0008* |
| RFI   | 524684  | 21  | rs43020736 | 29054823 | 0.371 | T/C     | 726 | −0.162 ± 0.07 | 0.0168& |
| DMI   | 524684  | 21  | rs43020736 | 29054823 | 0.371 | T/C     | 726 | −0.248 ± 0.08 | 0.0018* |
| RFI   | 524684  | 21  | rs43020769 | 29060759 | 0.478 | A/G     | 726 | 0.172 ± 0.07  | 0.0098& |
| MMWT  | 532512  | 25  | ss914082815 | 36278405 | 0.11  | T/C     | 719 | 1.555 ± 0.63  | 0.0148& |
| MMWT  | 532512  | 25  | ss914082816 | 36278050 | 0.02  | T/C     | 726 | 0.099 ± 1.31  | 0.0188& |
| MMWT  | 515895  | 27  | ss914082827 | 39798548 | 0.08  | A/G     | 726 | −2.298 ± 0.71 | 0.0013* |
| DMI   | 508697  | 28  | ss914082834 | 77277734 | 0.426 | A/G     | 726 | −0.211 ± 0.08 | 0.0067* |
| RFI   | 508697  | 28  | ss914082834 | 77277734 | 0.426 | A/G     | 726 | −0.183 ± 0.07 | 0.0054* |
| RFI   | 780878  | 28  | ss914082829 | 13580673 | 0.187 | T/A     | 726 | −0.208 ± 0.08 | 0.0099* |

1average daily gain (ADG), kg d⁻¹, average daily dry matter intake (DMI), kg d⁻¹, mid-point metabolic weight (MMWT), kg⁻¹, feed efficiency conversion ratio (FCR), kg gain/kg DM and residual feed intake (RFI) kg d⁻¹.
2is a significant SNP after adjusting for chromosome-wise 5% false discovery rate.
3is a suggestive SNP after adjusting for chromosome-wise 20% false discovery rate.
4Gene ID² = Entrez gene identifier.
5BTA³ = Bos taurus autosome.
6Ref. SNP⁴ = (rs#) is a reference SNP ID number and (ss#) ID is the National Center for Biotechnology Information (NCBI) assay ID number assigned by NCBI to submitted SNPs for discovered SNPs using RNA-Seq.
7Pos. (bp)⁵ = the SNP’s position in a base pair.
8MAF⁶ = minor allele frequency.
9Alleles⁷ = first allele/second allele, the second allele is the minor allele which the phenotypes regressed on its number (0, 1, and 2).
n⁸ = Number of animals’ phenotypes and genotypes for testing the association.
Estimate ± SE⁹ = allele substitution effect ± standard error.

(4), % subcutaneous fat within the rib section (SQFR) (4), and F1 (2).

Significant effects (at less 5% FDR) were found in 27 genes where gene ERCC5 (ID: 509602) had the highest proportion of the effects, revealing 8 of the significant associations with carcass traits (Table 4). The newly discovered SNP on BTA 12 (76889667 bp), within gene ERCC5 (ID: 509602), provided evidence of association with 5 of the studied carcass traits where the substitution of the minor allele was associated with increases of
Table 4 Significant SNP based on false discovery rate (FDR) q threshold of 0.05 for beef carcass traits using single locus regression model

| Trait      | Gene ID | BTA | Ref. SNP | BPPos  | MAF  | n    | Estimate ± SE | P-value |
|------------|---------|-----|----------|--------|------|------|---------------|---------|
| LR         | 539020  | 1   | rs43246339 | 81372644 | 0.165 | 664  | 1.151 ± 0.266 | 0.00002 |
| IFR        | 539020  | 1   | rs43246339 | 81372644 | 0.167 | 687  | -0.622 ± 0.172 | 0.0003  |
| IFR        | 614882  | 2   | rs43287969 | 1280728  | 0.320 | 648  | 0.494 ± 0.143  | 0.005   |
| F3         | 532545  | 2   | rs43307594 | 43392336 | 0.379 | 847  | 0.473 ± 0.15   | 0.0016  |
| IFR        | 538378  | 2   | rs42315485 | 58475918 | 0.035 | 687  | -0.968 ± 0.355  | 0.0065  |
| Marbling   | 522946  | 3   | ss914082841 | 2557106  | 0.379 | 837  | -0.109 ± 0.028  | 0.00066 |
| Marbling   | 532836  | 4   | rs43307594 | 43392336 | 0.379 | 847  | 0.473 ± 0.15   | 0.0016  |
| IFR        | 538378  | 2   | rs42315485 | 58475918 | 0.035 | 687  | -0.968 ± 0.355  | 0.0065  |
| Marbling   | 522946  | 3   | ss914082841 | 2557106  | 0.379 | 837  | -0.109 ± 0.028  | 0.00066 |
| Marbling   | 532836  | 4   | rs43307594 | 43392336 | 0.379 | 847  | 0.473 ± 0.15   | 0.0016  |
| IFR        | 538378  | 2   | rs42315485 | 58475918 | 0.035 | 687  | -0.968 ± 0.355  | 0.0065  |
| Marbling   | 522946  | 3   | ss914082841 | 2557106  | 0.379 | 837  | -0.109 ± 0.028  | 0.00066 |
| Marbling   | 532836  | 4   | rs43307594 | 43392336 | 0.379 | 847  | 0.473 ± 0.15   | 0.0016  |
| IFR        | 538378  | 2   | rs42315485 | 58475918 | 0.035 | 687  | -0.968 ± 0.355  | 0.0065  |
| Marbling   | 522946  | 3   | ss914082841 | 2557106  | 0.379 | 837  | -0.109 ± 0.028  | 0.00066 |
| Marbling   | 532836  | 4   | rs43307594 | 43392336 | 0.379 | 847  | 0.473 ± 0.15   | 0.0016  |
| IFR        | 538378  | 2   | rs42315485 | 58475918 | 0.035 | 687  | -0.968 ± 0.355  | 0.0065  |
| Marbling   | 522946  | 3   | ss914082841 | 2557106  | 0.379 | 837  | -0.109 ± 0.028  | 0.00066 |
| Marbling   | 532836  | 4   | rs43307594 | 43392336 | 0.379 | 847  | 0.473 ± 0.15   | 0.0016  |
| IFR        | 538378  | 2   | rs42315485 | 58475918 | 0.035 | 687  | -0.968 ± 0.355  | 0.0065  |
| Marbling   | 522946  | 3   | ss914082841 | 2557106  | 0.379 | 837  | -0.109 ± 0.028  | 0.00066 |
| Marbling   | 532836  | 4   | rs43307594 | 43392336 | 0.379 | 847  | 0.473 ± 0.15   | 0.0016  |
LYR and decreases in marbling, F3, GFR, IFR and SQFR (Table 4). Another newly discovered SNP in gene ERCC5 (76685563 bp) was strongly associated with three carcass traits where the substitution of the minor allele was associated with increases in F3, and GFR and decreases in LR (Table 4). Gene ERCC5 is involved in response to abiotic stimulus and negative regulation of programmed cell death and nucleotide excision repair pathway. In mice selected for high muscle mass, ERCC5 was located in QTTL for lean mass [48].

SNP on BTA 27 (39712547 bp), within gene solute carrier family 20 (phosphate transporter), member 2 (SLC20A2; ID: 518905), was associated with one carcass trait where the substitution of the minor allele was associated with an increase in BFR (Table 4). The SLC20A2 gene is involved in ion and cation transport. In human, mutations within SLC20A2 are associated with idiopathic basal ganglia calcification [49].

SNP rs43702346 on BTA 6, within gene polycystic kidney disease 2 (PKD2; ID: 530393), was significantly associated with two carcass traits where substitution with the minor allele was associated with a decrease in HCW and IFR (Table 4). The PKD2 gene is involved in negative regulation of G1/S transition of mitotic cell cycle process. Gene PKD2 is near an identified QTTL for bone percentage, fat percentage, meat percentage, meat-to-bone ratio, moisture content and subcutaneous fat [50]. In human, polymorphisms within PKD2 may take part in the development of gout [51].

The in silico functional analysis
In the current study, the 74 genes containing significant (P < 0.05) SNPs were submitted to DAVID for enrichment analysis. In total 39 genes out of the 74 genes were enriched in 35 biological process terms (Table 5). Ion transport and cation transport mechanisms contained the highest number of genes associated with feed efficiency traits. In addition, some genes affecting feed efficiency traits in the current study were involved in protein degradation, protein complex biogenesis, and protein amino acid glycosylation. The ion transport mechanism in conjunction with protein turnover and metabolism account for 37% of the variation in RFI [52].

In ruminants, protein synthesis accounts for 23% of total energy use in the whole body[53] and protein turnover accounts for 42% of total gastrointestinal tract energy use [54]. In the current study, some genes were involved in phosphorus metabolic processes, phosphorylation, and amino acid phosphorylation. Protein metabolism can be controlled by changing the phosphorylation status [55]. Genes involved in phosphorus metabolic processes and phosphorylation mechanisms regulate the metabolism of energy [56]. In the current study, regulation of transcription mechanisms contributed to variation in feed efficiency traits. The connection between a functional mutation in a specific transcription factor can increase or decrease expression of genes involved in glucose, amino acid, lipid, and cholesterol metabolism [57]. Other studies have demonstrated that genes that up-regulate in response to nutritional restriction are involved in transcription control [58].

The in silico functional study of genes having significant SNPs revealed potential pathways likely to contribute to variation in feed efficiency traits (Table 6). Mitogen-activated protein kinases (MAPK) signaling pathway included three of the identified genes (RASA1, CACNA1G and STK3). In a study of the differences in global gene expression between high and low RFI animals, the majority of up-regulated genes in low RFI animals were stimulated by MAPKs [59], where the MAPKs were involved in signal transduction pathways to activate different cellular processes, such as cell division, differentiation, and cell death as a response to hormones and stress [60]. The TYR gene is involved in Riboflavin metabolism, melanogenesis, tyrosine metabolism, and catecholamine biosynthesis, and the minor allele of SNP rs42402428, within gene TYR (ID: 280951) was associated with decreasing FCR. Polymorphisms in gene TYR have been associated with

| Table 4 Significant SNP based on false discovery rate (FDR) q threshold of 0.05 for beef carcass traits using single locus regression model (Continued) |
|------------------|---------|----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| LMA              | 540050  | 26             | rs42106947      | 37495213        | 0.488           | 848             | −1.766 ± 0.611  | 0.004           |
| BFR              | 518905  | 27             | ss914082824     | 39712547        | 0.015           | 684             | 0.714 ± 0.231   | 0.002           |
| IFR              | 515895  | 27             | ss914082827     | 39798548        | 0.076           | 687             | 0.654 ± 0.237   | 0.006           |
| SQFR             | 515895  | 27             | ss914082827     | 39798548        | 0.077           | 685             | 0.569 ± 0.208   | 0.006           |

1F1, subcutaneous fat depth between the 1st and 2nd quarter of the longissimus; F2, subcutaneous fat depth between 2nd and 3rd quarter of the longissimus; F3, subcutaneous fat depth between the 3rd and 4th quarter of the longissimus; Marbling was scored as ≤ 3.0 = devoid; 3.1 to 4.0 = traces; 4.1 to 5.9 = slight; 6.0 to 7.0 = small to moderate; and ≥ 7.0 = slightly abundant to abundant; HCW = Hot carcase weight (kg); LMA = Longissimus dorsi muscle area (cm2); LR = Lean meat within the rib section (%); LY = Lean yield grade (%); GRF = Grade fat (mm); IFR = Intermuscular fat (%); BFR = Body cavity fat within the rib section (%); SQFR = Proportion of subcutaneous fat from the rib section (%).
changing the coat colour of Braunvieh cattle [38]. Gene \(\text{GALNT13}\), affecting ADG, MMWT, DMI, F2, GRF, HCW, LMA, LY, and F3, is involved in mucin type O-Glycan biosynthesis. Gene \(\text{ATP6V1E2}\) (ID: 540113), which affects DMI and MMWT, plays an important role in various pathways and biological mechanisms. Gene \(\text{ATP6V1E2}\) is near an identified QTL for mycobacterium avium spp. Paratuberculosis resistance in Holstein cattle [61]. Gene \(\text{GTF2F2}\) (ID: 509259) affected RFI and is involved in basal transcription factors pathways, which regulate glucose, amino acids and protein, lipid metabolism and many other important metabolic processes. Changes in the function of \(\text{GTF2F2}\) would be associated with feed efficiency or metabolic diseases [57]. The minor allele of a newly discovered SNP (6: 37386084), within gene \(\text{ABCG2}\) (ID: 536203), was associated with decreasing IFR and marbling. The \textit{in silico} functional analysis showed that gene \(\text{ABCG2}\) is involved in ATP-binding cassette (ABC) transporters and bile

| Biological process                             | No | P value* | Genes                                                                 |
|------------------------------------------------|----|----------|----------------------------------------------------------------------|
| Ion transport                                  | 8  | 0.006    | 618639, 518905, 281701, 530393, 540113, 510792, 282411, 614299          |
| Cation transport                               | 7  | 0.004    | 618639, 518905, 530393, 540113, 510792, 282411, 614299                |
| Phosphorus metabolic process                   | 7  | 0.057    | 504429, 533815, 540329, 540113, 100048947, 281848, 512125             |
| Phosphorylation                                | 6  | 0.072    | 504429, 533815, 540113, 100048947, 281848, 512125                    |
| Metal ion transport                            | 5  | 0.034    | 618639, 518905, 530393, 282411, 614299                              |
| Regulation of transcription                    | 5  | 0.762    | 517336, 509259, 529124, 540474, 784720                              |
| Protein amino acid phosphorylation             | 5  | 0.126    | 504429, 533815, 100048947, 281848, 512125                          |
| Monovalent inorganic cation transport          | 4  | 0.060    | 618639, 518905, 540113, 614299                                    |
| Regulation of transcription, DNA-dependent     | 4  | 0.722    | 517336, 529124, 540474, 784720                                    |
| Transmembrane transport                        | 4  | 0.236    | 512725, 281701, 540113, 282411                                    |
| Proteolysis                                    | 3  | 0.756    | 617222, 524684, 534774                                           |
| Intracellular signalling cascade               | 3  | 0.643    | 530393, 614507, 281848                                           |
| Regulation of transcription from RNA polymerase II promoter | 3  | 0.290    | 517336, 540474, 784720                                           |
| Transcription                                  | 3  | 0.636    | 509259, 529124, 784720                                           |
| RNA processing                                 | 3  | 0.320    | 100048947, 512925, 281712                                         |
| Potassium ion transport                        | 2  | 0.359    | 618639, 614299                                                    |
| Nucleobase, nucleoside, nucleotide and nucleic acid biosynthetic process | 2  | 0.497    | 540113, 510792                                                    |
| Calcium ion transport                          | 2  | 0.279    | 530393, 282411                                                    |
| Regulation of homeostatic process              | 2  | 0.152    | 530393, 282411                                                    |
| Response to abiotic stimulus                   | 2  | 0.448    | 509602, 530393                                                    |
| Negative regulation of programmed cell death   | 2  | 0.476    | 509602, 282032                                                    |
| Protein complex biogenesis                     | 2  | 0.545    | 509259, 281848                                                    |
| Determination of symmetry                      | 2  | 0.067    | 497208, 530393                                                    |
| Microtubule-based process                      | 2  | 0.441    | 497208, 512287                                                    |
| Blood vessel morphogenesis                     | 2  | 0.351    | 282689, 282032                                                    |
| Protein transport                              | 2  | 0.833    | 282044, 614507                                                    |
| Protein amino acid autophosphorylation         | 2  | 0.130    | 281848, 512125                                                    |
| Neurological system process                    | 2  | 0.679    | 281701, 538198                                                    |
| Oxidation reduction                            | 2  | 0.899    | 280951, 532512                                                    |
| mRNA metabolic process                         | 2  | 0.495    | 100048947, 281712                                                 |
| Cell-cell adhesion                             | 1  | 1.000    | 540672                                                            |
| Protein amino acid glycosylation               | 1  | 1.000    | 532545                                                            |
| Muscle cell development                        | 1  | 1.000    | 529759                                                            |
| Amino acid transport                           | 1  | 1.000    | 511955                                                            |

*P value of the enriched biological process for genes’ list having significant SNP.
secretion pathways. The results of gene ABCG2 in the current study agree with reported gene ABCG2 as QTL for increasing milk yield and decreasing milk fat and protein [62-64]. The analysis also indicated that insulin-like growth factor 1 receptor gene IGF1R (ID: 281848) affecting ADG and marbling is involved in seven different pathways. Nonetheless, there was no association between production traits and the genotypes of IGF-IR/TaqI polymorphism [65-67]. This might be because a small number of animals was used to test the association in those analyses. Functional analysis allows a better understanding of the underlying mechanisms contributing to the genetic variation in feed efficiency, and it sheds light on potential pathways to target in future investigations.

Table 6 The pathways for 14 genes containing significant SNPs for one feed efficiency trait

| Pathway                                      | Genes                                                                 |
|----------------------------------------------|----------------------------------------------------------------------|
| bta04010: MAPK signalling pathway             | 282032 (RASA1), 282411 (CACNA1G), 533815 (STK3)                     |
| bta01100: Metabolic pathways                 | 280951 (TYR), 532545 (GALNT13), 540113 (ATP6V1E2)                   |
| bta04930: Type II diabetes mellitus          | 282411 (CACNA1G), 538996 (ABCC8)                                    |
| bta04145: Phagosome                          | 512287 (LOC512287), 540113 (ATP6V1E2)                               |
| bta02010: ABC transporters                   | 536203 (ABCG2), 538996 (ABCC8)                                      |
| bta04976: Bile secretion                     | 536203 (ABCG2)                                                       |
| bta03013: RNA transport                      | 616055 (CHADL)                                                       |
| bta03022: Basal transcription factors        | 509259 (GTF2F2)                                                      |
| bta04962: Vasopressin-regulated water reabsorption | 512287 (LOC512287)                                               |
| bta05132: Salmonella infection               | 512287 (LOC512287)                                                  |
| bta04514: Cell adhesion molecules (CAMs)     | 529759 (SDC1)                                                        |
| bta04512: ECM-receptor interaction           | 529759 (SDC1)                                                        |
| bta05144: Malaria                            | 529759 (SDC1)                                                        |
| bta04966: Collecting duct acid secretion     | 540113 (ATP6V1E2)                                                   |
| bta04721: Synaptic vesicle cycle             | 540113 (ATP6V1E2)                                                   |
| bta00190: Oxidative phosphorylation          | 540113 (ATP6V1E2)                                                   |
| bta05323: Rheumatoid arthritis               | 540113 (ATP6V1E2)                                                   |
| bta03420: Nucleotide excision repair         | 509602 (ERC5)                                                       |
| bta04510: Focal adhesion                     | 281848 (IGF1R)                                                       |
| bta04114: Oocyte meiosis, bta05214: Glioma   | 281848 (IGF1R)                                                       |
| bta05218: Melanoma, bta05200: Pathways in cancer | 281848 (IGF1R)                                                    |
| bta04914: Progesterone-mediated oocyte maturation | 281848 (IGF1R)                                                  |
| bta04520: Adherens junction                  | 281848 (IGF1R)                                                       |
| bta04730: Long-term depression,              | 281848 (IGF1R)                                                       |
| bta04144: Endocytosis                        | 281848 (IGF1R)                                                       |
| bta00740: Riboflavin metabolism              | 280951 (TYR)                                                        |
| bta04916: Melanogenesis                      | 280951 (TYR)                                                        |
| bta00350: Tyrosine metabolism                | 280951 (TYR)                                                        |
| bta03015: mRNA surveillance pathway          | 281712 (CPSF3)                                                      |
| bta03008: Ribosome biogenesis in eukaryotes   | 508697 (HEATR1)                                                     |
| bta05010: Alzheimer’s disease                | 534774 (BACE2)                                                       |
| bta04360: Axon guidance                      | 282032 (RASA1)                                                      |
| bta04740: Olfactory transduction             | 281701 (CNGA3)                                                      |
| bta00512: Mucin type O-Glycan biosynthesis   | 532545 (GALNT13)                                                    |
| bta05164: Influenza A                        | 100048947 (RNASEL)                                                  |
| bta05160: Hepatitis C                        | 100048947 (RNASEL)                                                  |
| bta04020: Calcium signalling pathway         | 282411 (CACNA1G)                                                    |
Genetic variation in RFI explained by candidate genes
The accuracy of a DNA panel to predict a trait like feed efficiency depends on the amount of genetic variation explained. The 98 SNP set associated (P < 0.05) with at least one feed efficiency trait included SNPs that did not pass the FDR threshold, although they significantly contributed towards building the prediction equation in GWAS. The 98 SNP set explained 26% of the genetic variance in RFI whereas the proportion explained by the set of 339 SNPs was 29.6%. The correlation between EBVs of RFI using ASReml and GEBV were 0.52 and 0.66 from the 98 and 399 SNP sets, respectively. Based on the proportion of the genetic variance explained by the 98 SNPs (26%), the corresponding Beef Improvement Federation (BIF) accuracy is 0.127. Nonetheless, the estimated genetic variance by the 98 SNPs might be overestimated as the additive polygenic animal effect was not included in the model. To improve the accuracy of the SNP panel developed from a crossbred population, a large number of phenotypes is required (~2000 animals) [68]. This might partially explain the relatively low estimated accuracy in the current study. In addition, large numbers of identified genes (83 out of 180) from fine mapping RFI were genotyped for only one SNP, and that decreases the probability of detecting the functional mutations. Nonetheless, combining validated SNPs from further fine mapping and the identified 98 SNPs may help develop a DNA test panel for commercial use.

Conclusion
This study reported SNPs that are significantly associated with RFI, performance, and carcass traits. We postulated that the identified significant SNPs, genes, biological mechanisms and pathways could be the direct cause of the variations in feed efficiency traits and carcass traits. The ability of the significant SNP to predict the genetic merit of feed efficiency and carcass traits should be measured in another population.

Additional files

Additional file 1: The list of 339 genotyped single nucleotide polymorphisms (SNPs) and their related information.

Additional file 2: Allele substitution effect estimates of SNPs influencing (P ≤ 0.05) growth and efficiency traits, and not passed chromosome wise false discovery rate (FDR) threshold q=0.2.

Additional file 3: Single nucleotide polymorphisms associated at P-value ≤ 0.05 using the genotypic model for growth and feed efficiency traits.

Additional file 4: Suggestive SNP based on false discovery rate (FDR) q threshold of 0.2 for beef carcass traits using single locus regression model (SLRM).

Abbreviations
SNP: Single nucleotide polymorphism; QTL: Quantitative trait loci; FDR: False discovery rate; BTA: Bos taurus autosome; RFI: Residual feed intake; ADG: Average daily gain; DMI: Average daily dry matter intake, MMWT: Mid-point metabolic weight; FCR: Feed efficiency conversion ratio (kg gain kg\(^{-1}\), DM); F1: Subcutaneous fat depth between the 1st and 2nd quarter of the longissimus; F2: Subcutaneous fat depth between 2nd and 3rd quarter of the longissimus; F3: Subcutaneous fat depth between the 3rd and 4th quarter of the longissimus; HCW: Hot carcass weight (kg); LMA: Longissimus dorsi muscle area (cm\(^2\)); LR: Lean meat within the rib section (%); LY: Lean yield grade (%); RF: Intramuscular fat (%); RFR: Body cavity fat within the rib section (%); SQFR: Proportion of subcutaneous fat from the rib section (%); EBRC: Elora Beef Research Center; KAP: the Agriculture and Agri-Food Canada Kapuskasing Research Centre; NLARS: New Liskeard Agriculture Research Station.
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