Exploring the Genetic Basis of Residual Feed Intake (RFI) for Predicting Feed Efficiency in Beef Bulls

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SUMMARY

Residual feed intake (RFI) is defined as the difference between actual feed consumption and the predicted feed intake based on a bull's live weight, growth, and maintenance needs. Bulls with low RFI values are considered more efficient because they have reduced feed costs compared to those with high RFI values. Identifying marker genes that control RFI is challenging due to the significant variation in differentially expressed genes (DEGs) and the antagonistic expression of genes that regulate the RFI trait in bulls. In this literature review, we searched for potential genes, their positional single nucleotide polymorphisms (SNPs), their chromosomal locations, and their expression patterns to better understand the regulation of RFI traits in bulls. Based on specific inclusion criteria, this review explored over 200 studies on RFI in beef bulls and steers published between 2012 and 2022. The review utilized genome-wide association studies (GWAS) and gene set enrichment analysis (GSEA) and identified 511 genes located on 240 chromosomal loci in 7,992 beef bulls. Of these genes, 52 were consistently reported as modulating RFI, while 469 were unique and only reported once. During this period, 228 of the 244 chromosomal loci were reported multiple times, while 16 were reported only once. The literature search revealed that 11 studies linked the bovine chromosome 6 (BTA6) to RFI quantitative trait loci (QTLs) in bulls. Similarly, eight studies linked BTA8, ten linked BTA7, and eight linked BTA11 to RFI QTLs. Additionally, 228 SNPs were identified across 30 chromosomal locations between 2012 and 2023. This review provides novel insights into the molecular mechanisms underlying feed efficiency (FE) regulation and lays the groundwork for identifying molecular markers associated with FE in bulls across all breeds and populations.

KEY WORDS

Beef cattle; residual feed intake; feed efficiency; genomics; GWAS; GSEA.

INTRODUCTION

In 2023, the United States ranked 9th globally in cattle population, with 94.4 million cattle. A significant portion of the financial resources allocated to cattle production is consumed by feed expenditures, which account for 55% to 75% of the overall costs in beef cattle farming (1). This makes feed efficiency (FE) a critical factor in the profitability of the livestock industry, especially since feeding costs are often volatile and beyond the direct control of producers (2). One of the key metrics used to evaluate FE is RFI, which measures the difference between an animal's actual feed intake and its expected feed intake based on maintenance and growth. Improving RFI is essential because it directly impacts FE and overall cost reduction in cattle production. For example, studies suggest that reducing the feed-to-gain ratio from 2.75 to 2.45 could save U.S. bull producers an estimated $500 million annually (5). The European Union similarly estimates that feed and sustainability account for about three-quarters of total costs (3, 4), highlighting the global importance of optimizing FE through metrics like RFI.

RFI is a heritable trait in bulls that can be selected to improve feed intake and feed conversion ratio (FCR) (6). Bulls with high RFI typically have higher daily dry matter intake (DMI) and a less efficient FCR, while bulls with low RFI exhibit the opposite pattern (7). Cow-calf producers also recognize the economic significance of RFI in bull sales (8).

RFI is a metric used to assess the efficiency of feed utilization in beef cattle. It is determined by calculating the discrepancy between the actual amount of feed consumed and the expected amount. The trait is influenced by both genetic and environmental factors, with heritability estimates ranging from 0.30 to 0.35 (9). RFI can serve as a selection criterion for optimizing animal efficiency and reducing feed costs while maintaining production levels. However, the effectiveness of its application in breeding programs is debated, with some suggesting that a more precise approach might involve selecting based on individual traits (10). Studies have explored the genetic basis of RFI and identified genes that are expressed differently in beef cattle with high and low RFI (11-14). These findings suggest

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that RFI could be valuable in animal breeding. Nevertheless, further research is needed to fully understand its genetic basis and enhance its application.

The focus of breeding goals has shifted from increasing the number of beef cattle to selecting feed-efficient bulls in order to obtain the best heritable traits in the beef industry (15-17). However, accurately estimating RFI is costly due to the need for expensive equipment, labor, and, most importantly, the use of individual animals for measurement (18). Selecting feed-efficient bulls based on RFI has significant economic and environmental advantages for the beef industry. By choosing bulls with lower RFI, producers can reduce bull maintenance costs by 9-10%, while simultaneously cutting methane emissions by 25-30% and lowering manure output (19). These combined benefits make RFI an important trait for improving overall sustainability in cattle farming. Additionally, multiple studies have shown that RFI has a moderate heritability, ranging from 0.18 to 0.41 in heifers (20, 21), making it a viable selection criterion to enhance FE alongside traits like faster growth and reduced body fat. While determining RFI phenotypes requires the costly and challenging collection of average daily feed intake (ADFI), identifying genes or markers associated with RFI would allow for more efficient, marker-assisted selection for FE at an early age, reducing reliance on direct ADFI measurements. Therefore, RFI could be an excellent alternative for improving FE in bulls (22). RFI has become a preferred metric for characterizing the FE of bulls because it offers energy savings beyond those related to growth and maintenance, accounting for variations between animals at different stages of production and development (23). This literature review will explore the genetic basis of RFI.

RESIDUAL FEED INTAKE (RFI) CALCULATION AND MEASUREMENT

RFI measures an animal's FE by calculating the difference between its actual feed intake and the expected intake based on its size and growth rate. A lower RFI indicates greater FE, as the animal consumes less feed without sacrificing growth (20, 24). This study explores the current knowledge on RFI, which has been shown to have moderate heritability. Selecting for low RFI can produce offspring that consume less feed while maintaining the same productivity levels as higher RFI cattle.

According to Nielsen et al. (4), accurately quantifying feed intake in national cattle evaluation systems is essential because variations in feed intake among cattle cannot be determined solely based on body weight and productivity levels. To address this, a standardized criterion has been developed for measuring, recording, and assessing FE, requiring RFI data over a period of at least 70 days (approximately 2.5 months) (25). Additionally, a 21-day acclimatization period, live weight measurements on two consecutive days at the start and end, and periodic measurements at irregular intervals have been included (26). Some recent studies have shortened the testing interval (27, 28), such as measuring body weight over 63 days (29) and 84 days, as defined by Manafiazar et al. (30). The shortest duration noted is between 35 and 42 days. However, reducing the RFI testing period may impact the accuracy of the results, as it has been shown to decrease the Spearman correlation coefficient by 5% to 7% (30). The accuracy of shorter test durations depends on factors such as animal growth rate and diet composition (31).

RFI is the difference between an animal's actual feed consumption and its expected feed consumption. A bull with a negative RFI is considered efficient, as it consumes less feed than expected based on its body weight and growth rate. However, the application of RFI as an indicator of FE is limited by the lack of facilities capable of recording daily feed intake for each bull, as well as the associated costs (32). While the regression-based calculation of RFI is independent of the traits used to calculate DMI phenotypically, it does not guarantee genotypic independence (33). The traditional multiple regression model used in many studies to predict DMI typically includes metabolic live weight and average daily gain (ADG).

OUTLINING THE GENETIC SELECTION OF RFI

RFI is a polygenic trait, meaning multiple genes contribute to its expression. Identifying key candidate genes or markers associated with RFI can facilitate marker-assisted selection (MAS) for FE, offering a cost-effective alternative to traditional methods like measuring ADFI. Recently, research has been focused on the development of selection lines for RFI to establish a resource population for studying the biological and genetic elements of RFI (34).

Next-generation sequencing technology and genome-wide association studies (GWAS) employing high-density single nucleotide polymorphism (SNP) genotypes are effective methodologies for identifying genes or genomic areas that account for the variability observed in livestock attributes (35). Using genomic methodologies presents new possibilities for identifying and selecting bulls with enhanced efficiency. By establishing the associations between genetic markers and FE, it becomes possible to extrapolate this knowledge to bulls who have been genotyped but have not undergone expensive phenotypic assessments of feed intake (36).

Since 2000, noteworthy progress has been made in high throughput genotyping and sequencing methods, leading to the development of high-density SNP chips. An example of such a chip is the Illumina Bovine SNP50 Bead Chip (37). Using the Bovine SNP50 in the context of beef cattle has enhanced precision in estimating animals' genetic worth (38). Implementing these advancements in bulls' production will yield advantages for several qualities, particularly those that are challenging to quantify or necessitate animal slaughter for phenotype recording, such as FE and carcass attributes (39). Multiple GWAS have provided evidence suggesting that numerous genes contribute to FE features, with the bulk of these genetic effects being of small magnitude (40-45). However, despite the extensive investigation of several SNPs, the comprehensive understanding of the genetic framework underlying FE remains incomplete. The Present study integrates the research of Yang et al. (46) and other researchers (34, 47-62) to predict 527 genes requiring further investigation to pinpoint the exact mutations causing differences in FE in steers or bulls, as shown in Table 1.

This paper reviews and gives an in-depth look at the genes linked to FE in bulls found in beef cattle through GWAS and Gene set enrichment analysis (GSEA) from 2012 to 2023. During this time frame, 511 genes related to regulating the RFI characteristic in bulls were identified among 30 chromosomes. Among the 511 identified genes, 52 had been repeatedly reported commonly in this investigation and considered very crucial in con-

trolling the RFI trait, while the other 469 were unique as reported single time. We looked at these genes in 7,992 bulls or steers using GWAS and GSEA analysis. Furthermore, this literature review identified that eleven studies linked the bovine chromosome 6 (BTA6) to quantitative trait loci (QTLs) that control the RFI trait in bulls. Ten studies linked BTA7 to QTLs that control the RFI trait, and eight studies linked BTA8 to QTLs that control the RFI trait. Lastly, eight studies linked BTA11 to QTLs that control the RFI trait. This review found 228 SNPs in 30 chromosomal locations between 2012 and 2023.

The study also covers the breed(s) of beef cattle /steers, sample size, country of research, and statistical method used to analyze the impact of different genes on FE in bulls during the specified period. Overall, the research has enhanced comprehension of the genetic elements impacting RFI in beef cattle, paving the way for enhanced breeding approaches to increase livestock production efficiency across all bull breeds and populations.

The current study also provides a chart-format overview of the corresponding genes, year, and beef breed used, as shown in Figure 1.

ECONOMIC IMPLICATIONS OF RFI FOR THE BEEF INDUSTRY

Currently, the focus of selection techniques is on enhancing the efficiency of breeding sires. The reason behind sires is that most genetic improvement occurs when sires transmit their traits to their offspring (15, 66). The potential cost reductions resulting from enhanced animal efficiency, particularly in the case of replacement of heifers with extended periods of herd tenure, would be substantial. The process of selecting for enhanced FE has the potential to yield several advantageous outcomes for the cow herd. These include a potential decrease of 9 to 10% in maintenance costs, a reduction of 10 to 12% in feed intake, a decrease in methane emissions by 25 to 30% (67, 68), and a reduction in manure production by 15 to 20%, all while maintaining ADG and mature cow size (69). The selection for enhanced efficiency yields substantial economic advantages. According to Crews (70), there is a cost difference of approximately $38 between feeding an efficient bull and an inefficient bull over 150 days. This cost difference will increase because of the rising grain and fuel costs.

The primary factor influencing the profitability of a beef operation is the reduction of input or production expenses, particularly those related to feeding. This is because cattle farmers have negligible control over the market value of their products (71). Integrating FE into breeding goals would enhance the genetic capacity of animals to exhibit reduced feed intake while sustaining equivalent production levels. Previous studies have provided evidence for the advantageous characteristics of more efficient beef cattle, including reduced DMI, decreased manure generation, and lower methane emissions (67, 68). According to the concept presented by Koch et al. (72) feed intake could be partitioned into two components: anticipated intake based on a specific output level and a residual component representing the disparity between observed and an-

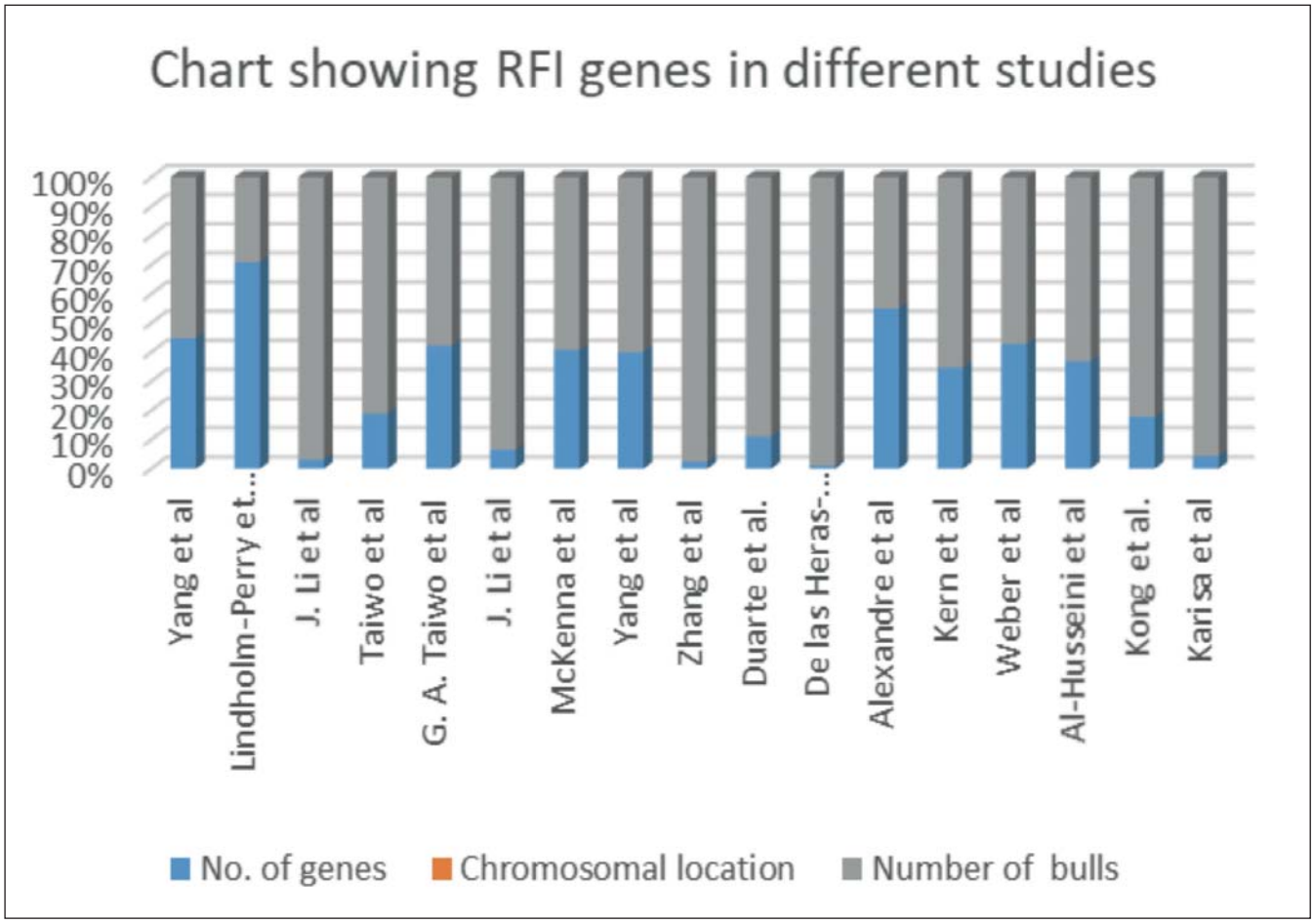

Figure 1 - RFI genes in different studies.

Table 1 - An overview of the RFI-linked genes predicted through genome-wide association studies (GWAS) in beef cattle.

Author & Title	Total No. & list of Genes controlling RFI in Bulls	*N*	Chromosome number	Beef Breed & Country	Statistical analysis
Yang et al. (55)	30 genes were identified that's controls the RFI trait in bulls: RNF170, MCC, LIMSC2, NEDD4L, B2M, MAN2BI, MPDZ, QSER1, TAOK1, TMEM245, CAMKK2, ATP5PD, TM9SF4, SEPTIN7, NSD1, RSF1, NR2C2, NDUFAF1, GAPVD1, AHCTF1, ENPP2, DIP2A, RBM33, ROCKS, ENPP2, DOT1L, ARHGAP5, GYG2, SLC39A14, TM9SF3	37	BTA 27, 10, -, 24, 8, 15, 19, 17,13,4, 7, 29, 22, 11, 16,14,1,4,14, 21, X, 26	China Charolais breed	GSEA
Taiwo et al. (59)	13 genes: CRAT, SLC27A5, SLC27A2, ACSBG2, ACADL, ACADSB, ACAA1, ACAA2, AADAT, MAT1A, GOT2. UQCRC1 and ATP5G1.	56	BTA 11, 18, 10, 7, 2, 22, 24, 8, 28, 18	Crossbreed beef steers were used in the USA	GSEA
Lindholm-Perry et al. (62)	83 genes were identified that control RFI: LOC789569, LOC101904916, TECR ATP6AP1, PAMR1, EGLN3, LOC100848775, LYPD3, KAT2B, KLK13, PLP2, HTRA1, RHOG, TUBA4A, CD52, SH3BGRL3, SESN3, ZDHHC5, ZNF750, RPS15, ODF21, SH3GLB2, HGS, MYL12A, ZDHHC3, ASB3, MYADM, LOC104976804, LYPD2, ASB2, CBX2, VARS, GLULP, RC3H1, HSPB1, ZNF146, LY6G6C, CYP1B1, PSMB5, ALPK1, DNM2, PSMB6, B3gNT3, C1QBP, NBEAL1, SH3GL1, 1L1RN, TUBB, SLC35D1, TMEM54, LOC104971374, CCDC66, MAN2B1, NDUFA9, CFL1, PIBF1, C7H5oRF46, LOC100848030, YPEL3, MTERF2, FRK, ATR, REXO5, RUVBL1, LOC104973218, PRR5, DNAJB1, MTAP, MAPK1, TMSB10, UACA, ARAF, DCUN1D4, GABARAP, MALL, RGS5, FAM107B, LOC100139345, PNPT1, RWDD3, SNX15, ELF5, S100A11	34	BTA 7,15,21,18,1, 26, 2, 19,11, 24, 22, 14,16, 25, 23, 3, 5, 29, 12, 9, 25, 17,10, 6, 13	Angus and Hereford crossbred steers of the USA and Canada	Meta-analysis of GWAS approach
Li et al. (61)	12 candidate genes associated with RFI traits in bulls were identified namely: CYP2E1, FAM13A, FAM184A, GALNTL6, GPRC5A, KCNJ16, LINC01588, LOC101903052, LOC101903477, LOC101904559, LOC101905089, LOC101906021. Canada:	368	BTA 18, 6, 9, 8, 5, 19	Charolais, Hereford-Angus crosses, and beef booster	GWAS
Taiwo et al. (60)	41 genes: HBA, HBA1, HBB, LOC101907518, RPL39, IOC101902490, UBE2D1, FUCA2, B4GALT6, FBXL3, SOCS3, COMMD8, RPLP2, RPL34, HSPA1A, HSPHI, BAG2, DNAJA1, JUN, HSPA4, UBE2D1, DNAJB1, H3C13, H2BC7, H4C2, ELOC, ELOB, H2AC8, SIRT1, FLCN, ATP6V1G1, HSPA14, H2BU1, HSPA1A, HSPH1, BAG2, DNAJA1, JUN, HSPA4, UBED1.	56	BTA 25, 15, 4, 9, 24, 12, 19, 6, 29, 23, 18, 8, 3, 7, 26, BTA 2, 16, 14, 25, 28, 13	Canada & USA Cross breed beef steers	GSEA
Li et al. (57)	26 genes: ADGRF1, ADGRF5, ANXA8L1, ATG3, BOC, CD2AP, DAB1, DYNC1LI1, ESR2, ITPR2, KATNA1, LATS1, NEDD4, SHROOM3, SPICE1, SYNE2, ADGRF5, ATG3, BOC, CD2AP, ESR2, NEDD4, SLC9A9, SYNE2, ADGRF1, ADGRF5	368	BTA 23, 28, 1, 3, 22, 10, 5, 9, 6, 1	Canadian Cross breeds: Charolais, Hereford-angus and beef booster	GWAS
McKenna et al. (56)	11 genes were identified as key genes controlling the RFI trait. The genes were: HSPA5, CRELD2, HYOU1, MANF, ACTA2, DNAJB11, GMPPB, GNPNAT1, LIMS2, GSTT1 and DBP.	16	BTA 11, 5, 15, 22, 26, 1, 10, 2, 17, 18	Simmental steers from Ireland	GWAS
Yang et al. (55)	20 genes: SSH2, CHD8, PCBP2, IOC407163, TDP2, CERS5, WDR11, STYX, NDUFS1, H2AFY, VPS37C, TADA2A, ATP2B4, SLC6A20, LRRC28, BAZ2A, WAC, CLOCK, TXLNA, SMTN	30	BTA 19, 5, 23, 26, 10, 2, 28, 29, 19, 22, 21, 13, 6, 1, 17	China Qinchuan bulls	WGCNA
Zhang et al. (53)	Identified 100 genes having key role for RFI trait: AMPH, ARHGAP32, ATL1, BID, C3AR1, CAMP, CCND1, CD4, CFTR, CHL1, CLEC11A, CLIC4, CNTFR, CSTB, CTHRC1, CUL3, DVL1, EPO, FGL1, GDF3, GSDMD, HAND1, HAUS4, HELLS, IFNA2, INHA, INTU, KCNE2, KCNK2, KIF11, KIF13B, KIFC1, LGALS1, LIF, LIMK2, MAPK1, MAPT, MMP20,NDUFAB1,NEFHNFIA, NGFR, NMNAT3, NTRK2, OSMR, P2RY12, PALLD, PARD3, PARD6B, PCTP, PEG10, PKP1, PLXNB2, POLG, PPARGC1A, PPARGC1B, PTHLH, PTPN1, RIPK1, RNF4, RXRB, SCYL1, SERPINA3, SERPINE2, SGCE, TRAK2, UCP1UPK2, VDAC1, ADNP, ATG4B, ATG4C, BID, CAMP, CBLB, CCND1, CD4, CHL1, CLEC11A, CLIC4, CTHRC1, ENC1, EXO5, FSCN1, HAND1, IDE, KCNK2, KIF11, KIFC1, KLHDC8B, LANCL1, LGALS1, MAPT, NDUFAB1, NDUFS2, NEFH, NGFR, NLGN1, NR5A1, NTRK2, OLA1, P2RY12, PARD3, POLG, PPARGC1A, PPARGC1B, SERPINA3, SLC25A5, SRCIN1, SS18, SSNA1, TP53INP1, TTR, UCP1, VDAC1, LANCL1, ST8SIA1, PARD3, ATL1, PPARGC1A, CCDC103, PARD6B, CD4, SS18, RIPK1,	3984	BTA 4, 29, 10, 5, 22, 29, 18, 2, 8, 1, 14, 16, 25, 27, 7, 26, 17, 23, 19, 15, 20,13,4, 21,6,3,11,6, 24	Canada Angus, Charolais, Kinsella Composite, Elora crossbred	GWAS

Author & Title	Total No. & list of Genes controlling RFI in Bulls	*N*	Chromosome number	Beef Breed & Country	Statistical analysis
	CELSR2, CLEC11A, UCP1, COQ7, CTHRC1, LIF, SERPINA3, NFIA, NDUFAB1, CCDC39, EPO, CHL1, CCND1, BID, KCNK2, VDAC1, LGALS1, TP53INP1, TCF7L1, CAMP, KIF11, KIF13B, P2RY12, NLGN1, PPARGC1B, POLG, PLXNB2, ARMC4, CLIC4, MAPT, NTRK2, IFNA2, FSCN1, TRAK2, DVL1, NMNAT3, HAND1, NEFH, NDUFS2, IDE, FCGR2B, NGFR, ARHGAP32, KIFC1, TFCP2L1, ACSL6, AGMO, AKR1C3, AKR1C4, AKR1C1/AKR1C2, ALPI, ANGPTL4, ANGPTL6, ATP5PF, BID, BMP7, CAMP, CD4, CERS5, CFTR, CLDN16, CLEC11A, CNTFR, CTDNEP1, CYP2C18, CYP2J2, CYP7B1, DEGS2, DHRS4, ELOVL4, ERLIN1, FCGR2B, FGL1, GNAI1, GPC3, IL1RN, INHA, KCNE1B, KIF13B, LGALS1, LIF, MAPK1, MOGAT2, MRAS, NGFR, NR5A1, NTRK2, P2RY12, P2RY13, PARD3, PCTP, PDK2, PIGP, PIK3CB, PLA2G2A, PLEKHA3, PLVAP, POLG, PPARGC1A, PPARGC1B, PRKCB, PTHLH, PTPN1, RGS2, SERPINE2, ST8SIA1, TFCP2L1, TRHR, TTR, UCP1, UGT2B4, UGT2B11, UGT2B17, GPC3, ST8SIA1, KLF15, MRAS, INHA, PIK3CB, ANGPTL4, CLDN16, PPARGC1A, IL1RN, PDK2, P2RY13, PRKCB, FGL1, CD4, CA4, CTDNEP1, PCSK2, CLEC11A, UCP1, MOGAT2, DIO3, LIF, DUOXA2, SLC37A2, ANGPTL6, PTPN1, HBA1/HBA2, CFTR, BID, PLA2G2A, TTR, GNAI1, KCNE2, VDAC1, ALPI, LGALS1, PKN1, TRHR, CAMP, TP53INP1, KIF13B, PPARGC1B, POLG, CLIC4, NTRK2, NR5A1, BMP7, GCNT4, SLC22A6, PTGER1, KCNE1B, SLC20A2, PCTP, FCGR2B, AGMO, PLVAP, NGFR, IP6K1, MAPK1, AOC3, GRPR, PTHLH				
Duarte et al. (63)	3 key genes were identified: MCCC1, AOX1, PCCA	02	BTA 1, 02 &12	Angus Bulls, UK	GWAS
de las Heras-Saldana et al. (51)	24 genes: DUSP1, ERGIC1, RPL26L1, STK10, ATP6V0E1, STC2, CPEB4, NEURL1B and BOD1(Genomic region BTA20, 3.88-5.88). SDS, SDSL, DTX1, SLC8B1, OAS2, PTPN11, RPL6, LHX5, TPCN1 (Genomic region BTA17-6.26-6.46). XKR4 and SOX17 (Genomic region BTA14, 2.31-2.51). VEPH1, PTX3 and MFSD1 (Genomic region BTA1, 1.10-1.11) LOC104968862 and LOC104968863 (Genomic region BTA6, 5.41-5.61). MINPP1 (BTA26, 7.90-9.90)	2190	BTA 20, 17, 1,6, 26 (Identified SNPs=57)	Genomic Data from 2190 Australian Angus steers were used in this study	GWAS
Alexandre et al. (52)	22 genes: NR2F6, and TGFB1, SST, SNORA73, ENSBTAG00000047700, ENSBTAG00000047121, ENSBTAG00000047816, ENSBTAG00000039928, ANXA13, FST, PBLD, ENSBTAG0000001368, JCHAIN, IGFBP1, SBK2, ACTC1, MYH1, HR, TAGLN, SFRP2, FN1, CAV1	18	BTA 7, 1, 18, 19, 20, 11, 14, 28, 6, 18, 10, 8, 15, 17, 2	Brazil Nelore Bulls	GWAS
Kern et al. (50)	17 genes: ARHGAP27, ACAT1, BOK, CTSD, DGCR6, GSTA4, HSPB1, KLK10, MIF, MRPL41, NDUFS8, NME3, NQO1, RAB25, RGS5, TRABD, RNH1	32	BTA 19, 15, 3, 29, 17, 23, 25,18,11, 5	USA Angus and Hereford steers	NGS-SAS
Weber et al. (48)	Total 12 genes controlling the RFI was identified: APOA2, CCL2, CDKN2A, E2F1, GC, HHEX, IGFBP2, IL8, MYOD1, PCSK2, SHC3 and ZEB1.	16	BTA 3, 19, 8, 13, 6, 26, 2, 24, 15	USA Angus steers	GWAS
Al-Husseini et al. (64)	Total 35 genes including: AVPR1A, CNN1, CXCR7, EDNRB, FGA, GHR, IGFBP3, NKIRAS1, RGS2, AHR, CD4, gSTM1, S100A10, HELZ, HLA-DRB1, POSTN, AP3B2, ESPN, MAOA, CPEB1, AHSG, COL3A1, CYP2C18, MEP1B, SLC27A6, ABCC4, ABHD5, COL4A6, MAP2K6, SNAI2, DDC, DHRS3, SLC22A7, SOD3.	60	BTA 5, 7, 3, 12, 17, 20, 4, 27,19, 23, 21, 16, X, 1, 2, 26, 24, 22, X,14, 6	Australian Angus bull breed	NGS DEseq
Kong et al. (65)	Total 38 genes: TPI, TECR, COX8A, SLC25A39, PKM2, SUZ12, TMSB10, TECR, TUBA4A, RPL10, HSPB1, PSMB6, DNAJB1, RPS15, TUBB5, TUBB5, RPL36, CLPTM1, ETHE1, HGS, HSF1, CFL1, CAPNS1, PSMD5, ACTB, UBC, UBA52, mYL9, TP11, GNB2, UBE2V1, DSTN, GNB1, DNM2, GTF21, SUCLG2, TMSB4, UACA.	175	BTA 5, 7, 29, 19, 23,11, 2, X, 25, 19, X, 18,14, 8, 17, 13, 16, 22, 10	Canada, Hereford × Aberdeen Angus hybrid steers	GWAS
Karisa et al. (47)	Total 24 genes: PQLC2, NECAP2, CAST, INSIG1, UMPS, OSMR, LRP5, LIFR, UGT3A1, PARP14, ACAD11, UBA5, BIN1, ASNSD1, MKI67IP, AOX1, SMARCAL1, PLEKHA7, APAIP, CYP2B, OCLN, GHR, SLC45A2, MYO10.	531	BTA 2, 4, 7, 15, 18, 20, 29 (SNPs, =24)	Canadian steers from Angus and Charolais and hybrid bulls	GWAS

Note: GSEA (Gene set enrichment analysis), GWAS (Genome Wide Association studies), Qpcr (Quantitative Polymerase Chain Reaction)

ticipated intake. The residual can be used to identify animals exhibiting low (negative) RFI or those displaying high (positive) RFI (73).

Bull selection is the primary way of achieving genetic advancements in the cattle sector. In conjunction with the expansion of growth characteristics, there has been a growing emphasis among buyers of bulls on attributes related to the quality of carcasses (74). Recent developments in whole GWAS have led to a novel metric for assessing individual animal feed consumption, known as RFI. The RFI, independent of growth traits, is determined by subtracting the projected feed intake from the actual feed intake. An animal exhibiting a harmful RFI demonstrates a reduced consumption of feed in comparison to the anticipated amount, indicating a higher level of FE (35). The present review study has shown that machine learning algorithms can discern the most and least feed-efficient groups of beef cattle by utilizing genomic information, thus obviating the need for costly and challenging-to-measure features like feed intake and performance measures. The results of our study indicate that the highest and lowest percentiles (1%, 5%, 10%, and 15%) of the bull population may be identified as the most and least feed-efficient groups through the utilization of SNP markers. This classification method demonstrates high accuracy and can enhance the productivity and competitiveness of the beef industry. Therefore, the enhancement of FE by selecting breeding animals with lower RFI values can impact the profitability and competitiveness of the beef sector. This improvement can account for around 55-75% of the overall production costs as stated earlier (75).

CHALLENGES IN THE ADOPTION OF RFI

The adoption of RFI in cattle breeding programs faces significant challenges, primarily due to the high costs and technical complexities involved in evaluating this trait (4). In contrast to the utilization of feed conversion as a selection criterion, the utilization of RFI for selection appears to favor animals with reduced feed intake and decreased maintenance needs without any discernible impact on adult weight or weight gain (76-78). According to Berry et al. (33), utilizing molecular information in genetically assisted selection methods can enhance selection precision and expedite genetic advancement in bull breeding.

Extensive investigation is currently being conducted to ascertain the genetic underpinnings of RFI, and the findings thus far have shown promise (17, 41, 42). Nevertheless, the number of published studies on this topic still needs to be higher. One investigation conducted by Barendse et al. (40), conducted a comprehensive analysis of the entire genome using the Meg Allele Genotyping Bovine 10K SNP panel, as previously described by Hardenbol et al. (79) The average marker spacing on this chip was 325 kilobase pairs (kbp). The genotyping chip was used to analyze the genetic makeup of 189 cattle. This group included various breeds such as Angus, Brahman, Belmont Red, Hereford, Murray Grey, Santa Gertrudis, and Shorthorn. These animals were selected explicitly for having extreme RFI values. It is important to note that this group of bulls was a subset taken from a larger population of 1,472 cattle. In the study above, a total of 161 SNPs were identified as having a significant association ($P < 0.01$) with RFI when assessed individually. 76% of total genetic variation was noted among the 20 identified SNPs, positively associated with the RFI trait.

According to the meta-analysis conducted by Berry and Crowley (12), the overall heritability estimates for RFI in developing beef cattle were found to be 0.33, with a range of 0.07 to 0.62. Nevertheless, gene prediction accuracy in male cattle must be higher to select candidates without a suitable phenotypic measurement Kenny et al. (25). The estimation of breeding values that incorporate genomic information relies on the establishment of a reference population in which the trait of interest (such as FE) should have been measured, and bulls have been genotyped using suitable genomic markers (38, 80, 81). However, to our understanding, there is much lacking in the reference population data for beef cattle regarding the validation of the genomic data. The formation of such a population would require addressing various challenges, including diverse breeds, age variations, and nutritional management differences among beef cattle across the different research groups (25).

Currently, the primary emphasis of research in the field of genetic regulation of FE in bulls is the discovery of sets of genetic variants that have biological relevance to this feature (82, 62, 83). Extensive studies have been conducted on the genetic underpinnings of RFI in male bovines. In a study conducted by Chen et al. (84), some genes, namely GSTM1, GSTM2, and S100A10, were discovered as exhibiting differential expression in bulls characterized by high and low RFI. In a study conducted Cowan et al. (85), compelling evidence was discovered regarding the presence of a previously unidentified growth hormone allele that is linked to RFI in Holstein bulls. Similarly, another study by Herd and Bishop (86), provided empirical evidence highlighting the heritability of RFI in British Hereford cattle, as well as its positive associations with FCR and predicted maintenance energy expenditure. In a study conducted by Wang et al. (87), the researcher examined the consequences of choosing bulls with low RFI on breeding soundness and reproductive performance. The findings of the study indicated that there were no adverse impacts seen. The findings collectively indicate a multifaceted genetic foundation for RFI in male cattle, which may have significant ramifications for both the efficiency of feed use and reproductive capabilities.

A comprehensive study was conducted by Yang et al. (46), to display the integration and comparison of various transcriptome sequence data through the utilization of differential analysis, including functional enrichment analysis, protein-protein interaction (PPI) network analysis, weighted co-expression network analysis (WGCNA), and GSEA methodology. The researchers made predictions regarding the potential genes and functional analysis pathways strongly associated with beef cattle's RFI. In addition, their study's findings showed the expression of 20,002 genes, encompassing 345 genes that exhibited differential expressions (DEGs). Among these DEGs, 167 genes were upregulated, while 178 genes were observed to be downregulated in their group. Table 2 lists the 50 most upregulated genes and the 10 most downregulated genes and their gene locations. Out of the DEGs analyzed, four candidate genes (SHC1, GPX4, ACADL, and IGF1) were successfully identified and validated as marker genes for RFI in beef cattle.

Nevertheless, these variations must exhibit appropriate robustness across various bull breeds, developmental stages, and nutrition regimens, if they prove advantageous to the overall beef business. In a recent investigation by Seabury et al. (80),

a genome-wide association analysis was performed to investigate the relationship between QTLs and FE-related traits. The study utilized the Illumina Bovine HD (778K) and SNP50 assay platforms to identify QTLs that could potentially be utilized for genomic selection. In addition, some programs seek to integrate global DNA sequence data, such as the Global initiatives, the Canadian Cattle Genome Project, aim to integrate vast amounts of DNA sequence data, providing a foundation for the development of genomics-driven tools that can enhance the efficiency and sustainability of beef production (81), to create genomics-driven tools to improve beef production's effectiveness and long-term viability. The primary objective of joint investigations should center on identifying functional variants, with the support of imputation if required, to establish the association between these variants and economically significant traits such as FE and related characteristics (8). The future achievement in enhancing FE in beef cattle breeding will rely on integrating genetic data into national and international breeding programs that utilize multi-trait genomic selection.

CONCLUSION

This literature review concludes that RFI is an effective measure of FE in beef bulls and steers that is independent of growth and body measurements. The review analyzed over 200 studies conducted from 2012 to 2023, ultimately including 17 research papers that met the inclusion criteria. It identified 511 genes associated with RFI traits, distributed across 30 chromosomes, along with QTL regions for all identified genes. Notably, the study linked QTLs associated with RFI traits to chromosomes BTA6, BTA7, BTA8, and BTA11. Additionally, the review found 228 SNPs across these 30 chromosomal locations between 2012 and 2022. These findings highlight the potential to predict efficient beef bulls without compromising reproductive performance and fertility in multi-sire groups, pending further validation in other populations.

Conflicts of interest

The authors declare that they have no conflict of interest

Authors Contributions

All Authors who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the conception and design of this work or the analysis and interpretation of the data, as well as the writing of the manuscript, to take public responsibility for it. Authors believe the manuscript represents valid work. Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication.

References

1. Wendimu, A., and Tekalign, W. 2023. Conventional beef cattle farming practices in Wolaita and Sidama, Southern Ethiopia. *Am. J. Anim. Vet. Sci.*, 18:199-209.
2. Mahanta, S. K., Garcia, S. C., and Islam, M. R. 2020. Forage based feeding systems of dairy animals: issues, limitations and strategies. Range Manage. *Agrofor.*, 41:188-199.
3. Onteru, S. K., Gorbach, D. M., Young, J. M., Garrick, D. J., Dekkers, J. C. M., and Rothschild, M. F. 2013. Whole genome association studies of residual feed intake and related traits in the pig. *PLoS ONE*, 8:e61756. https://doi.org/10.1371/journal.pone.0061756
4. Li, J., Wang, Y., Mukiibi, R., Karisa, B., Plastow, G. S., and Li, C. 2022. Integrative analyses of genomic and metabolomic data reveal genetic mechanisms associated with carcass merit traits in beef cattle. *Sci. Rep.,* 12: Article 1. https://doi.org/10.1038/s41598-022-06567-z
5. Nielsen, M. K., MacNeil, M. D., Dekkers, J. C. M., Crews, D. H., Jr., Rathje, T. A., Enns, R. M., and Weaber, R. L. 2013. Review: Life-cycle, total-industry genetic improvement of feed efficiency in beef cattle: Blueprint for the Beef Improvement Federation. *Prof. Anim. Sci*., 29.
6. Foroutan, A., Fitzsimmons, C., Mandal, R., Berjanskii, M. V., and Wishart, D. S. 2020. Serum metabolite biomarkers for predicting residual feed intake (RFI) of young Angus bulls. *Metabolites,* 10: Article 12. https://doi.org/10.3390/metabo10120491
7. Fitzsimons, C., Kenny, D. A., and McGee, M. 2014. Visceral organ weights, digestion, and carcass characteristics of beef bulls differing in residual feed intake offered a high concentrate diet. *Animal*, 8:949-959. https://doi.org/10.1017/S1751731114000652
8. Taylor, R. F., McGee, M., Kelly, A. K., and Crosson, P. 2020. Bioeconomic and greenhouse gas emissions modelling of the factors influencing technical efficiency of temperate grassland-based suckler calf-to-beef production systems. *Agricultural Systems,* 183:102860.
9. Martin, P., Ducrocq, V., Faverdin, P., and Friggens, N. C. 2021. Invited review: Disentangling residual feed intake-Insights and approaches to make it more fit for purpose in the modern context. *J. Dairy Sci*., 104:6329-6342.
10. Terry, S. A., Basarab, J. A., Guan, L. L., and McAllister, T. A. 2020. Strategies to improve the efficiency of beef cattle production. *Can. J. Anim. Sci*., 101:1-19.
11. Chen, Y., Gondro, C., Quinn, K., Herd, R. M., Parnell, P. F., and Vanselow, B. 2011. Global gene expression profiling reveals genes expressed differentially in cattle with high and low residual feed intake. *Anim. Genet*., 42:475-490. https://doi.org/10.1111/j.1365-2052.2011.02182.x
12. Berry, D. P., and Crowley, J. J. 2013. Cell biology symposium: Genetics of feed efficiency in dairy and beef cattle. *J. Anim. Sci*., 91:1594-1613. https://doi.org/10.2527/jas2012-5862
13. Hardie, L. C., VandeHaar, M. J., Tempelman, R. J., Weigel, K. A., Armentano, L. E., Wiggans, G. R., Veerkamp, R. F., de Haas, Y., Coffey, M. P., Connor, E. E., Hanigan, M. D., Staples, C., Wang, Z., Dekkers, J. C. M., and Spurlock, D. M. 2017. The genetic and biological basis of feed efficiency in mid-lactation Holstein dairy cows. *J. Dairy Sci.*, 100. https://doi.org/10.3168/jds.2017-12604
14. Kenny, D. A., Fitzsimons, C., Waters, S. M., and McGee, M. 2018. Invited review: Improving feed efficiency of beef cattle-The current state of the art and future challenges. *Animal*, 12:1815-1826. https://doi.org/10.1017/S1751731118000976
15. Wood, B. J., Archer, J. A., and Van Der Werf, J. H. J. 2004. Response to selection in beef cattle using IGF-1 as a selection criterion for residual feed intake under different Australian breeding objectives. *Livest. Prod. Sci.*, 91:69-81.
16. Kahi, A. K., and Hirooka, H. 2007. Effect of direct and indirect selection criteria for efficiency of gain on profitability of Japanese Black cattle selection strategies. *J. Anim. Sci.*, 85:2401-2412.
17. Moore, S. S., Mujibi, F. D., and Sherman, E. L. 2009. Molecular basis for residual feed intake in beef cattle. *J. Anim. Sci*., 87:E41-E47. https://doi.org/10.2527/jas.2008-1418
18. Mononen, J., Kostensalo, J., Pesonen, M., Huuskonen, A., and Manni, K. 2022. Assessing the reliability of optimized residual feed intake measurements in beef cattle. *Ruminants*, 2:407-419.
19. Terry, S. A., Basarab, J. A., Guan, L. L., and McAllister, T. A. 2020. Strategies to improve the efficiency of beef cattle production. *Can. J. Anim. Sci*., 101:1-19.
20. Herd, R. M., Archer, J. A., and Arthur, P. F. 2003. Reducing the cost of beef production through genetic improvement in residual feed intake: Opportunity and challenges to application. *J. Anim. Sci*., 81: E10-E17. https://academic.oup.com/jas/article/81/13_suppl_1/E9/4789599
21. Archer, J. A., Reverter, A., Herd, R. M., and Arthur, P. F. 2023. Phenotypic and genetic relationships for feed intake, feed efficiency, body composition, and cow milk yield measured post-weaning and in mature beef cows. *Anim. Prod. Sci*., 63:1473-1482.
22. Foroutan, A., Fitzsimmons, C., Mandal, R., Berjanskii, M. V., and Wishart, D. S. 2020. Serum metabolite biomarkers for predicting residual feed intake (RFI) of young Angus bulls. *Metabolites*, 10:491.
23. Jorge-Smeding, E., Bonnet, M., Renand, G., Taussat, S., Graulet, B., Ortigues-Marty, I., and Cantalapiedra-Hijar, G. 2021. Common and diet-specific metabolic pathways underlying residual feed intake in fattening Charolais yearling bulls. *Sci. Rep.,* 11:24346.

24. Brunes, L. C., Baldi, F., Lopes, F. B., Lobo, R. B., Espigolan, R., Costa, M. F. O., and Magnabosco, C. U. 2021. Selection criteria for feed efficiency-related traits and their association with growth, reproductive, and carcass traits in Nelore cattle. *Anim. Prod. Sci*., 61:1633-1642.
25. Kenny, D. A., Fitzsimons, C., Waters, S. M., and McGee, M. 2018. Invited review: Improving feed efficiency of beef cattle - The current state of the art and future challenges. *Animal*, 12:1815-1826. https://doi.org/10.1017/S1751731118000976
26. Beef Improvement Federation. 2010. Guidelines for uniform beef improvement programs. *Beef Improvement Federation*, North Carolina State University, Raleigh, NC, USA. https://scholar.google.com/scholar?q=Beef%20Improvement%20Federation%202010.%20Animal%20evaluation.%20In%20Guidelines%20for%20uniform%20beef%20improvement%20programs%20(ed.%20LV%20Cundiff%2C%20LD%20Van%20Vleck%20and%20WD%20Hohenboken)%2C%20pp.%2016%E2%80%9355.%20Beef%20Improvement%20Federation%2C%20North%20Carolina%20State%20University%2C%20Raleigh%2C%20NC%2C%20USA.
27. Culbertson, M. M., Speidel, S. E., Peel, R. K., Cockrum, R. R., Thomas, M. G., and Enns, R. M. 2015. Optimum measurement period for evaluating feed intake traits in beef cattle. J. *Anim. Sci.*, 93:2482-2487.
28. Cassady, C. J., Felix, T. L., Beever, J. E., Shike, D. W., Taylor, J., Kerley, M., Schnabel, R., Marques, E., Garrick, D., Hansen, S., Loy, D., Weaber, R., Seabury, C., Beever, J., Shike, D., Fahrenkrug, S., Spangler, M., Johnson, K., Neibergs, H., Pollak, J. 2016. Effects of timing and duration of test period and diet type on intake and feed efficiency of Charolais-sired cattle. *J. Anim. Sci*., 94. https://doi.org/10.2527/jas.2016-0633
29. Wang, Z., Nkrumah, J. D., Li, C., Basarab, J. A., Goonewardene, L. A., Okine, E. K., Crews, D. H., and Moore, S. S. 2006. Test duration for growth, feed intake, and feed efficiency in beef cattle using the GrowSafe System. *J. Anim. Sci*., 84:2289-2298. https://doi.org/10.2527/jas.2005-715
30. Manafiazar, G., Basarab, J., McKeown, L., Stewart-Smith, J., Baron, V. S., MacNeil, M., and Plastow, G. 2017. Optimizing feed intake recording and feed efficiency estimation to increase the rate of genetic gain for feed efficiency in beef cattle. *Can. J. Anim. Sci*., 97. https://doi.org/10.1139/CJAS-2016-0118
31. Goonewardene, L. A., Okine, E., Wang, Z., Spaner, D., Mir, P. S., Mir, Z., and Marx, T. 2004. Residual metabolizable energy intake and its association with diet and test duration. *J. Anim. Sci.*
32. Sartori, L. V. C., Gurgeira, D. N., Crisóstomo, C., de Paz, C. C. P., Ferreira, J., and da Costa, R. L. D. 2024. Performance, feed efficiency, feeding behavior, and cortisol concentration of lambs ranked for residual feed intake and residual intake and gain. *Trop. Anim. Health Prod.*, 56:51.
33. Berry, D. P., Garcia, J. F., and Garrick, D. J. 2016. Development and implementation of genomic predictions in beef cattle. *Anim. Front*., 6:32-38. https://doi.org/10.2527/af.2016-0005
34. Al Husseini, W., Gondro, C., Quinn, K., Herd, R. M., Gibson, J. P., and Chen, Y. 2014. Expression of candidate genes for residual feed intake in Angus cattle. *Anim. Genet.,* 45:12-19. https://doi.org/10.1111/age.12092
35. Tan, W. L. A., Neto, L. R. P., Reverter, A., McGowan, M., and Fortes, M. R. S. 2023. Sequence level genome-wide associations for bull production and fertility traits in tropically adapted bulls. *BMC Genomics*, 24:365. https://doi.org/10.1186/s12864-023-09475-2
36. Meuwissen, T. H., Hayes, B. J., and Goddard, M. E. 2001. Prediction of total genetic value using genome-wide dense marker maps. *Genetics*, 157:1819-1829.
37. Matukumalli, L. K., Lawley, C. T., Schnabel, R. D., Taylor, J. F., Allan, M. F., Heaton, M. P., O'Connell, J., Moore, S. S., Smith, T. P. L., Sonstegard, T. S., and Van Tassell, C. P. 2009. Development and characterization of a high-density SNP genotyping assay for cattle. *PLoS ONE*, 4:e5350. https://doi.org/10.1371/journal.pone.0005350
38. Hayes, B. J., Bowman, P. J., Chamberlain, A. J., and Goddard, M. E. 2009. Invited review: Genomic selection in dairy cattle: Progress and challenges. *J. Dairy Sci*., 92:433-443. https://doi.org/10.3168/jds.2008-1646
39. Dekkers, J. C. M., and Hospital, F. 2002. The use of molecular genetics in the improvement of agricultural populations. *Nat. Rev. Genet*., 3:22-32. https://doi.org/10.1038/nrg701
40. Barendse, W., Reverter, A., Bunch, R. J., Harrison, B. E., Barris, W., and Thomas, M. B. 2007. A validated whole-genome association study of efficient food conversion in cattle. *Genetics*, 176:1893-1905. https://doi.org/10.1534/genetics.107.072637
41. Nkrumah, J. D., Sherman, E. L., Li, C., Marques, E., Crews, D. H., Bartusiak, R., Murdoch, B., Wang, Z., Basarab, J. A., and Moore, S. S. 2007. Primary genome scan to identify putative quantitative trait loci for feedlot growth rate, feed intake, and feed efficiency of beef cattle. *J. Anim. Sci*., 85(12). https://doi.org/10.2527/jas.2007-0234.
42. Sherman, E. L., Nkrumah, J. D., and Moore, S. S. 2010. Whole genome single nucleotide polymorphism associations with feed intake and feed efficiency in beef cattle. J. Anim. Sci., 88(1):16-22. https://doi.org/10.2527/jas.2008-1759.
43. Bolormaa, S., Hayes, B. J., Savin, K., Hawken, R., Barendse, W., Arthur, P. F., Herd, R. M., and Goddard, M. E. 2011. Genome-wide association studies for feedlot and growth traits in cattle. *J. Anim. Sci*., 89(6):1684-1697. https://doi.org/10.2527/jas.2010-3079.
44. Mujibi, F. D. N., Nkrumah, J. D., Durunna, O. N., Grant, J. R., Mah, J., Wang, Z., Basarab, J., Plastow, G., Crews, D. H., and Moore, S. S. 2011. Associations of marker panel scores with feed intake and efficiency traits in beef cattle using preselected single nucleotide polymorphisms. *J. Anim. Sci.,* 89(11):3362-3371. https://doi.org/10.2527/jas.2010-3362.
45. Snelling, W. M., Allan, M. F., Keele, J. W., Kuehn, L. A., Thallman, R. M., Bennett, G. L., Ferrell, C. L., Jenkins, T. G., Freetly, H. C., Nielsen, M. K., and Rolfe, K. M. 2011. Partial-genome evaluation of postweaning feed intake and efficiency of crossbred beef cattle. *J. Anim. Sci.,* 89(6):1731-1741. https://doi.org/10.2527/jas.2010-3526.
46. Yang, C., Zhu, Y., Ding, Y., Huang, Z., Dan, X., Shi, Y., and Kang, X. 2022. Identifying the key genes and functional enrichment pathways associated with feed efficiency in cattle. *Gene,* 807:145934. https://doi.org/10.1016/j.gene.2021.145934.
47. Karisa, B. K., Thomson, J., Wang, Z., Stothard, P., Moore, S. S., and Plastow, G. S. 2013. Candidate genes and single nucleotide polymorphisms associated with variation in residual feed intake in beef cattle. *J. Anim. Sci*., 91(8):3502-3513. https://doi.org/10.2527/jas.2012-6170.
48. Weber, K. L., Welly, B. T., Van Eenennaam, A. L., Young, A. E., Porto-Neto, L. R., Reverter, A., and Rincon, G. 2016. Identification of gene networks for residual feed intake in Angus cattle using genomic prediction and RNA-seq. *PLOS ONE*, 11(3):e0152274. https://doi.org/10.1371/journal.pone.0152274.
49. Fecteau, R. E., Kong, J., Kresak, A., Brock, W., Song, Y., Fujioka, H., Elston, R., Willis, J. E., Lynch, J. P., Markowitz, S. D., Guda, K., and Chak, A. 2016. Association between germline mutation in VSIG10L and familial Barrett neoplasia. *JAMA Oncol.,* 2(10):1333-1339. https://doi.org/10.1001/jamaoncol.2016.2054.
50. Kern, R. J., Zarek, C. M., Lindholm-Perry, A. K., Kuehn, L. A., Snelling, W. M., Freetly, H. C., Cunningham, H. C., and Meyer, A. M. 2017. Ruminal expression of the NQO1, RGS5, and ACAT1 genes may be indicators of feed efficiency in beef steers. *Anim. Genet*., 48(1):90-92. https://doi.org/10.1111/age.12490.
51. de las Heras-Saldana, S., Clark, S. A., Duijvesteijn, N., Gondro, C., van der Werf, J. H. J., and Chen, Y. 2019. Combining information from genome-wide association and multi-tissue gene expression studies to elucidate factors underlying genetic variation for residual feed intake in Australian Angus cattle. *BMC Genomics*, 20(1):939. https://doi.org/10.1186/s12864-019-6270-4
52. Alexandre, P. A., Naval-Sanchez, M., Porto-Neto, L. R., Ferraz, J. B. S., Reverter, A., and Fukumasu, H. 2019. Systems Biology Reveals NR2F6 and TGFB1 as Key Regulators of Feed Efficiency in Beef Cattle. *Front. Genet.*, 10. https://www.frontiersin.org/journals/genetics/articles/10.3389/fgene.2019.00230
53. Zhang, F., Wang, Y., Mukiibi, R., Chen, L., Vinsky, M., Plastow, G., Basarab, J., Stothard, P., and Li, C. 2020. Genetic architecture of quantitative traits in beef cattle revealed by genome wide association studies of imputed whole genome sequence variants: I: feed efficiency and component traits. *BMC Genomics*, 21:36. https://doi.org/10.1186/s12864-019-6362-1
54. Rathert, A. R., Meyer, A. M., Foote, A. P., Kern, R. J., Cunningham-Hollinger, H. C., Kuehn, L. A., and Lindholm-Perry, A. K. 2020. Ruminal transcript abundance of the centromere-associated protein E gene may influence residual feed intake in beef steers. *Anim. Genet*., 51(3):453-456. https://doi.org/10.1111/age.12926
55. Yang, C., Han, L., Li, P., Ding, Y., Zhu, Y., Huang, Z., Dan, X., Shi, Y., and Kang, X. 2021. Characterization and Duodenal Transcriptome Analysis of Chinese Beef Cattle With Divergent Feed Efficiency Using RNA-Seq. *Front. Genet.*, 12. https://www.frontiersin.org/journals/genetics/articles/10.3389/fgene.2021.741878
56. McKenna, C., Keogh, K., Porter, R. K., Waters, S. M., Cormican, P., and Kenny, D. A. 2021. An examination of skeletal muscle and hepatic tissue transcriptomes from beef cattle divergent for residual feed intake. *Sci. Rep.,* 11(1):8942. https://doi.org/10.1038/s41598-021-87842-3
57. Li, J., Mukiibi, R., Wang, Y., Plastow, G. S., and Li, C. 2021. Identification of candidate genes and enriched biological functions for feed efficiency

traits by integrating plasma metabolites and imputed whole genome sequence variants in beef cattle. *BMC Genomics*, 22:823. https://doi.org/10.1186/s12864-021-08064-5
58. Foroutan, A., Wishart, D. S., and Fitzsimmons, C. 2021. Exploring Biological Impacts of Prenatal Nutrition and Selection for Residual Feed Intake on Beef Cattle Using Omics Technologies: A Review. *Front. Genet.*, 12:720268. https://doi.org/10.3389/fgene.2021.720268
59. Taiwo, G. A., Idowu, M., Denvir, J., Cervantes, A. P., and Ogunade, I. M. 2022. Identification of Key Pathways Associated With Residual Feed Intake of Beef Cattle Based on Whole Blood Transcriptome Data Analyzed Using Gene Set Enrichment Analysis. *Front. Vet. Sci.*, 9. https://www.frontiersin.org/articles/10.3389/fvets.2022.848027
60. Taiwo, G., Idowu, M. D., Wilson, M., Pech-Cervantes, A., Estrada-Reyes, Z. M., and Ogunade, I. M. 2022. Residual Feed Intake in Beef Cattle Is Associated With Differences in Hepatic mRNA Expression of Fatty Acid, Amino Acid, and Mitochondrial Energy Metabolism Genes. *Front. Anim. Sci.*, 3. https://www.frontiersin.org/articles/10.3389/fanim.2022.828591
61. Li, J., Wang, Y., Mukiibi, R., Karisa, B., Plastow, G. S., and Li, C. 2022. Integrative analyses of genomic and metabolomic data reveal genetic mechanisms associated with carcass merit traits in beef cattle. *Sci. Rep.*, 12(1): Article 1. https://doi.org/10.1038/s41598-022-06567-z
62. Lindholm-Perry, A. K., Meyer, A. M., Kern-Lunbery, R. J., Cunningham-Hollinger, H. C., Funk, T. H., and Keel, B. N. 2022. Genes involved in feed efficiency identified in a meta-analysis of rumen tissue from two populations of beef steers. *Animals*, 12(12): 1514. https://doi.org/10.3390/ani12121514
63. Duarte, D. a. S., Newbold, C. J., Detmann, E., Silva, F. F., Freitas, P. H. F., Veroneze, R., and Duarte, M. S. 2019. Genome-wide association studies pathway-based meta-analysis for residual feed intake in beef cattle. *Anim. Genet.*, 50(2): 150-153. https://doi.org/10.1111/age.12761
64. Al-Husseini, W., Chen, Y., Gondro, C., Herd, R. M., Gibson, J. P., and Arthur, P. F. 2016. Characterization and profiling of liver microRNAs by RNA-sequencing in cattle divergently selected for residual feed intake. Asian-Australas. *J. Anim. Sci.*, 29(10): 1371-1382. https://doi.org/10.5713/ajas.15.0605
65. Kong, R. S. G., Liang, G., Chen, Y., Stothard, P., and Guan, L. L. 2016. Transcriptome profiling of the rumen epithelium of beef cattle differing in residual feed intake. *BMC Genomics*, 17(1): 592. https://doi.org/10.1186/s12864-016-2935-4
66. Kahi, A. K., Barwick, S. A., and Graser, H. U. 2003. Economic evaluation of Hereford cattle breeding schemes incorporating direct and indirect measures of feed intake. *Aust. J. Agric. Res.*, 54(10). https://doi.org/10.1071/AR03025
67. Hegarty, R. S., Goopy, J. P., Herd, R. M., and McCorkell, B. 2007. Cattle selected for lower residual feed intake have reduced daily methane production. *J. Anim. Sci.,* 85(6). https://doi.org/10.2527/jas.2006-236
68. Nkrumah, J. D., Okine, E. K., Mathison, G. W., Schmid, K., Li, C., Basarab, J. A., Price, M. A., Wang, Z., and Moore, S. S. 2006. Relationships of feedlot feed efficiency, performance, and feeding behavior with metabolic rate, methane production, and energy partitioning in beef cattle. *J. Anim. Sci.*, 84: 145-153. https://academic.oup.com/jas/article/84/1/145/4804175
69. Basarab, J. A., Price, M. A., and Okine, E. K. 2002. Commercialization of net feed efficiency. In Proceedings of the 23rd Western Nutritional Conference, Edmonton, Alberta, Canada, 183-194.
70. Crews, D. H. 2005. Genetics of efficient feed utilization and national cattle evaluation: A review. *Genet. Mol. Res.*, 4(2).
71. Herd, R. M., Archer, J. A., and Arthur, P. F. 2003. Reducing the cost of beef production through genetic improvement in residual feed intake: Opportunity and challenges to application. *J. Anim. Sci.*, 81(13_suppl_1): E10-E17. https://academic.oup.com/jas/article/81/13_suppl_1/E9/4789599
72. Koch, R. M., Swiger, L. A., Chambers, D., and Gregory, K. E. 1963. Efficiency of feed use in beef cattle. *J. Anim. Sci.,* 22(2): 486-494. https://doi.org/10.2527/jas1963.222486x
73. McDonald, T. J., Brester, G. W., Bekkerman, A., and Paterson, J. A. 2010. CASE STUDY: Searching for the ultimate cow: The economic value of residual feed intake at bull sales. *Prof. Anim. Sci.,* 26(6): 655-660.
74. Butler, M. L., Hartman, A. R., Bormann, J. M., Weaber, R. L., Grieger, D. M., and Rolf, M. M. 2022. Genome-wide association study of beef bull semen attributes. *BMC Genomics*, 23(1): 74. https://doi.org/10.1186/s12864-021-08256-z
75. Shirzadifar, A., Miar, Y., Plastow, G., Basarab, J., Li, C., Fitzsimmons, C., Riazi, M., and Manafiazar, G. 2023. A machine learning approach to predict the most and the least feed-efficient groups in beef cattle. *Smart Agric. Technol.*, 5: 100317. https://doi.org/10.1016/j.atech.2023.100317
76. Basarab, J. A., Price, M. A., Aalhus, J. L., Okine, E. K., Snelling, W. M., and Lyle, K. L. 2003. Residual feed intake and body composition in young growing cattle. *Can. J. Anim. Sci.*, 83(2). https://doi.org/10.4141/A02-065
77. Carstens, G. E., Theis, C. M., White, M. B., Welsh Jr., T. H., Warrington, B. G., Randel, R. D., Forbes, T. D. A., Lippke, H., Greene, L. W., and Lunt, D. K. 2002. Relationships between net feed intake and ultrasound measures of carcass composition in growing beef steers. *Beef Cattle Res. Texas*, 2: 31-34.
78. Paulino, P. V., Castro, F. C., Magnabosco, A. C., and Sainz, R. D. 2004. Performance and residual feed intake differences between steers housed in individual or group pens. *J. Dairy Sci.,* 87: 43-43.
79. Hardenbol, P., Yu, F., Belmont, J., MacKenzie, J., Bruckner, C., Brundage, T., Boudreau, A., Chow, S., Eberle, J., Erbilgin, A., Falkowski, M., Fitzgerald, R., Ghose, S., Iartchouk, O., Jain, M., Karlin-Neumann, G., Lu, X., Miao, X., Moore, B., Gibbs, R. A. 2005. Highly multiplexed molecular inversion probe genotyping: Over 10,000 targeted SNPs genotyped in a single tube assay. *Genome Res.*, 15(2): 269-275. https://doi.org/10.1101/gr.3185605
80. Seabury, C. M., Oldeschulte, D. L., Saatchi, M., Beever, J. E., Decker, J. E., Halley, Y. A., Bhattarai, E. K., Molaei, M., Freetly, H. C., Hansen, S. L., Yampara-Iquise, H., Johnson, K. A., Kerley, M. S., Kim, J., Loy, D. D., Marques, E., Neibergs, H. L., Schnabel, R. D., Shike, D. W., Taylor, J. F. 2017. Genome-wide association study for feed efficiency and growth traits in U.S. beef cattle. *BMC Genomics*, 18(1): 386. https://doi.org/10.1186/s12864-017-3754-y
81. Stothard, P., Liao, X., Arantes, A. S., De Pauw, M., Coros, C., Plastow, G. S., Sargolzaei, M., Crowley, J. J., Basarab, J. A., Schenkel, F., Moore, S., and Miller, S. P. 2015. A large and diverse collection of bovine genome sequences from the Canadian Cattle Genome Project. *GigaScience,* 4: 49. https://doi.org/10.1186/s13742-015-0090-5
82. Fitzsimons, C., McGee, M., Keogh, K., Waters, S. M., and Kenny, D. A. 2017. Molecular physiology of feed efficiency in beef cattle. In C. G. Scanes and R. A. Hill (Eds.), Biology of Domestic Animals (1st ed., pp. 122-165). *CRC Press*. https://doi.org/10.1201/9781315152080-6
83. Lu, D., Sargolzaei, M., Li, C., Abo-Ismail, M., Vander Voort, G., Wang, Z., Plastow, G., Moore, S., and Miller, S. P. 2013. Association analysis for feed efficiency traits in beef cattle using preserved haplotypes. *Genome,* 56(10): 586-591. https://doi.org/10.1139/gen-2013-0072
84. Chen, Y., Arthur, P. F., Herd, R. M., Quinn, K., and Barchia, I. M. 2012. Using genes differentially expressed in bulls to classify steers divergently selected for high and low residual feed intake. *Anim. Prod. Sci.*, 52(7): 608-612. https://doi.org/10.1071/AN11266
85. Cowan, C. M., Dentine, M. R., Ax, R. L., and Schuler, L. A. 1989. Restriction fragment length polymorphisms associated with growth hormone and prolactin genes in Holstein bulls: Evidence for a novel growth hormone allele. *Anim. Genet.,* 20(3): 157-165. https://doi.org/10.1111/j.1365-2052.1989.tb00853.x
86. Herd, R. M., and Bishop, S. C. 2000. Genetic variation in residual feed intake and its association with other production traits in British Hereford cattle. *Livest. Prod. Sci.*, 63(2). https://doi.org/10.1016/S0301-6226(99)00122-0
87. Wang, Z., Colazo, M. G., Basarab, J. A., Goonewardene, L. A., Ambrose, D. J., Marques, E., Plastow, G., Miller, S. P., and Moore, S. S. 2012. Impact of selection for residual feed intake on breeding soundness and reproductive performance of bulls on pasture-based multisire mating. *J. Anim. Sci.*, 90(9): 2963-2969. https://doi.org/10.2527/jas.2011-4521

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