UNIVERSIDAD NACIONAL AUTÓNOMA DE MÉXICO
DOCTORADO EN CIENCIAS DE LA SALUD Y PRODUCCIÓN ANIMAL

EVALUACIÓN GENÓMICA DE CARACTERÍSTICAS REPRODUCTIVAS Y CRECIMIENTO EN GANADO SIMMENTAL Y SIMBRAH

TESIS
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DEDICATORIAS

Para mi esposa **Karen M. Reyes Briones** y mis queridos hijos **René** y **Rebeca**:

Quiero expresarles la profunda gratitud y el amor que siento por cada uno de ustedes. A lo largo de todos estos años, su apoyo incondicional y su presencia constante a mi lado han sido un gran impulso en mi vida.

No importa lo que el futuro nos depare, tengan la certeza de que siempre estaré para ustedes. Los llevo en lo más profundo de mi ser y mi amor por ustedes solo crece.

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RESUMEN

El objetivo de esta investigación fue identificar regiones genómicas asociadas a características de crecimiento y reproductivas en bovinos Simmental y Simbrah a través de GWAS (estudio de asociación del genoma completo). El estudio incluyó datos fenotípicos de características de crecimiento y reproductivas, así como datos genómicos usan paneles de alta densidad (GGP Bovine 150k).

En el primer capítulo se encontró una diferencia en la magnitud de las probabilidades posteriores entre las razas entre los análisis de asociación del genoma y de los cromosomas. Un total de 110, 143 y 302 SNP se asociaron con GWAS y CWAS (estudio de asociación por cromosoma) para características de crecimiento en los análisis de datos de Simmental, Simbrah y conjuntos, respectivamente. Se destaca del análisis de enriquecimiento de las vías de ARN polimerasa (POLR2G, POLR3E) y sinapsis GABAérgica (GABRR1, GABRR3) para ganado Simmental y vía de señalización de p53 (BID, SERPINB5) para ganado Simbrah.

Conclusión: Sólo el 6.265% de los marcadores asociados con características de crecimiento se encontraron usando CWAS y GWAS. Los marcadores asociados mediante el análisis CWAS, que no se asociaron mediante el GWAS, representan información que debido al modelo y antecedentes no se asoció con las características.

En el segundo capítulo después del control de calidad, se utilizaron 105,129 SNP autosómicos de 967 animales. Los bloques de haplotipos se definieron en función del desequilibrio de ligamiento. La asociación entre haplotipos y SNP para características reproductivas y tamaño corporal se realizó utilizando modelos bayesianos y frecuentistas. 23, 13, 7 y 2 SNP mostraron asociaciones con talla corporal (FS), circunferencia escrotal (SC), fertilidad en vaquillas (HF) y permanencia productiva (STAY), respectivamente.

Además, los haplotipos 7, 8, 7 y 1 mostraron asociaciones con FS, SC, HF y STAY, respectivamente. Dentro de estos segmentos genómicos delineados, se asociaron genes candidatos potenciales.

Las regiones asociadas tienen el potencial de brindar información acerca de las características de interés económico en el ganado Simmental y Simbrah. Además, los genes propuestos pueden ser útiles para descubrir las rutas genéticas a través de técnicas de análisis de enriquecimiento.

Palabras clave: GWAS, SNP, Ganado de Carne, Genética, Genómica.

ABSTRACT

The objective of this research was to identify genomic regions associated with growth and reproductive traits in Simmental and Simbrah cattle through GWAS (genome-wide association study). The study included phenotypic data on growth and reproductive traits, as well as genomic data using high-density panels (GGP Bovine 150k).

In the first chapter, a difference in the magnitude of posterior probabilities between breeds was found between the genome and chromosome association analyses. A total of 110, 143, and 302 SNPs were associated with GWAS and CWAS (chromosome-based association study) for growth traits in the Simmental, Simbrah, and ensemble data analyses, respectively. It stands out from the enrichment analysis of the RNA polymerase pathways (POLR2G, POLR3E) and GABAergic synapse (GABRR1, GABRR3) for Simmental cattle and p53 signaling pathway (BID, SERPINB5) for Simbrah cattle.

Conclusion: Only 6.265% of the markers associated with growth traits were found using CWAS and GWAS. The markers associated by the CWAS analysis, which were not associated by the GWAS, represent information that due to the model and background was not associated with the traits.

In the second chapter after quality control, 105,129 autosomal SNPs from 967 animals were used. Haplotype blocks were defined based on linkage disequilibrium. The comparison between haplotypes and SNPs for reproductive traits and FS (frame score) was performed using Bayesian and frequentist models. 23, 13, 7 and 2 SNPs showed associations with FS, scrotal circumference (SC), heifer fertility (HF) and productive stay (STAY), respectively. Furthermore, haplotypes 7, 8, 7, and 1 showed associations with FS, SC, HF, and STAY, respectively. Within these delineated genomic segments, potential candidate genes were associated.

The associated regions have the potential to provide information about traits of economic interest in Simmental and Simbrah cattle. Furthermore, the proposed genes may be useful for discovering genetic pathways through enrichment analysis techniques.

Key words: GWAS, SNP, CATTLE, GENETICS, GENOMICS, GROWTH TRAITS, REPRODUCTIVE TRAITS

PERMISOS DE REIMPRESIÓN

Date: 29/10/2023

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Dear Dr. RENE CALDERON CHAGOYA:

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Dear Dr. CALDERON-CHAGOYA,

Thank you very much for your e-mail. The Editorial Office agreed to the inclusion of the article you accepted for publication in Genes, in your doctoral thesis.

Please note that the published paper should be cited as Genes' publication in your doctoral thesis references' section.

Please do not hesitate to contact us if you have any questions.

Congratulations on finishing your doctoral thesis!

Kind regards,

Mr. Jason Li

Assistant Editor

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INTRODUCCIÓN

La producción de carne bovina es una actividad económica de gran importancia en todo el mundo. El sector ganadero busca constantemente mejorar su producción, lo que ha llevado al mejoramiento genético a convertirse en un área de estudio fundamental para los sistemas de producción. En este sentido, la selección genética se presenta como una estrategia que busca la identificación de animales con características deseables y su uso como progenitores para mejorar la siguiente generación.

Actualmente, gracias al desarrollo de nuevas tecnologías y la disponibilidad de información genómica de alta densidad en el ganado bovino, tenemos acceso a nuevas herramientas para el estudio de características de interés económico en el ganado bovino. Un claro ejemplo de esto son los análisis de asociación del genoma completo (GWAS, por sus siglas en inglés), los cuales se ha utilizado como una herramienta para identificar variantes genéticas asociadas con características de interés económico.

El uso del GWAS nos permite comprender mejor la arquitectura genética de las características de interés económico en diversas especies (Korte y Farlow, 2013), lo que puede llevar a un mejor conocimiento de los mecanismos biológicos que subyacen a estas características. Sin embargo, uno de los principales problemas en los GWAS son las asociaciones falsas. Estas pueden disminuir si se tiene un buen control de calidad de los datos, no hay estratificación en la población y los individuos muestreados son unidades estadísticamente independientes tomadas de la población (Sharma *et al*., 2015). Si no se tienen en cuenta estos factores, las

pruebas de asociación pueden dar lugar a asociaciones espurias o pueden tener tasas de error de tipo I infladas.

El objetivo principal de esta investigación es identificar regiones asociadas a través del GWAS a características de crecimiento y reproductivas en bovinos Simmental y Simbrah.

Para cumplir este objetivo, se recopilaron datos genómicos y fenotípicos de bovinos Simmental y Simbrah de México. Los fenotipos fueron obtenidos a través de la Asociación Mexicana Simmental-Simbrah de México A.C. Los datos genéticos se han obtenido a través de la genotipificación con paneles de alta densidad. Los datos fenotípicos incluyen información de peso al nacer, peso al destete, peso al año, talla corporal, circunferencia escrotal, fertilidad en vaquillas y permanencia productiva.

CAPÍTULO 1: REVISIÓN LITERARIA

DIVERSIDAD GENÉTICA ENTRE LAS RAZAS MODERNAS

Se considera que el ganado bovino actual desciende del extinto aurochs (*Bos primigenius*), con sus principales exponentes, el ganado *Bos taurus* y *Bos indicus*. A través del estudio del ADN mitocondrial, se aprecia que ambos grupos proceden de diferentes poblaciones de *Bos primigenius* de hace más de 200,000 años (Loftus *et al*., 1994).

La arqueología ha mostrado evidencia de la domesticación del ganado bovino en la época del Neolítico. En el caso del ganado *Bos indicus* existe evidencia de su presencia en Jordania hace más de 3000 años, misma región donde se encontraba Mesopotamia. Dicha zona, era también conocida por su intercambio comercial, lo que pudo apoyar al intercambio de material genético en el ganado de la región (Neumann y Parpola, 1987). Esta región geográfica, tuvo un periodo de calentamiento y aridez, factores que pudieron haber favorecido una mejor adaptación del ganado a zonas áridas (Loftus *et al*., 1999).

En el caso del ganado europeo, este se extendió por toda Europa a través de la migración de los primeros agricultores, donde a medida que se establecieron se produjo un mestizaje esporádico entre el ganado doméstico y ganado europeo nativo, que persistió en algunas regiones hasta la Edad Media (Upadhyay *et al*., 2017).

Esto coincide con los estudios sobre el tamaño efectivo de la población a través de las generaciones, lo cuales sugieren dos puntos de tiempo distintos. El primero, hace ~2000 generaciones (~ 12,000 años), momento en el que todos los tamaños de población parecen converger, en comparación con períodos anteriores (Villa-

Angulo *et al*., 2009). El segundo punto distintivo se encuentra en las 100 generaciones más recientes, que muestran una fuerte disminución en el tamaño efectivo de la población, lo que sugiere que todas las razas en este estudio experimentaron un cuello de botella poblacional (Villa-Angulo *et al*., 2009). Dos eventos pueden haber contribuido sustancialmente a esta reducción en el tamaño efectivo de la población en este segundo evento: El primero fue la intensificación del aislamiento de la población, principalmente en Europa. Lo cual inicio con la Gran Hambruna de 1315–1322, seguida de una serie de crisis a gran escala a principios del siglo XIV, que provocó reducciones significativas en la población humana debido a una gran escasez de alimentos, y una reducción dramática en el tamaño de la población de ganado principalmente debido a la plaga de Murrain (Kershaw, 1973). El segundo evento, la alta presión de selección de características específicas y el uso de la inseminación artificial, que han reducido drásticamente el número de sementales útiles en los últimos 50 años (Villa-Angulo *et al*., 2009).

Los cambios fisiológicos relacionados con el aumento en la producción durante las últimas décadas, como el balance energético negativo, la atenuación del estrés por calor, entre otros, constituyen cambios en la expresión de nuevos genes polimórficos, que incorporan alelos favorables a través de la selección (Weller *et al*., 2017). La expresión de dichas regiones puede ser debida a un grupo reciente de mutaciones con grandes efectos, los cuales se diseminan rápidamente en la población y a otro grupo grande de genes con bajas frecuencias de alelos menores los cuales permanecen silenciados hasta poder expresarse en un entorno apropiado, lo cual se ha denominado "adaptación poligénica" (Druet *et al*., 2014).

Estos cambios en la historia demográfica junto con la deriva genética, las migraciones, la subdivisión de las poblaciones, la selección, las tasas de mutación variables y la conversión de genes podrían modificar la relación entre las estimaciones de desequilibrio de ligamiento (LD) y podría explicar la variabilidad observada entre razas (Cañas-Álvarez *et al*., 2016).

LA ARQUITECTURA GENETICA DEL GANADO BOVINO

A partir de la década de los años 1950, se implementaron esquemas de prueba de progenie en los programas ganaderos en la mayoría de los países desarrollados (Robertson y Rendel, 1950). Sin embargo, aunque los toros alcanzan la madurez sexual a una edad temprana, se debe esperar un periodo de tiempo prolongado para que los registros de la primera generación de crías estén disponibles, aproximadamente 5 años, lo cual es la principal desventaja del esquema de prueba de progenie.

En la década de 1960, surgió el uso de la electroforesis en gel para estudiar polimorfismos de proteínas, lo que permitió estudiar la variación genética en las poblaciones de ganado. Con la llegada de la genética molecular en la década de 1970, se contemplaron nuevas posibilidades para identificar genes o regiones genómicas que regulan características de interés (Smith y Simpson, 1986). Durante la década de 1980, el desarrollo de la PCR y los métodos de secuenciación permitieron el surgimiento de la genómica como disciplina.

A principios del siglo XXI, con el primer borrador de la secuencia del genoma humano, se inició una nueva etapa para la genómica (Venter *et al*., 2001). El genoma del ganado bovino (*Bos taurus*) fue secuenciado y ensamblado en 2009

(Tellam *et al*., 2009). El genoma bovino consiste en alrededor de 3 mil millones de pares de bases y ~22 000 genes, de los cuales más del 60% son similares a todos los mamíferos, y el 80 % de los genes codificadores de proteínas dentro del genoma bovino tiene homólogos humanos.

Las secuencias genómicas de referencia son necesarias para comprender la biología del ganado bovino, estudiar la diversidad genética e implementar la selección genómica en los programas de mejoramiento animal (Saravanan, Panigrahi, Kumar, Nayak, *et al*., 2022). Hay ensamblajes de genoma actualmente disponibles para el ganado *Bos taurus*: Bos_taurus_UMD3.1.1 de la Universidad de Maryland, ARS-UCD1.3 de la USDA-ARS, Btau_5.0.1 y Btau_4.6.1 de Cattle Genome Sequencing International Consortium; en cuanto al genoma de las razas *Bos indicus* existe el panel de referencia Bos_indicus_1.0 de Genoa Biotecnologia SA y para el ganado cruzado está el panel de referencia UOA_Brahman_1 de la University of Adelaide. Todos los paneles de referencia antes mencionados se encuentran visibles en la herramienta Genome Data Viewer del NCBI, el cual es un navegador de genomas que permite analizar, explorar y comparar ensamblajes de diversas especies (Rangwala *et al*., 2021).

Con la introducción de estas secuencias genómicas a través de paneles de marcadores polimorfismo de un solo nucleótido (SNP) de alta densidad, el uso de la genómica en la ganadería se ha convertido en una realidad (Van Tassell *et al*., 2008). En los países más desarrollados, los costos de genotipificación están en un punto en que puede justificarse económicamente para las decisiones de gestión a nivel de hato (Thomasen *et al*., 2014).

Esto ha desencadenado el desarrollo en abundancia de nuevas metodologías, modelos estadísticos de locus único y multilocus, con enfoques bayesianos y machine learning. Sin embargo, actualmente no hay acuerdo sobre cuál es el “mejor” método. Las principales aplicaciones de los datos genómicos se pueden dividir en: (i) investigación de la diversidad genética y la composición de la raza/estructura de la población; (ii) identificación de variantes genéticas y loci de características cuantitativas (QTL) relacionados con características de importancia económica; (iii) mejorar los programas de mejoramiento genético por selección genómica (Saravanan, Panigrahi, Kumar, Nayak, *et al*., 2022). No obstante, con las nuevas herramientas genómicas, el principal factor que limita la precisión es el número de toros con genotipos y registros de hijas (VanRaden *et al*., 2009).

Antes del uso de la genómica, la mayoría de los estudios que intentaron simular los genes subyacentes a características de interés, asumieron una distribución que postulaba unos pocos QTL grandes y muchos pequeños (Weller, 2009).

Los avances en la genómica han resultado en una mayor comprensión de la arquitectura genética (Saravanan, Panigrahi, Kumar, Nayak, *et al*., 2022). Fisher (1918), demostró que, si muchos genes afectan una característica, entonces el muestreo aleatorio de alelos en cada gen produce un fenotipo continuo normalmente distribuido en la población. A medida que la cantidad de genes crece mucho, la contribución de cada gen se vuelve correspondientemente más pequeña, lo que lleva al límite del conocido "modelo infinitesimal".

Sin embargo, los SNP que contribuyen con la mayor parte de la heredabilidad tienden a estar repartidos por todo el genoma y no están cerca de los genes con funciones específicas. Para dar sentido a estas observaciones, se ha propuesto un

modelo "omnigénico", este divide los genes no por vía, sino por su proximidad en términos de causalidad al fenotipo. Los genes “básicos” son aquellos en los que el producto génico tiene un efecto directo sobre el fenotipo. Por lo general, hay pocos genes de este tipo y, por lo tanto, las variantes genéticas que afectan la función o la regulación de esos genes ("variantes centrales") explican una pequeña proporción de la heredabilidad. Por el contrario, los genes "periféricos" afectan al fenotipo indirectamente, a través de una red de interacciones con otros genes periféricos y centrales. Debido a que hay muchos más genes de este tipo, la mayor parte de la heredabilidad de cualquier característica en particular se explica por variantes que afectan a los genes periféricos, en lugar de centrales ("variantes periféricas") (Boyle *et al*., 2017).

Por otro lado, la diversidad genética entre las razas de ganado es muy importante para la adaptación a las condiciones ambientales cambiantes (Saravanan, Panigrahi, Kumar, y Bhushan, 2022). Estudiar esta diversidad a través de la caracterización genética de las razas permite determinar la variabilidad genética, elemento fundamental en los programas de mejoramiento y conservación de razas. Esta variación se mantiene mediante el aumento de la frecuencia de alelos raros, nuevas mutaciones y cambios en los objetivos de selección y manejo (Weller *et al*., 2017).

Debido a la diferente arquitectura genética entre las razas y la naturaleza poligénica de las características complejas, se encuentran diferentes regiones y diferentes genes asociados con la misma característica en diferentes razas de la misma especie. Los GWAS han demostrado ser un método ideal para identificar genes

asociados con varios fenotipos y dilucidar los mecanismos de las características complejas (Sharma *et al*., 2015).

Se han generado mapas de LD de alta resolución y caracterizaciones de la estructura de bloques de haplotipos para diferentes organismos, lo que confirma que dilucidar en escala fina la estructura de LD a nivel de población es crucial para comprender la naturaleza de la asociación entre genes y características fenotípicas, como enfermedades complejas y QTL (Villa-Angulo *et al*., 2009).

A través de repositorios digitales como Cattle QTL, conocemos información sobre regiones asociadas a características de interés económico. Actualmente Cattle QTL contiene 193,898 QTL o asociaciones de 1130 publicaciones para 680 características diferentes (Hu *et al*., 2022).

No obstante, algunas investigaciones podrían proporcionar asociaciones falsas. El control de calidad de los datos es uno de los pasos más importantes para minimizar los errores en un estudio GWAS. Los enfoques para la elaboración del análisis se basan en dos suposiciones fundamentales: primero, la población bajo estudio debe ser genéticamente homogénea, es decir, no debe haber estratificación de la población; segundo, todos los sujetos de las muestras deben representar unidades estadísticamente independientes extraídas de esa población. Otro escenario es que los individuos relacionados comparten alelos tanto causales como no causales, y que el LD entre estos sitios puede conducir a malinterpretaciones de los marcadores (den Berg *et al*., 2019; Sharma *et al*., 2015).

Si a lo anterior le aunamos que en los modelos multirraciales podemos encontrar diferencias en el LD, con la disimilitud más clara entre las poblaciones de *Bos taurus*

y *Bos indicus*, ya que, a distancias cortas del marcador, las razas *Bos indicus* tienen un LD más bajo en comparación con las razas *Bos taurus* (Porto-Neto *et al*., 2014). La variabilidad entre diferentes razas también se puede observar en el comportamiento de los valores de LD entre cromosomas. Una amplia variación en las tasas de recombinación autosómica puede conducir a una marcada diversidad en el patrón de LD en diferentes regiones genómicas y en cromosomas, pero las diferencias también pueden deberse a niveles de heterocigosidad, deriva genética o selección (Cañas-Álvarez *et al*., 2016).

La disminución de LD en el genoma determina el poder de detección en los estudios de asociación de genoma completo e indica la densidad de marcadores necesaria para una selección genómica precisa (Cañas-Álvarez *et al*., 2016). Se ha señalado que para tener el mismo poder de detectar la asociación entre el QTL y el marcador, el tamaño de la muestra debe incrementarse aproximadamente 1/r2 en comparación con el tamaño de la muestra para detectar directamente la asociación con la mutación causal (Pritchard y Przeworski, 2001). En el contexto de la selección genómica, la precisión depende tanto de la cantidad de LD entre QTL y marcadores como del número de registros disponibles para estimar los efectos de los marcadores (Toosi *et al*., 2010).

MÉTODOS ESTADÍSTICOS PARA GWAS

Los GWAS tienen como objetivo asociar SNP con una característica de interés para comprender mejor la arquitectura genética y mejorar la precisión y persistencia de la predicción genómica.

Con el aumento del número de SNP utilizados para GWAS, especialmente hasta las secuencias imputadas del genoma completo, se espera que aumente el número de asociaciones de falsos positivos y la elección de un umbral de significación apropiado se convierte en un reto. Aunque todo el concepto de umbrales significativos no debe malinterpretarse para asumir la causalidad y la reproducibilidad de los efectos de los SNP (Baker, 2016), es un concepto útil para la cría de animales para preseleccionar y ponderar diferencialmente los SNP en la predicción genómica entre razas (Raymond *et al*., 2018).

Como ya se mencionó anteriormente, la eficacia del GWAS en el estudio de características complejas está determinada por múltiples factores que deben tenerse en cuenta al realizar los estudios. Entre estos se encuentran, la variación fenotípica, tamaño de población, estructura de la población, LD, densidad de marcadores, frecuencias alélicas, umbral de significancia y el modelo estadístico.

En cuanto al modelo estadístico, los GWAS buscan encontrar marcadores genéticos que estén significativamente asociados con la variación en el fenotipo. Básicamente, el concepto de GWAS se deriva de una prueba estadística simple (por ejemplo, ANOVA) donde el modelo prueba cada marcador individualmente para una posible asociación (Bush y Moore, 2012). Sin embargo, una limitante con estos modelos son la presencia de falsos positivos, por lo que se han desarrollado varios procedimientos estadísticos para controlar las tasas de error de tipo I y tipo II mediante la incorporación de la estructura (matriz Q) y el parentesco (matriz K) como cofactores en los modelos (Tibbs Cortes *et al*., 2021). Pero, la sobre corrección de la estructura de la población puede conducir a una mayor tasa de falsos negativos. Esto ha causado el desarrollo de múltiples métodos en los que se

incorporan diferentes cofactores y se reduce el tiempo de cálculo. Entre los modelos más comúnmente utilizados podemos encontrar modelos estadísticos de locus único y multilocus, y con enfoques bayesianos.

Modelos de locus único

El método estándar utilizado en GWAS es el análisis de locus único, como el que se utiliza un modelo lineal mixto. A pesar de su simplicidad y velocidad, el análisis de un solo locus asume firmemente que solo un QTL tiene efecto. Esto es en gran medida válido para las características poligénicas, donde los QTL distintos del que se prueban pueden explicarse adecuadamente por el término poligénico (Tibbs Cortes *et al*., 2021).

La detección de SNP basada en un modelo aditivo es la primera recomendación para elegir un algoritmo genético apropiado (Manolio, 2013). Después de seleccionar el algoritmo genético adecuado, se pueden implementar diferentes pruebas estadísticas como el análisis de varianza (ANOVA), la prueba t, la prueba exacta de Fisher, la prueba de chi-cuadrado, la prueba de tendencia de Cochran-Armitage y la prueba de razón de probabilidades para las pruebas de un solo locus. (Manolio, 2013).

El primer modelo GWAS desarrollado fue un modelo lineal general (GLM), que incluía el control genómico, la asociación estructurada y las pruebas de modelos de asociación basadas en familias, que tenían en cuenta la estructura de la población para reducir el sobreajuste y los falsos descubrimientos en las regiones genómicas (Pritchard *et al*., 2000). Sin embargo, GLM tiende a no identificar adecuadamente relaciones como el parentesco, lo que condujo al desarrollo de nuevos métodos de

GWAS basados en un modelo lineal mixto (MLM) que incorpora simultáneamente la estructura de la población y el parentesco en los análisis (Z. Zhang *et al*., 2010). En los modelos MLM, la estructura de la población o los componentes principales se consideran como un efecto fijo y el parentesco se ajusta como una estructura de varianza-covarianza aleatoria entre genotipos (Yu *et al*., 2006).

Para aumentar el poder estadístico de la detección y reducir el tiempo de cálculo en MLM, se desarrollaron modelos como MLM comprimido (CMLM) y modelos CMLM enriquecidos (ECMLM). CMLM tiene en cuenta la agrupación de genotipos en diferentes grupos y el método ECMLM se basa en CMLM con un parámetro adicional, que investiga alternativas para medir el parentesco entre un grupo diferente de genotipos como el promedio de parentesco individual por parejas (Li *et al*., 2014).

Uno de los principales problemas con los modelos basados en MLM es el tiempo de cálculo, lo que llevo a los modelos como: asociación eficiente de modelos mixtos (EMMA), la asociación eficiente de modelos mixtos acelerada (EMMAX) y la asociación eficiente de modelos mixtos en todo el genoma (GEMMA).

El modelo EMMA reduce el tiempo de cálculo al convertir la optimización bidimensional de los componentes de la varianza residual y genética en una optimización unidimensional al calcular la probabilidad en función de su relación (Kang *et al*., 2008). EMMAX estiman los componentes de la varianza o la relación sin iteraciones y luego los ajustan a los marcadores de prueba (Wen *et al*., 2018). El modelo GEMMA tiene la misma estrategia informática que EMMAX, pero calcula los parámetros de población para cada marcador genético probado (Z. Zhang *et al*., 2010).

En GWAS de locus único, una preocupación clave es la alta tasa de falsos positivos. Para reducirlo, la corrección de Bonferroni se aplica con frecuencia en los métodos de locus único, incluidos EMMAX, GEMMA, ECMLM y MLM (Y.-M. Zhang *et al*., 2019).

En genética humana, el umbral del valor p de significancia para todo el genoma de 5×10^{-8} se ha convertido en un estándar para GWAS de variante común (Y.-M. Zhang *et al*., 2019). Sin embargo, esta corrección o el valor de p crítico en genética humana es demasiado estricto para detectar ciertas regiones asociados en características de interés económica en el ganado. Para abordar este problema, se ha propuesto una corrección de Bonferroni modificada; es decir, se reemplaza el número de marcadores (m) en las fórmulas de corrección por el número efectivo de marcadores (me) (S.-B. Wang *et al*., 2016). En el análisis de datos reales con ganado bovino, se aplican con frecuencia algunos umbrales de valor p subjetivos y menos estrictos para un nivel significativo debido a un gran error experimental (Xu *et al*., 2018).

Modelos Multilocus

En muchos estudios, los modelos GWAS de locus único no excedieron significativamente el umbral de significancia, por lo que recurren a métodos de GWAS de múltiples locus. Dado que el método de locus único tiene menos poder para detectar SNP con efectos menores e ignora la presencia de QTL en características cuantitativas. Sin embargo, los modelos multilocus consideran múltiples QTL y los tratan como efectos aleatorios, lo que se acerca al modelo genético real en el ganado (Zhao *et al*., 2022).

Teóricamente, la corrección para pruebas múltiples es innecesaria en GWAS de locus múltiples porque todos los genes o loci potenciales para características complejas se ajustan a un solo modelo lineal y sus efectos se estiman y prueban simultáneamente (Xu *et al*., 2018). Además, las pruebas multilocus pueden ser adecuadas para detectar regiones relevantes asociadas con características complejas (Segura *et al*., 2012). Sin embargo, el principal problema de las pruebas multilocus surge al trabajar con conjuntos de datos con un número de marcadores genéticos mayor que el número de genotipos (Segura *et al*., 2012).

Para considerar la estructura de la población en los análisis, se desarrolló el método de modelo mixto multilocus (MLMM) basado en la reestimación de la varianza del modelo en cada paso a través de un método de regresión *forward, backward* y *stepwise* (Segura *et al*., 2012). Los marcadores genéticos en este método GWAS se tratan como cofactores de efectos fijos (Mihalyov *et al*., 2017). Aunque MLMM tiene un desempeño aceptable con un mayor poder estadístico, la posibilidad de perder marcadores genéticos valiosos aún existe debido al uso del método de regresión *forward, backward* y *stepwise* (Mihalyov *et al*., 2017; Segura *et al*., 2012). El EMMA de efecto SNP aleatorio multilocus rápido (FASTmrEMMA) y el mapeo de intervalo compuesto de todo el genoma (GCIM) son métodos GWAS multilocus que se desarrollan bajo el marco MLM para considerar los efectos de los marcadores genéticos como aleatorios y construir la nueva y rápida transformación de matriz (Wen *et al*., 2018). Estos métodos son útiles para cubrir la matriz de covarianza de la matriz K poligénica y reducir el ruido causado por el medio ambiente (Wen *et al*., 2018).

Otro modelo multilocus que actualmente se implementa en una amplia gama de estudios es el modelo fijo y aleatorio de unificación de probabilidad circulante (Farm-CPU) que divide el modelo MLMM en un modelo de efectos aleatorios y un modelo de efectos fijos, luego los emplea iterativamente para lograr el mejor resultado en un conjunto de datos dado (Liu *et al*., 2016).

Modelos bayesianos

Los modelos bayesianos pueden cuantificar la incertidumbre, a través de las probabilidades de distribución, junto con la información a priori. Su aplicación reciente en GWAS también ha mostrado un mayor poder de detección al ajustar simultáneamente múltiples efectos de marcador y corregir implícitamente las estructuras biológicas (Zhao *et al*., 2019).

Un desafío asociado con los GWAS es el problema de “p grande n pequeño”, en cuyo caso como alternativa, los métodos bayesianos también juegan un papel destacado en la resolución de problemas de selección de variables. Entre los métodos de selección de variables bayesianos, encontramos comúnmente y con algoritmos de simulación posterior la selección de variables de Gibbs y la selección de variables de búsqueda estocástica (O’Hara y Sillanpää, 2009).

Lo anterior requiere especificaciones previas, como la distribución de la característica de interés y la probabilidad de marcadores genéticos asociados (Stephens y Balding, 2009). A los coeficientes de regresión, se les pueden asignar valores a priori no informativos o informativos. Esos coeficientes asignados a priori no informativos, son los efectos fijos, se estiman con base únicamente en la información contenida en la verosimilitud. Para los coeficientes a priori informativos asignados, la elección del a priori juega un papel importante en la determinación del

tipo de contracción de las estimaciones de los efectos inducidos (Pérez y de los Campos, 2014).

Se han desarrollado diferentes modelos bayesianos para detectar regiones genómicas asociadas con características de interés. La mayoría de los modelos desarrollados son divergentes en función de sus suposiciones de especificación previa (e Silva *et al*., 2013). Los modelos de regresión logística penalizados fueron los primeros modelos Bayesianos desarrollados, que se construyeron sobre la base de imponer una penalización a los marcadores genéticos para seleccionar el marcador más relevante asociado con una característica de interés (Y. Wang *et al*., 2009).

El modelo de regresión de crestas bayesiano, usa los a priori gaussianos lo que induce una reducción de la estimación similar a la de regresión de crestas, donde todos los efectos se reducen en un grado similar (Pérez y de los Campos, 2014). Esto significa que se basa en la consideración del coeficiente cercano a cero para variables con efectos menores, pero que incluyen todas las variables en el modelo final (Fort y Lambert-Lacroix, 2005).

Otro modelo importante es el de contracción mínima absoluta (LASSO), la cual se basa en forzar a las variables con efectos menores a tener exactamente un coeficiente cero, y solo las variables significativas se incluyen en el modelo final (Hans, 2009). Esto a través de diferentes modelos jerárquicos, donde se considera la distribución normal para los efectos genéticos y la distribución a priori exponencial doble para sus varianzas en el algoritmo MCMC para detectar regiones más relevantes asociadas a características de interés (Park y Casella, 2008). Uno de los principales inconvenientes de LASSO bayesiano es que utiliza los mismos criterios

de reducción para los marcadores genéticos con efectos grandes y pequeños (Zou, 2006).

BayesA, considera distribuciones univariadas independientes e idénticas para efectos de marcadores genéticos con una media nula y una densidad t de student (Meuwissen *et al*., 2001). Esto significa que el efecto del marcador genético del locus "A" tiene la distribución t de Student normal e independiente con la media nula y la varianza específica del locus desconocida.

Además, existen dos a priori de mezcla finita: una mezcla de un punto de masa en cero y una densidad Gaussiana, un modelo denominado como BayesC (Habier *et al*., 2011) y una mezcla de un punto de masa en cero y una densidad de t escalada, un modelo conocido como BayesB (Meuwissen *et al*., 2001). Al asignar una probabilidad previa no nula para que el efecto del marcador sea igual a cero, los antecedentes utilizados en BayesB y BayesC tienen potencial para inducir la selección de variables. En sí, BayesB y BayesC extienden a BayesA y la regresión de crestas bayesiano, respectivamente, mediante la introducción de un parámetro adicional π que representa la proporción a priori de efectos distintos de cero.

Uno de los principales desafíos entre todos los modelos Bayesianos GWAS es que suelen ser computacionalmente exigentes a pesar de la gran mejora en los métodos de simulación MCMC. Por lo tanto, se requieren esfuerzos significativos para aumentar la velocidad computacional en los modelos Bayesianos (Zhao *et al*., 2019).

Validación de GWAS

Actualmente, no existe consenso sobre un umbral para los estudios de asociación en el sector pecuario, ya que este pudiera minimizar el número de falsos positivos

mediante una combinación de control de calidad de la información a través de un umbral apropiado (den Berg *et al*., 2019). A pesar de los esfuerzos para controlar la estructura de la población y el uso de umbrales bastante estrictos, aún ocurrirán falsos positivos en GWAS dada la enorme cantidad de SNP, lo que significa una alta posibilidad de que al menos uno de estos esté asociado con alguna estructura no explicada en los datos.

La única evidencia de que una asociación significativa detectada en un GWAS es real es la validación en una población independiente. La relación entre el conjunto de descubrimiento y validación también debe considerarse cuidadosamente. Por ejemplo, si se descubre un SNP significativo en una población, y el SNP se valida en sus hijas, existe una alta probabilidad de que exista la misma estructura de población en ambos conjuntos de datos, lo que lleva a una aparente validación de lo que realmente es un resultado falso positivo. En ganadería, la validación más convincente es entre razas, ya que la estructura de pedigrí debe ser independiente. Sin embargo, si un SNP no se valida entre razas, puede deberse a que la región subyacente no se segrega entre ellas (Hayes, 2013).

La replicación es un principio importante en estadística. Dentro del paradigma frecuentista, se puede usar una muestra de replicación independiente junto con un umbral a menudo menos estricto. Una muestra de replicación puede implicar menos genotipificación, ya que solo es necesario genotipar los loci seleccionados en la primera etapa (Ball, 2013).

JUSTIFICACIÓN

Actualmente en los países más desarrollados los costos de genotipificación con paneles de baja densidad están en un punto en que puede justificarse económicamente para las decisiones de gestión a nivel de hato (Thomasen *et al*., 2014). Sin embargo, no se ha obtenido el mismo grado de beneficio en países en vías de desarrollo, especialmente en términos de mejoramiento genético. En países en desarrollo como México, la mayor parte de la producción tiene lugar en sistemas de pequeños propietarios, que se caracterizan por problemas de baja producción, sustentabilidad, rentabilidad y competitividad, atribuidos al escaso uso de tecnología (Cárdenas-Bejarano *et al*., 2016). Por tal motivo, el uso de nuevas herramientas para el mejoramiento genético solo será posible a través de las asociaciones de criadores de bovinos de registro, los cuales integran bases de datos que permitan la realización de evaluaciones genéticas nacionales, las cuales podrán ser usadas por parte de los hatos comerciales para la identificación de animales genéticamente superiores.

A través de herramientas como el GWAS, se podrá conocer mejor la arquitectura genética de las características de interés económico, los cuales beneficiarán a la industria ganadera. Además, será posible identificar nuevas regiones asociadas a características de interés económico, identificar nuevos mecanismos biológicos a través de genes que aún no se ha descrito su función, obtener información sobre la variación de razas sobre la misma característica, investigar variantes raras o de baja frecuencia, estudiar diferentes tipos de marcadores, además de otras aplicaciones (Tam *et al*., 2019).

OBJETIVOS

Estudiar regiones genómicas asociadas con características de crecimiento (peso al nacer, peso al destete directo, peso al destete materno, peso al año y talla corporal) y reproductivas (circunferencia escrotal, fertilidad en vaquillas y permanencia productiva) en las razas Simmental y Simbrah en México.

OBJETIVOS ESPECÍFICOS

- Generar mapas de LD e identificar las estructuras de bloques de haplotipos del ganado Simmental y Simbrah para comparar las diferencias en ambas razas.
- Evaluar los modelos de asociación del genoma para cada una de las características de crecimiento y reproductivas con la información por cromosoma y del genoma completo en las razas Simmental y Simbrah.
- Identificar marcadores genéticos (SNPs o haplotipos) a través de estudios de asociación del genoma para características de crecimiento y reproductivas en el ganado Simmental y Simbrah.
- Identificar genes candidatos para características de crecimiento y reproductivas en el ganado Simmental y Simbrah.
- Realizar un análisis de enriquecimiento funcional para identificar posibles redes de genes.

CAPITULO 2: Genome and chromosome wide association studies for growth traits in Simmental and Simbrah cattle

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Genome and chromosome wide association studies for growth traits in Simmental and Simbrah cattle

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Objective: The objective of this study was to perform genome (genome wide association studies [GWAS]) and chromosome (CWAS) wide association analyses to identify single nucleotide polymorphisms (SNPs) associated with growth traits in registered Simmental and Simbrah cattle.
Methods: The phenotypes were deregressed BLUP EBVs for birth weight, weaning weight direct, weaning weight maternal, and yearling weight. The genotyping was performed with the GGP Bovine 150k chip. After the quality control analysis, 105,129 autosomal SNP from 967 animals (473 Simmental and 494 Simbrah) were used to carry out genotype association tests. The two association analyses were performed per breed and using combined information of the two breeds. The SNP associated with growth traits were mapped to their corresponding genes at 100 kb on either side.
Results: A difference in magnitude of posterior probabilities was found across breeds between genome and chromosome wide association analyses. A total of 110, 143, and 302 SNP were associated with GWAS and CWAS for growth traits in the Simmental-, Simbrah- and joint -data analyses, respectively. It stands out from the enrichment analysis of the pathways for RNA polymerase (POLR2G, POLR3E) and GABAergic synapse (GABRR1, GABRR3) for Simmental cattle and p53 signaling pathway (BID, SERPINB5) for Simbrah cattle.
Conclusion: Only 6,265% of the markers associated with growth traits were found using CWAS and GWAS. The associated markers using the CWAS analysis, which were not associated using the GWAS, represents information that due to the model and priors was not associated with the traits.

Keywords: Genes; Growth Traits; Genome Wide Association Studies (GWAS); Simbrah; Simmental; Single Nucleotide Polymorphism (SNP)

INTRODUCTION

Simmental and Simbrah cattle are some of the most widespread breeds for meat production in Mexico. Growth traits are traditionally included as selection criteria in beef cattle breeding programs, due to their association with meat production and therefore are of great economic importance for both breeders and industry [1]. The most common type of growth trait used in the selection process is the body weight measurement, which can be taken at birth and throughout an animal's life [2]. Growth traits usually present heritability and genetic correlations from moderate to strong [3,4]. Genetic associations are caused by linkage disequilibrium (LD) and pleiotropic effects of genes [5]. The LD is important for experimental designs to increase genome wide association studies (GWAS) efficiency in studied populations. Linkage disequilibrium patterns and scale within and between populations/breeds can be influenced by several factors, such as marker a

frequencies, selection history, population structure, effective population size, marker type and density, and LD measure used [6]. Additionally, inter-chromosome epistasis effects are expected to be unaffected by LD between the two single nucleotide polymorphisms (SNPs) of each SNP pair but some effects still could have contributions from LD between an SNP adjacent to another SNP that had a significant inter-chromosome epistasis effect [7]. The aim of this research was to implement GWAS and chromosome-wide association (CWAS) analyses to identify SNPs associated with growth traits in registered Simmental and Simbrah cattle.

MATERIALS AND METHODS

The genotype and phenotype of 1,130 animals (547 Simmental and 583 Simbrah), provided by the Mexican Simmental-Simbrah Breeders Association, were used. The phenotypes were deregressed BLUP EBV [8] for birth weight (BW), weaning weight direct (WWD), weaning weight maternal (WWM), and yearling weight (YW).

Blood samples were taken from all the animals in the study. Samples were individually identified and sent to Neogen's GeneSeek Laboratory (Lincoln, NE, USA) for DNA extraction and genotyping using the GGP Bovine 150k chip with 138,962 SNP.

All SNP with a call rate <0.95 and a minor allele frequency <0.05 were excluded. Individuals with a call rate less than 0.95 were also deleted. After the quality control analysis, 105,129 autosomal SNP from 967 animals (473 Simmental and 494 Simbrah) were used to carry out genotype association tests. Additionally, chromosome marker databases were performed to calculate their effect on the different traits individually. Intra-chromosomal LD were evaluated by means of pair-wise coefficients of determination (r^2) in Plink 1.9. Marker pairs were grouped based on their pairwise physical distance into bins of 1 kb, starting from 0 to 5,000 kb. The average r^2 for SNP pairs in each bin was estimated as the arithmetic mean of all r^2.

A comparison was made between the GWAS and CWAS analyses using a Bayes B model through the BGLR statistical package of the R program. These association analyses were carried out separately for the two breeds and combining the information of both breeds (joint analysis).

For a continuous response (y_i; i = 1, ..., n) the data equation is represented as $y_i = \eta_i + \varepsilon_i$, where η_i is a linear predictor (the expected value of y_i given predictors) and ε_i are the residuals, independent and normally distributed with mean zero and variance $w_i^2\sigma_\varepsilon^2$. The linear predictor represents the conditional expectation function, and it is structured as

$$\boldsymbol{\eta} = 1\mu + \sum_{j=1}^{J} \boldsymbol{X_j}\boldsymbol{\beta}_j ,$$

where μ is the intercept, $\boldsymbol{X_j}$ are design matrices for predictors, $\boldsymbol{X_j} = \{x_{ijk}\}$, and $\boldsymbol{\beta_j}$ are vectors of effects associated with the columns of $\boldsymbol{X_j}$. For the joint analysis model, $\boldsymbol{X_1}$ is a design matrix for the effects of breed, $\boldsymbol{\beta_1}$ is the corresponding vector of effects, $\boldsymbol{X_2}$ is the matrix with marker genotypes, and $\boldsymbol{\beta_2}$ is the corresponding vector of marker effects. Collecting the above assumptions, we have the following conditional distribution of the data:

$$p(\boldsymbol{y}|\boldsymbol{\theta}) = \prod_{i=1}^{n} N\left(y_i|\mu + \sum_{j=1}^{J}\sum_{k=1}^{K_j} x_{ijk}\beta_{jk}\,,\ \sigma_\varepsilon^2 w_i^2\right)$$

where $\boldsymbol{\theta}$ represents the collection of unknowns, including the intercept, regression coefficients ($\boldsymbol{\beta_{jk}}$) and the residual variance.

This analysis uses Markov Chain Monte Carlo (MCMC) methods to calculate posterior mean estimates of marker effects and variances. The chains included 100,000 iterations with the first 25,000 samples used for burn-in.

The models were evaluated with the Gelman–Rubin diagnostic, which evaluates MCMC convergence by analyzing the difference between multiple Markov chains. The convergence is assessed by comparing the estimated between-chains and within-chain variances for each model parameter. For this, the potential scale reduction factor ($\widehat{\boldsymbol{R}}$) was adjusted. The key parameter for this adjustment is the estimated degrees of freedom, d, for a Student-t approximation to the posterior inference based upon the simulations [9],

$$\widehat{\boldsymbol{R}}_{\boldsymbol{c}} = \frac{\boldsymbol{d}+\mathbf{3}}{\boldsymbol{d}+\mathbf{1}}\widehat{\boldsymbol{R}}$$

Large differences between these variances indicate non-convergence ($\widehat{\boldsymbol{R}}_{\boldsymbol{c}} > \mathbf{1.1}$). When the model did not converge, the number of iterations and burn-in were doubled. Once the effects of the markers were estimated, 95% confidence intervals and posterior probabilities for the markers' effects were calculated. Marker effects equal to zero reflect no marker's effect.

The SNP associated with growth traits were mapped at 100 kb pairs on either side, because of the average LD (r^2 = 0.2) previously found in beef cattle [10]. With these SNP windows, genes and quantitative trait loci (QTLs) in the same regions were found. After that, pathway enrichment analyses were conducted using the Database for Annotation, Visualization and Integrated Discovery (DAVID). A p-value <0.05 determined by Fisher's exact test was set as the criterion

for significance. The pathway analyses were carried out using the official symbols of genes and the *Bos taurus* species as reference.

RESULTS

The intra-chromosomal LD (r^2) tended to decrease with increasing genomic distance in both breeds and joint data. Simmental showed higher LD than Simbrah in the nearest distances (<100 kb). For larger distances between SNP (>150 kb), Simbrah showed slightly higher average r^2 than Simmental. For adjacent markers (<1 kb), average r^2 were 0.515, 0.587, and 0.469 for joint-, Simmental- and Simbrah-data analyses, respectively (Figure 1).

There were differences also in the average r^2 at a particular marker distance depending on the chromosome. Average r^2 ranged from 0.019 (BTA26) to 0.057 (BTA14) in the joint analysis, from 0.018 (BTA28) to 0.040 (BTA6) in the Simmental-data analysis, and from 0.023 (BTA26) to 0.068 (BTA14) in the Simbrah-data analysis.

Gelman-Rubin's shrink factors of all the models converged to 1 as the number of iterations increased, which indicates that five chains converged to each other. To select those markers associated with a trait, posterior probabilities were used. Even though the order of the most associated markers was similar in both GWAS and CWAS, there was a clear difference between the posterior probabilities obtained with both analyses, e.g., in Simmental, the marker BovineHD1300014404 was associated with YW using both CWAS and GWAS; the difference between posterior probabilities was 0.6805 (Table 1). In almost all cases, when a marker was associated with a trait using GWAS, it was also associated with the same trait using CWAS. In contrast, other markers were associated at chromosome-wide level, but were not associated with a trait at genome-wide level.

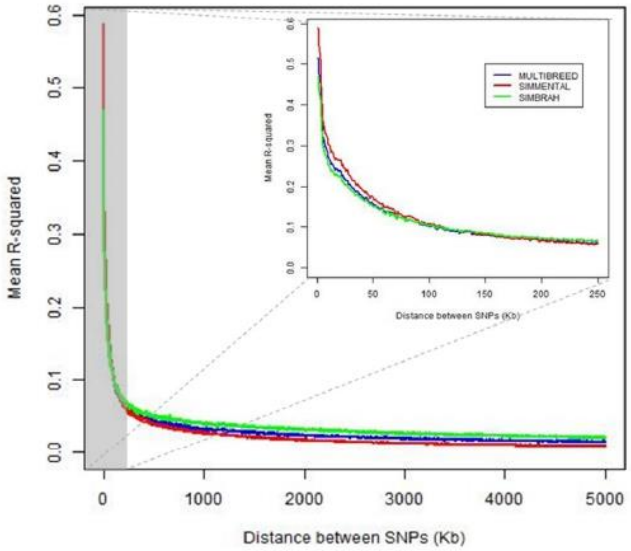

Figure 1. Average coefficients of determination (r^2) for distance bins of 1 kb for Simmental-, Simbrah- and joint- data analyses plotted against physical distance (kb) between single nucleotide polymorphism.

In both, GWAS and CWAS, SNP were found to be associated with growth traits in the Simmental population (Supplementary Table S1). A total of 23 (16 for GWAS and 7 for CWAS), 22 (11 for GWAS and 11 for CWAS), 28 (21 for GWAS and 7 for CWAS), and 37 (20 for GWAS and 17 for CWAS) SNP were associated with BW, WWD, WWM, and YW, respectively. Additionally, four of the SNP associated with WWM, and WWD were the same and another four SNP shared the same regions (within 100 kb).

In the Simbrah population, a total of 61 (27 for GWAS and 34 for CWAS), 39 (23 for GWAS and 16 for CWAS), 23 (13 for GWAS and 10 for CWAS), and 20 (14 for GWAS and 6 for CWAS) SNP were associated with BW, WWD, WWM, and YW, respectively (Supplementary Table S1); 9 of these SNPs were the same for WWM and WWD. Another four SNP shared the same regions (within 100 kb) for the same traits.

In the joint analysis, 95 (60 for GWAS and 35 for CWAS), 76 (52 for GWAS and 24 for CWAS), 60 (41 for GWAS and 19 for CWAS), and 71 (42 for GWAS and 29 for CWAS) SNP were associated with BW, WWD, WWM and YW, respectively (Supplementary Table S1). Also, 19 and 1 of the SNPs associated with WWM and YW were the same for WWD. Another 3, 1, and 1 SNPs for WWM, BW, and YW shared the same regions (within 100 kb) with SNPs associated with WWD. Within the SNP windows, QTLs were previously associated with other traits, 183, 162, 18, and 302 within the regions associated with BW, WWD, WWM and YW, respectively (Supplementary Table S2). In the same way, a total of 51, 61, 25, and 40 genes were found within these regions (Supplementary Table S2).

In each type of analysis, markers associated with growth traits were found in at least 10 chromosomes, however, there is no clear difference between which chromosome had more associated regions. Displaying all SNP for Simmental, Simbrah and joint model, the SNP for WWD matched 34 and 2 SNP for BW, WWM, and YW, respectively. Also, 3, 2, and 1 SNP windows for BW matched with the SNPs for WWD, WWM, and YW; 5 and 1 SNP windows for WWD matched with the SNPs for WWM and YW; finally, 1 SNP window matched between WWM and YW. Additionally, 14 and 1 of the SNPs associated with WWM and YW were the same for WWD. However, these SNP windows are not close enough to match three or more traits at the same time.

Through the database QTL_ARS_UCD1, 280, 271, 156, and 402 QTLs previously described were found within the SNP windows for BW, WWD, WWM, and YW, respectively

Table 1. Single nucleotide polymorphisms (SNP) with the highest posterior probabilities (>0.15) associated with growth traits in both genome- (GWAS) and chromosome-wide analysis (CWAS)

SNP	BW		WWD		WWM		YW	
	GWAS	CWAS	GWAS	CWAS	GWAS	CWAS	GWAS	CWAS
Joint analysis								
BovineHD0400015064							0.155	0.660
BovineHD0700022164	0.269	0.552						
BovineHD1100018479			0.448	0.794	0.405	0.907		
BovineHD1200007354			0.188	0.226				
BovineHD1900010762			0.428	0.964				
BovineHD2000005310							0.287	0.914
BovineHD2200002151	0.750	0.860						
BovineHD2900012617	0.664	0.338						
BTB-00218987	0.251	0.482						
BTB-00397480			0.225	0.476				
Simbrah analysis								
ARS-BFGL-NGS-3343	0.288	0.345						
ARS-BFGL-NGS-40907			0.253	0.318	0.152			
ARS-BFGL-NGS-75279			0.210	0.476		0.157		
BovineHD0100005053	0.259	0.750						
BovineHD0200037022				0.272	0.150			
BovineHD0300022871				0.368	0.200	0.687		
BovineHD0400014726			0.171		0.291	0.236		
BovineHD0700030669							0.170	0.694
BovineHD1100018735							0.241	0.903
BovineHD2000005310							0.220	0.503
Simmental analysis								
BovineHD1100018476			0.171	0.675				
BovineHD1100028536							0.338	0.821
BovineHD1300014404							0.151	0.831
BovineHD2100010794			0.153	0.590				
BovineHD2100012099	0.543	0.609						
BovineHD2800009062							0.179	0.471

BW, birth weight; WWD, weaning weight direct; WWM, weaning weight maternal; YW, yearling weight.

(Supplementary Table S2). For all the traits, QTLs associated with conformation, health, meat, carcass, milk, and reproduction traits in cattle were found. Over the database ARS-UCD1.2, 131, 102, 64, and 98 genes were found within the SNP windows for BW, WWD, WWM, and YW, respectively (Supplementary Table S2). Four of these genes were found within SNP windows for WWD and YW.

The posterior probability for gene inclusion is always greater than or equal to the probability that any SNP is included [11]. For this reason, genes within SNP windows were used to search for networks that could be associated with growth traits. Functional enrichment analysis was carried out to identify genes that are over-represented in a large group of genes and may have a connection with the studied phenotypes (Table 2).

DISCUSSION

The LD estimates at various distances were of the magnitude of those reported by Villa-Angulo et al [12] in several dairy and beef cattle breeds using less dense SNP panels. The difference in the decline of the average r^2 between Simmental and Simbrah could be an effect of the indicine breeds. It has been observed that indicine breeds had lower r^2 at short distances and higher r^2 at longer distances between markers than taurine breeds [13]. Higher LD in taurine breeds has been attributed to smaller effective population size and stronger genetic bottleneck during breed formation [14].

Means of r^2 were obtained for each chromosome averaged across breeds ranging from 0.019 (BTA26) to 0.057 (BTA14) in the joint model, from 0.018 (BTA28) to 0.040 (BTA6) in Simmental, and from 0.023 (BTA26) to 0.068 (BTA14) in Simbrah. In the present study, the higher LD values detected in some chromosomes in comparison to others can be indicative of the presence of QTLs affecting traits that have been under intense selection in both breeds [6]. A wide variation in autosomal recombination rates can lead to a marked diversity in the pattern of LD in different genomic regions and

Table 2. Reactome and KEGG pathways significantly enriched using genes associated with growth traits

Data	Trait	Category	Pathway	Count	p-value	Candidate genes
Joint	WWD	Reactome	Hemostasis-Thrombin signalling through proteinase activated receptors	2	0.02	*GNA11, GNA15*
			Hemostasis-Thromboxane signalling through TP receptor	2	0.0096	*GNA11, GNA15*
			Hemostasis-ADP signalling through P2Y purinoceptor 1	2	0.012	*GNA11, GNA15*
			Hemostasis-Platelet homeostasis-Platelet sensitization by LDL	2	0.011	*GNA11, GNA15*
			Metabolism-Fatty Acids bound to GPR40 regulate insulin secretion	2	0.0096	*GNA11, GNA15*
Simmental	BW	KEGG	RNA polymerase	2	0.035	*POLR2G, POLR3E*
		Reactome	Metabolism of proteins-N-glycan trimming in the endoplasmic reticulum and Calnexin/ Calreticulin cycle	2	0.017	*UBXN1, GANAB*
	WWD	KEGG	Nicotine addiction	2	0.022	*GABRR1, GABRR2*
			GABAergic synapse	2	0.045	*GABRR1, GABRR2*
			Morphine addiction	2	0.048	*GABRR1, GABRR2*
Simbrah	BW	KEGG	p53 signaling pathway	2	0.046	*BID, SERPINB5*

KEGG, Kyoto encyclopedia of genes and genomes; *GNA11*,G protein subunit alpha 11; *GNA15*, G protein subunit alpha 15; WWD, weaning weight direct; BW, birth weight; *POLR2G*, RNA polymerase II subunit G; *POLR3E*, RNA polymerase III subunit E; *UBXN1*, UBX domain protein 1; *GANAB*, glucosidase II alpha subunit; *GABRR1*, gamma-aminobutyric acid type A receptor subunit rho1; *GABRR2*, gamma-aminobutyric acid type A receptor subunit rho2; *BID*, BH3 interacting domain death agonist; *SERPINB5*, serpin family B member 5.

chromosomes [15]. The causes may have acted differently at specific genomic regions at singular locations among the Simmental and Simbrah populations. The different LD patterns across chromosomes have been assumed that exist, and therefore, it is also expected different genomic inflation factors across chromosomes [16].

The posterior probabilities do not define with clarity the extent of association of an SNP with a trait, however, if we compare with frequentist models, studies have been carried out where it is shown that around half of the published associations with $p<5\times10^{-7}$ had posterior probabilities less than 0.5 [17]. The posterior probabilities are being conditioned on the model and the priors, however, while posterior probabilities provide a measure of evidence for hypotheses for the marker effects, it is difficult to judge them separately, as individual model probabilities may be "diluted" as the number of markers grows receiving small probability (both prior and posterior) [11,18]; this could have been what affected the posterior probabilities of the GWAS and CWAS; if this is the case, a lot of useful information could be missing.

The change in posterior probabilities was probably due to the density of the markers used in each of the three analyses, with the GWAS giving lower values compared to those of the CWAS [19]. However, a study applying a mixed linear association model with a leave-one-chromosome-out approach, suggests that even if the genomic inflation factors do not differ a lot between the different SNP densities, genomic inflation factors varied largely across the chromosomes [16]. An explanation might be that there was a different level of association between the SNP on the chromosome and the trait of interest, also, because using the total number of SNPs can result in too conservative thresholds since it violates the assumption of independence between tests [20,21].

For all growth traits, markers were found in regions previously associated with QTLs for production, reproduction, health, and conformation traits (Supplementary Table S2). However, it is of greater interest to focus on the QTLs that are correlated with growth traits.

In the Simmental-data analysis, within the SNP windows, QTL were previously associated with other traits; in total, there were 69, 30, 135, and 71 QTLs within the regions associated with BW, WWD, WWM, and YW, respectively (Supplementary Table S2). A total of 60, 17, 34, and 50 genes were associated with BW, WWD, WWM, and YW, respectively (Supplementary Table S2). For BW, in the associated SNP windows, some QTLs were previously reported with the length of productive life, body depth, net merit, muscle phosphorus and potassium content, shear force, and tenderness score in Holstein, Angus, and Nelore. For WWD, one SNP window on BTA 10 were reported QTLs associated with body weight in Charolais and Gelbvieh cattle. In the case of WWM, inside the SNP windows QTLs were previously associated with average daily gain, body weight gain, body depth, rump width, body weight, carcass weight, fat thickness, hip height, longissimus muscle area, marbling score, metabolic body weight, residual feed intake, withers height, and dry matter intake. For YW, it was found in SNP windows QTLs previously associated with length of productive life, net merit, and dry matter intake in Holstein cattle.

In Simbrah cattle, inside the SNP windows, 28, 79, 3, and 29 QTL were previously associated with other traits within the regions associated with BW, WWD, WWM, and YW, respectively (Supplementary Table S2). Also, a total of 20, 24,

5, and 8 genes were found within these regions (Supplementary Table S2). Within regions associated with BW QTLs were previously found for maturity rate in Brahman cattle and net merit and length of productive life in Holstein cattle. For WWD, in the SNP windows QTLs were previously associated with body weight (birth) in Brangus cattle, weaning weight in Blanco Orejinegro cattle and lean meat yield in Holstein cattle. For WWM, on BTA 24, QTL previously associated with bodyweight and maturity rate were found. For YW, in a SNP window of BTA 14 a QTL previously associated with birth weight in Charolais and Chianina cattle and carcass weight in Hanwoo cattle was found.

From the results of the joint model, several coincidences were found within the regions associated with BW, WWD, and YW, with the databases of QTLs. For BW, in the associated SNP windows, some QTLs previously reported with maturity rate in Brahman cattle, body weight (birth) in Charolais and Chianina cattle, yearling weight in Charolais and Gelbvieh cattle, subcutaneous fat in Hanwoo cattle, body depth, lean meat yield, length of productive life, net merit, PTA type and rump width in Holstein cattle, and dry matter intake and metabolic weight in beef cattle. In the case of WWD inside the SNP windows, QTLs were previously associated with average daily feed intake, carcass weight, fat thickness, marbling score, residual feed intake, and, average daily gain in beef cattle, body weight (yearling) in Charolais, and Chianina cattle, maturity rate in Braham cattle, tenderness score in Angus cattle and, lean meat yield, growth index, average daily gain, length of productive life and net merit in Holstein cattle. For WWM, inside the SNP, windows were reported QTLs associated with muscle sodium content in Angus cattle, maturity rate in Brahman cattle, and dry matter intake in Holstein cattle. For YW it was found in SNP windows QTLs previously associated with marbling score, muscle creatine content, tenderness score in Angus cattle, bodyweight in Charolais, Chianina, and Gelbvieh cattle, carcass weight in Wagyu cattle, dry matter intake, dressed carcass, and body mass in a beef cattle population, and body depth, lean meat yield, length of productive life, net merit and rump width and lactation persistency in Holstein cattle.

The joint analysis of two breeds increases the statistical power to detect more significant SNPs rather than a single analysis. Also, the Simmental and Simbrah analyses give different significant genes. These differences can be associated with the genomic architecture changes with hybridization and subsequent inter-se mating during the formation of a composite breed, this means that alleles at some loci increase in frequency more than others in the newly hybridized population [22]. Additionally, differences were found between the enrichment analyzes, mainly because no similar genes were found between the different association analyses. Furthermore, the more diverse the number of genes, the greater the number of pathways that were found.

In the joint analysis, inside the SNP windows, there are some genes relevant to growth traits (Supplementary Table S2). Among these stand out special AT-rich sequence-binding protein-1 (*SATB1*), prominin mouse-like 1 (*PROM1*), CUB and Sushi multiple domains 1 (*CSMD1*), phosphatidylserine synthase 1 (*PTDSS1*), and ubiquinol-cytochrome c reductase binding protein (*UQCRB*) (candidate genes for BW).

SATB1 has been associated with the concentration of triiodothyronine, a hormone linked with physiological processes, including growth and development [23]. Also, *SATB1* has shown differences in its expression in fetal adipose tissues, depending on the maternal diet [24]. *PROM1* has been selected as a candidate gene for BW in goats, this is a protein-coding gene, which plays a role in cell differentiation, proliferation, and apoptosis [25]. In Hanwoo cattle, *CSMD1* was more highly expressed in muscle samples from animals with increasing carcass weight in intramuscular fat and eye muscle area [26]. Additionally, *PTDSS1* and *UQCRB* tend to be expressed more highly in muscle with increasing intramuscular fat content [26].

Reactome pathways for WWD in the joint analysis included the metabolism through the regulation of insulin secretion by fatty acids bound to G protein-coupled receptor 40 (*GPR40*) fatty acids augment the glucose-triggered secretion of insulin through two mechanisms: intracellular metabolism and activation of free fatty acid receptor 1 (*FFAR1*).

Also, in the Simmental-data analysis, for BW, a reactome pathway associated with the metabolism of proteins-N-glycan trimming in the endoplasmic reticulum and Calnexin/Calreticulin cycle was identified; in this process, the N-glycan is progressively trimmed off by the three glucoses and some of the mannoses before the protein is transported to the cis-Golgi.

In Simmental cattle, inside the SNP windows, there are some genes relevant to growth traits (Supplementary Table S2). Among these stand out *SATB1* (candidate gene for WWD), proenkephalin (*PENK*), collagen type IV alpha 1 chain (*COL4A1*), short chain dehydrogenase/reductase family 16C member 6 (*SDR16C6*), and cell division cycle 5 like (*CDC5L*) (candidate genes for WWM).

PENK has been associated as a candidate gene for growth traits along with RB1 inducible coiled-coil 1 (*RB1CC1*), neuropeptides B and W receptor 1 (*NPBWR1*), and pleiomorphic adenoma gene 1 (*PLAG1*) in Nellore cattle, according to these studies, *PLAG1* seems to be the major gene due to its role in regulating insulin-like growth factors, and *RB1CC1*, *NPBWR1*, and *PENK* are also involved in processes that can contribute to determining the uniformity of growth traits, like YW [27]. *COL4A1* is related to developmental biology, protein digestion, and protein absorption have been indicated

as a candidate gene for weaning weight and YW [28]. *SDR16C6* has been associated as a candidate gene for weaning weight and daily weight gain between birth and weaning in Blanco Orejinero cattle [29]. *CDC5L* has been associated as a candidate gene of muscular growth and homeostasis during puberty in conjunction with MYC proto-oncogene (*MYC*), transcription factor 3 (*TCF3*), RUNX family transcription factor 2 (*RUNX2*), activating transcription factor 2 (*ATF2*), and cAMP responsive element binding protein 1 (*CREB1*) [30].

The RNA polymerase pathway was associated with Simmental cattle for BW and take part in the transcription in the genetic information processing. In a study the RNA polymerase pathway was observed downregulated in overfed moderate-energy diet (OVE) cows; also, the gene *POLR2G* (polymerase II gene) and other polymerases III genes were affected. To lower polymerase II gene expression, OVE cows also experienced suppression of the RNA transport pathway. RNA transport allows mRNA transcribed in the nucleus to be processed and translated later in the cytoplasm [31]. This result does not necessarily mean that there was less overall transcription. In eukaryotes, there are 3 distinct RNA polymerases, these transcription complexes are composed of heterogeneous subunits, which can individually affect the transcription complex [32].

The GABAergic synapse pathway was associated with WWD in Simmental cattle. GABA is a neurotransmitter widely distributed in the central nervous system, which is synthesized from glutamate through decarboxylation39 and plays an important role in regulating feeding behavior in the hypothalamus. Other studies have found that this pathway was significantly associated with live weight in Simmental cattle [33]. Additionally, it was suggested that neuronal sensitivity to GABA is related to the control of feeding behavior in ruminant animals [34].

An interesting term that has been found in Simmental cattle for WWD is nicotine and morphine addiction. Both terms are found as significant Kyoto encyclopedia of genes and genomes pathways associated with substance dependence in humans extrapolated to bovines. Other studies have observed these pathways in their analysis [33,35,36]. However, given the origin, all agree that the pathway regulation is ambiguous and requires further validation.

In Simbrah cattle, inside the SNP windows, there are some genes relevant to growth traits (Supplementary Table S2). Among these stand out vacuolar protein sorting 4 homolog B (*VPS4B*) (candidate gene for BW), cadherin 20 (*CDH20*) (candidate gene for WWM), hedgehog acyltransferase (*HHAT*), phosphodiesterase 4B (*PDE4B*), tripartite motif containing 63 (*TRIM63*), high mobility group AT-hook 2 (*HMGA2*) (candidate genes for WWD), and thymocyte selection associated high mobility group box (*TOX*) (candidate gene for YW).

In pigs, *VPS4B* and *CDH20* have been described as a candidate gene that composes the underlying genetic architecture of porcine growth and fatness traits, this gene is crucial for the degradation of membrane receptors, regulation of epidermal growth factor receptors, and insulin receptors [37].

HHAT is a gene previously associated with weaning weight in Zebú cattle [38]. *PDE4B* encodes the phosphodiesterase enzyme type 4 that hydrolyses the cyclic adenosine monophosphate, which is related to energy modulation processes in the body, and is linked with lipolysis control, regulating body composition, also this gene has been associated with average daily gain [39]. *TRIM63* is part of the ubiquitin-proteasome system in the main proteolytic pathway in muscle, and the muscle-specific ligases tripartite motif-containing, also there is a supposition that *TRIM63* (MuRF-1) may play a role in the control of protein degradation and probably also contributes to skeletal muscle metabolism [40]. *HMGA2* has been detected for BW in Brangus, the *HMGA* proteins are architectural transcription factors that regulate the transcription of a variety of genes and direct cellular growth, proliferation, and differentiation [41], also the regulation of insulin like growth factor 2 (*IGF2*) by *HMGA2* has been proved to occur directly or through increased expression of *PLAG1* [42].

The *TOX* gene has previously been linked to *PLAG1*, coiled-coil-helix-coiled-coil-helix domain containing 7 (*CHCHD7*), short chain dehydrogenase/reductase family 16C member 5 (*SDR16C5*), *SDR16C6*, *PENK*, family with sequence similarity 110 member B (*FAM110B*), cytochrome P450 family 7 subfamily A member 1 (*CYP7A1*), and syndecan binding protein (*SDCBP*) as candidate genes for carcass weight in Hanwoo cattle. According to them, a denser LD structure was found in and around *TOX* gene rather than a region that surrounds *PLAG1* gene, this result might be due to a multigene effect in which multiple genes in the same QTL region are affecting correlated traits in cattle [43].

In Simbrah, the p53 signaling pathway was significantly associated with BW. This pathway is induced by several stress signals (DNA damage, oxidative stress, and activated oncogenes). The p53 protein is employed as a transcriptional activator of p53-regulated genes. Also, p53 is a gene that has been proposed as a part of a network that influences puberty, making supports the relevance of tumor-related genes for puberty [44]. There is evidence of the correlation of pubertal traits (standardized age at first oestrus and scrotal circumference) with growth characteristics, such as YW and the maternal component of weaning weight and BW [45].

CONCLUSION

Only 6,265% of the markers associated with growth traits were found using CWAS and GWAS. The associated markers

found just in the CWAS could be used for the identification of candidate genes. No significantly associated regions were found between breeds. Although Simbrah is a synthetic breed derived from Simmental, no common regions were found, however, in the joint analysis, some common regions were found.

These regions may be useful in providing insight into growth traits in Simmental and Simbrah cattle with related phenotypic measurements. Also, candidate genes helped identify gene pathways through enrichment analysis. These pathways can help us understand how they are connected to growth traits.

CONFLICT OF INTEREST

We certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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SUPPLEMENTARY MATERIAL

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Supplementary Table S1. Marker effects ( ) and their posterior probabilities (PP) of SNPs associated with growth traits with the use of genome-wide association (GWA) as well as a chromosome-wide association (CWA) in simmental and simbrah cattle

Supplementary Table S2. QTLs and genes previously described within the regions associated with growth traits in simmental and simbrah cattle

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CAPITULO 3: Discovering genomic regions associated with reproductive traits and frame score in mexican Simmental and Simbrah cattle through individual SNP and haplotype markers

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Discovering Genomic Regions Associated with Reproductive Traits and Frame Score in Mexican Simmental and Simbrah Cattle Using Individual SNP and Haplotype Markers

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Abstract: Reproductive efficiency stands as a critical determinant of profitability within beef production systems. The incorporation of molecular markers can expedite advancements in reproductive performance. While the use of SNPs in association analysis is prevalent, approaches centered on haplotypes can offer a more comprehensive insight. The study used registered Simmental and Simbrah cattle genotyped with the GGP Bovine 150 k panel. Phenotypes included scrotal circumference (SC), heifer fertility (HF), stayability (STAY), and frame score (FS). After quality control, 105,129 autosomal SNPs from 967 animals were used. Haplotype blocks were defined based on linkage disequilibrium. Comparison between haplotypes and SNPs for reproductive traits and FS was conducted using Bayesian and frequentist models. 23, 13, 7, and 2 SNPs exhibited associations with FS, SC, HF, and STAY, respectively. In addition, seven, eight, seven, and one haplotypes displayed associations with FS, SC, HF, and STAY, respectively. Within these delineated genomic segments, potential candidate genes were associated.

Keywords: genes; genome-wide association study (GWAS); haplotypes; Simbrah; Simmental; single nucleotide polymorphism (SNP)

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1. Introduction

Reproductive efficiency is essential for the profitability of beef production systems. High reproductive rates significantly increases the biological and economic efficiency of cow–calf production systems [1]. The main factors that significantly impact reproductive efficiency in cattle include the timing of puberty and first conception, the duration of post-partum anoestrus, and the overall lifetime productivity. This metric encapsulates the combined effects of cow survival and reproductive performance as well as the survival and growth rate of their offspring [2].

Genetic evaluations can expedite improvements in reproductive performance and other traits with low heritability [3]. Additionally, the utilization of molecular markers can enhance the accuracy of heritability estimations. Genotypes obtained via SNP panels have applications in the study of complex traits, the exploration of linkage disequilibrium patterns, QTL mapping, genomic selection, and genetic gain calculation [4]. The availability of individuals genotyped with high-density SNP panels simplifies the identification of genomic regions linked to economically significant traits, improving the detection of QTLs and genetic variation.

While SNPs are commonly used in association analyses, haplotype-based methods offer more comprehensive information. In contrast to SNPs, which can have a maximum of two alleles, haplotype blocks can encompass more than two haplotypes. Haplotype blocks consist of two or more closely located loci, making them prone to co-inheritance due to their high linkage disequilibrium. Haplotype-based methodologies, aimed at enhancing the efficacy of identifying causal haplotypes, are rational, considering that genes operate as coherent gene sets, rather than as individual SNPs within the set. These haplotype-based techniques are anticipated to provide improved control over false positives when compared to single-SNP methods as they concentrate on the complete haplotype block rather than on the individual SNPs within that block [5]. Haplotype construction compresses multiple SNPs into a haplotype locus and optimizes the design of genomic selection and GWAS [6].

The ability to replicate the regions is associated with the economically significant traits reported in other studies [7–11], which enables us to validate these associations as there is a possibility of false positives in the association analyses [12]. Hence, without this validation, the number and identity of the regions and genes influencing the expression of reproductive traits remain uncertain. In beef cattle, this situation has also been emphasized where it is necessary to test these genomic regions to determine whether their use in genomic selection will be beneficial in crossbreeding programs [13].

Also, a multi-breed reference population has the potential to significantly enhance the precision of genomic predictions by enabling breeds with limited reference population data to leverage information from other breeds [14]. Notably, improvements in the accuracy of genomic predictions are achieved when the breeds included in the multi-breed reference population share close genetic relationships [14].

The objective of this study was to compare the results of an association analysis with haplotypes and SNPs for reproductive traits and frame score (FS) in Simmental and Simbrah cattle using the EMMAX, BayesB, and BayesC methods.

2. Materials and Methods

2.1. Phenotypic Data

The phenotypes employed in the current study were:

- Frame score (FS): Hip height converted to frame score represents a linear measurement employed by cattle producers to assess the potential lean-to-fat ratio of an individual animal within a performance-oriented program. Calculated using the reference tables provided by the Beef Improvement Federation [15].
- Scrotal circumference (SC): For yearling bulls, scrotal circumference measurement entails encircling the broadest section of the scrotum with a scrotal tape while the testicles are in a fully extended state.
- Heifer fertility (HF): Represents the probability that the daughters of a sire have their first calving at the age of 3 years or earlier.
- Stayability (STAY): Indicates the probability that the daughters of a sire, having had a calf before 3 years of age, will have at least a second calf before 6 years of age.

Estimated breeding values (EBV) for all traits were computed using data from the Mexican Simmental-Simbrah Breeders Association, which was subsequently submitted to Mexico's National Institute for Forestry, Agriculture, and Livestock Research (INIFAP) for the National Genetic Evaluation.

In line with the protocols detailed by Garrick et al. [16], these EBV were deregressed (DEBV). Following the deregression process, males with low DEBV were excluded from the analysis. This resulted in a total of 547 Simmental and 583 Simbrah animals that were considered for further analyses.

2.2. Genotypic Data

Blood samples were obtained from each of the animals participating in the study. These samples were individually labeled and subsequently dispatched to Neogen's Gene-Seek Laboratory, located in Lincoln, NE, USA, for the purpose of DNA extraction and

genotyping. The GGP Bovine 150 k chip, consisting of 138,962 SNP markers, was employed for genotyping. All SNPs with a call rate lower than 0.95 and a minor allele frequency below 0.05 were excluded. Furthermore, individuals with a call rate lower than 0.95 were removed from the dataset. Following the quality control assessment, a total of 105,129 autosomal SNPs from 967 animals (473 Simmental and 494 Simbrah) were employed for genotype association tests [17].

Haplotype blocks were defined as regions smaller than 200 kb, with at least 90% of the comparisons between SNPs within the block in "strong LD". The 90% confidence interval for LD was established between 0.70 and 0.98. A total of 16,651 haplotype blocks (each block had between 2 and 48 SNPs) containing 57,202 haplotypes were inferred and used for the association analysis. Quality control and haplotypes were determined with Plink 1.07 [18].

2.3. Association Analyses

A comparison was made between haplotypes and SNPs for reproductive traits and FS in Simmental and Simbrah cattle. The association analyses were carried out separately for each breed, combining the information of both breeds (joint analysis). Two different approaches were used, a single-marker GWAS and two Bayesian GWAS.

2.3.1. Single-Marker GWAS

For the single-marker GWAS, EMMAX was implemented using SNP & Variation Suite 7 (Golden Helix, Inc., Bozeman, MT, USA); this is a single-locus mixed model GWAS approach that fits a genomic relationship matrix to account for genetic covariance among animals [19]. In single-locus GWAS, one primary concern is the elevated false positive rate. To mitigate this concern, the Bonferroni correction is commonly employed in single-locus models. We set the false discovery rate to 0.05 to correct for multiple testing. The response variables used were the corrected phenotypes (y-Xb). In the case of this data type, the Mixed Model approach is highly suitable. It allows us to account for relatedness by incorporating the random effects component of the model, utilizing a kinship matrix (IBS), and also enables the inclusion of supplementary fixed effects (such as Breed for joint analyses).

The *p*-values for the Bonferroni-corrected thresholds at the suggestive and 5% genome-wide significance levels were determined by dividing 1 and 0.05, respectively, by the total number of markers utilized in the GWAS. The concept of the suggestive level was originally introduced by Lander and Kruglyak [20] and signifies the threshold at which, assuming the null hypothesis, one false positive is anticipated per genome scan [21]. Following the analysis, none of the SNP or haplotype markers surpassed the significance thresholds at the genome-wide level in both the Simmental and Simbrah data analyses as well as in the joint-data analysis. Consequently, the suggestive threshold level was employed as a reference to identify associations between the markers and economically significant traits.

2.3.2. Bayesian GWAS

The Bayesian models were implemented via the BGLR statistical package of the R program [22]. Two a priori finite mixture models were employed: one comprising a mass point at zero and a Gaussian density, referred to as BayesC [23], and another featuring a mass point at zero along with a scaled t density, known as BayesB [24]. By assigning a nonzero prior probability for the marker effect to equal zero, the principles underlying BayesB and BayesC have the capacity to initiate variable selection.

For a continuous response (y_i; $i = 1, \ldots, n$), the data equation is formulated as follows: $y_i = \eta_i + \varepsilon_i$, where η_i represents a linear predictor, the expected value of y_i given the predictors, and ε_i denotes the residuals. These residuals are independent and conform to a normal distribution with a mean of zero and a variance $w_i^2\sigma_\varepsilon^2$. The linear predictor serves as the conditional expectation function and is structured as:

$$\eta = 1\mu + X_1\beta_1, \quad (1)$$

$$\eta = 1\mu + X_1\beta_1 + X_2\beta_2, \quad (2)$$

μ represents the intercept and X_j stands for the design matrices for the predictors, denoted as $X_j = \left\{x_{ijk}\right\}$, where x_{ijk} is the marker in the region j from the breed k of the individual i and β_j are vectors of the effects associated with the columns of X_j. For the Simmental and Simbrah analysis model (1) X_1 is the matrix with marker genotypes, and β_1 is the corresponding vector of marker effects. For the joint analysis model (2), X_1 is a design matrix for the effects of breed, β_1 is the corresponding vector of effects, X_2 is the matrix with marker genotypes, and β_2 is the corresponding vector of marker effects. Bringing together these assumptions, we obtain the following conditional distribution of the data:

$$p(y|\theta) = \prod_{i=1}^{n} N\left(y_i|\mu + \sum_{j=1}^{J}\sum_{k=1}^{K_j} x_{ijk}\beta_{jk}, \sigma_\varepsilon^2 w_i^2\right)$$

where θ represents the collection of unknowns, including the intercept, regression coefficients $\left(\beta_{jk}\right)$, and the residual variance. The analysis employs Markov chain Monte Carlo (MCMC) methods to calculate posterior mean estimates of marker effects and variances. The MCMC chains consist of 100,000 iterations, with the initial 25,000 samples designated for burn-in.

The Gelman–Rubin diagnostic was employed to evaluate the Bayesian models, which evaluates MCMC convergence by analyzing the difference between multiple Markov chains. The convergence is assessed by comparing the estimated between-chains and within-chain variances for each model parameter. To facilitate this process, adjustments were made to the potential scale reduction factor, with the estimated degrees of freedom (d) serving as the pivotal parameter for this adaptation. This adjustment relies on a Student-t approximation for posterior inference derived from the simulations [22],

$$\hat{R}_c = \frac{d+3}{d+1}\hat{R}$$

Significant disparities in these variances signal non-convergence $\left(\hat{R}_c > 1.1\right)$. In cases where the model failed to converge, the number of iterations and burn-ins were doubled. After estimating marker effects, 95% confidence intervals and posterior probabilities for these effects were calculated. Marker effects that equal zero signify the absence of any marker's influence. To select those markers associated with a trait, posterior probabilities and confidence intervals were used.

2.4. Candidate Gene Annotations and Previously Reported QTL

The SNP and haplotypes associated were mapped at 100 kb intervals on both sides, given the average LD (r^2 = 0.2) previously observed in beef cattle [13]. Potential candidate genes were identified and linked to the associations using the latest genetic annotations from ENSEMBL (release 104), based on the *Bos taurus* ARS-UCD1.2 genome assembly [25]. A gene was considered a candidate if at least one marker window overlapped with it.

Furthermore, a search was conducted for QTLs previously associated with these SNP and haplotype windows within the same regions. The identified QTLs were compared to those recorded in the Cattle QTL Database [26].

3. Results

Except for the analysis conducted on STAY in Simbrah cattle, which generated no identified associated markers, the Quantile–Quantile (Q-Q) plots did not reveal any substantial deviations (Figure 1). The close alignment of observed values with the expected values is evident, with most data points residing along or in close proximity to the central line

between the x-axis and the y-axis. This absence of early divergence between expected and observed values indicates the absence of population stratification [27].

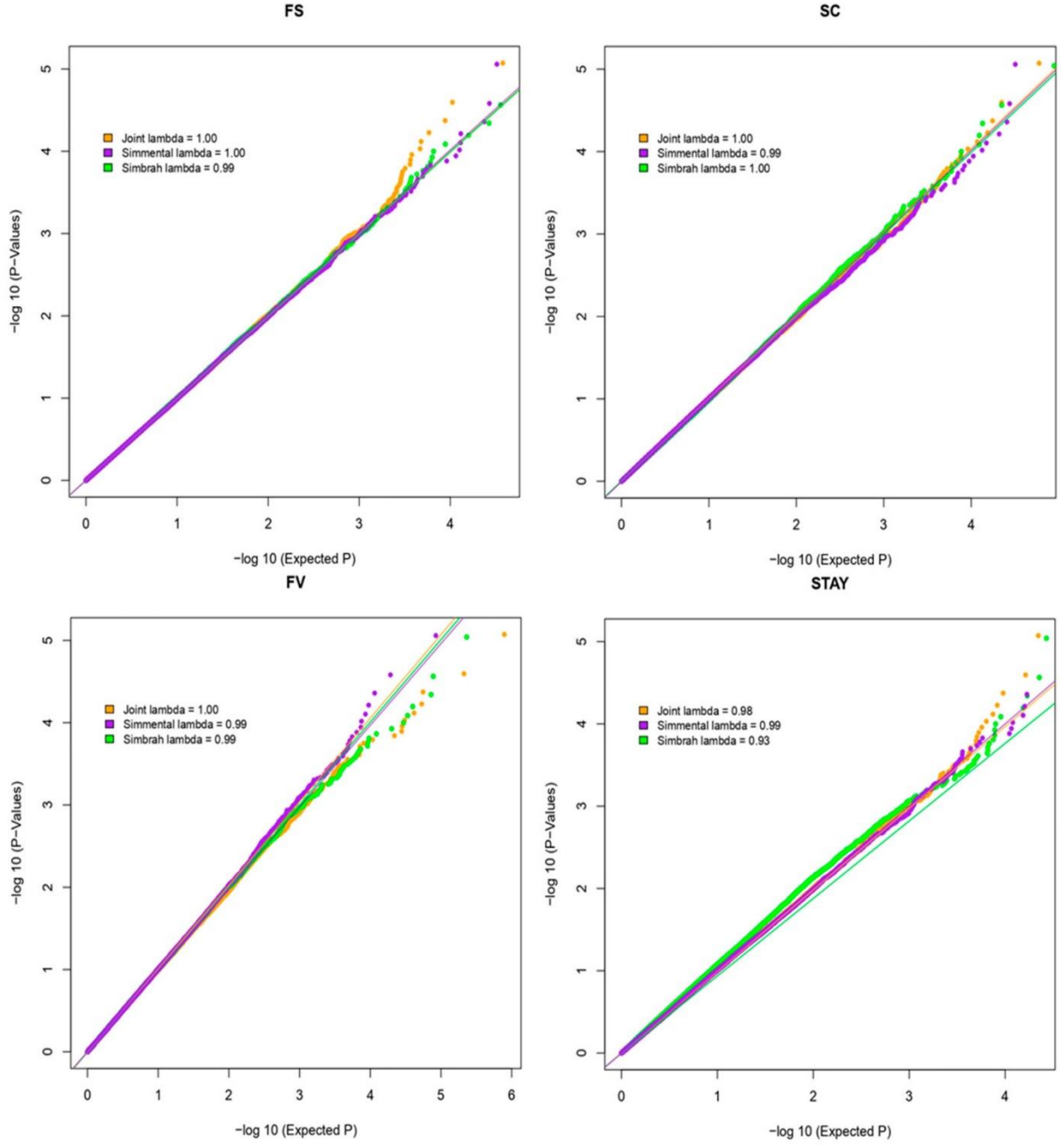

Figure 1. Quantile–Quantile (Q-Q) plot with the haplotype association analysis for frame score (FS), scrotal circumference (SC), heifer fertility (HF), and stayability (STAY) using the EMMAX method in Simmental, Simbrah, and Joint Analysis.

Figure 2 displays a bar plot representing the distribution of SNP markers and haplotypes associated with FS, SC, HF, and STAY in Simmental, Simbrah, and the Joint Analysis. Also, by using the Cattle QTL Database [26], 118, 74, 45, and 28 QTLs previously described were found within the SNP windows for FS, SC, HF, and STAY, respectively; also, 50, 83, 63, and 16 QTLs previously described were found within the haplotype windows for FS, SC,

HF, and STAY, respectively (Table S1). For all the traits, QTLs associated with conformation, health, meat, carcass, milk, and reproduction traits in cattle were found. Over the database ARS-UCD1.2, 18, 11, 6, and 2 genes were found within the SNP windows for FS, SC, HF, and STAY, respectively; also, 2, 22, 7, and 1 QTLs previously described were found within the haplotype windows for FS, SC, HF, and STAY, respectively (Table S1).

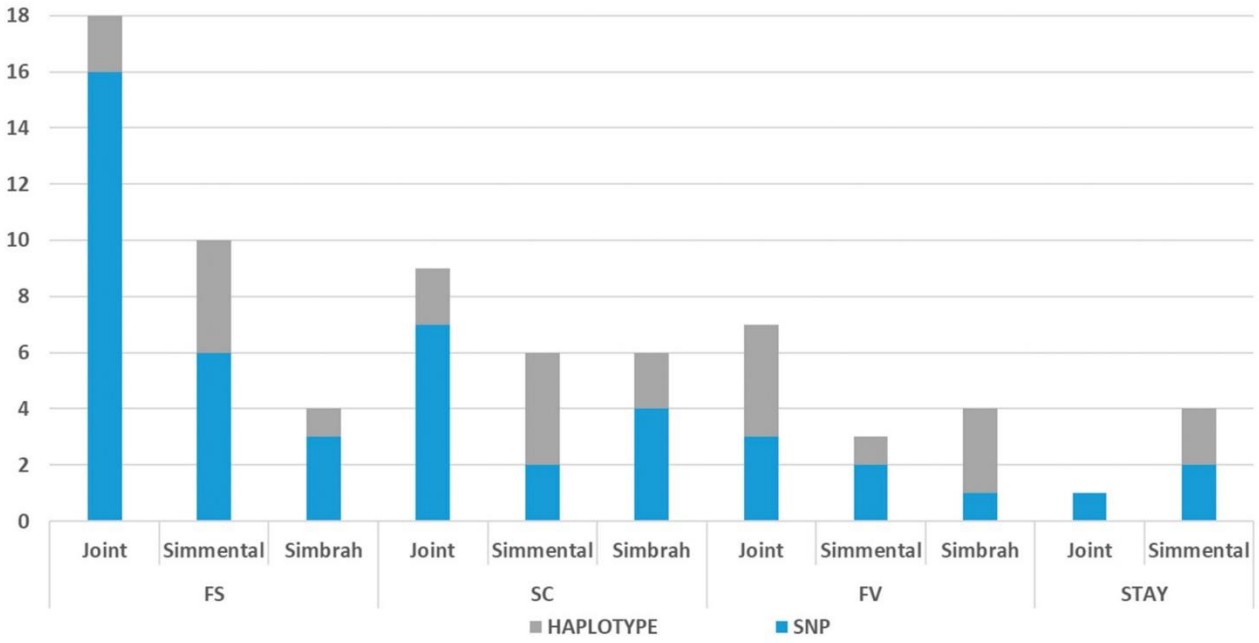

Figure 2. SNP markers and haplotypes associated with frame score (FS), scrotal circumference (SC), heifer fertility (HF), and stayability (STAY) in Simmental, Simbrah, and Joint Analysis.

3.1. Frame Score

In the joint association analysis of FS with SNPs, 15 associated regions were located on chromosomes 4, 5, 6, 7, 8, 11, 16, 17, and 22 (Table S2). Only one marker located on chromosome 17 was associated with all models (BayesB, BayesC, and EMMAX). Three regions were identified with the BayesC model on chromosomes 6, 7, and 8, and the remaining regions were linked with the Bayesian models.

In the Simmental data analysis with SNPs, six associated regions were found on chromosomes 2, 17, 19, and 20 (Table S2). The associated regions on chromosomes 17 and 19 were determined using the BayesC model, and the remaining regions were determined with both the BayesB and BayesC models.

For Simbrah cattle, associated regions were found on chromosomes 3, 17, and 18 (Table S2). There was only one associated region using the BayesB model on chromosome 17. The remaining regions were found with both BayesB and BayesC models.

In the haplotype association analysis with the joint analysis, two regions were identified on chromosomes 4 and 8, both with the BayesC model (Table S3). In addition, the region located on chromosome 8 was associated with the BayesB model (Figure 3).

In the haplotype analysis of the Simbrah cattle, only one region on chromosome 3 was identified with the three models (Table S3). In Simmental cattle, four regions were located on chromosomes 1, 2, 4, and 12 with the two Bayesian models (Figure 3).

By contrasting the regions associated with SNPs and haplotypes, we found two regions in common in the joint analysis (Table S3). For the individual analyses of Simmental and Simbrah, one region was found to be common in each breed (Figure 3).

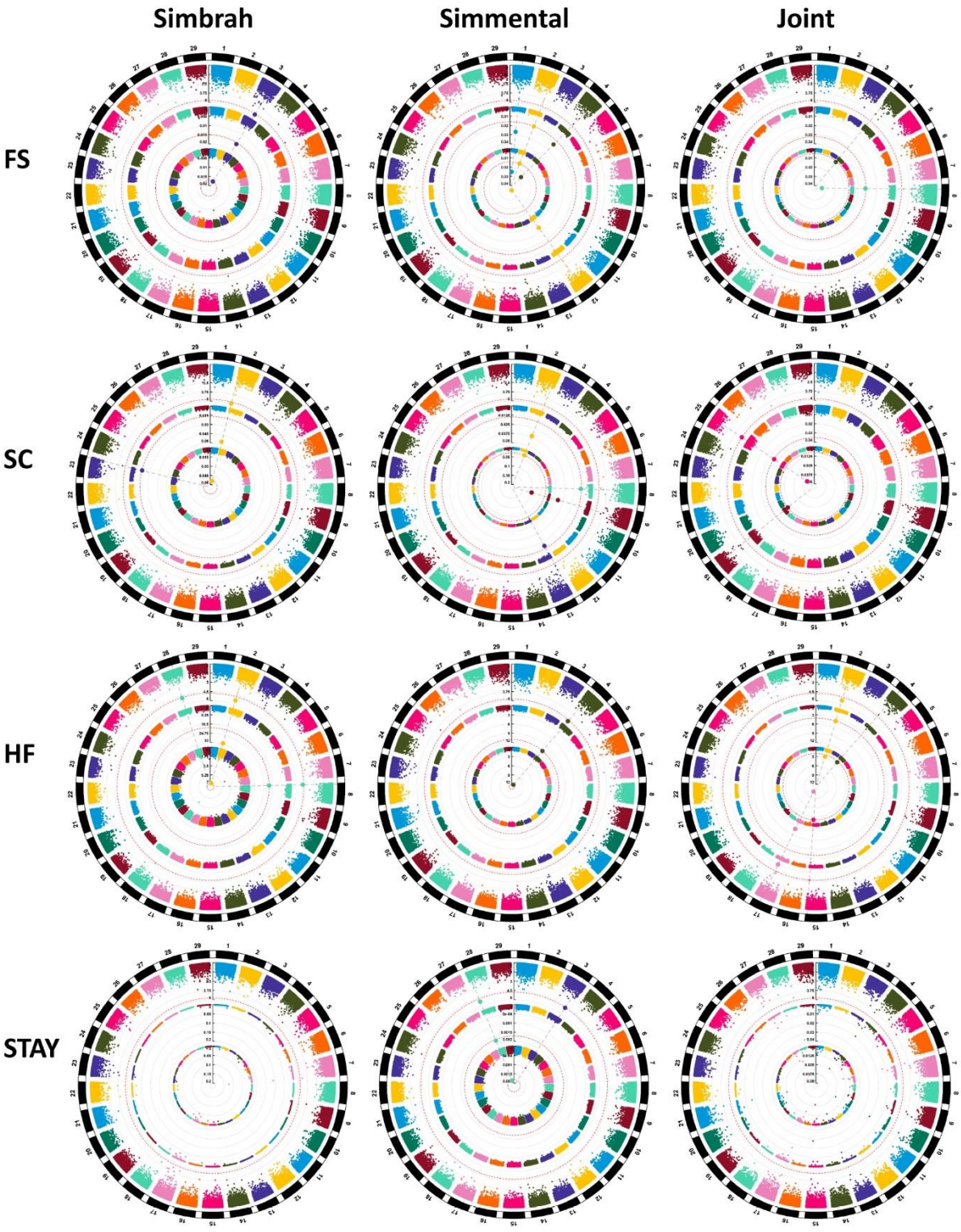

Figure 3. Circle Manhattan Plot with the haplotype association analysis for frame score (FS), scrotal circumference (SC), heifer fertility (HF), and stayability (STAY) with the EMMAX (outer circle, $-\log_{10}$ *p*-values), BayesB (middle circle, posterior probabilities), and BayesC (inner circle, posterior probabilities) model in Simbrah, Simmental, and joint cattle. The associated haplotypes are above the red line with big dots in each analysis.

3.2. Scrotal Circumference

According to the joint association analysis of scrotal circumference with SNPs, seven associated regions were located on chromosomes 1, 3, 6, 10, and 17 (Table S2). With the three models (BayesB, BayesC, and EMMAX), only one marker was associated with chromosome 10. The other regions were associated with BayesB and BayesC, except the one located on chromosome 1, which was only associated with BayesC.

Two associated regions were found on chromosomes 10 and 13 in the association analysis with SNPs for Simmental cattle (Table S2). All models determined the associated region on chromosome 10, and Bayesian models determined the remaining regions.

There were associated regions on chromosomes 6, 10, 17, and 23 for Simbrah cattle (Table S2). On chromosomes 17 and 23, there were two regions associated with BayesC. The remaining regions were detected by BayesB and BayesC.

On chromosomes 19 and 25, the joint analysis revealed two haplotype associated regions (Table S3). Each of the three models determined the associated region on chromosome 25, and the BayesC model determined the remaining region (Figure 3).

The haplotype analysis of Simbrah cattle identified two regions on chromosomes 2 and 23 (Table S3). With all models, we determined the associated region on chromosome 2, and BayesB determined the remaining region (Figure 3).

Four regions were found on chromosomes 2, 8, 9, and 13 of Simmental cattle (Table S3). Chromosomes 8 and 13 were associated with the BayesB model. The remaining regions were found with both BayesB and BayesC models (Figure 3).

By contrasting the regions associated with SNPs and haplotypes, we found no regions in common in the joint analysis. For the individual analyses of Simmental and Simbrah, one region was found to be common in each case. In addition, there was a region in the SNP analysis in common between Simmental and Simbrah with the joint analysis in chromosomes 10 and 6, respectively.

3.3. Heifer Fertility

The joint association analysis of heifer fertility with SNPs identified four associated regions on chromosomes 4, 17, and 18 (Table S2). With the three models (BayesB, BayesC, and EMMAX), only one region on chromosome 17 was associated. On chromosome 4, BayesC identified two regions, while BayesB and BayesC were linked to the remaining regions.

In the SNP association analysis for Simmental cattle, two associated regions were found on chromosomes 4 and 21 (Table S2). The associated region on chromosome 4 was determined using the BayesC model, and the remaining region was determined by all models. As for Simbrah cattle, an associated region was found on chromosome 17 with all models.

Based on the haplotype association analysis with the joint analysis, four regions were identified on chromosomes 2, 4, 15, and 17 (Table S3). Two regions were identified with the BayesC model on chromosomes 4 and 15, and the remaining regions were linked with all models (Figure 3).

The haplotype analysis of Simbrah cattle identified only three regions on chromosomes 2, 8, and 28 (Table S3). All regions were associated with the EMMAX model. BayesB was linked with chromosomes 2 and 8. The BayesC model also determined the region associated with chromosome 2. Simmental cattle showed a region on chromosome 4 with all models (Figure 3).

Comparing the regions associated with SNPs and haplotypes, we found one region in common. Additionally, the Simbrah and joint analyses shared a region on chromosome 17.

3.4. Stayability

In the joint association analysis of STAY with SNPs, one associated region was located on chromosome 21 with the BayesC model (Table S2). In Simmental cattle, associated SNPs were found on chromosomes 1 and 28 using the two Bayesian models (Table S2). In addition, the EMMAX model was linked to the chromosome 28 region. The EMMAX

model identified an additional region on chromosomes 3 in the Simmental cattle haplotype analysis. In Bayesian models, the region associated with chromosome 28 was located as well.

Our analysis of Simmental individual analyses of chromosome 28 revealed a region common to both haplotypes and SNPs (Table S2).

4. Discussion

4.1. Frame Score

In the Simmental data analysis, within the SNP windows on chromosome 2, QTLs were previously associated with a body form composite index in Holstein cattle; this index contemplates the height of the animal, which is a measure that is also used to calculate FS [28]. Also, inside of an SNP window on chromosome 19, three different traits were previously associated, these included a QTL for body weight (yearling) in Angus cattle [8], which is a trait correlated with FS [29]. In the same way, in the same study, they associated this region with another QTL for SC [8], which is also related to FS [29], and stature through an association analysis in Holstein cattle [30]. Finally, within a haplotype window, a QTL was also associated with body weight (yearling) in Angus cattle [8].

From the results of the joint model, several coincidences were found within the regions associated with FS, with the databases of QTLs. On chromosome 5 and 7, associations with SC in Angus cattle [8] were found, which is a trait correlated with FS [29]. Also, QTLs associated with body weight (yearling) were found within chromosome 6 and 22; the first one was in crossbred beef cattle [31] and the second in Angus cattle [8], and as already mentioned, this is a trait correlated with FS [29].

The ligand-dependent nuclear receptor corepressor-like (LCORL) gene on chromosome 6 has been reported to be associated with body frame size (height) at puberty in Japanese Black and Charolais x German Holstein cattle [32]; it is the same region associated in the present work with FS (Table S1).

4.2. Scrotal Circumference

In the Simbrah data analyses, two QTL associated with body weight (yearling) inside of the haplotypes windows were found on chromosome 2 in Angus × Brahman cattle [33] and 23 in Angus cattle [8] In the same region of chromosome 23, a QTL associated with SC in Angus cattle was found [8].

In Simmental cattle, associations with body weight (yearling) were found within two haplotype windows on chromosomes 8 in crossbreed cattle [31] and 13 in Angus × Brahman cattle [34]. The same region of chromosome 13 was found with the SNP analysis. In addition, within an SNP window, two regions associated with SC and sexual precocity [7] in tropically adapted breeds were found.

In the joint-data analysis, associations were found in two SNPs windows on chromosome 1 in Angus × Brahman cattle [34] and 17 in Angus cattle [8] associated with body weight (yearling). On chromosome 10, associations with SC and sexual precocity were reported; this is the same region found in the current Simmental data analysis. For haplotypes windows, on chromosome 19, two QTLs associated with SC in Angus cattle [8] and the ovulation rate [35] were found. Finally, a haplotype window on chromosome 25 was found in the same region as a QTL associated with body weight (yearling) in Angus cattle [8].

In Iranian Holstein cattle [36], on chromosome 13, the recombination signal binding protein for the immunoglobulin kappa J region-like (RBPJL) gene associated with calving to first service was identified, which is the same gene that was associated in the present work with SC (Table S1).

4.3. Heifer Fertility

In the Simmental data analysis, within the SNP windows on chromosome 21, QTLs were previously reported to SC in Angus cattle [8], which is a trait correlated with FS [29].

From the results of the joint model, in the SNP window on chromosome 18, a QTL was associated with the pregnancy rate and length of productive life in Holstein cattle [37]; also, on chromosome 15 within a haplotype window, a QTL associated with age at puberty in crossbreed cattle was reported [38].

In Iranian Holstein cattle [36], on chromosome 2, the ADP ribosylation factor-like GTPase 5A (ARL5A), calcium voltage-gated channel auxiliary subunit β 4 (CACNB4) gene associated with calving to first service was identified, which is the same gene that was associated in the present work with HF (Table S1).

RUN Domain Containing 3B (RUNDC3B) on chromosome 4 had been reported to the retained placenta signals with associations related to milk production, productive life, and health and reproduction traits, including calving ease and stillbirth [30,39]. In Holstein cattle on chromosome 4, the Inner Mitochondrial Membrane Peptidase 2-Like Gene (IMMP2L) had a negative effect on the cow conception rate [40]; in mouse, homozygous IMMP2L females were infertile due to defects in folliculogenesis and ovulation, whereas mutant males were severely subfertile due to erectile dysfunction [41].

In goats, the expression of the CKLF-like MARVEL transmembrane domain-containing 2 (CMTM2) gene on chromosome 18 was more elevated in the ovaries of multiple prolific goats at first kidding compared to non-prolific goats [42].

4.4. Stayability

In the Simmental data analysis, within the SNP windows on chromosome 1, QTLs were previously reported for the interval to first estrus after calving in Holstein cattle [43]. With the severe body condition loss, there can be longer intervals to the first ovulation and first estrus, lower first service conception rates, and more days open [44]. On chromosome 28 in the same region that an SNP and haplotype window were found, a QTL was previously associated to the pregnancy rate [45].

In Costeño con Cuernos cattle from Colombia, on chromosome 21, the cathepsin H (CTSH) gene associated with age at first calving was identified [46], which is the same gene that was associated in the present study with STAY (Table S1).

4.5. Single-Marker GWAS and Two Bayesian GWAS

As shown in the results, none of the SNPs crossed the threshold level at the genome level for the EMMAX model. Nonetheless, this is not an isolated case, as in many studies, single locus GWAS models, such as EMMAX, did not significantly exceed the threshold of significance, so they resort to other methodologies [47]. Although the whole concept of significant thresholds should not be misinterpreted to assume causality and reproducibility of SNP effects [48], it is a useful concept to preselect and differentially weigh SNPs in a genomic prediction between breeds [49].

According to our dataset, while using a single marker with EMMAX makes it more stringent to assert significance, employing Bayesian models offers a superior understanding of how LD affects the outcome. However, as Legarra et al. [50] mentions, the strength of the evidence that combines information from several consecutive markers increases with Bayesian models and decreases with EMMAX. These approaches could benefit frequentist models by offering an improved mixture of evidence among markers. Yet, their suitability for primary detection remains uncertain due to the absence of clearly defined rejection thresholds.

In GWAS, a frequent issue arises when the number of parameters (p) is significantly larger than the number of samples (N). Consequently, conventional methods of maximizing the likelihood based on effect sizes often result in severe overfitting. To address this problem, a common approach is to introduce a regularization term into the log likelihood, encouraging many components of β (effect sizes) to approach zero. From a Bayesian perspective, this can be viewed as maximizing the posterior distribution $p(\beta \mid X)$ [51]. This advantage of Bayesian models over single locus models allows for better handling of overfitting in GWAS.

4.6. SNP- and Haplotype-Based Association Analyses

In the present study, we identified several significant SNPs and favorable haplotypes using SNP and haplotype-GWAS approaches, respectively, that regulate FS, SC, HF, and STAY in Simmental and Simbrah cattle. The idea of utilizing haplotype-based GWAS has been suggested as an additional method to enhance the advantages gained from LD [52]. This is because these studies have the potential to offer a new perspective on genetic factors that are not identified via the analysis with SNPs, which allows us to investigate the genetic architecture of traits of economic interest [52].

SNP- and Hap-window approaches to identify important genomic regions accounted for LD and better characterized QTL than the individual effects [53]. For all traits, markers were found in regions previously associated with genes and QTLs for production, reproduction, health, and conformation traits. However, it is of greater interest to focus on the QTLs that are correlated with each trait.

Association analyses have identified many common genetic variants associated with traits of interest, but these variants typically have small effect sizes and account for only a small fraction of the heritability of most traits. This missing heritability revealed in many well-powered analyses associations suggests that there are many important architectural details of traits that remain to be discovered. However, an association that explains only a small proportion of heritability may nonetheless provide valuable biological insights [54]; therefore, the lack of overlapping genomic regions identified for shared traits between Simmental and Simbrah cattle suggests that these breeds have distinct genetic architectures for these traits.

Our study provides new insights into the genetic basis of reproductive traits and FS in Simmental and Simbrah cattle. We identified positional candidate genes with functional evidence that could improve bull genomic prediction for these traits. It has been proven that GWAS-selected sequence variants improve genomic prediction reliability [14], which could have a major impact on the beef cattle industry as it would allow producers to breed more productive and efficient animals.

5. Conclusions

A total of 23, 13, 7, and 2 SNPs were associated with FS, SC, HF, and STAY, respectively. Also, seven, eight, seven, and one haplotypes were associated with FS, SC, HF, and STAY, respectively. Through these regions, we identified possible candidate genes for the different traits used in this study. These regions may be useful in Mexican Simmental and Simbrah cattle. No regions were found to be common between Simmental and Simbrah cattle, which indicate that we are dealing with two completely different genetic architectures.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/genes14112004/s1, Table S1: Traits and candidate genes previously identified within the regions associated with reproductive traits and frame score in Simmental and Simbrah cattle; Table S2: SNPs associated with reproductive traits and frame score with the models BAYESB, BAYESC and EMMAX in Simmental and Simbrah cattle; Table S3: Haplotypes associated with reproductive traits and frame score with the models BAYESB, BAYESC, and EMMAX in Simmental and Simbrah cattle.

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DISCUSIÓN GENERAL

En el presente estudio observamos como existe una diferencia en las frecuencias alélicas del ganado Simmental y Simbrah, lo cual se puede observar desde que se muestran las tendencias de LD. De manera que, aunque el ganado Simbrah desciende de ganado Simmental, existe una diferenciación en ambas poblaciones.

Lo anterior coincide con lo encontrado por otros autores que comparan diferentes LD en varias razas (Villa-Angulo *et al*., 2009). Además, la presencia de valores más altos de LD observados en ciertos cromosomas en comparación con otros puede sugerir la existencia de QTL que influyen en las características que han sufrido una fuerte selección en ambas razas (Biegelmeyer *et al*., 2016).

La variación en las tasas de recombinación entre autosomas puede resultar en una diversidad significativa en los patrones de LD observados en varias regiones genómicas y cromosomas (Cañas-Álvarez *et al*., 2016). Lo que puede haber afectado regiones genómicas específicas y ubicaciones individuales de manera diferente dentro de las poblaciones Simmental y Simbrah. De manera que resulta relevante identificar regiones que pudieran estar asociadas a características de interés económico.

Un enfoque alternativo y lógico para emplear en los análisis de asociación es a través pruebas que evalúen los efectos de múltiples marcadores en una región genómica. Para una prueba basada en una región, el poder depende en gran medida de la arquitectura genética, y su estimación requiere modelar esta arquitectura genética y el LD entre las variables (Wu *et al*., 2011). De manera que, agrupar SNP por genes, vías metabólicas o bloques de haplotipo, pudiera apoyarnos a tener una nueva perspectiva sobre factores genéticos que no se

identifican mediante el análisis individual de SNP. Además, el uso de conjuntos de SNP también puede reducir el número de predictores y aliviar el problema de la colinealidad. Dado que la gran cantidad de variantes puede conducir a limitaciones informáticas para el cálculo de LD y la selección de todas las variantes, así como a un sobreajuste debido a la alta colinealidad entre las variantes, la cual puede dar como resultado efectos variantes condicionales muy sobreestimados y valores de p inflados (Veerkamp *et al*., 2016).

Otro enfoque utilizado en el capítulo 1 es el realizar análisis de asociación individuales por cromosoma, de manera que reducimos las dimensiones del análisis a regiones específicas del genoma. Sin embargo, se ha encontrado que, aunque los factores de inflación genómica no muestran diferencias significativas entre las diferentes densidades de SNP, existe una variación considerable en los factores de inflación genómica entre los cromosomas (den Berg *et al*., 2019). Esta observación podría explicarse potencialmente por los diferentes niveles de asociación entre los SNP en cada cromosoma y la característica de interés. Además, utilizar el número total de SNP puede conducir a umbrales demasiado conservadores, ya que viola el supuesto de independencia entre las pruebas (Duggal *et al*., 2008; Nicodemus *et al*., 2005).

En cuanto a los modelos utilizados, se observó en el segundo capítulo que el modelo que utiliza un solo locus (EMMAX), no pudo identificar marcadores asociados a las características reproductivas mediante un umbral a nivel de genoma, dicha información concuerda con lo encontrado por diversos autores (Zhao *et al*., 2022) y es una de las razones por las que se han desarrollado muchas otras metodologías como las de múltiples locus (Zhao *et al*., 2022). En cuanto a los modelos bayesianos

estos participan activamente dentro de las nuevas metodologías que se han realizado año con año, desde su incorporación en la selección genómica con Meuwisen *et al*. (2001) hasta los modelos más actuales de machine learning. Esto se debe principalmente a su capacidad de solventar el problema de dimensiones que se presenta al tener un número mucho mayor de parámetros que dé muestras (Banerjee *et al*., 2018).

CONCLUSIONES

Se encontraron diferencias entre las regiones asociadas a las características de interés económico en Simmental y Simbrah. Lo que muestra que, aunque el origen del ganado Simbrah es el Simmental, la arquitectura genética entre ambas razas es diferente.

En las características estudiadas en este trabajo se encontraron asociaciones en el genoma. En las de crecimiento, que tienen heredabilidad moderada, fue mayor la cantidad de marcadores asociados, en comparación con las características reproductivas que generalmente tienen una heredabilidad baja.

Se pudo observar en el caso de los modelos bayesianos (BayesA y BayesB), tienden a tener asociaciones similares. Además de que tienen mayor poder de detección que el modelo de un solo locus (EMMAX). El uso de otros tipos de marcadores, como los haplotipos, puede ser beneficioso para la identificación de regiones asociadas a características de interés económico, ya que pueden proporcionar más información, ya que un bloque de haplotipos constan de dos o más loci y puede tener más de dos haplotipos, lo que proporciona mayor diversidad dentro de una región determinada.

El uso de análisis por cromosoma para complementar los análisis del genoma completo, dado que, al tomar la información de todo el genoma, la varianza individual de los marcadores se puede ver diluida, lo que imposibilita su detección. Las regiones asociadas pueden ser útiles para proporcionar información sobre las características de crecimiento en el ganado Simmental y Simbrah con mediciones fenotípicas relacionadas. Además, los genes candidatos pueden ayudar a identificar las vías de los genes a través del análisis de enriquecimiento. Estos estudios pueden ayudarnos a entender mejor las rutas metabólicas de las características de interés económico.

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Table S1. Marker effects ($\hat{b}_j$) and their posterior probabilities (PP) of SNPs associated with growth traits with the use of genome-wide association (GWA) as well as a chromosome-wide association (CWA) in simmental and simbrah cattle.

Model	Chr[a]	Pos[b]	SNPs[c]	BW[d]				WWD[e]				WWM[f]				YW[g]			
				GWA		CWA		GWA		CWA		GWA		CWA		GWA		CWA	
				$\hat{b}_j$	PP	$\hat{b}_j$	PP	$\hat{b}_j$	PP	$\hat{b}_j$	PP	$\hat{b}_j$	PP	$\hat{b}_j$	PP	$\hat{b}_j$	PP	$\hat{b}_j$	PP
Joint	1	6,952,436	BovineHD0100002043			-0.026	0.129												
Joint	1	17,148,366	BovineHD0100005053	0.012	0.066	0.068	0.301												
Joint	1	18,258,818	BovineHD0100005339	-0.040	0.240														
Joint	1	24,168,476	ARS-BFGL-BAC-6737									0.034	0.043	0.126	0.128				
Joint	1	41,455,680	Hapmap23514-BTA-150593					-0.097	0.098			0.083	0.127						
Joint	1	49,567,103	BovineHD0100014058			0.014	0.061												
Joint	1	49,634,079	BovineHD0100014071			0.013	0.053												
Joint	1	50,665,945	BovineHD0100014362	-0.010	0.071	-0.016	0.107												
Joint	1	53,241,119	ARS-BFGL-NGS-94761					0.042	0.029	1.713	0.621			-0.112	0.092				
Joint	1	54,038,526	BTB-00217542															0.803	0.351
Joint	1	58,000,696	ARS-BFGL-NGS-40337					0.139	0.150			-0.037	0.065						
Joint	1	78,127,259	BovineHD0100022657			-0.016	0.064												
Joint	1	115,897,261	BovineHD0100033028											0.088	0.130				
Joint	1	118,821,328	BovineHD0100033867					-0.105	0.106										
Joint	1	118,912,426	BovineHD0100033896					-0.116	0.125	-0.623	0.451					-0.089	0.101	-0.466	0.424
Joint	1	119,151,202	BovineHD4100000688													-0.045	0.046		
Joint	1	131,680,356	BovineHD0100037820					0.058	0.060										
Joint	1	147,542,196	BovineHD0100043239									-0.029	0.054						
Joint	1	155,615,450	ARS-BFGL-NGS-54653	0.017	0.111	0.078	0.408												
Joint	1	157,593,001	BovineHD0100012784													0.044	0.040		
Joint	1	157,605,027	BovineHD1100023814													0.034	0.054		
Joint	2	6,912,773	BovineHD0200002005					0.048	0.032	0.284	0.200								
Joint	2	13,346,155	BTA-20457-no-rs									0.036	0.053						
Joint	2	13,367,301	BovineHD4100001011					-0.042	0.034			0.090	0.110	0.337	0.313				
Joint	2	28,366,129	BovineHD0200008331							0.190	0.148								
Joint	2	30,228,551	BovineHD0200008901							0.238	0.184								
Joint	2	57,203,290	BovineHD0200016269			-0.014	0.054												
Joint	2	92,668,354	BovineHD0200026560							-0.106	0.100								
Joint	2	94,636,270	Hapmap50979-BTA-48487													-0.132	0.152		
Joint	2	122,900,223	BovineHD0200035799			-0.013	0.090												
Joint	2	133,487,750	BovineHD0200039106									0.054	0.068	0.187	0.169				
Joint	3	328,058	BovineHD0300000063									0.045	0.080						

Joint	3	15,763,689	BovineHD4100001879			-0.016	0.094												
Joint	3	34,241,835	BovineHD0300035533			0.014	0.102												
Joint	3	43,071,852	BovineHD0300013160	-0.008	0.038	-0.028	0.102												
Joint	3	71,037,098	BovineHD0300020955			-0.013	0.053												
Joint	3	73,463,469	BovineHD0300021473	-0.020	0.112	-0.053	0.259												
Joint	3	101,605,832	BovineHD0300029255													-0.036	0.045		
Joint	4	10,025,067	BovineHD0400003025					-0.037	0.043										
Joint	4	34,087,094	BovineHD0400009726	0.016	0.101														
Joint	4	39,299,282	BTB-01780264					0.044	0.037	0.361	0.170								
Joint	4	45,694,800	BovineHD0400012548					0.095	0.088			-0.203	0.245						
Joint	4	48,070,266	BovineHD0400013290					0.107	0.073	1.844	0.838			-0.701	0.473				
Joint	4	52,341,148	BovineHD0400014536			-0.151	0.412												
Joint	4	52,350,959	BovineHD0400014539	0.007	0.045														
Joint	4	53,943,257	BovineHD0400014943													-0.043	0.045		
Joint	4	54,668,072	BovineHD0400015064													0.160	0.155	0.964	0.660
Joint	4	88,650,637	BovineHD0400024784	0.011	0.074														
Joint	4	111,112,243	BovineHD0400032138													0.057	0.074	0.279	0.261
Joint	4	112,844,573	BovineHD0400032781					-0.039	0.029			0.047	0.070						
Joint	5	4,559,923	ARS-BFGL-NGS-41385							0.829	0.632	-0.029	0.050	-0.246	0.303				
Joint	5	8,878,483	BTB-00218987	0.044	0.251	0.097	0.482												
Joint	5	28,142,436	BovineHD0500008288													0.126	0.131	0.573	0.458
Joint	5	37,375,959	BovineHD0500010721											-0.055	0.052				
Joint	5	43,173,154	BovineHD0500012424													-0.037	0.048	-0.274	0.211
Joint	5	43,254,214	BTB-01477571													-0.047	0.064	-0.683	0.548
Joint	5	46,106,048	BovineHD0500013307			-0.035	0.219												
Joint	5	47,114,993	BovineHD0500013676	0.008	0.037	0.056	0.155												
Joint	5	47,920,992	BovineHD0500013910					-0.152	0.172			0.084	0.136	0.072	0.096				
Joint	5	109,153,222	ARS-BFGL-NGS-16738									0.032	0.054	0.106	0.146				
Joint	5	109,639,214	BovineHD0500031760									-0.035	0.063	-0.085	0.116				
Joint	5	109,676,735	BovineHD0500031776									-0.040	0.056	-0.063	0.087				
Joint	6	206,650	BovineHD0600000030	0.009	0.045														
Joint	6	22,449,056	BovineHD0600006577	0.009	0.054														
Joint	6	24,537,233	BovineHD4100004318	-0.008	0.057	-0.106	0.543												
Joint	6	31,922,816	Hapmap27500-BTC-032985	0.012	0.075														
Joint	6	35,575,862	BovineHD4100004463							0.318	0.211								
Joint	6	42,770,292	BovineHD0600012095							-0.125	0.103								
Joint	6	66,299,180	ARS-BFGL-NGS-72592							-0.194	0.138								
Joint	6	73,018,262	BovineHD0600020776													-0.035	0.049		

Joint	6	86,762,457	BovineHD0600024201													0.033	0.044		
Joint	6	111,363,016	BovineHD0600033010	-0.009	0.062														
Joint	6	112,448,301	BovineHD0600033358					-0.042	0.057										
Joint	7	7,011,872	BovineHD0700002043													0.043	0.053	0.076	0.058
Joint	7	10,456,355	BovineHD0700002995															0.098	0.078
Joint	7	10,619,615	BovineHD0700003030													0.034	0.035	0.319	0.250
Joint	7	18,446,391	BovineHD0700005476					0.131	0.112										
Joint	7	20,673,981	BovineHD0700006039					-0.077	0.069	-0.305	0.205								
Joint	7	26,294,867	BovineHD0700007673															0.077	0.093
Joint	7	71,945,283	BovineHD0700021817			0.015	0.053												
Joint	7	73,180,407	BovineHD0700022161			-0.019	0.110												
Joint	7	73,197,856	BovineHD0700022164	-0.046	0.269	-0.112	0.552												
Joint	7	73,286,379	BovineHD0700022183	-0.017	0.108	-0.028	0.131												
Joint	7	102,495,062	BovineHD0700030660															0.121	0.138
Joint	7	102,564,741	BovineHD0700030692													0.059	0.077	0.183	0.186
Joint	7	105,857,552	BTB-00115134															0.203	0.133
Joint	8	6,189,677	ARS-BFGL-NGS-104101													0.107	0.140		
Joint	8	8,989,368	BovineHD0800002828	-0.021	0.142														
Joint	8	11,078,911	BovineHD0800003578	-0.015	0.095														
Joint	8	60,290,538	ARS-BFGL-NGS-112663					0.043	0.048										
Joint	8	67,033,400	ARS-BFGL-NGS-100986			-0.087	0.270												
Joint	8	84,579,963	BovineHD0800025526															-0.550	0.201
Joint	8	105,641,396	BovineHD0800032157					-0.046	0.042			0.068	0.085	0.116	0.143				
Joint	9	11,997,198	ARS-BFGL-NGS-57235													0.044	0.051	0.290	0.302
Joint	9	17,288,971	BovineHD0900004742			0.013	0.079												
Joint	9	33,787,578	BovineHD0900009384													0.049	0.053	0.306	0.302
Joint	9	38,735,093	BovineHD0900010916	0.007	0.050														
Joint	9	60,827,498	BTB-00397480					0.259	0.225	0.793	0.476	-0.037	0.063						
Joint	9	67,744,737	BovineHD0900019004															-0.183	0.151
Joint	9	68,870,505	BovineHD0900019298															-0.141	0.132
Joint	9	70,289,809	BovineHD0900019735			0.008	0.053												
Joint	9	88,192,486	BovineHD0900025200	-0.008	0.044														
Joint	9	94,143,252	BovineHD4100007685			0.007	0.040												
Joint	10	8,127,430	BovineHD1000002661													-0.157	0.178		
Joint	10	62,797,711	BovineHD1000018187					0.278	0.272										
Joint	10	62,841,361	BovineHD1000018212					0.041	0.033										
Joint	10	62,884,887	BovineHD1000018235					0.046	0.053										
Joint	10	66,652,170	ARS-BFGL-NGS-119477	-0.021	0.138														

Joint	10	67,686,585	BovineHD1000019457					0.047	0.048										
Joint	10	73,845,211	BovineHD1000021104													-0.056	0.073		
Joint	10	86,431,884	BovineHD1000024739	-0.007	0.049														
Joint	10	100,924,131	ARS-BFGL-NGS-3343	0.010	0.072														
Joint	11	23,992,969	BovineHD1100007232	-0.022	0.155														
Joint	11	24,662,197	BovineHD1100007434													0.038	0.028	0.440	0.234
Joint	11	35,039,180	BovineHD1100010338					-0.141	0.130	-0.695	0.518	0.055	0.056	0.140	0.156				
Joint	11	52,029,467	BovineHD1100015270											0.184	0.177				
Joint	11	54,076,261	BovineHD1100015725									-0.042	0.064	-0.278	0.347				
Joint	11	64,511,310	BovineHD1100018285													0.066	0.087	0.335	0.337
Joint	11	65,438,305	BovineHD1100018470									0.029	0.032						
Joint	11	65,466,018	BovineHD1100018476					-0.141	0.123	-0.286	0.175	0.029	0.046						
Joint	11	65,476,648	BovineHD1100018479					-0.544	0.448	-1.242	0.794	0.333	0.405	0.941	0.907				
Joint	11	88,018,340	ARS-BFGL-BAC-16207					-0.126	0.105										
Joint	11	92,059,776	BovineHD1100026733	-0.011	0.076														
Joint	11	93,632,997	BovineHD1100027287					0.039	0.031										
Joint	11	98,859,170	ARS-BFGL-NGS-1504													0.040	0.040		
Joint	11	98,929,180	BovineHD1100028767					0.117	0.119	0.200	0.170								
Joint	12	9,614,438	BovineHD1200002648	0.017	0.100	0.075	0.317												
Joint	12	14,939,312	BovineHD1200004459					-0.055	0.067										
Joint	12	19,910,693	BovineHD1200006022													0.045	0.064		
Joint	12	24,453,018	BovineHD1200007354					-0.198	0.188	-0.403	0.226								
Joint	12	56,034,163	ARS-BFGL-NGS-104509									-0.031	0.032						
Joint	12	56,683,360	BovineHD1200015726					0.046	0.052			-0.104	0.149	-0.198	0.230				
Joint	12	56,939,408	BovineHD1200028035					-0.069	0.080	-0.509	0.410								
Joint	12	58,592,180	BovineHD1200016189	-0.011	0.065														
Joint	12	59,106,604	BovineHD1200016310					-0.101	0.098			0.059	0.096						
Joint	12	65,399,981	BovineHD1200018025									-0.054	0.091						
Joint	13	1,007,186	BovineHD1300000145	0.020	0.135														
Joint	13	1,055,763	BovineHD1300000159	-0.010	0.067														
Joint	13	3,792,105	BovineHD4100009863					0.045	0.046			-0.059	0.074						
Joint	13	16,380,572	BovineHD1300004626															0.035	0.051
Joint	13	73,129,519	BovineHD4100010407									-0.031	0.042						
Joint	13	78,533,511	BovineHD1300022916									0.034	0.055						
Joint	14	22,518	BovineHD0600000008	0.007	0.044														
Joint	14	13,328,209	BovineHD1400004176									0.054	0.070						
Joint	14	23,607,944	BovineHD4100011295	-0.010	0.065														
Joint	14	28,344,330	BovineHD1400024444	-0.017	0.087														

Joint	14	28,438,412	BovineHD1400008725	-0.017	0.085													
Joint	14	41,275,153	Hapmap42426-BTA-110900			0.031	0.151											
Joint	14	67,912,806	BovineHD1400019721	0.009	0.076	0.071	0.326											
Joint	15	2,854,992	BovineHD1500000701									0.041	0.061					
Joint	15	4,857,417	Hapmap42143-BTA-23359	0.008	0.047													
Joint	15	18,637,239	Hapmap44329-BTA-98197									-0.103	0.132	-0.226	0.221			
Joint	15	36,609,370	ARS-BFGL-NGS-108699														0.185	0.210
Joint	15	41,077,053	BovineHD1500011406	0.008	0.061													
Joint	15	52,246,245	BovineHD1500015330					0.058	0.049	0.637	0.427							
Joint	15	55,414,359	BovineHD1500016269					0.044	0.039									
Joint	15	65,140,618	ARS-BFGL-NGS-29708													0.056	0.052	1.403	0.742
Joint	15	65,148,971	BovineHD1500018910															0.329	0.224
Joint	15	68,479,023	BTB-00612553					-0.296	0.233									
Joint	15	72,473,829	Hapmap47929-BTA-37615	-0.011	0.080													
Joint	15	83,228,283	BovineHD1500024815	0.009	0.062													
Joint	16	11,761,343	BovineHD1600003306			-0.095	0.347											
Joint	16	14,177,173	BovineHD1600004027	0.014	0.102													
Joint	16	69,421,830	BTB-00658688	0.067	0.394													
Joint	16	72,830,063	BovineHD1600021349	0.012	0.076													
Joint	16	76,408,519	ARS-BFGL-NGS-30589													-0.035	0.031		
Joint	17	54,907,144	BovineHD1700016212	0.007	0.031														
Joint	17	63,860,049	ARS-BFGL-NGS-94330					0.053	0.066	0.801	0.563							
Joint	17	63,950,062	ARS-BFGL-BAC-36611			0.093	0.180											
Joint	17	65,618,037	BovineHD1700019693					-0.054	0.047									
Joint	18	4,772,831	BovineHD1800001433	0.023	0.144													
Joint	18	6,864,571	BTA-42870-no-rs									-0.032	0.062					
Joint	18	7,691,780	BTA-44411-no-rs													-0.071	0.076		
Joint	18	20,659,854	BTA-42769-no-rs									0.039	0.052					
Joint	18	46,276,728	Hapmap50691-BTA-43520	-0.028	0.187													
Joint	18	46,311,016	BovineHD1800013676	-0.007	0.044													
Joint	19	18,623,450	BovineHD1900005438					0.037	0.051									
Joint	19	20,134,133	BovineHD1900005935	-0.010	0.070													
Joint	19	36,467,014	BovineHD1900010762					-0.494	0.428	-1.608	0.964							
Joint	19	59,245,784	UA-IFASA-8216					0.039	0.032									
Joint	19	62,556,282	BovineHD1900018249					0.049	0.056			-0.098	0.129					
Joint	20	17,591,241	BovineHD2000005310													-0.286	0.287	-1.276	0.914
Joint	20	22,651,571	BTA-95455-no-rs															0.288	0.221
Joint	20	26,706,016	BovineHD2000007953															-0.168	0.160

Joint	20	48,820,669	BovineHD2000013587	0.015	0.099													
Joint	20	60,637,163	BovineHD2000017040									-0.088	0.137					
Joint	21	33,958,935	BovineHD2100009841	-0.007	0.058													
Joint	21	39,874,490	BovineHD2100011516					-0.141	0.150	-0.983	0.601							
Joint	21	46,971,798	ARS-BFGL-NGS-19437	-0.011	0.073													
Joint	22	6,983,538	BovineHD2200002151	-0.205	0.750	-0.252	0.860											
Joint	22	7,005,226	Hapmap57734-rs29023397	-0.040	0.164													
Joint	22	7,615,852	BovineHD2200002310									0.032	0.052					
Joint	22	8,374,341	BovineHD2200002533													-0.045	0.045	
Joint	22	32,091,984	ARS-BFGL-NGS-68862													0.034	0.048	
Joint	22	32,279,858	BovineHD2200009264													0.078	0.086	0.647	0.482
Joint	22	49,836,856	ARS-BFGL-NGS-15965													-0.094	0.083		
Joint	23	16,132,392	BovineHD2300004168	0.008	0.051													
Joint	24	3,673,081	BovineHD2400001090					0.039	0.041									
Joint	24	21,855,713	BovineHD2400005992													-0.062	0.065	
Joint	24	45,599,385	BovineHD2400012691					0.049	0.056			-0.043	0.055					
Joint	24	45,625,444	BovineHD2400012696									-0.047	0.063					
Joint	25	24,586,554	BovineHD2500007018									0.037	0.055					
Joint	25	27,159,249	BovineHD2500007661													-0.034	0.044	
Joint	25	30,331,706	Hapmap27064-BTC-028223					-0.092	0.088									
Joint	26	26,877,456	BovineHD2600007223					-0.089	0.103			0.073	0.108					
Joint	26	41,389,219	ARS-BFGL-NGS-27004	-0.007	0.047													
Joint	27	3,993,708	BovineHD2700000961	-0.010	0.066													
Joint	27	4,209,953	BovineHD2700001041	-0.077	0.414													
Joint	28	4,045,281	BTB-00974697													0.040	0.051	
Joint	28	12,534,832	BovineHD2800003638	-0.010	0.058													
Joint	28	26,661,955	ARS-BFGL-NGS-1594					0.050	0.049									
Joint	29	39,734,672	Hapmap58798-rs29016922	0.022	0.126	0.166	0.682											
Joint	29	41,063,582	BovineHD2900012617	0.158	0.664	0.087	0.338											
Joint	29	42,093,690	BovineHD2900012868					-0.087	0.055									
Joint	29	44,308,524	BovineHD2900013427													-0.090	0.105	
Joint	29	45,254,795	BovineHD2900013642													-0.089	0.109	
Joint	29	45,294,962	BovineHD2900013649													-0.050	0.062	
Joint	29	46,630,938	BovineHD2900014007													0.048	0.072	
Joint	29	46,700,354	ARS-BFGL-NGS-18176													0.057	0.085	
Simbrah	1	17,148,366	BovineHD0100005053	0.071	0.259	0.259	0.750											
Simbrah	1	24,168,476	ARS-BFGL-BAC-6737					-0.096	0.066	-1.930	0.848	0.117	0.119	1.459	0.900			
Simbrah	1	50,665,945	BovineHD0100014362	-0.015	0.056													

Simbrah	1	77,723,763	BovineHD0100022553													0.060	0.056	0.218	0.168
Simbrah	1	105,630,169	Hapmap27036-BTA-163250			-0.075	0.259												
Simbrah	1	105,655,281	BovineHD0100030188			-0.066	0.241												
Simbrah	1	113,227,837	Hapmap55381-rs29025399	0.014	0.067														
Simbrah	1	130,520,535	BTA-51376-no-rs			-0.041	0.135												
Simbrah	1	144,528,438	ARS-BFGL-NGS-76373	-0.020	0.097														
Simbrah	2	2,434,950	BovineHD0200000670	0.014	0.071														
Simbrah	2	57,203,290	BovineHD0200016269			-0.089	0.189												
Simbrah	2	59,904,495	BovineHD0200017150							-0.225	0.146								
Simbrah	2	83,004,959	BovineHD0200023844			-0.055	0.190												
Simbrah	2	121,510,489	BovineHD0200030201	0.030	0.138														
Simbrah	2	126,956,287	BovineHD0200037022					0.195	0.126	0.524	0.272	-0.171	0.150	-0.163	0.134				
Simbrah	2	126,959,242	ARS-BFGL-NGS-75279					0.343	0.210	0.974	0.476	-0.166	0.149	-0.185	0.157				
Simbrah	3	43,733,400	BovineHD0300013378							0.357	0.228			-0.109	0.111				
Simbrah	3	50,662,691	BovineHD0300015419			0.086	0.274												
Simbrah	3	52,416,306	ARS-BFGL-NGS-83439					-0.119	0.084	-0.183	0.102			0.114	0.103				
Simbrah	3	52,416,878	BovineHD0300015876					-0.084	0.072	-0.212	0.113								
Simbrah	3	52,417,560	BovineHD0300015877					-0.135	0.096	-0.219	0.123								
Simbrah	3	52,418,852	BovineHD0300015878					-0.129	0.099	-0.239	0.152								
Simbrah	3	52,419,897	BovineHD0300015879					-0.104	0.074										
Simbrah	3	79,022,233	BovineHD0300022871					-0.106	0.096	-0.573	0.368	0.180	0.200	0.803	0.687				
Simbrah	3	95,913,981	BovineHD0300027678			-0.127	0.332												
Simbrah	3	97,394,480	BovineHD0300028111											-0.186	0.166				
Simbrah	4	5,031,881	BovineHD0400001381			0.056	0.092												
Simbrah	4	31,991,755	BovineHD0400009179									-0.046	0.052						
Simbrah	4	53,098,825	BovineHD0400014726					-0.226	0.171			0.297	0.291	0.267	0.236				
Simbrah	4	54,668,072	BovineHD0400015064													0.080	0.056	1.044	0.569
Simbrah	5	6,592,231	BovineHD0500001781			-0.016	0.049												
Simbrah	5	12,104,374	ARS-BFGL-NGS-29426											0.329	0.276				
Simbrah	5	13,013,473	BovineHD0500003932			0.016	0.074												
Simbrah	5	13,022,277	BovineHD0500003937			0.022	0.104												
Simbrah	5	19,431,606	ARS-BFGL-NGS-116388					0.069	0.055										
Simbrah	5	23,023,551	BovineHD0500006748							1.457	0.725								
Simbrah	5	47,920,992	BovineHD0500013910					-0.127	0.107										
Simbrah	5	48,404,403	BovineHD0500014027													-0.073	0.069		
Simbrah	5	61,740,946	BovineHD0500017392											0.286	0.195				
Simbrah	5	64,043,861	BovineHD0500018000			-0.059	0.184												
Simbrah	5	103,845,399	BovineHD0500029816			-0.022	0.072												

Simbrah	5	109,058,472	ARS-BFGL-NGS-63306	-0.014	0.047														
Simbrah	6	26,061,286	BovineHD0600007586			0.084	0.228												
Simbrah	6	66,299,180	ARS-BFGL-NGS-72592					-0.118	0.098										
Simbrah	6	73,481,332	ARS-BFGL-NGS-101891															0.646	0.323
Simbrah	6	100,695,560	BovineHD0600028510	-0.025	0.110	-0.160	0.551												
Simbrah	6	112,861,438	BovineHD0600033525									0.046	0.062						
Simbrah	7	467,956	BovineHD0700000069	-0.018	0.087														
Simbrah	7	53,143,975	BovineHD0700015866			0.057	0.210												
Simbrah	7	60,601,468	BovineHD0700018057	0.015	0.072														
Simbrah	7	60,660,405	BovineHD0700018070			0.069	0.221												
Simbrah	7	60,688,281	BovineHD0700018078			0.074	0.222												
Simbrah	7	68,783,389	BovineHD0700020842			-0.094	0.287												
Simbrah	7	71,945,283	BovineHD0700021817			0.208	0.595												
Simbrah	7	94,642,456	BovineHD0700028320	-0.024	0.105	-0.093	0.309												
Simbrah	7	95,124,226	BovineHD0700028470	0.019	0.097														
Simbrah	7	96,746,068	BovineHD0700029014	0.047	0.193														
Simbrah	7	102,529,075	BovineHD0700030669													0.194	0.170	1.027	0.694
Simbrah	7	105,411,287	BovineHD0700031468			0.080	0.252												
Simbrah	8	11,078,911	BovineHD0800003578	-0.016	0.076	-0.113	0.370												
Simbrah	8	21,572,629	BovineHD0800006587	0.027	0.106	0.080	0.248												
Simbrah	8	53,884,363	BovineHD0800016303			-0.044	0.177												
Simbrah	8	107,236,795	ARS-BFGL-NGS-41550							-0.415	0.240								
Simbrah	9	49,257,679	BTB-02006579					0.070	0.055										
Simbrah	9	71,359,980	BovineHD0900020122	-0.025	0.076														
Simbrah	10	7,799,488	BTA-118104-no-rs													0.080	0.080		
Simbrah	10	64,816,309	ARS-BFGL-NGS-62905			-0.080	0.210												
Simbrah	10	100,924,131	ARS-BFGL-NGS-3343	0.073	0.288	0.091	0.345												
Simbrah	11	155,522	BovineHD1100000016							0.911	0.470								
Simbrah	11	23,992,969	BovineHD1100007232	-0.020	0.103	0.254	0.792												
Simbrah	11	47,008,188	ARS-BFGL-NGS-40907					0.373	0.253	0.525	0.318	-0.143	0.152						
Simbrah	11	66,281,456	BovineHD1100018735													0.541	0.241	2.662	0.903
Simbrah	12	2,618,638	BTB-01103269					0.080	0.056										
Simbrah	12	31,449,808	BovineHD1200009267	0.016	0.045														
Simbrah	13	37,243,918	BovineHD1300010845													0.113	0.107		
Simbrah	13	80,054,531	BovineHD1300023400	-0.028	0.141														
Simbrah	14	14,586,053	BovineHD1400004575	-0.028	0.111	-0.136	0.410												
Simbrah	14	22,341,542	BovineHD4100011291			-0.085	0.182												
Simbrah	14	25,259,499	BovineHD4100011361													0.061	0.046		

Simbrah	15	6,233,678	BovineHD1500001629					0.073	0.062			-0.088	0.076					
Simbrah	15	72,473,829	Hapmap47929-BTA-37615	-0.052	0.218													
Simbrah	16	73,010,856	BovineHD1600021426					0.084	0.064									
Simbrah	17	62,581,666	BovineHD1700018671			-0.144	0.428											
Simbrah	18	25,185,199	BovineHD1800007788	-0.016	0.071													
Simbrah	19	3,880,877	BovineHD1900000960													0.283	0.238	
Simbrah	19	21,849,452	BovineHD1900006407	0.016	0.068													
Simbrah	20	16,815,306	BovineHD2000005088													0.091	0.070	
Simbrah	20	17,591,241	BovineHD2000005310													-0.263	0.220	-0.695	0.503
Simbrah	20	35,259,879	BovineHD2000010095					-0.136	0.111	-0.418	0.246							
Simbrah	21	59,162,526	ARS-BFGL-NGS-16275	0.034	0.104													
Simbrah	21	62,121,957	BovineHD2100018719	-0.026	0.117													
Simbrah	21	66,284,836	BovineHD2100019902					0.093	0.076									
Simbrah	22	11,083,535	BovineHD2200003294					0.090	0.080									
Simbrah	22	33,432,901	BovineHD2200009669					-0.102	0.078			0.086	0.093					
Simbrah	23	15,783,127	BovineHD2300004035			0.151	0.499											
Simbrah	24	3,673,081	BovineHD2400001090													0.255	0.222	
Simbrah	24	4,051,421	BovineHD2400001180									0.047	0.059					
Simbrah	24	4,074,679	BovineHD2400001190									0.110	0.122					
Simbrah	24	14,964,805	BovineHD2400004198													-0.153	0.152	
Simbrah	24	32,576,870	BTB-01623856	-0.015	0.072													
Simbrah	24	53,702,809	BovineHD2400015420													-0.203	0.197	
Simbrah	24	59,990,135	BovineHD2400017485									0.054	0.051					
Simbrah	24	61,732,249	BovineHD2400018109			-0.093	0.276											
Simbrah	27	31,269,649	BTB-00966795					-0.099	0.064	-1.434	0.527							
Simmental	1	4,615,149	BTB-00002966							0.974	0.573							
Simmental	1	30,449,967	ARS-BFGL-NGS-14285															0.652	0.267
Simmental	1	39,638,269	BovineHD0100011262									0.089	0.083					
Simmental	1	115,487,178	BTA-108007-no-rs									0.056	0.061					
Simmental	1	155,461,258	ARS-BFGL-NGS-39036							-0.232	0.117							
Simmental	2	20,637,894	ARS-BFGL-NGS-27536			-0.031	0.077											
Simmental	2	24,759,987	BTB-00083874			0.023	0.070											
Simmental	2	32,163,209	ARS-BFGL-NGS-77689											-0.294	0.273			
Simmental	3	8,271,067	BovineHD0300002718											0.250	0.215			
Simmental	3	11,445,314	BTA-26230-no-rs													-0.110	0.097	
Simmental	3	96,214,989	BovineHD0300027779											-0.277	0.171			
Simmental	3	99,860,543	BovineHD0300028809											-0.192	0.123			
Simmental	4	10,025,067	BovineHD0400003025					-0.089	0.067									

Simmental	4	82,072,066	BovineHD0400022891											-0.109	0.099				
Simmental	4	114,805,260	BovineHD0400033491											0.134	0.124				
Simmental	5	12,192,068	BovineHD0500003615													0.114	0.096	0.947	0.576
Simmental	5	27,758,354	BovineHD0500008183															0.399	0.190
Simmental	5	68,696,282	BovineHD0500019361															-0.560	0.361
Simmental	5	99,889,487	BovineHD0500028730															0.432	0.232
Simmental	5	113,010,737	BovineHD0500032783															0.234	0.155
Simmental	6	12,002,585	BovineHD0600003405													-0.087	0.074		
Simmental	7	92,877,894	BovineHD0700027753	0.022	0.105														
Simmental	8	3,229,083	BovineHD0800001007													0.103	0.079		
Simmental	8	6,189,677	ARS-BFGL-NGS-104101													0.079	0.062		
Simmental	8	40,320,705	BovineHD0800012081							-0.268	0.140								
Simmental	8	78,200,098	BovineHD0800023786									-0.058	0.067						
Simmental	8	78,299,132	BovineHD0800023822									-0.108	0.118						
Simmental	9	21,845,628	BovineHD0900005901													-0.120	0.073	-3.039	0.967
Simmental	9	52,842,486	BovineHD0900014769															-0.860	0.430
Simmental	9	60,827,498	BTB-00397480					0.335	0.225			-0.255	0.225						
Simmental	10	9,243,642	ARS-BFGL-NGS-5218													0.098	0.068		
Simmental	10	45,764,666	BovineHD1000013758	-0.011	0.054														
Simmental	10	52,771,028	ARS-BFGL-NGS-14607	0.035	0.148	0.148	0.462												
Simmental	10	55,739,309	BovineHD1000016562					0.251	0.141										
Simmental	10	62,870,803	Hapmap53237-rs29021167					0.069	0.054										
Simmental	10	66,578,924	BovineHD1000019217			0.037	0.133												
Simmental	10	76,421,733	BovineHD1000021867					0.079	0.052										
Simmental	10	77,297,598	BovineHD1000022170													0.074	0.067		
Simmental	11	24,662,197	BovineHD1100007434													0.244	0.113	2.737	0.875
Simmental	11	65,014,198	BovineHD1100018385															0.822	0.508
Simmental	11	65,438,305	BovineHD1100018470					-0.114	0.092			0.054	0.052						
Simmental	11	65,466,018	BovineHD1100018476					-0.244	0.171	-1.345	0.675	0.057	0.062						
Simmental	11	65,476,648	BovineHD1100018479					-0.134	0.102	-0.342	0.182	0.088	0.075	0.525	0.423				
Simmental	11	67,895,920	BovineHD1100019193			0.045	0.123												
Simmental	11	76,334,598	BovineHD1100021866					-0.104	0.077	-1.358	0.683								
Simmental	11	80,850,526	BovineHD1100023198													0.112	0.097		
Simmental	11	85,981,496	BovineHD1100024691			-0.067	0.209												
Simmental	11	98,094,178	BovineHD1100028536													-0.589	0.338	-1.833	0.821
Simmental	11	98,222,190	BovineHD1100028591													-0.249	0.177		
Simmental	11	104,173,821	BovineHD1100030298															0.607	0.323
Simmental	12	84,848,183	BTB-00508549									0.082	0.084						

Simmental	13	35,025,679	BovineHD1300010246	-0.017	0.096														
Simmental	13	49,369,652	BovineHD1300014404													0.230	0.151	1.800	0.831
Simmental	14	16,336,431	BovineHD1400005136															6.288	0.846
Simmental	14	23,539,175	BTB-00559128									-0.056	0.064						
Simmental	14	23,540,117	BovineHD1400007305									-0.092	0.088						
Simmental	14	23,548,867	BovineHD1400007308									-0.064	0.066						
Simmental	14	23,550,648	BovineHD1400007309									-0.070	0.066						
Simmental	15	31,588,113	BovineHD1500008710									-0.085	0.098						
Simmental	15	36,609,370	ARS-BFGL-NGS-108699													0.079	0.059		
Simmental	16	62,275,255	BovineHD1600017881															0.981	0.593
Simmental	16	73,216,135	BovineHD1600021470	-0.012	0.065														
Simmental	17	5,895,955	BTB-01002430							0.419	0.250								
Simmental	17	41,889,885	BovineHD1700011883	-0.049	0.245														
Simmental	17	63,860,049	ARS-BFGL-NGS-94330							1.126	0.641								
Simmental	18	5,082,859	BovineHD1800001572	0.027	0.106														
Simmental	18	8,845,340	BovineHD1800003058	0.021	0.094														
Simmental	18	60,918,681	ARS-BFGL-NGS-11218	0.024	0.130														
Simmental	21	36,357,577	BovineHD2100010794					-0.221	0.153	-1.308	0.590								
Simmental	21	41,969,536	BovineHD2100012081	-0.011	0.050														
Simmental	21	42,032,839	BovineHD2100012099	-0.133	0.543	-0.161	0.609												
Simmental	21	42,043,390	Hapmap42487-BTA-26592	-0.019	0.085														
Simmental	22	6,983,538	BovineHD2200002151	-0.011	0.056														
Simmental	23	17,791,358	BovineHD2300004479									0.117	0.128						
Simmental	25	19,912,086	BovineHD2500005568	-0.047	0.212														
Simmental	25	24,586,554	BovineHD2500007018									0.142	0.141						
Simmental	25	24,613,223	ARS-BFGL-NGS-97895									0.065	0.066						
Simmental	25	30,331,706	Hapmap27064-BTC-028223					-0.262	0.158			0.160	0.136						
Simmental	25	40,152,700	BovineHD2500011470													0.070	0.048		
Simmental	27	7,754,398	BovineHD2700002124									0.061	0.082						
Simmental	27	11,205,123	BovineHD2700003046									0.147	0.158						
Simmental	27	18,808,741	BovineHD2700005194							0.339	0.205								
Simmental	27	26,428,979	BovineHD2700007194															1.071	0.307
Simmental	27	39,714,460	BovineHD2700011482							-0.222	0.150								
Simmental	28	12,352,710	BovineHD2800003602													0.092	0.087		
Simmental	28	33,405,318	BovineHD2800009010													0.075	0.058		
Simmental	28	33,588,312	BovineHD2800009062													0.227	0.179	0.909	0.471
Simmental	28	33,608,386	BovineHD2800009066													0.140	0.129		
Simmental	28	42,051,760	BovineHD2800011945	-0.016	0.079														

Simmental	29	7,859,363	BovineHD2900002232				-0.081	0.086		
Simmental	29	41,063,582	BovineHD2900012617	0.016	0.071					
Simmental	29	45,254,795	BovineHD2900013642						-0.072	0.069

[a] Chromosome; [b] Position; [c] single nucleotide polymorphism; [d] birth weight; [e] weaning weight direct; [f] weaning weight maternal; [g] yearly weight.

Table S2. QTLs and genes previously described within the regions associated with growth traits in simmental and simbrah cattle.

Model	Trait	Chr[a]	Pos[b]	SNPs[c]	QTLs[d]	Genes[e]
Joint	BW[f]	1	155,615,450	ARS-BFGL-NGS-54653	MILK: Milk fat yield (PUBMED_ID=22449276), Milk protein yield (PUBMED_ID=22449276); PRODUCTION: Maturity rate (PUBMED_ID=26445451); REPRODUCTION: Conception rate (PUBMED_ID=31718557)	LOC101908237, LOC112448155, LOC112448186, SATB1
		2	122,900,223	BovineHD0200035799	HEALTH: Bovine respiratory dise (PUBMED_ID=30229962); MILK: Milk kappa-casein perce (PUBMED_ID=27485317), Milk zinc content (PUBMED_ID=25989905)	LOC104971336, LOC112442418, LAPTM5, MATN1
		6	111,363,016	BovineHD0600033010		LOC104968940, TAPT1, PROM1
		8	67,033,400	ARS-BFGL-NGS-100986	HEALTH: Bovine respiratory dise (PUBMED_ID=30229962); MILK: Milk casein percentage (PUBMED_ID=28711251), Milk fat percentage (PUBMED_ID=28711251), Milk fat yield (PUBMED_ID=28711251), Milk protein percentage (PUBMED_ID=28711251), Milk protein-to-fat rat (PUBMED_ID=28711251)	LOC100298923, LOC100848109, LOC784966, LPL
		9	94,143,252	BovineHD4100007685		ZDHHC14
		10	100,924,131	ARS-BFGL-NGS-3343		FOXN3
		11	92,059,776	BovineHD1100026733	HEALTH: Anti-Müllerian hormone (PUBMED_ID=30007805); PRODUCTION: Body weight (birth) (PUBMED_ID=30290764); REPRODUCTION: Conception rate (PUBMED_ID=31718557)	
		12	58,592,180	BovineHD1200016189		TRNAC-GCA_157, LOC784127
		14	22,518	BovineHD0600000008		LOC100299844
		14	67,912,806	BovineHD1400019721		LOC112449543, PTDSS1, MTERF3, UQCRB
		15	83,228,283	BovineHD1500024815	REPRODUCTION: Conception rate (PUBMED_ID=27209127)	MS4A3, LOC112441667, LOC112441666, LOC107133207, MS4A2, MS4A7, MS4A14, MS4A5, MS4A1
		17	63,950,062	ARS-BFGL-BAC-36611	MILK: 305-day milk yield (PUBMED_ID=29521460), Milk fat percentage (PUBMED_ID=29521460), Milk fat yield (PUBMED_ID=29521460), Milk protein percentage (PUBMED_ID=29521460), Milk protein yield (PUBMED_ID=21831322), Milk yield (PUBMED_ID=21831322); REPRODUCTION: Non-return rate (PUBMED_ID=29178833), Sire conception rate (PUBMED_ID=29486732), Sperm motility (PUBMED_ID=27610941)	ACACB, UNG, ALKBH2, USP30, SVOP
		20	48,820,669	BovineHD2000013587		LOC112443046, CDH10
		22	7,005,226	Hapmap57734-rs29023397	MEAT AND CARCASS: Lean meat yield (PUBMED_ID=25273628), Subcutaneous fat (PUBMED_ID=27221246); PRODUCTION: Dry matter intake (PUBMED_ID=23851991), Metabolic body weight (PUBMED_ID=23851991)	LOC107131649, LOC514651, CMTM6, DYNC1LI1

	23	16,132,392	BovineHD2300004168	CONFORMATION: Feet and leg conformati (PUBMED_ID=21831322), Foot angle (PUBMED_ID=21831322), Rear leg placement - re (PUBMED_ID=21831322), Rear leg placement - si (PUBMED_ID=21831322), Stature (PUBMED_ID=21831322), Strength (PUBMED_ID=21831322), Teat length (PUBMED_ID=21831322); HEALTH: Somatic cell score (PUBMED_ID=21831322); MEAT AND CARCASS: Lean meat yield (PUBMED_ID=25273628); MILK: Milk fat percentage (PUBMED_ID=21831322), Milk fat yield (PUBMED_ID=21831322), Milk protein percentage (PUBMED_ID=21831322, 31139206), Milk protein yield (PUBMED_ID=21831322), Milk yield (PUBMED_ID=21831322); PRODUCTION: Body depth (PUBMED_ID=21831322), Net merit (PUBMED_ID=21831322), PTA type (PUBMED_ID=21831322); REPRODUCTION: Calving ease (PUBMED_ID=21831322), Calving ease (maternal) (PUBMED_ID=21831322)	LOC112443875, LOC112443876, LOC112443924, TRERF1
	26	41,389,219	ARS-BFGL-NGS-27004	CONFORMATION: Feet and leg conformati (PUBMED_ID=21831322), Foot angle (PUBMED_ID=21831322), Rear leg placement - re (PUBMED_ID=21831322), Stature (PUBMED_ID=21831322), Strength (PUBMED_ID=21831322), Teat length (PUBMED_ID=21831322), Udder attachment (PUBMED_ID=21831322), Udder depth (PUBMED_ID=21831322), Udder height (PUBMED_ID=21831322); MILK: Milk C16 index (PUBMED_ID=31563305), Milk fat percentage (PUBMED_ID=21831322), Milk fat yield (PUBMED_ID=21831322), Milk palmitoleic acid c (PUBMED_ID=31563305), Milk protein percentage (PUBMED_ID=21831322), Milk protein yield (PUBMED_ID=21831322); PRODUCTION: Body depth (PUBMED_ID=21831322), Body weight (yearling) (PUBMED_ID=19966163), Length of productive li (PUBMED_ID=21831322), Net merit (PUBMED_ID=21831322), PTA type (PUBMED_ID=21831322), Rump width (PUBMED_ID=21831322); REPRODUCTION: Calf size (PUBMED_ID=21183059), Calving ease (PUBMED_ID=21183059, 21831322), Calving ease (maternal) (PUBMED_ID=21831322), Stillbirth (PUBMED_ID=21831322)	FGFR2
	27	4,209,953	BovineHD2700001041	REPRODUCTION: Conception rate (PUBMED_ID=31299913), Reproductive efficiency (PUBMED_ID=26286463)	CSMD1, LOC782601
WWD[g]	4	112,844,573	BovineHD0400032781	HEALTH: Tick resistance (PUBMED_ID=28619006); MEAT AND CARCASS: Carcass weight (PUBMED_ID=22479267), Fat thickness at the 12 (PUBMED_ID=22479267), Marbling score (PUBMED_ID=22479267); PRODUCTION: Average daily feed inta (PUBMED_ID=22479267), Average daily gain (PUBMED_ID=22479267), Body weight (yearling) (PUBMED_ID=30290764), Residual feed intake (PUBMED_ID=22479267)	ZBED6CL, LOC112446454, ZNF775, LOC511617, LRRC61, GIMAP8, GIMAP7, RARRES2, REPIN1
	6	112,448,301	BovineHD0600033358	MILK: Milk kappa-casein perce (PUBMED_ID=27485317)	LOC112447132, LOC112447222
	7	20,673,981	BovineHD0700006039	CONFORMATION: Udder depth (PUBMED_ID=21831322); HEALTH: Somatic cell score (PUBMED_ID=21831322); MEAT AND CARCASS: Lean meat yield (PUBMED_ID=25273628); PRODUCTION: Length of productive li (PUBMED_ID=21831322), Net merit (PUBMED_ID=21831322); REPRODUCTION: Age at first calving (PUBMED_ID=25178291), Calving ease (maternal) (PUBMED_ID=21831322), Daughter pregnancy rate (PUBMED_ID=21831322), Stillbirth (maternal) (PUBMED_ID=21831322)	CELF5, TRNAM-CAU_5, LOC112447372, AES, TLE2, S1PR4, TLE6, NCLN, GNA15, GNA11

	11	98,929,180	BovineHD1100028767		SWI5, LOC107132969, TRNAR-UCU_5, LOC112448949, TRNAW-CCA_18, LOC112448915, GOLGA2, MIR199B, MIR3604-2, MIR3154, COQ4, MIR219-1, CERCAM, DNM1, TRUB2, SLC27A4, URM1
	12	59,106,604	BovineHD1200016310	MILK: Milk riboflavin content (PUBMED_ID=25771056)	
	13	3,792,105	BovineHD4100009863	REPRODUCTION: Conception rate (PUBMED_ID=31299913)	LOC112449424, SLX4IP, MKKS
	15	68,479,023	BTB-00612553	CONFORMATION: Rump angle (PUBMED_ID=21831322); HEALTH: Serotonin level (PUBMED_ID=32292413); PRODUCTION: Maturity rate (PUBMED_ID=26445451)	
	17	65,618,037	BovineHD1700019693	REPRODUCTION: Conception rate (PUBMED_ID=28814769), Non-return rate (PUBMED_ID=29178833)	LOC112442055, MYO18B
	19	62,556,282	BovineHD1900018249	MEAT AND CARCASS: Lean meat yield (PUBMED_ID=25273628); MILK: Milk fat yield (PUBMED_ID=21831322), Milk protein yield (PUBMED_ID=21831322, 22449276), Milk yield (PUBMED_ID=21831322); PRODUCTION: Body weight (yearling) (PUBMED_ID=24906442); REPRODUCTION: Non-return rate (PUBMED_ID=24265800)	CEP112, APOH
	24	45,599,385	BovineHD2400012691	HEALTH: Abomasum displacement (PUBMED_ID=23548285)	LOC101903660, EPG5, MIR6523A, MIR6523B, SIGLEC15
	25	30,331,706	Hapmap27064-BTC-028223	MILK: Milk protein yield (PUBMED_ID=22449276), Milking speed (PUBMED_ID=29705414)	AUTS2
	26	26,877,456	BovineHD2600007223	MILK: Milk C14 index (PUBMED_ID=25511820, 26364108, 30243637, 31563305), Milk C16 index (PUBMED_ID=31563305), Milk fat yield (PUBMED_ID=31139206), Milk myristoleic acid c (PUBMED_ID=25511820, 26364108, 31563305), Milk palmitoleic acid c (PUBMED_ID=31563305), Milk protein percentage (PUBMED_ID=22449276); REPRODUCTION: Inseminations per conce (PUBMED_ID=20477799)	
	28	26,661,955	ARS-BFGL-NGS-1594	REPRODUCTION: First service conceptio (PUBMED_ID=32650431), Inseminations per conce (PUBMED_ID=32650431)	PALD1, LRRC20, EIF4EBP2, NODAL
	29	42,093,690	BovineHD2900012868	CONFORMATION: Conformation score (PUBMED_ID=27136002); MEAT AND CARCASS: Tenderness score (PUBMED_ID=29163638); MILK: Milk protein percentage (PUBMED_ID=20630249); PRODUCTION: Average daily gain (PUBMED_ID=27136002), Growth index (PUBMED_ID=27136002); REPRODUCTION: Gestation length (PUBMED_ID=29178833), Interval to first estru (PUBMED_ID=29178833)	C29H11orf95, LOC112444891, PLA2G16, RTN3, ATL3, SPINDOC
WWM[h]	1	147,542,196	BovineHD0100043239	MILK: Colostrum albumin conce (PUBMED_ID=33255903)	LOC112448047
	2	133,487,750	BovineHD0200039106	MILK: Milk fat yield (PUBMED_ID=22449276), Milk zinc content (PUBMED_ID=25989905)	LOC112443641, LOC788425, AKR7L, EMC1, MRTO4, UBR4
	5	109,676,735	BovineHD0500031776	CONFORMATION: Conformation score (PUBMED_ID=24341352); MILK: Milk fat percentage (PUBMED_ID=27287773), Milk protein yield (PUBMED_ID=31139206); PRODUCTION: Maturity rate (PUBMED_ID=26445451)	LOC101905166, H1F0, GALR3, MIR658, EIF3L, C5H22orf23, TRIOBP, GCAT, ANKRD54, MICALL1, POLR2F, SOX10
	8	105,641,396	BovineHD0800032157		ASTN2, PAPPA

	13	78,533,511	BovineHD1300022916	MILK: Milk protein percentage (PUBMED_ID=22497459), Milk urea nitrogen yiel (PUBMED_ID=22497459)	LOC101907588, LOC101907513, RIPOR3, PTPN1
	18	20,659,854	BTA-42769-no-rs	PRODUCTION: Dry matter intake (PUBMED_ID=23031337)	
	20	60,637,163	BovineHD2000017040	MEAT AND CARCASS: Muscle sodium content (PUBMED_ID=29163638); REPRODUCTION: First service conceptio (PUBMED_ID=32650431), Inseminations per conce (PUBMED_ID=32650431)	
YW[i]	1	157,605,027	BovineHD1100023814		LOC107131289, PRDM9, ZNF596
	2	94,636,270	Hapmap50979-BTA-48487	MEAT AND CARCASS: Muscle creatine content (PUBMED_ID=29163638); MILK: Milk kappa-casein perce (PUBMED_ID=27485317), Milk protein percentage (PUBMED_ID=25148050); PRODUCTION: Body weight (birth) (PUBMED_ID=19966163), Body weight gain (PUBMED_ID=19966163), Dry matter intake (PUBMED_ID=23851991), Metabolic body weight (PUBMED_ID=23851991)	LOC112442953, ZDBF2, GPR1, ADAM23
	3	101,605,832	BovineHD0300029255	MILK: Milk kappa-casein perce (PUBMED_ID=27485317), Milk unglycosylated kap (PUBMED_ID=27485317)	RNF220, ERI3
	4	111,112,243	BovineHD0400032138	MEAT AND CARCASS: Yield grade (PUBMED_ID=22394233); MILK: Milk protein percentage (PUBMED_ID=27506634); PRODUCTION: Body weight (yearling) (PUBMED_ID=19966163)	CNTNAP2
	6	86,762,457	BovineHD0600024201	CONFORMATION: Angularity (PUBMED_ID=29115939), Feet and leg conformati (PUBMED_ID=21831322), Foot angle (PUBMED_ID=21831322), Rear leg placement - si (PUBMED_ID=21831322), Teat placement - front (PUBMED_ID=21831322), Udder attachment (PUBMED_ID=21831322), Udder depth (PUBMED_ID=21831322); HEALTH: Bovine tuberculosis sus (PUBMED_ID=26960806), Clinical mastitis (PUBMED_ID=23647142, 27760518), Ketosis (PUBMED_ID=31311492), Somatic cell count (PUBMED_ID=27534682, 21831322, 31139206); MILK: Cheese fat recovery (PUBMED_ID=27889122), Milk alpha-S2-casein pe (PUBMED_ID=27485317), Milk fat yield (PUBMED_ID=31139206), Milk glycosylated kappa (PUBMED_ID=27485317), Milk kappa-casein perce (PUBMED_ID=27485317), Milk phosphorylated alp (PUBMED_ID=27485317), Milk protein percentage (PUBMED_ID=20630249, 22449276, 27287773, 31139206), Milk protein yield (PUBMED_ID=27760518, 28358110, 29751743, 29921979, 30696404, 31139206), Milk rennet coagulation (PUBMED_ID=26947304), Milk unglycosylated kap (PUBMED_ID=27485317), Milk yield (PUBMED_ID=25084281, 25151887, 31139206), Time to curd firmness (PUBMED_ID=26947304); PRODUCTION: Lactation persistency (PUBMED_ID=27889128), Length of productive li (PUBMED_ID=21831322, 27889128), Net merit (PUBMED_ID=21831322); REPRODUCTION: Calving ease (PUBMED_ID=21831322), Calving ease (maternal) (PUBMED_ID=21831322), Conception rate (PUBMED_ID=31139206), Daughter pregnancy rate (PUBMED_ID=27209127, 31139206), Interval to first estru (PUBMED_ID=20477799, 28814769), Stillbirth (maternal) (PUBMED_ID=21831322)	SLC4A4
	7	105,857,552	BTB-00115134	MILK: Milk protein yield (PUBMED_ID=22449276), Milk tridecylic acid co (PUBMED_ID=27506634)	
	8	84,579,963	BovineHD0800025526	MEAT AND CARCASS: Carcass weight (PUBMED_ID=22607022); MILK: Milking speed (PUBMED_ID=29705414)	LOC112447923, CARD19, WNK2, NINJ1
	9	68,870,505	BovineHD0900019298		SMLR1, EPB41L2
	12	19,910,693	BovineHD1200006022	HEALTH: Bovine tuberculosis sus (PUBMED_ID=30763354); MEAT AND CARCASS: Lean meat yield (PUBMED_ID=25273628)	LOC112449043

		15	65,148,971	BovineHD1500018910	MILK: Milk C14 index (PUBMED_ID=31563305), Milk capric acid conten (PUBMED_ID=30841852, 31563305), Milk fat percentage (PUBMED_ID=31139206), Milk fat yield (PUBMED_ID=29751743, 30696404, 31139206), Milk lauric acid conten (PUBMED_ID=31563305); PRODUCTION: Body weight (yearling) (PUBMED_ID=30290764)	ELF5, EHF
		16	76,408,519	ARS-BFGL-NGS-30589	CONFORMATION: Dairy form (PUBMED_ID=21831322), Teat length (PUBMED_ID=21831322); HEALTH: Somatic cell score (PUBMED_ID=21831322); MEAT AND CARCASS: Marbling score (PUBMED_ID=29163638), Tenderness score (PUBMED_ID=29163638); PRODUCTION: Length of productive li (PUBMED_ID=21831322); REPRODUCTION: Daughter pregnancy rate (PUBMED_ID=21831322)	LOC112441872, DENND1B, MIR2284N, CRB1
		18	7,691,780	BTA-44411-no-rs		LOC101902820, LOC112442253, LOC112442481, PKD1L2, CMC2, CENPN, C18H16orf46, GCSH, ATMIN
		20	26,706,016	BovineHD2000007953	PRODUCTION: Body weight (yearling) (PUBMED_ID=19966163), Length of productive li (PUBMED_ID=27889128)	
		22	49,836,856	ARS-BFGL-NGS-15965	CONFORMATION: Hoof and leg disorders (PUBMED_ID=27344389); HEALTH: Ketosis (PUBMED_ID=31311492)	LOC104975568, HEMK1, C22H3orf18, CACNA2D2, MAPKAPK3, CISH
		29	46,700,354	ARS-BFGL-NGS-18176		LOC112444901
Simbrah	**BW**	3	95,913,981	BovineHD0300027678		LOC112446108, FAF1, DMRTA2
		5	109,058,472	ARS-BFGL-NGS-63306	CONFORMATION: Foot angle (PUBMED_ID=18565942)	LOC112446914, TRNAE-UUC_32, LOC104972584, CECR2, BCL2L13, ATP6V1E1, BID
		13	80,054,531	BovineHD1300023400	MILK: Milk glycerophosphochol (PUBMED_ID=25670729)	
		19	21,849,452	BovineHD1900006407	REPRODUCTION: Conception rate (PUBMED_ID=31299913), First service conceptio (PUBMED_ID=31299913)	ABR, TIMM22, NXN
		21	62,121,957	BovineHD2100018719	MILK: Milk conjugated linolei (PUBMED_ID=24909189); REPRODUCTION: Calving ease (PUBMED_ID=29178833)	LOC112443345
		24	61,732,249	BovineHD2400018109	CONFORMATION: Feet and leg conformati (PUBMED_ID=21831322), Foot angle (PUBMED_ID=21831322), Rear leg placement - re (PUBMED_ID=21831322), Rear leg placement - si (PUBMED_ID=21831322), Rump angle (PUBMED_ID=21831322), Stature (PUBMED_ID=21831322), Strength (PUBMED_ID=21831322), Teat length (PUBMED_ID=21831322), Udder depth (PUBMED_ID=21831322); HEALTH: Somatic cell score (PUBMED_ID=21831322); MILK: Milk fat percentage (PUBMED_ID=21831322), Milk fat yield (PUBMED_ID=21831322), Milk potassium content (PUBMED_ID=25989905), Milk protein percentage (PUBMED_ID=21831322), Milk protein yield (PUBMED_ID=21831322), Milk yield (PUBMED_ID=21831322); PRODUCTION: Length of productive li (PUBMED_ID=21831322), Maturity rate (PUBMED_ID=26445451), Net merit (PUBMED_ID=21831322); REPRODUCTION: Calving ease (PUBMED_ID=21831322), Calving ease (maternal) (PUBMED_ID=21831322), Stillbirth (PUBMED_ID=21831322)	LOC112444232, LOC107131790, SERPINB12, VPS4B, KDSR, SERPINB5

	WWD	2	126,959,242	ARS-BFGL-NGS-75279	CONFORMATION: Rump angle (PUBMED_ID=31633203); MILK: Milk fat yield (PUBMED_ID=31139206), Milk lactose content (PUBMED_ID=29246110), Milk tetracosanoic acid (PUBMED_ID=27506634), Milk zinc content (PUBMED_ID=25989905); REPRODUCTION: Conception rate (PUBMED_ID=31299913)	LOC112443410, LOC112443411, LOC107131877, CATSPER4, CEP85, CNKSR1, ZNF593, FAM110D, PDIK1L, TRIM63, SLC30A2, EXTL1
		3	79,022,233	BovineHD0300022871	MILK: Milk yield (PUBMED_ID=22449276)	LOC101902048, PDE4B
		5	47,920,992	BovineHD0500013910	CONFORMATION: Stature (PUBMED_ID=21212230, 29459679), Teat thickness (PUBMED_ID=28727049), Udder cleft (PUBMED_ID=28727049); PRODUCTION: Body weight (birth) (PUBMED_ID=24906442); REPRODUCTION: Gestation length (PUBMED_ID=22034999), Inhibin level (PUBMED_ID=23785023), Interval to first estru (PUBMED_ID=22100599), Pregnancy rate (PUBMED_ID=26020876)	HMGA2, MIR763
		11	155,522	BovineHD1100000016		LOC112448861
		16	73,010,856	BovineHD1600021426	PRODUCTION: Body weight (weaning) (PUBMED_ID=25158260), Lactation persistency (PUBMED_ID=20412936)	LOC112441917, LOC112441868, HHAT, SERTAD4
		20	35,259,879	BovineHD2000010095	HEALTH: Abomasum displacement (PUBMED_ID=23548285), Respiratory rate (PUBMED_ID=26198991); MEAT AND CARCASS: Lean meat yield (PUBMED_ID=25273628); MILK: Milk fat content (PUBMED_ID=30459810), Milk fat percentage (PUBMED_ID=20630249, 31139206), Milk fat yield (PUBMED_ID=22449276, 30459810), Milk protein percentage (PUBMED_ID=20630249, 21048968, 22449276, 27287773, 28377602, 31139206), Milk protein yield (PUBMED_ID=22449276), Milk yield (PUBMED_ID=31139206); REPRODUCTION: Calving to conception i (PUBMED_ID=28259397), Inseminations per conce (PUBMED_ID=28259397)	FYB1
		21	66,284,836	BovineHD2100019902	HEALTH: Immunoglobulin G level (PUBMED_ID=30241501)	LOC112443172
		22	33,432,901	BovineHD2200009669	HEALTH: Somatic cell score (PUBMED_ID=25288516)	FAM19A1
	WWM	6	112,861,438	BovineHD0600033525	REPRODUCTION: Retained placenta (PUBMED_ID=31931710)	QDPR, CLRN2
		24	59,990,135	BovineHD2400017485	PRODUCTION: Body weight (yearling) (PUBMED_ID=19966163), Maturity rate (PUBMED_ID=26445451)	LOC112444177, LOC101902622, CDH20
	YW	14	25,259,499	BovineHD4100011361	HEALTH: Insulin-like growth fac (PUBMED_ID=22811567); MEAT AND CARCASS: Carcass weight (PUBMED_ID=24116007, 25164077, 26104396, 27221246); MILK: Milking speed (PUBMED_ID=29705414); PRODUCTION: Body weight (birth) (PUBMED_ID=30290764); REPRODUCTION: Age at puberty (PUBMED_ID=22100599), Interval to first estru (PUBMED_ID=22100599), Scrotal circumference (PUBMED_ID=22811567)	TRNAC-GCA_175, TOX
		19	3,880,877	BovineHD1900000960	HEALTH: Bovine tuberculosis sus (PUBMED_ID=30763354)	
		24	53,702,809	BovineHD2400015420		MBD2, LOC104975792, LOC112441476, STARD6, POLI, C24H18orf54
Simmental	**BW**	16	73,216,135	BovineHD1600021470	MEAT AND CARCASS: Muscle phosphorus conte (PUBMED_ID=29163638), Muscle potassium conten (PUBMED_ID=29163638)	
		16	73,216,135	BovineHD1600021470		SYT14

	18	60,918,681	ARS-BFGL-NGS-11218	CONFORMATION: Foot angle (PUBMED_ID=21831322), Rear leg placement - si (PUBMED_ID=21831322), Strength (PUBMED_ID=21831322); HEALTH: Bovine tuberculosis sus (PUBMED_ID=26960806), Somatic cell score (PUBMED_ID=21831322); MILK: Milk fat percentage (PUBMED_ID=21831322), Milk fat yield (PUBMED_ID=21831322), Milk protein percentage (PUBMED_ID=21831322), Milk protein yield (PUBMED_ID=21831322), Milk tridecylic acid co (PUBMED_ID=27506634); PRODUCTION: Body depth (PUBMED_ID=21831322), Length of productive li (PUBMED_ID=27889128), Net merit (PUBMED_ID=21831322); REPRODUCTION: Calving ease (PUBMED_ID=21831322, 28109604), Conception rate (PUBMED_ID=28814769), Interval from first to (PUBMED_ID=28814769), Stayability (PUBMED_ID=29471369), Stillbirth (PUBMED_ID=21831322, 28109604)	
	18	60,918,681	ARS-BFGL-NGS-11218		LOC532048, LOC504704, LOC615600, LOC515600, LOC506868, MGC139164, MIR371, MGC157082, NLRP12
	25	19,912,086	BovineHD2500005568	HEALTH: Anti-Müllerian hormone (PUBMED_ID=29729909); MILK: Average daily milk yiel (PUBMED_ID=28857209), Milk tridecylic acid co (PUBMED_ID=27506634)	LOC112444373, SDR42E2, LOC112444300, TRNAL-UAG_3, TRNAL-AAG_9, VWA3A, POLR3E, EEF2K, CDR2
	28	42,051,760	BovineHD2800011945	MEAT AND CARCASS: Shear force (PUBMED_ID=28727016)	LOC112444747, LOC112444750, LOC112444720, LOC101907562, ANXA8L1, ANTXRL
	29	41,063,582	BovineHD2900012617	MEAT AND CARCASS: Tenderness score (PUBMED_ID=29163638); MILK: 305-day milk yield (PUBMED_ID=ISU0100), Milk fat percentage (PUBMED_ID=20630249), Milk protein percentage (PUBMED_ID=20630249, 27485317, 32998688), Milk yield (PUBMED_ID=20630249); REPRODUCTION: Interval to first estru (PUBMED_ID=29178833)	LOC112444961, LBHD1, LOC112444859, LOC112444936, LOC104976274, LOC112444959, LOC112444957, LOC112444955, LOC112444950, LOC112444960, LOC112444952, LOC112444953, LOC112444954, LOC112444948, C29H11orf98, ZBTB3, UQCC3, HNRNPUL2, TTC9C, B3GAT3, GANAB, INTS5, CSKMT, UBXN1, LRRN4CL, BSCL2, GNG3, POLR2G, TAF6L, TMEM179B, TMEM223, NXF1, STX5, WDR74, SLC3A2
WWD	1	155,461,258	ARS-BFGL-NGS-39036	MILK: Milk fat yield (PUBMED_ID=22449276), Milk protein yield (PUBMED_ID=22449276)	LOC112448269, LOC101908237, LOC112448155, SATB1
	9	60,827,498	BTB-00397480	MILK: Milk alpha-S2-casein pe (PUBMED_ID=27485317), Milk phosphorylated alp (PUBMED_ID=27485317); REPRODUCTION: Inseminations per conce (PUBMED_ID=24428918)	LOC101903075, LOC100847428, LOC112448207, ANKRD6, MIR2903, GABRR1, RRAGD, UBE2J1, GABRR2
	10	76,421,733	BovineHD1000021867	MILK: Milk glycosylated kappa (PUBMED_ID=27485317); PRODUCTION: Body weight (yearling) (PUBMED_ID=19966163), Body weight gain (PUBMED_ID=19966163); REPRODUCTION: Conception rate (PUBMED_ID=31718557), Inseminations per conce (PUBMED_ID=31718557)	LOC112448595, LOC100297513, SYNE2, ESR2
	27	39,714,460	BovineHD2700011482	MILK: Milk fat percentage (PUBMED_ID=29284405)	

WWM	3	99,860,543	BovineHD0300028809	MILK: Milk kappa-casein perce (PUBMED_ID=27485317), Milk unglycosylated kap (PUBMED_ID=27485317)	LOC104971814, LOC101902049, LOC112446064, NSUN4, UQCRH, LRRC41, LURAP1, POMGNT1, PIK3R3, RAD54L, TSPAN1
	4	114,805,260	BovineHD0400033491	HEALTH: Somatic cell score (PUBMED_ID=25288516); MEAT AND CARCASS: Carcass weight (PUBMED_ID=30290764); PRODUCTION: Average daily gain (PUBMED_ID=24730749), Body weight gain (PUBMED_ID=19966163)	CCT8L2, KMT2C
	11	65,476,648	BovineHD1100018479	MILK: Milk fat percentage (PUBMED_ID=25511820)	LOC100139826
	12	84,848,183	BTB-00508549	CONFORMATION: Feet and leg conformati (PUBMED_ID=21831322), Foot angle (PUBMED_ID=21831322), Rear leg placement - re (PUBMED_ID=21831322), Stature (PUBMED_ID=21831322), Strength (PUBMED_ID=21831322), Udder attachment (PUBMED_ID=21831322), Udder cleft (PUBMED_ID=21831322), Udder depth (PUBMED_ID=21831322), Udder height (PUBMED_ID=21831322); PRODUCTION: Body depth (PUBMED_ID=21831322), PTA type (PUBMED_ID=21831322), Rump width (PUBMED_ID=21831322)	COL4A1
	14	23,550,648	BovineHD1400007309	CONFORMATION: Stature (PUBMED_ID=21212230); HEALTH: Insulin-like growth fac (PUBMED_ID=22811567, 23785023); MEAT AND CARCASS: Carcass weight (PUBMED_ID=22497335, 22607022, 27112906), Fat thickness at the 12 (PUBMED_ID=22497335), Longissimus muscle area (PUBMED_ID=22497335), Marbling score (PUBMED_ID=22497335); PRODUCTION: Average daily gain (PUBMED_ID=22497335), Body weight (PUBMED_ID=26641032), Body weight (birth) (PUBMED_ID=19966163), Body weight (weaning) (PUBMED_ID=19966163), Body weight (yearling) (PUBMED_ID=19966163), Body weight gain (PUBMED_ID=19966163), Hip height (PUBMED_ID=31179577), Metabolic body weight (PUBMED_ID=28521758, 31931702), Residual feed intake (PUBMED_ID=22497335), Withers height (PUBMED_ID=31179577); REPRODUCTION: Age at puberty (PUBMED_ID=22100599, 26641032, 30997484), Calving ease (PUBMED_ID=24906442), Interval to first estru (PUBMED_ID=22100599, 26641032), Scrotal circumference (PUBMED_ID=22811567), Sexual precocity (PUBMED_ID=30053002)	SDR16C6, PENK
	15	31,588,113	BovineHD1500008710	PRODUCTION: Body weight (yearling) (PUBMED_ID=19966163)	LOC785951, GRIK4, TBCEL
	23	17,791,358	BovineHD2300004479	MILK: Milk protein percentage (PUBMED_ID=31139206), Milk yield (PUBMED_ID=28358110, 29921979); PRODUCTION: Body weight gain (PUBMED_ID=19966163), Dry matter intake (PUBMED_ID=24183684)	LOC101905117, MYMX, LOC101905365, SPATS1, TCTE1, CAPN11, HSP90AB1, TMEM151B, SLC29A1, SLC35B2, NFKBIE, AARS2, CDC5L
	27	11,205,123	BovineHD2700003046	PRODUCTION: Average daily gain (PUBMED_ID=22497295), Lactation persistency (PUBMED_ID=20412936)	
	29	7,859,363	BovineHD2900002232	REPRODUCTION: Conception rate (PUBMED_ID=31718557), Inseminations per conce (PUBMED_ID=31718557)	LOC112444877

YW	5	113,010,737	BovineHD0500032783	CONFORMATION: Dairy form (PUBMED_ID=21831322), Feet and leg conformati (PUBMED_ID=21831322), Foot angle (PUBMED_ID=21831322), Rear leg placement - re (PUBMED_ID=21831322), Rear leg placement - si (PUBMED_ID=21831322), Strength (PUBMED_ID=21831322), Teat length (PUBMED_ID=21831322); HEALTH: Somatic cell score (PUBMED_ID=21831322); MILK: Milk fat percentage (PUBMED_ID=21831322), Milk fat yield (PUBMED_ID=21831322), Milk protein percentage (PUBMED_ID=21831322), Milk protein yield (PUBMED_ID=21831322); PRODUCTION: Length of productive li (PUBMED_ID=21831322), Net merit (PUBMED_ID=21831322); REPRODUCTION: Calving ease (PUBMED_ID=21831322), Calving ease (maternal) (PUBMED_ID=21831322), Daughter pregnancy rate (PUBMED_ID=21831322), Inseminations per conce (PUBMED_ID=32271764), Interval to first estru (PUBMED_ID=22100599), Stillbirth (PUBMED_ID=21831322)	LOC535121, LOC785804, MGC127055, CYP2D14, MIR2442, CENPM, 37865, WBP2NL, NAGA, PHETA2, SMDT1, NDUFA6, TCF20
	10	77,297,598	BovineHD1000022170		LOC112448644, MAX
	11	104,173,821	BovineHD1100030298	MILK: 305-day milk yield (PUBMED_ID=ISU0100), Cheese protein recovery (PUBMED_ID=27889122), Milk beta-lactoglobulin (PUBMED_ID=27485317, 29571285), Milk butyric acid conte (PUBMED_ID=29391528), Milk kappa-casein perce (PUBMED_ID=27485317)	LOC101902839, LOC101902895, LOC107132967, LOC112448923, LOC112448928, LOC100848307, LOC112448857, LOC112448956, LOC112448907, LOC112448908, LOC112448904, LOC112448903, LOC112448905, EGFL7, FAM69B, LOC789606, LOC100139115, SURF2, MIR126, SURF4, AGPAT2, ABO, SURF6, MED22, RPL7A
	13	49,369,652	BovineHD1300014404	MILK: Milk protein percentage (PUBMED_ID=31139206), Milk yield (PUBMED_ID=22449276)	LOC112449233
	25	40,152,700	BovineHD2500011470	PRODUCTION: Dry matter intake (PUBMED_ID=24183684)	SDK1, MIR2390
	27	26,428,979	BovineHD2700007194	HEALTH: Bovine tuberculosis sus (PUBMED_ID=31480266)	LOC101906081, LOC112441503, LOC112444672, DCTN6, RBPMS
	28	33,608,386	BovineHD2800009066	MILK: Time to curd firmness (PUBMED_ID=26947304)	DLG5, POLR3A

[a] Chromosome; [b] Position; [c] single nucleotide polymorphism; [d] QTLs found in the NAGRP CattleQTLdb database (Available online: https://www.animalgenome.org/cgi-bin/QTLdb/BT/index.); [e] genes found in the assembly ARS-

Supplementary

Table S1. Traits and genes previously described within the regions associated with reproductive traits and frame score in Simmental and Simbrah cattle.

Trait	Chr [a]	Marker	Position	Traits previously associated	Genes
SC	1	BovineHD0100007238	24964189	Exterior= Rump angle (PUBMED_ID= 12605852), Udder cleft (PUBMED_ID= 16167984), Teat length (PUBMED_ID= 15377635), Meat_and_Carcass= Marbling score (PUBMED_ID= 20477797), Oleic acid content (PUBMED_ID= 20477785), Milk= Milk protein yield (PUBMED_ID= 9691050), Milk yield (PUBMED_ID= 7713441), Milk protein yield (PUBMED_ID= 7713441), Milk fat percentage (PUBMED_ID= 14762092), Milk fat yield (PUBMED_ID= 11178740), Production= Height (mature) (PUBMED_ID= 20477797), Body weight (birth) (PUBMED_ID= 20477797), Reproduction= Calving ease (PUBMED_ID= 20477797), Non-return rate (PUBMED_ID= 15377635),	ROBO2
SC	1	BovineHD0100020122	69664149	Health= Infectious bovine keratoconjunctivitis susceptibility (PUBMED_ID= 17093209), Meat_and_Carcass= Oleic acid content (PUBMED_ID= 20477785), Linoleic acid content (PUBMED_ID= 20416790), Linolenic acid content (PUBMED_ID= 20416790), Polyunsaturated fatty acid content (PUBMED_ID= 20416790), Marbling score (PUBMED_ID= 20477797), Carcass weight (PUBMED_ID= 12926775), Fat thickness at the 12th rib (PUBMED_ID= 17894565), Milk= Milk alpha-casein percentage (PUBMED_ID= 19397519), Production= Body weight (yearling) (PUBMED_ID= 12926775), Body weight (slaughter) (PUBMED_ID= 12926775), Body weight (weaning) (PUBMED_ID= 20477797), Reproduction= Fertility treatments (PUBMED_ID= 19841231), Conception rate (PUBMED_ID= 12605852),	SLC12A8, ZNF148
SC	2	HAPLOTYPE	41538841-41567719	Exterior=Udder depth (PUBMED_ID= 17433017), Teat placement (PUBMED_ID= 12605852), Dairy form (PUBMED_ID= 16167984), Health=Immunoglobulin G level (PUBMED_ID= 21138580), Somatic cell score (PUBMED_ID= 25288516), Meat_and_Carcass=Lung percentage (PUBMED_ID= 20477785), Fat thickness at the 12th rib (PUBMED_ID= 14677852), Yield grade (PUBMED_ID= 14677852), Milk=Milk fat yield (PUBMED_ID= 17433017), Milk yield (PUBMED_ID= 12778594), Milk protein yield (PUBMED_ID= 16167984), Milk fat percentage (PUBMED_ID= 14762090), Milk fat yield (PUBMED_ID= 9691050), Milk kappa-casein percentage (PUBMED_ID= 27485317), Production=Body weight (birth), (PUBMED_ID= 14677852), Chest depth (PUBMED_ID= 12605852), Body weight (mature), (PUBMED_ID= 20477797), Body weight (birth), (PUBMED_ID= 20477797),	
SC	2	HAPLOTYPE	5747611-5759652	Exterior=Udder depth (PUBMED_ID= 17433017), Udder attachment (PUBMED_ID= 16230715), Strength (PUBMED_ID= 16230715), Meat_and_Carcass=Longissimus muscle area (PUBMED_ID= 17596127), Retail product yield (PUBMED_ID= 9498354), Longissimus muscle area (PUBMED_ID= 9498354), Yield grade (PUBMED_ID= 9498354), Marbling score (PUBMED_ID= 9498354), Fat thickness at the 12th rib (PUBMED_ID= 9498354), Kidney, pelvic, and heart fat percentage (PUBMED_ID= 9498354), Conjugated linoleic acid content (PUBMED_ID= 17894565), Beef flavor intensity (PUBMED_ID= 17894565), Monounsaturated fatty acid content (PUBMED_ID= 17894565), Oleic acid to stearic acid ratio (PUBMED_ID= 17894565), Carcass weight (PUBMED_ID= 22303340), Lean meat yield (PUBMED_ID= 30290764), Yield grade (PUBMED_ID= 30290764), Longissimus muscle area (PUBMED_ID= 31931697), Milk=Milk fat yield (PUBMED_ID= 16167984), Milk sodium content (PUBMED_ID= 33824377), Production=Body weight (weaning), (PUBMED_ID= 22303340), Body weight (birth), (PUBMED_ID= 9498354), Thurl width (PUBMED_ID= 16230715), Body weight (yearling), (PUBMED_ID= 22303340), Body weight (slaughter), (PUBMED_ID= 22303340), Calving ease (PUBMED_ID= 26065883),	NEMP2
SC	3	BovineHD0300004685	14395023	Health= Somatic cell count (PUBMED_ID= 11845286), Meat_and_Carcass= Marbling score (PUBMED_ID= 14677852), Longissimus muscle area (PUBMED_ID= 20477797), Carcass weight (PUBMED_ID= 20477797), Shear force (PUBMED_ID= 33101375), Milk= Milk protein percentage (PUBMED_ID= 12605852), Milk protein percentage (PUBMED_ID= 27287773), Production= Body weight (weaning) (PUBMED_ID= 20477797), Body weight (mature) (PUBMED_ID= 20477797), Body weight (birth) (PUBMED_ID= 20477797), Reproduction= Non-return rate (PUBMED_ID= 18717969), Non-return rate (PUBMED_ID= 17257192),	MEF2D, RHBG
SC	6	BovineHD0600009601	32965679	Health= Somatic cell score (PUBMED_ID= 15514072), Abomasum displacement (PUBMED_ID= 18946144), Clinical mastitis (PUBMED_ID= 11845286), Bovine spongiform encephalopathy (PUBMED_ID= 15342524), Meat_and_Carcass= Kidney, pelvic, and heart fat percentage (PUBMED_ID= 20477785), Kidney, pelvic, and heart fat weight (PUBMED_ID= 20477785), Kidney fat weight (PUBMED_ID= 20477785), Fat thickness at the 12th rib (PUBMED_ID= 20477797), Marbling score (PUBMED_ID= 20477797), Longissimus muscle area (PUBMED_ID= 20477797), Kidney, pelvic, and heart fat percentage (PUBMED_ID= 18791160), Hematin pigment concentration (PUBMED_ID= 18254735), Carcass weight (PUBMED_ID= 19653884), Milk= Milk fat yield (PUBMED_ID= 11167525), Milk protein percentage (PUBMED_ID= 15514072), Milk solids (PUBMED_ID= 22058003), Milk protein percentage (PUBMED_ID= ISU0040), Milk yield (PUBMED_ID= 19603057), Milk protein yield (PUBMED_ID= 19603057), Milk protein	

				percentage (PUBMED_ID= 8978065), Milk protein percentage (PUBMED_ID= 16702292), Milk protein yield (PUBMED_ID= 16702292), Milk yield (PUBMED_ID= 16702292), Milk yield (PUBMED_ID= 12778594), Milk protein percentage (PUBMED_ID= 12778594), Milk fat percentage (PUBMED_ID= 9691050), Milk fat percentage (PUBMED_ID= 11178740), Milk yield (PUBMED_ID= 11167525), Milk fat yield (PUBMED_ID= 16428646), Milk fat percentage (PUBMED_ID= 16428646), Milk protein percentage (PUBMED_ID= ISU0040), Milk fat yield (PUBMED_ID= 19603057), Milk fat percentage (PUBMED_ID= 19603057), Milk protein percentage (PUBMED_ID= 22742505), Production= Body weight (weaning) (PUBMED_ID= 20477797), Body weight (slaughter) (PUBMED_ID= 19653884), Body weight (birth) (PUBMED_ID= 19016677), Body weight (birth) (PUBMED_ID= 10764062), Body weight (weaning) (PUBMED_ID= 20477797), Body length (birth) (PUBMED_ID= 18791160), Body weight (birth) (PUBMED_ID= 18791160), Body weight (birth) (PUBMED_ID= 15537758), Average daily gain (PUBMED_ID= 15537758), Hip height (PUBMED_ID= 12605852), Rump width (PUBMED_ID= 12605852), Reproduction= Calving ease (PUBMED_ID= 20477797), Gestation length (PUBMED_ID= 19016677),	
SC	8	HAPLOTYPE	38363220-38366097	Exterior=Rump angle (PUBMED_ID= 21831322), Meat_and_Carcass=Fat thickness at the 12th rib (PUBMED_ID= 11325189), Carcass weight (PUBMED_ID= 20477797), Milk=Milking speed (PUBMED_ID= 12605852), Lactation persistency (PUBMED_ID= 19646150), Milk fat yield (PUBMED_ID= 21831322), Milk yield (PUBMED_ID= 21831322), Milk protein yield (PUBMED_ID= 21831322), Production=Body length (birth), (PUBMED_ID= 18791160), Body weight (mature), (PUBMED_ID= 20477797), Body weight (birth), (PUBMED_ID= 20477797), Net merit (PUBMED_ID= 21831322), Body weight (yearling), (PUBMED_ID= 19966163), Reproduction=Stillbirth (PUBMED_ID= 12613879),	UHRF2
SC	9	HAPLOTYPE	15900318-15919300	Health=Clinical mastitis (PUBMED_ID= 18832229), Meat_and_Carcass=Longissimus muscle area (PUBMED_ID= 20477797), Marbling score (PUBMED_ID= 17347893), Milk=Milk fat yield (PUBMED_ID= 11167525), Production=Length of productive life (PUBMED_ID= 18650300), Reproduction=Conception rate (PUBMED_ID= 31299913),	
SC	10	ARS-BFGL-NGS-74837	18541772	Exterior= Angularity (PUBMED_ID= 10791796), Meat_and_Carcass= Fat percentage (PUBMED_ID= 18791160), Marbling score (PUBMED_ID= 14677852), Carcass weight (PUBMED_ID= 14677852), cis-Vaccenic acid content (PUBMED_ID= 20416790), Milk= Milk protein yield (PUBMED_ID= 18298934), Milk fat yield (PUBMED_ID= 7713441), Production= Veterinary treatments (PUBMED_ID= 19389971), Height (mature) (PUBMED_ID= 20477797), Body weight (birth) (PUBMED_ID= 20477797), Reproduction= Conception rate (PUBMED_ID= 31299913), First service conception (PUBMED_ID= 31299913),	THSD4
SC	10	BovineHD1000007178	22308257	Exterior= Social separation--Vocalization (PUBMED_ID= 18784067), Udder attachment (PUBMED_ID= 15377635), Teat length (PUBMED_ID= 15377635), Meat_and_Carcass= Marbling score (PUBMED_ID= 14677852), Carcass weight (PUBMED_ID= 14677852), Longissimus muscle area (PUBMED_ID= 20477797), Muscle pH (PUBMED_ID= 18254735), Muscle nitrogen content (PUBMED_ID= 18254735), Gastrointestinal tract weight (PUBMED_ID= 20477785), Carcass weight (PUBMED_ID= 17347893), Milk= Milk protein yield (PUBMED_ID= 18298934), Milk fat yield (PUBMED_ID= 7713441), Milk yield (PUBMED_ID= 18700999), Milk fat yield (PUBMED_ID= 15377635), Milk protein yield (PUBMED_ID= 15377635), Production= Height (mature) (PUBMED_ID= 20477797), Body weight (birth) (PUBMED_ID= 20477797), Body weight (weaning) (PUBMED_ID= 20477797), Body weight (birth) (PUBMED_ID= 32053968), Reproduction= Calving ease (PUBMED_ID= 20477797), Scrotal circumference (PUBMED_ID= 30997484), Sexual precocity (PUBMED_ID= 30053002),	
SC	13	BovineHD1300021455	73602949	Exterior= Teat length (PUBMED_ID= 14691316), Udder attachment (PUBMED_ID= 16230715), Udder height (PUBMED_ID= 16230715), Udder width (PUBMED_ID= 16230715), Udder depth (PUBMED_ID= 16230715), Udder composite index (PUBMED_ID= 16230715), Meat_and_Carcass= Marbling score (PUBMED_ID= 20477797), Milk= Milk yield (PUBMED_ID= 14762090), Milk protein yield (PUBMED_ID= 14762090), Production= PTA type (PUBMED_ID= 16230715), Body weight (yearling) (PUBMED_ID= 12926775),	MATN4, RBPJL, WFDC15B, MATN4, RBPJL, WFDC15B
SC	13	HAPLOTYPE	73602949-73620495	Exterior=Teat length (PUBMED_ID= 14691316), Udder attachment (PUBMED_ID= 16230715), Udder height (PUBMED_ID= 16230715), Udder width (PUBMED_ID= 16230715), Udder depth (PUBMED_ID= 16230715), Udder composite index (PUBMED_ID= 16230715), Meat_and_Carcass=Marbling score (PUBMED_ID= 20477797), Milk=Milk yield (PUBMED_ID= 14762090), Milk protein yield (PUBMED_ID= 14762090), Production=PTA type (PUBMED_ID= 16230715), Body weight (yearling), (PUBMED_ID= 12926775),	
SC	17	BovineHD1700002151	7548169	Exterior= Rump angle (PUBMED_ID= 12605852), Health= PCVI minus PCVF (PUBMED_ID= 12805560), PCVF minus PCVM (PUBMED_ID= 12805560), PCV variance (PUBMED_ID= 12805560), Final packed red blood cell volume (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 150 after challenge (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 100	DCLK2, LRBA

				after challenge (PUBMED_ID= 12805560), Immunoglobulin G level (PUBMED_ID= 22438944), Meat_and_Carcass= Longissimus muscle area (PUBMED_ID= 20477797), Marbling score (PUBMED_ID= 10764062), Carcass weight (PUBMED_ID= 19937580), Fat thickness at the 12th rib (PUBMED_ID= 19937580), Milk= Milk alpha-casein percentage (PUBMED_ID= 19397519), Milking speed (PUBMED_ID= 29705414), Production= Average daily gain (PUBMED_ID= 17596127), Body weight (birth) (PUBMED_ID= 20477797), Residual feed intake (PUBMED_ID= 17709790),	
SC	17	BovineHD1700004678	15972230	Exterior= Rump angle (PUBMED_ID= 12605852), Health= PCVI minus PCVF (PUBMED_ID= 12805560), PCVF minus PCVM (PUBMED_ID= 12805560), PCV variance (PUBMED_ID= 12805560), Final packed red blood cell volume (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 150 after challenge (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 100 after challenge (PUBMED_ID= 12805560), Meat_and_Carcass= Longissimus muscle area (PUBMED_ID= 20477797), Marbling score (PUBMED_ID= 10764062), Carcass weight (PUBMED_ID= 20477797), Milk= Milk alpha-casein percentage (PUBMED_ID= 19397519), Production= Average daily gain (PUBMED_ID= 17596127), Body weight (yearling) (PUBMED_ID= 20477797),	
SC	19	HAPLOTYPE	43058602-43162697	Exterior=Rump angle (PUBMED_ID= 12605852), Social separation--Standing alert (PUBMED_ID= 18784067), Social separation--Vocalization (PUBMED_ID= 18784067), Teat length (PUBMED_ID= 16230715), Health=Somatic cell score (PUBMED_ID= 15514072), Gastrointestinal nematode burden (PUBMED_ID= 19254385), Meat_and_Carcass=Oleic acid content (PUBMED_ID= 17242864), Stearic acid content (PUBMED_ID= 20477785), Myristic acid content (PUBMED_ID= 17242864), Marbling score (PUBMED_ID= 20477797), Longissimus muscle area (PUBMED_ID= 20477797), Muscle pH (PUBMED_ID= 18254735), Subcutaneous fat thickness (PUBMED_ID= 9720178), Intramuscular fat (PUBMED_ID= 9720178), Myristic acid content (PUBMED_ID= 27112906), Oleic acid content (PUBMED_ID= 27112906), Myristic acid content (PUBMED_ID= 23607548), Oleic acid content (PUBMED_ID= 27112906), Myristic acid content (PUBMED_ID= 27112906), Oleic acid content (PUBMED_ID= 27112906), Marbling score (PUBMED_ID= 33101375), Milk=Milk fat percentage (PUBMED_ID= 15514072), Milk protein percentage (PUBMED_ID= 15514072), Milk stearic acid content (PUBMED_ID= 17242864), Milk trans-vaccenic acid content (PUBMED_ID= 17242864), Milk conjugated linoleic acid content (PUBMED_ID= 17242864), Milk oleic acid content (PUBMED_ID= 17242864), Milk myristic acid content (PUBMED_ID= 17242864), Milk linoleic acid content (PUBMED_ID= 17242864), Milk caproic acid content (PUBMED_ID= 17242864), Milk fat yield (PUBMED_ID= 12605852), Milk caprylic acid content (PUBMED_ID= 17242864), Milk capric acid content (PUBMED_ID= 17242864), Milk lauric acid content (PUBMED_ID= 17242864), Milk fat percentage (PUBMED_ID= 12778594), Production=Body weight (mature), (PUBMED_ID= 20477797), Height (yearling), (PUBMED_ID= 20477797), Body weight (weaning), (PUBMED_ID= 20477797), Body weight (birth), (PUBMED_ID= 20477797), Residual feed intake (PUBMED_ID= 17709790), Reproduction=Ovulation rate (PUBMED_ID= 10656928), Dystocia (PUBMED_ID= 19912419), Scrotal circumference (PUBMED_ID= 20477797),	AARSD1, BRCA1, IFI35, NBR1, RND2, RPL27, RUNDC1, TMEM106A, U2, VAT1
SC	23	BovineHD2300006211	23730493	Exterior= Teat placement - front (PUBMED_ID= 16230715), Health= Parasite detection rate (PUBMED_ID= 12805560), Immunoglobulin G level (PUBMED_ID= 21138580), Meat_and_Carcass= Carcass weight (PUBMED_ID= 20477797), Marbling score (PUBMED_ID= 20477797), Milk= Milk fat yield (PUBMED_ID= 15514072), Milk protein yield (PUBMED_ID= 15514072), Milk yield (PUBMED_ID= 15514072), Milk protein percentage (PUBMED_ID= 10430670), Milk protein percentage (PUBMED_ID= 12778594), Milking speed (PUBMED_ID= 10791796), Milk yield (PUBMED_ID= 12729552), Milking speed (PUBMED_ID= 10430670), Production= Body weight (weaning) (PUBMED_ID= 20477797), Body weight (yearling) (PUBMED_ID= 20477797), Body weight (birth) (PUBMED_ID= 20477797), Body weight (birth) (PUBMED_ID= 15537758), Average daily gain (PUBMED_ID= 15537758), Residual feed intake (PUBMED_ID= 18791150), Reproduction= Percentage live sperm after thawing (PUBMED_ID= 19630877), Twinning (PUBMED_ID= 11003703), Twinning (PUBMED_ID= 15147392), Scrotal circumference (PUBMED_ID= 20477797),	
SC	23	HAPLOTYPE	23730493-23745977	Exterior=Teat placement - front (PUBMED_ID= 16230715), Health=Parasite detection rate (PUBMED_ID= 12805560), Immunoglobulin G level (PUBMED_ID= 21138580), Meat_and_Carcass=Carcass weight (PUBMED_ID= 20477797), Marbling score (PUBMED_ID= 20477797), Milk=Milk fat yield (PUBMED_ID= 15514072), Milk protein yield (PUBMED_ID= 15514072), Milk yield (PUBMED_ID= 15514072), Milk protein percentage (PUBMED_ID= 12778594), Milking speed (PUBMED_ID= 10791796), Milk yield (PUBMED_ID= 12729552), Milking speed (PUBMED_ID= 10430670), Production=Body weight (weaning), (PUBMED_ID= 20477797), Body weight (yearling), (PUBMED_ID= 20477797), Body weight (birth), (PUBMED_ID= 15537758), Average daily gain (PUBMED_ID= 15537758), Residual feed intake (PUBMED_ID= 18791150), Reproduction=Percentage live sperm after thawing (PUBMED_ID= 19630877), Twinning (PUBMED_ID= 15147392), Scrotal circumference (PUBMED_ID= 20477797),	
SC	25	HAPLOTYPE	27577974-27654242	Exterior=Udder attachment (PUBMED_ID= 10791796), Flight from feeder (PUBMED_ID= 18784067), Social separation--Vocalization (PUBMED_ID= 18784067), Health=Gastrointestinal nematode burden (PUBMED_ID= 19254385), Immunoglobulin G level (PUBMED_ID= 21138580), Bovine tuberculosis susceptibility (PUBMED_ID= 26960806), Bovine respiratory disease	AHSP, MRPS17, NIPSNAP2,

				susceptibility (PUBMED_ID= 30229962), Meat_and_Carcass=Carcass weight (PUBMED_ID= 20477797), Tenderness score (PUBMED_ID= 18254735), Milk=Milk yield (PUBMED_ID= 18650300), Production=Body weight (yearling), (PUBMED_ID= 20477797), Body weight (weaning), (PUBMED_ID= 20477797), Reproduction=Calving ease (PUBMED_ID= 20477797), Sperm average path velocity (PUBMED_ID= 19630877),	OR7A153, OR7A53, PSPH, RUSF1, SEPTIN14, ZNF713
FS	1	HAPLOTYPE	60895445-60899823	Health=Initial packed red blood cell volume (PUBMED_ID= 12805560), Meat_and_Carcass=Oleic acid content (PUBMED_ID= 20477785), Linoleic acid content (PUBMED_ID= 20416790), Linolenic acid content (PUBMED_ID= 20416790), Polyunsaturated fatty acid content (PUBMED_ID= 20416790), Marbling score (PUBMED_ID= 20477797), Fat percentage (PUBMED_ID= 14731222), Retail product yield (PUBMED_ID= 14731222), Yield grade (PUBMED_ID= 14731222), Marbling score (PUBMED_ID= 33101375), Milk=Milk protein yield (PUBMED_ID= 11178740), Milk yield (PUBMED_ID= 11178740), Milk alpha-casein percentage (PUBMED_ID= 19397519), Production=Body weight (mature), (PUBMED_ID= 20477797), Reproduction=Fertility treatments (PUBMED_ID= 19841231), Conception rate (PUBMED_ID= 12605852),	
FS	2	ARS-BFGL-NGS-60458	28349857	Exterior= Udder depth (PUBMED_ID= 17433017), Body form composite index (PUBMED_ID= 16230715), Teat placement (PUBMED_ID= 12605852), Meat_and_Carcass= Lung percentage (PUBMED_ID= 20477785), Fat thickness at the 12th rib (PUBMED_ID= 14677852), Milk= Milk fat yield (PUBMED_ID= 17433017), Milk fat yield (PUBMED_ID= 16167984), Milk protein percentage (PUBMED_ID= 14762090), Milk yield (PUBMED_ID= 12778594), Production= Body depth (PUBMED_ID= 16230715),	
FS	2	BTB-01145846	56674297	Exterior= Udder depth (PUBMED_ID= 17433017), Health= Immunoglobulin G level (PUBMED_ID= 21138580), Initial packed red blood cell volume (PUBMED_ID= 12805560), PCVI minus PCVF (PUBMED_ID= 12805560), PCVI minus PCVM (PUBMED_ID= 12805560), Minimum packed red blood cell volume (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 150 after challenge (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 100 after challenge (PUBMED_ID= 12805560), Percentage decrease in body weight up to day 150 after challenge (PUBMED_ID= 12805560), Tick resistance (PUBMED_ID= 20433753), Meat_and_Carcass= Lung percentage (PUBMED_ID= 20477785), Fat thickness at the 12th rib (PUBMED_ID= 14677852), Yield grade (PUBMED_ID= 14677852), Carcass weight (PUBMED_ID= 20477797), Fat thickness at the 12th rib (PUBMED_ID= 20477797), Milk= Milk fat yield (PUBMED_ID= 17433017), Milk yield (PUBMED_ID= 12778594), Milk fat percentage (PUBMED_ID= 14762090), Milk fat yield (PUBMED_ID= 9691050), Production= Body weight (birth) (PUBMED_ID= 14677852), Body weight (initial) (PUBMED_ID= 12805560), Reproduction= Non-return rate (PUBMED_ID= 18717969),	LRP1B
FS	2	HAPLOTYPE	28329020-28349857	Exterior=Udder depth (PUBMED_ID= 17433017), Body form composite index (PUBMED_ID= 16230715), Teat placement (PUBMED_ID= 12605852), Meat_and_Carcass=Lung percentage (PUBMED_ID= 20477785), Fat thickness at the 12th rib (PUBMED_ID= 14677852), Milk=Milk fat yield (PUBMED_ID= 16167984), Milk protein percentage (PUBMED_ID= 14762090), Milk yield (PUBMED_ID= 12778594), Production=Body depth (PUBMED_ID= 16230715),	
FS	3	BovineHD0300029985	104074474	Exterior= Structural soundness (PUBMED_ID= 17183116), Health= Clinical mastitis (PUBMED_ID= 11845286), Meat_and_Carcass= Carcass weight (PUBMED_ID= 20477797), Marbling score (PUBMED_ID= 20477797), Reproduction= Stillbirth (PUBMED_ID= 18420641),	
FS	3	HAPLOTYPE	104074474-104081372	Exterior=Structural soundness (PUBMED_ID= 17183116), Health=Clinical mastitis (PUBMED_ID= 11845286), Meat_and_Carcass=Carcass weight (PUBMED_ID= 20477797), Marbling score (PUBMED_ID= 20477797), Reproduction=Stillbirth (PUBMED_ID= 18420641),	
FS	4	BTB-00190917	59503146	Exterior= Social separation--Vocalization (PUBMED_ID= 18784067), Social separation--Standing alert (PUBMED_ID= 18784067), Health= FMDV peptide-induced cell proliferation (PUBMED_ID= 21138580), Meat_and_Carcass= Marbling score (PUBMED_ID= 19781039), Longissimus muscle area (PUBMED_ID= 15537759), Marbling score (PUBMED_ID= 15537759), Milk= Milking speed (PUBMED_ID= 15377635), Milk protein yield (PUBMED_ID= 15377635), Milk fat percentage (PUBMED_ID= 9621249), Milk caproic acid content (PUBMED_ID= 34091779), Production= Body weight (weaning) (PUBMED_ID= 20477797), Body weight (slaughter) (PUBMED_ID= 22303340), Reproduction= Calving ease (PUBMED_ID= 18420641),	
FS	4	HAPLOTYPE	59489126-59503146	Exterior=Social separation--Vocalization (PUBMED_ID= 18784067), Social separation--Standing alert (PUBMED_ID= 18784067), Health=FMDV peptide-induced cell proliferation (PUBMED_ID= 21138580), Meat_and_Carcass=Marbling score (PUBMED_ID= 19781039), Longissimus muscle area (PUBMED_ID= 15537759), Marbling score (PUBMED_ID= 15537759), Milk=Milking speed (PUBMED_ID= 15377635), Milk protein yield (PUBMED_ID= 15377635), Milk fat percentage (PUBMED_ID= 9621249), Milk caproic	

				acid content (PUBMED_ID= 34091779), Production=Body weight (weaning), (PUBMED_ID= 20477797), Body weight (slaughter), (PUBMED_ID= 22303340), Reproduction=Calving ease (PUBMED_ID= 18420641),	
FS	4	HAPLOTYPE	6351817-6418053	Meat_and_Carcass=Tenderness score (PUBMED_ID= 33101375), Production=Body depth (PUBMED_ID= 16230715), Body weight gain (PUBMED_ID= 19966163), Reproduction=Inseminations per conception (PUBMED_ID= 32650431),	
FS	5	BovineHD0500035146	118776285	Meat_and_Carcass= Carcass weight (PUBMED_ID= 20477797), Reproduction= Scrotal circumference (PUBMED_ID= 20477797),	
FS	6	BovineHD4100004588	37588140	Health= Somatic cell score (PUBMED_ID= 15514072), Clinical mastitis (PUBMED_ID= 11845286), Bovine spongiform encephalopathy (PUBMED_ID= 15342524), Meat_and_Carcass= Kidney, pelvic, and heart fat percentage (PUBMED_ID= 20477785), Kidney, pelvic, and heart fat weight (PUBMED_ID= 20477785), Kidney fat weight (PUBMED_ID= 20477785), Fat thickness at the 12th rib (PUBMED_ID= 20477797), Marbling score (PUBMED_ID= 20477797), Longissimus muscle area (PUBMED_ID= 20477797), Kidney, pelvic, and heart fat percentage (PUBMED_ID= 18791160), Hematin pigment concentration (PUBMED_ID= 18254735), Carcass weight (PUBMED_ID= 19653884), Longissimus muscle area (PUBMED_ID= 31931697), Subcutaneous fat thickness (PUBMED_ID= 31931697), Carcass weight (PUBMED_ID= 31931697), Lean meat yield (PUBMED_ID= 31931697), Subcutaneous fat thickness (PUBMED_ID= 31931697), Longissimus muscle area (PUBMED_ID= 31931697), Carcass weight (PUBMED_ID= 31931697), Bone weight (PUBMED_ID= 34912371), 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19603057), Milk protein percentage (PUBMED_ID= 8978065), Milk protein percentage (PUBMED_ID= 16702292), Milk protein yield (PUBMED_ID= 16702292), Milk yield (PUBMED_ID= 16702292), Milk yield (PUBMED_ID= 12778594), Milk protein percentage (PUBMED_ID= 12778594), Milk fat percentage (PUBMED_ID= 9691050), Milk fat percentage (PUBMED_ID= 11178740), Milk yield (PUBMED_ID= 11167525), Milk fat yield (PUBMED_ID= 16428646), Milk fat percentage (PUBMED_ID= 16428646), Milk protein percentage (PUBMED_ID= ISU0040), Milk yield (PUBMED_ID= 16428646), Milk protein percentage (PUBMED_ID= 19397519), Milk protein yield (PUBMED_ID= 16428646), Milk yield (PUBMED_ID= ISU0040), Milk protein percentage (PUBMED_ID= 27760518), Milk fat percentage (PUBMED_ID= 27760518), Milk protein percentage (PUBMED_ID= 27760518), Milk fat percentage (PUBMED_ID= 27760518), Milk protein percentage (PUBMED_ID= 27760518), Milk fat percentage (PUBMED_ID= 32635893), Milk protein percentage (PUBMED_ID= 27760518), Milk fat percentage (PUBMED_ID=	LCORL

				27760518), Milk protein percentage (PUBMED_ID= 27760518), Production= Body weight (weaning) (PUBMED_ID= 20477797), Body weight (slaughter) (PUBMED_ID= 19653884), Body weight (birth) (PUBMED_ID= 19016677), Body weight (birth) (PUBMED_ID= 10764062), Body weight (weaning) (PUBMED_ID= 20477797), Body length (birth) (PUBMED_ID= 18791160), Body weight (birth) (PUBMED_ID= 18791160), Body weight (birth) (PUBMED_ID= 15537758), Average daily gain (PUBMED_ID= 15537758), Hip height (PUBMED_ID= 12605852), Rump width (PUBMED_ID= 12605852), Metabolic body weight (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Dry matter intake (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Dry matter intake (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Average daily feed intake (PUBMED_ID= 22168586), Average daily gain (PUBMED_ID= 22168586), Metabolic body weight (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Dry matter intake (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Dry matter intake (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Dry matter intake (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Dry matter intake (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 30290764), Body weight (birth) (PUBMED_ID= 30290764), Average daily gain (PUBMED_ID= 30290764), Body weight (birth) (PUBMED_ID= 30290764), Body weight (birth) (PUBMED_ID= 19966163), Body weight (weaning) (PUBMED_ID= 19966163), Body weight (yearling) (PUBMED_ID= 19966163), Body weight gain (PUBMED_ID= 19966163), Metabolic body weight (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Dry matter intake (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Dry matter intake (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Dry matter intake (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Dry matter intake (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Dry matter intake (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Dry matter intake (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Body weight (birth) (PUBMED_ID= 23851991), Body weight (weaning) (PUBMED_ID= 23851991), Body weight (birth) (PUBMED_ID= 19966163), Body weight gain (PUBMED_ID= 19966163), Metabolic body weight (PUBMED_ID= 31931702), Dry matter intake (PUBMED_ID= 31931702), Metabolic body weight (PUBMED_ID= 31931702), Average daily gain (PUBMED_ID= 31931702), Reproduction= Calving ease (PUBMED_ID= 20477797), Gestation length (PUBMED_ID= 19016677), Calf size (PUBMED_ID= 25935543), Calving index (PUBMED_ID= 25935543),	
FS	7	BovineHD0700000068	467158	Meat_and_Carcass= Marbling score (PUBMED_ID= 20477797), Carcass weight (PUBMED_ID= 17596127), Fat thickness at the 12th rib (PUBMED_ID= 22303340), Longissimus muscle area (PUBMED_ID= 32180796), Milk= Milk beta-casein percentage (PUBMED_ID= 19397519), Milk fat yield (PUBMED_ID= 14762091), Milk fat percentage (PUBMED_ID= 14762091), Production= Body weight (weaning) (PUBMED_ID= 20477797), Reproduction= Scrotal circumference (PUBMED_ID= 20477797), Dystocia (PUBMED_ID= 12613879), Stillbirth (PUBMED_ID= 12613879),	5S_rRNA, FLT4
FS	8	BovineHD0800015325	50833954	Health= Clinical mastitis (PUBMED_ID= 11845286), Somatic cell count (PUBMED_ID= 11845286), Meat_and_Carcass= Carcass weight (PUBMED_ID= 20477797), Longissimus muscle area (PUBMED_ID= 20477797), Muscle anserine content (PUBMED_ID= 29163638), Milk= Milking speed (PUBMED_ID= 12605852), Production= Body length (birth) (PUBMED_ID= 18791160), Body weight (birth) (PUBMED_ID= 20477797), Height (yearling) (PUBMED_ID= 20477797), Height (mature) (PUBMED_ID= 20477797), Body weight (yearling) (PUBMED_ID= 19966163), Reproduction= Dystocia (PUBMED_ID= 12613879),	TRPM6
FS	8	BovineHD0800019879	65744992	Exterior= Structural soundness (PUBMED_ID= 16167984), Foot angle (PUBMED_ID= 17183116), Health= Clinical mastitis (PUBMED_ID= 11845286), Somatic cell count (PUBMED_ID= 11845286), Gastrointestinal nematode burden (PUBMED_ID= 24303892), Somatic cell count (PUBMED_ID= 16167984), Milk= Milk kappa-casein percentage (PUBMED_ID= 27485317), Milk unglycosylated kappa-casein percentage (PUBMED_ID= 27485317), Production= Body weight (birth) (PUBMED_ID= 20477797), Body weight (birth) (PUBMED_ID= 19966163), Reproduction= Dystocia (PUBMED_ID= 12613879), Calving ease (PUBMED_ID= 18420641), Stillbirth (PUBMED_ID= 18420641), Age at puberty (PUBMED_ID= 22100599),	
FS	8	BovineHD0800027652	91458487	Exterior= Foot angle (PUBMED_ID= 17183116), Structural soundness (PUBMED_ID= 16167984), Meat_and_Carcass= Carcass weight (PUBMED_ID= 20477797), Marbling score (PUBMED_ID= 20477797), Longissimus muscle area (PUBMED_ID= 20477797),	GRIN3A

				Intramuscular fat (PUBMED_ID= 21421834), Milk= Milk protein yield (PUBMED_ID= 29751743), Milk protein yield (PUBMED_ID= 30696404), Production= Body weight (birth) (PUBMED_ID= 20477797), Height (mature) (PUBMED_ID= 20477797), Reproduction= Calving ease (PUBMED_ID= 18420641), Stillbirth (PUBMED_ID= 18420641), Twinning (PUBMED_ID= 16026340), Calving ease (PUBMED_ID= 20477797),	
FS	8	BovineHD4100007105	102704398	Exterior= Foot angle (PUBMED_ID= 17183116), Structural soundness (PUBMED_ID= 16167984), Meat_and_Carcass= Carcass weight (PUBMED_ID= 20477797), Marbling score (PUBMED_ID= 20477797), Longissimus muscle area (PUBMED_ID= 20477797), Production= Body weight (birth) (PUBMED_ID= 20477797), Height (mature) (PUBMED_ID= 20477797), Rump width (PUBMED_ID= 12605852), Reproduction= Calving ease (PUBMED_ID= 18420641), Stillbirth (PUBMED_ID= 18420641), Twinning (PUBMED_ID= 16026340), Calving ease (PUBMED_ID= 20477797),	C8H9orf43, POLE3, RGS3, SNORA72
FS	8	HAPLOTYPE	65744992-65802549	Exterior=Structural soundness (PUBMED_ID= 16167984), Foot angle (PUBMED_ID= 17183116), Health=Clinical mastitis (PUBMED_ID= 11845286), Somatic cell count (PUBMED_ID= 11845286), Gastrointestinal nematode burden (PUBMED_ID= 24303892), Somatic cell count (PUBMED_ID= 16167984), Milk=Milk kappa-casein percentage (PUBMED_ID= 27485317), Milk unglycosylated kappa-casein percentage (PUBMED_ID= 27485317), Milk kappa-casein percentage (PUBMED_ID= 27485317), Production=Body weight (birth), (PUBMED_ID= 19966163), Reproduction=Dystocia (PUBMED_ID= 12613879), Calving ease (PUBMED_ID= 18420641), Stillbirth (PUBMED_ID= 18420641), Age at puberty (PUBMED_ID= 22100599), Conception rate (PUBMED_ID= 31718557), Inseminations per conception (PUBMED_ID= 31718557),	
FS	11	BovineHD1100027596	94731004	Health= Immunoglobulin G level (PUBMED_ID= 19016677), Meat_and_Carcass= Marbling score (PUBMED_ID= 20477797), Longissimus muscle area (PUBMED_ID= 20477797), Milk= Cheese protein recovery (PUBMED_ID= 27889122), Milk fat yield (PUBMED_ID= 34828436), Cheese protein recovery (PUBMED_ID= 27889122), Production= Body weight (mature) (PUBMED_ID= 20477797), Body weight (weaning) (PUBMED_ID= 20477797),	DENND1A
FS	12	HAPLOTYPE	50678326-50689493	Exterior=Structural soundness (PUBMED_ID= 17183116), Health=Gastrointestinal nematode burden (PUBMED_ID= 24303892), Meat_and_Carcass=Retail product yield (PUBMED_ID= 14677852), Longissimus muscle area (PUBMED_ID= 20477797), Milk=Milk fat yield (PUBMED_ID= 12778594), Production=Body weight (yearling), (PUBMED_ID= 20477797), Height (mature), (PUBMED_ID= 20477797), Body weight (mature), (PUBMED_ID= 20477797), Body weight (birth), (PUBMED_ID= 20477797), Body weight (mature), (PUBMED_ID= 20477797), Body weight (weaning), (PUBMED_ID= 20477797), Reproduction=Stillbirth (PUBMED_ID= 19912419),	LMO7, UCHL3
FS	16	BovineHD1600003330	11855136	Exterior= Structural soundness (PUBMED_ID= 17183116), Meat_and_Carcass= Fat thickness at the 12th rib (PUBMED_ID= 20477797), Carcass weight (PUBMED_ID= 20477797), Milk= 305-day milk yield (PUBMED_ID= 17582132), Milk protein yield (PUBMED_ID= 17582132), Production= Length of productive life (PUBMED_ID= 9691050), Body weight (weaning) (PUBMED_ID= 20477797), Height (mature) (PUBMED_ID= 20477797), Reproduction= Stillbirth (PUBMED_ID= 19912419), Interval to first estrus after calving (PUBMED_ID= 22100599),	
FS	17	ARS-BFGL-NGS-118918	18626728	Exterior= Rump angle (PUBMED_ID= 12605852), Health= PCVI minus PCVF (PUBMED_ID= 12805560), PCVF minus PCVM (PUBMED_ID= 12805560), PCV variance (PUBMED_ID= 12805560), Final packed red blood cell volume (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 150 after challenge (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 100 after challenge (PUBMED_ID= 12805560), Meat_and_Carcass= Marbling score (PUBMED_ID= 10764062), Milk= Milk alpha-casein percentage (PUBMED_ID= 19397519), Milk yield (PUBMED_ID= 21607666), Lactation persistency (PUBMED_ID= 21607666), Milk yield (PUBMED_ID= 21607666), Production= Average daily gain (PUBMED_ID= 17596127), Body weight (weaning) (PUBMED_ID= 20477797), Reproduction= Calving ease (PUBMED_ID= 20477797),	NOCT
FS	17	BTB-01087937	19461407	Exterior= Rump angle (PUBMED_ID= 12605852), Health= PCVI minus PCVF (PUBMED_ID= 12805560), PCVF minus PCVM (PUBMED_ID= 12805560), PCV variance (PUBMED_ID= 12805560), Final packed red blood cell volume (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 150 after challenge (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 100 after challenge (PUBMED_ID= 12805560), Meat_and_Carcass= Marbling score (PUBMED_ID= 10764062), Milk= Milk alpha-casein percentage (PUBMED_ID= 19397519), Production= Average daily gain (PUBMED_ID= 17596127), Body weight (weaning) (PUBMED_ID= 20477797), Reproduction= Calving ease (PUBMED_ID= 20477797), Early embryonic survival (PUBMED_ID= 19456315),	SLC7A11
FS	17	BovineHD1700006112	20844627	Exterior= Rump angle (PUBMED_ID= 12605852), Health= PCVI minus PCVF (PUBMED_ID= 12805560), PCVF minus PCVM (PUBMED_ID= 12805560), PCV variance (PUBMED_ID= 12805560), Final packed red blood cell volume (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 150 after challenge (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 100 after challenge (PUBMED_ID= 12805560), Gastrointestinal nematode burden (PUBMED_ID= 24303892), Meat_and_Carcass=	

				Marbling score (PUBMED_ID= 10764062), Milk= Milk alpha-casein percentage (PUBMED_ID= 19397519), Production= Average daily gain (PUBMED_ID= 17596127), Body weight (weaning) (PUBMED_ID= 20477797), Reproduction= Calving ease (PUBMED_ID= 20477797),	
FS	17	BovineHD1700007095	24825598	Health= PCVI minus PCVF (PUBMED_ID= 12805560), PCVF minus PCVM (PUBMED_ID= 12805560), PCV variance (PUBMED_ID= 12805560), Final packed red blood cell volume (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 150 after challenge (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 100 after challenge (PUBMED_ID= 12805560), Meat_and_Carcass= Marbling score (PUBMED_ID= 10764062), Milk= Milk alpha-casein percentage (PUBMED_ID= 19397519), Production= Average daily gain (PUBMED_ID= 17596127), Body weight (weaning) (PUBMED_ID= 20477797), Reproduction= Calving ease (PUBMED_ID= 20477797),	
FS	18	ARS-BFGL-NGS-103183	47994061	Exterior= Foot angle (PUBMED_ID= 16167984), Teat length (PUBMED_ID= 16167984), Health= Immunoglobulin G level (PUBMED_ID= 21138580), Somatic cell score (PUBMED_ID= 19725965), Bovine respiratory disease susceptibility (PUBMED_ID= 34409086), Bovine respiratory disease susceptibility (PUBMED_ID= ISU0120), Meat_and_Carcass= Palmitic acid content (PUBMED_ID= 20477785), Omega-6 to omega-3 fatty acid ratio (PUBMED_ID= 20416790), Milk= Milk fat yield (PUBMED_ID= 15514072), Milk protein yield (PUBMED_ID= 12487480), Milk yield (PUBMED_ID= 16533362), Production= Body weight (birth) (PUBMED_ID= 20477797), Reproduction= Stillbirth (PUBMED_ID= 18420641),	DPF1, SIPA1L3, U6
FS	19	BovineHD1900017112	59345427	Exterior= Foot angle (PUBMED_ID= 21831322), Feet and leg conformation (PUBMED_ID= 21831322), Teat placement - front (PUBMED_ID= 21831322), Udder attachment (PUBMED_ID= 21831322), Rear leg placement - rear view (PUBMED_ID= 21831322), Teat placement - rear (PUBMED_ID= 21831322), Udder height (PUBMED_ID= 21831322), Stature (PUBMED_ID= 21831322), Strength (PUBMED_ID= 21831322), Udder cleft (PUBMED_ID= 21831322), Udder depth (PUBMED_ID= 21831322), Health= Somatic cell score (PUBMED_ID= 15514072), Abomasum displacement (PUBMED_ID= 18946144), Bovine spongiform encephalopathy (PUBMED_ID= 15342524), Meat_and_Carcass= Myristic acid content (PUBMED_ID= 17242864), Marbling score (PUBMED_ID= 20477797), Subcutaneous fat thickness (PUBMED_ID= 15080315), Longissimus muscle area (PUBMED_ID= 20477797), Milk= Milk protein percentage (PUBMED_ID= 15514072), Milk conjugated linoleic acid content (PUBMED_ID= 17242864), Milk fat yield (PUBMED_ID= 12605852), Milk yield (PUBMED_ID= 22449276), Milk tricosanoic acid content (PUBMED_ID= 27506634), Production= Body weight (birth) (PUBMED_ID= 9720178), Body weight (yearling) (PUBMED_ID= 20477797), Body weight (mature) (PUBMED_ID= 26445451), Body depth (PUBMED_ID= 21831322), PTA type (PUBMED_ID= 21831322), Net merit (PUBMED_ID= 21831322), Rump width (PUBMED_ID= 21831322), Reproduction= Calving ease (PUBMED_ID= 20477797), Scrotal circumference (PUBMED_ID= 20477797), Conception rate (PUBMED_ID= 31718557), Calving ease (maternal) (PUBMED_ID= 21831322), Calving ease (PUBMED_ID= 21831322), Conception rate (PUBMED_ID= 31299913),	
FS	19	BovineHD1900018261	62590391	Health= Bovine spongiform encephalopathy (PUBMED_ID= 15342524), Milk= Milk fat yield (PUBMED_ID= 21831322), Milk yield (PUBMED_ID= 21831322), Milk protein yield (PUBMED_ID= 21831322), Milk protein yield (PUBMED_ID= 22449276),	APOH, CEP112
FS	20	BovineHD2000020384	69702259	Meat_and_Carcass= Marbling score (PUBMED_ID= 20477797), Shear force (PUBMED_ID= 28727016), Milk= Milk protein yield (PUBMED_ID= 18298934), Colostrum albumin concentration (PUBMED_ID= 33255903), Reproduction= Calving ease (PUBMED_ID= 20477797),	
FS	22	Hapmap53119-rs29018	29120539	Health= Minimum packed red blood cell volume (PUBMED_ID= 12805560), Meat_and_Carcass= Intramuscular fat (PUBMED_ID= 18254735), Marbling score (PUBMED_ID= 18791160), Myristic acid content (PUBMED_ID= 20416790), Palmitic acid content (PUBMED_ID= 20416790), Palmitoleic acid content (PUBMED_ID= 20416790), Stearic acid content (PUBMED_ID= 20416790), Oleic acid content (PUBMED_ID= 20416790), Conjugated linoleic acid content (PUBMED_ID= 20416790), Total fatty acid content (PUBMED_ID= 20416790), Saturated fatty acid content (PUBMED_ID= 20416790), Polyunsaturated to saturated fatty acid ratio (PUBMED_ID= 20416790), Carcass weight (PUBMED_ID= 20477797), Milk= Milk protein yield (PUBMED_ID= 14762090), Production= Body weight (yearling) (PUBMED_ID= 20477797), Reproduction= Non-return rate (PUBMED_ID= 19389971),	
FS	22	BovineHD2200009696	33624719	Exterior= Udder depth (PUBMED_ID= 18832229), Health= Minimum packed red blood cell volume (PUBMED_ID= 12805560), Somatic cell score (PUBMED_ID= 18832229), Meat_and_Carcass= Beef flavor intensity (PUBMED_ID= 18254735), Fat percentage (PUBMED_ID= 18791160), Marbling score (PUBMED_ID= 33101375), Production= Body weight (yearling) (PUBMED_ID= 20477797), Height (mature) (PUBMED_ID= 20477797), Reproduction= Calf size (PUBMED_ID= 18420641),	
FS	22	BovineHD2200009726	33760924	Exterior= Udder depth (PUBMED_ID= 18832229), Rump angle (PUBMED_ID= 16230715), Health= Minimum packed red blood cell volume (PUBMED_ID= 12805560), Somatic cell score (PUBMED_ID= 18832229), Meat_and_Carcass= Beef flavor intensity (PUBMED_ID= 18254735), Fat percentage (PUBMED_ID= 18791160), Production= Body weight (yearling) (PUBMED_ID= 20477797), Height (mature) (PUBMED_ID= 20477797), Reproduction= Calf size (PUBMED_ID= 18420641),	

HF	2	HAPLOTYPE	44282846-44313656	Exterior=Udder depth (PUBMED_ID= 17433017), Teat placement (PUBMED_ID= 12605852), Dairy form (PUBMED_ID= 16167984), Health=Immunoglobulin G level (PUBMED_ID= 21138580), Initial packed red blood cell volume (PUBMED_ID= 12805560), PCVI minus PCVF (PUBMED_ID= 12805560), PCVI minus PCVM (PUBMED_ID= 12805560), Minimum packed red blood cell volume (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 150 after challenge (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 100 after challenge (PUBMED_ID= 12805560), Percentage decrease in body weight up to day 150 after challenge (PUBMED_ID= 12805560), Meat_and_Carcass=Lung percentage (PUBMED_ID= 20477785), Fat thickness at the 12th rib (PUBMED_ID= 14677852), Yield grade (PUBMED_ID= 14677852), Milk=Milk fat yield (PUBMED_ID= 17433017), Milk yield (PUBMED_ID= 12778594), Milk protein yield (PUBMED_ID= 16167984), Milk fat percentage (PUBMED_ID= 14762090), Milk fat yield (PUBMED_ID= 9691050), Production=Body weight (birth), (PUBMED_ID= 14677852), Chest depth (PUBMED_ID= 12605852), Body weight (birth), (PUBMED_ID= 20477797), Body weight (initial), (PUBMED_ID= 12805560),	ARL5A, CACNB4
HF	2	HAPLOTYPE	44292504-44317544	Exterior=Udder depth (PUBMED_ID= 17433017), Teat placement (PUBMED_ID= 12605852), Dairy form (PUBMED_ID= 16167984), Health=Immunoglobulin G level (PUBMED_ID= 21138580), Initial packed red blood cell volume (PUBMED_ID= 12805560), PCVI minus PCVF (PUBMED_ID= 12805560), PCVI minus PCVM (PUBMED_ID= 12805560), Minimum packed red blood cell volume (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 150 after challenge (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 100 after challenge (PUBMED_ID= 12805560), Percentage decrease in body weight up to day 150 after challenge (PUBMED_ID= 12805560), Meat_and_Carcass=Lung percentage (PUBMED_ID= 20477785), Fat thickness at the 12th rib (PUBMED_ID= 14677852), Yield grade (PUBMED_ID= 14677852), Milk=Milk fat yield (PUBMED_ID= 17433017), Milk yield (PUBMED_ID= 12778594), Milk protein yield (PUBMED_ID= 16167984), Milk fat percentage (PUBMED_ID= 14762090), Milk fat yield (PUBMED_ID= 9691050), Production=Body weight (birth), (PUBMED_ID= 14677852), Chest depth (PUBMED_ID= 12605852), Body weight (birth), (PUBMED_ID= 20477797), Body weight (initial), (PUBMED_ID= 12805560),	ARL5A, CACNB4
HF	4	BovineHD0400009320	32656334	Exterior= Stature (PUBMED_ID= 16230715), Health= Immunoglobulin G level (PUBMED_ID= 21138580), Somatic cell score (PUBMED_ID= 9691050), Somatic cell score (PUBMED_ID= 14556700), Meat_and_Carcass= Tenderness score (PUBMED_ID= 11325189), Meat-to-bone ratio (PUBMED_ID= 18791160), Bone percentage (PUBMED_ID= 18791160), Carcass weight (PUBMED_ID= 11325189), Marbling score (PUBMED_ID= 19781039), Production= Average daily gain (PUBMED_ID= 11325189), Residual feed intake (PUBMED_ID= 18791150), Length of productive life (PUBMED_ID= 27889128),	RUNDC3B
HF	4	BovineHD0400015866	57768518	Exterior= Social separation--Vocalization (PUBMED_ID= 18784067), Social separation--Standing alert (PUBMED_ID= 18784067), Health= FMDV peptide-induced cell proliferation (PUBMED_ID= 21138580), Meat_and_Carcass= Marbling score (PUBMED_ID= 19781039), Longissimus muscle area (PUBMED_ID= 15537759), Marbling score (PUBMED_ID= 15537759), Milk= Milking speed (PUBMED_ID= 15377635), Milk protein yield (PUBMED_ID= 15377635), Milk fat percentage (PUBMED_ID= 9621249), Production= Body weight (weaning) (PUBMED_ID= 20477797), Body weight (slaughter) (PUBMED_ID= 22303340), Reproduction= Calving ease (PUBMED_ID= 18420641),	IMMP2L
HF	4	HAPLOTYPE	32641770-32656334	Exterior=Stature (PUBMED_ID= 16230715), Health=Immunoglobulin G level (PUBMED_ID= 21138580), Somatic cell score (PUBMED_ID= 14556700), Meat_and_Carcass=Tenderness score (PUBMED_ID= 11325189), Meat-to-bone ratio (PUBMED_ID= 18791160), Bone percentage (PUBMED_ID= 18791160), Carcass weight (PUBMED_ID= 11325189), Marbling score (PUBMED_ID= 19781039), Production=Average daily gain (PUBMED_ID= 11325189), Residual feed intake (PUBMED_ID= 18791150), Length of productive life (PUBMED_ID= 27889128),	RUNDC3B
HF	4	HAPLOTYPE	57701711-57701711	Exterior=Social separation--Vocalization (PUBMED_ID= 18784067), Social separation--Standing alert (PUBMED_ID= 18784067), Health=FMDV peptide-induced cell proliferation (PUBMED_ID= 21138580), Meat_and_Carcass=Marbling score (PUBMED_ID= 19781039), Longissimus muscle area (PUBMED_ID= 15537759), Marbling score (PUBMED_ID= 15537759), Milk=Milking speed (PUBMED_ID= 15377635), Milk protein yield (PUBMED_ID= 15377635), Milk fat percentage (PUBMED_ID= 9621249), Production=Body weight (weaning), (PUBMED_ID= 20477797), Body weight (slaughter), (PUBMED_ID= 22303340), Reproduction=Calving ease (PUBMED_ID= 18420641),	IMMP2L
HF	8	HAPLOTYPE	34351802-34400070	Exterior=Foot angle (PUBMED_ID= 21831322), Feet and leg conformation (PUBMED_ID= 21831322), Teat placement - front (PUBMED_ID= 21831322), Udder attachment (PUBMED_ID= 21831322), Rear leg placement - rear view (PUBMED_ID= 21831322), Teat placement - rear (PUBMED_ID= 21831322), Udder height (PUBMED_ID= 21831322), Stature (PUBMED_ID= 21831322), Strength (PUBMED_ID= 21831322), Udder cleft (PUBMED_ID= 21831322), Udder depth (PUBMED_ID= 21831322), Foot angle (PUBMED_ID= 21831322), Feet and leg conformation (PUBMED_ID= 21831322), Udder attachment (PUBMED_ID= 21831322), Stature (PUBMED_ID= 21831322), Strength (PUBMED_ID= 21831322), Udder depth (PUBMED_ID= 21831322), Health=Somatic cell score (PUBMED_ID= 18832229), Meat_and_Carcass=Fat thickness at the 12th rib (PUBMED_ID= 11325189), Marbling score	

				(PUBMED_ID= 20477797), Milk=Milking speed (PUBMED_ID= 29705414), Milk fat yield (PUBMED_ID= 21831322), Production=Body length (birth), (PUBMED_ID= 18791160), Body depth (PUBMED_ID= 21831322), PTA type (PUBMED_ID= 21831322), Net merit (PUBMED_ID= 21831322), Rump width (PUBMED_ID= 21831322), Body depth (PUBMED_ID= 21831322), PTA type (PUBMED_ID= 21831322), Rump width (PUBMED_ID= 21831322), Body weight (yearling), (PUBMED_ID= 30290764), Reproduction=Stillbirth (PUBMED_ID= 12613879), Stillbirth (maternal), (PUBMED_ID= 21831322),	
HF	15	HAPLOTYPE	82616506-82629156	Meat_and_Carcass=Carcass weight (PUBMED_ID= 20477797), Reproduction=Calving ease (PUBMED_ID= 20477797), Calf size (PUBMED_ID= 18420641), Age at puberty (PUBMED_ID= 22100599),	OR5A1, OR5AN1, OR5AN1M
HF	17	BovineHD1700007641	26596450	Health= PCVI minus PCVF (PUBMED_ID= 12805560), PCVF minus PCVM (PUBMED_ID= 12805560), PCV variance (PUBMED_ID= 12805560), Final packed red blood cell volume (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 150 after challenge (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 100 after challenge (PUBMED_ID= 12805560), Meat_and_Carcass= Marbling score (PUBMED_ID= 10764062), Milk= Milk alpha-casein percentage (PUBMED_ID= 19397519), Milk caproic acid content (PUBMED_ID= 29391528), Production= Average daily gain (PUBMED_ID= 17596127), Body weight (weaning) (PUBMED_ID= 20477797), Reproduction= Calving ease (PUBMED_ID= 20477797),	
HF	17	HAPLOTYPE	26596450-26603052	Health=PCVI minus PCVF (PUBMED_ID= 12805560), PCVF minus PCVM (PUBMED_ID= 12805560), PCV variance (PUBMED_ID= 12805560), Final packed red blood cell volume (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 150 after challenge (PUBMED_ID= 12805560), Percentage decrease in PCV up to day 100 after challenge (PUBMED_ID= 12805560), Meat_and_Carcass=Marbling score (PUBMED_ID= 10764062), Milk=Milk alpha-casein percentage (PUBMED_ID= 19397519), Milk caproic acid content (PUBMED_ID= 29391528), Production=Average daily gain (PUBMED_ID= 17596127), Body weight (weaning), (PUBMED_ID= 20477797), Reproduction=Calving ease (PUBMED_ID= 20477797),	
HF	18	ARS-BFGL-NGS-107813	34260554	Exterior= Udder attachment (PUBMED_ID= 16230715), Udder height (PUBMED_ID= 16230715), Udder depth (PUBMED_ID= 16230715), Udder composite index (PUBMED_ID= 16230715), Health= Immunoglobulin G level (PUBMED_ID= 21138580), Meat_and_Carcass= Palmitic acid content (PUBMED_ID= 20477785), Omega-6 to omega-3 fatty acid ratio (PUBMED_ID= 20416790), Marbling score (PUBMED_ID= 27221246), Intramuscular fat (PUBMED_ID= 29163638), Milk= Milk yield (PUBMED_ID= 12487480), Production= Residual feed intake (PUBMED_ID= 18791150), Body weight (weaning) (PUBMED_ID= 20477797), Length of productive life (PUBMED_ID= 16734691), Reproduction= Dystocia (PUBMED_ID= 12613879), Stillbirth (PUBMED_ID= 19912419), Pregnancy rate (PUBMED_ID= 16734691),	BEAN1, CKLF, CMTM2, TK2
HF	21	BovineHD2100003533	13241858	Health= Clinical mastitis (PUBMED_ID= 14762087), Somatic cell count (PUBMED_ID= 16167984), Milk= Milk yield (PUBMED_ID= 12778594), Production= Body weight (birth) (PUBMED_ID= 15537758), Average daily gain (PUBMED_ID= 15537758), Reproduction= Stillbirth (PUBMED_ID= 19912419), Gestation length (PUBMED_ID= 19016677), Scrotal circumference (PUBMED_ID= 20477797),	
STAY	1	ARS-BFGL-BAC-14872	136386893	Exterior= Teat placement - front (PUBMED_ID= 16230715), Udder cleft (PUBMED_ID= 16230715), Meat_and_Carcass= Fat thickness at the 12th rib (PUBMED_ID= 20477797), Longissimus muscle area (PUBMED_ID= 20477797), Milk= Milk alpha-casein percentage (PUBMED_ID= 19397519), Milk fat yield (PUBMED_ID= 16533362), Milk fat yield (PUBMED_ID= 19841231), Production= Body weight (birth) (PUBMED_ID= 14677852), Body weight (yearling) (PUBMED_ID= 20477797), Body weight (weaning) (PUBMED_ID= 20477797), Veterinary treatments (PUBMED_ID= 19389971), Reproduction= Interval to first estrus after calving (PUBMED_ID= 19389971),	
STAY	21	BovineHD2100007401	25151974	Exterior= Udder width (PUBMED_ID= 16167984), Teat placement - front (PUBMED_ID= 16167984), Udder attachment (PUBMED_ID= 16167984), Teat length (PUBMED_ID= 16167984), Health= Clinical mastitis (PUBMED_ID= 14762087), Meat_and_Carcass= Fat thickness at the 12th rib (PUBMED_ID= 20477797), Carcass weight (PUBMED_ID= 20477797), Longissimus muscle area (PUBMED_ID= 20477797), Milk= Milk yield (PUBMED_ID= 12778594), Production= Body weight (weaning) (PUBMED_ID= 20477797), Body weight (birth) (PUBMED_ID= 15537758), Body weight (yearling) (PUBMED_ID= 20477797), PTA type (PUBMED_ID= 16167984), Reproduction= Stillbirth (PUBMED_ID= 19912419), Gestation length (PUBMED_ID= 19016677),	CTSH
STAY	28	BovineHD2800001953	6493973	Exterior= Udder cleft (PUBMED_ID= 12605852), Teat placement - front (PUBMED_ID= 12605852), Meat_and_Carcass= Fat thickness at the 12th rib (PUBMED_ID= 20477797), Longissimus muscle area (PUBMED_ID= 20477797), Carcass weight (PUBMED_ID= 20477797), Carcass weight (PUBMED_ID= 29103288), Milk= Milk lactose content (PUBMED_ID= 31178181), Milk mid-infrared spectra (PUBMED_ID= 31178181), Milk lactose content (PUBMED_ID= 31447150), Milk lactose content (PUBMED_ID= 29246110), Milk potassium content (PUBMED_ID= 33824377), Milk sodium content (PUBMED_ID= 33824377), Milk lactose content (PUBMED_ID= 31447150), Production= Body weight (initial) (PUBMED_ID= 12805560), Body weight (mean)	KCNK1

				(PUBMED_ID= 12805560), Body weight (weaning) (PUBMED_ID= 20477797), Body weight gain (PUBMED_ID= 19966163), Reproduction= Pregnancy rate (PUBMED_ID= 12605852), Gestation length (PUBMED_ID= 22034999),	
STAY	28	HAPLOTYPE	6480000-6493973	Exterior=Udder cleft (PUBMED_ID= 12605852), Teat placement - front (PUBMED_ID= 12605852), Meat_and_Carcass=Fat thickness at the 12th rib (PUBMED_ID= 20477797), Longissimus muscle area (PUBMED_ID= 20477797), Carcass weight (PUBMED_ID= 29103288), Milk=Milk protein yield (PUBMED_ID= 18650300), Milk lactose content (PUBMED_ID= 31178181), Milk mid-infrared spectra (PUBMED_ID= 31178181), Milk lactose content (PUBMED_ID= 29246110), Milk potassium content (PUBMED_ID= 33824377), Milk sodium content (PUBMED_ID= 33824377), Milk lactose content (PUBMED_ID= 31447150), Production=Body weight (initial), (PUBMED_ID= 12805560), Body weight (mean), (PUBMED_ID= 12805560), Body weight (weaning), (PUBMED_ID= 20477797), Body weight gain (PUBMED_ID= 19966163), Reproduction=Pregnancy rate (PUBMED_ID= 12605852), Gestation length (PUBMED_ID= 22034999),	KCNK1

[a] Chromosome; FS= Frame score; SC= Scrotal circumference; HF= Heifer fertility; STAY= Stayability.

Table S2. SNPs associated with reproductive traits and frame score with the models BAYESB, BAYESC and EMMAX in Simmental and Simbrah cattle.

Trait	Breed	Chr[a]	Position	SNP[b]	Model	PP[c]	P-value
FS[d]	Joint	4	59503146	BTB-00190917	BAYESB	0.08	
					BAYESC	0.07	
		5	118776285	BovineHD0500035146	BAYESB	0.32	
					BAYESC	0.30	
		6	37588140	BovineHD4100004588	BAYESC	0.04	
		7	467158	BovineHD0700000068	BAYESC	0.09	
		8	50833954	BovineHD0800015325	BAYESC	0.06	
			65744992	BovineHD0800019879	BAYESB	0.73	
					BAYESC	0.70	
			91458487	BovineHD0800027652	BAYESB	0.07	
					BAYESC	0.07	
			102704398	BovineHD4100007105	BAYESB	0.08	
					BAYESC	0.09	
		11	94731004	BovineHD1100027596	BAYESB	0.12	
					BAYESC	0.13	
		16	11855136	BovineHD1600003330	BAYESB	0.30	
					BAYESC	0.32	
		17	18626728	ARS-BFGL-NGS-118918	BAYESB	0.09	
					BAYESC	0.09	
			20844627	BovineHD1700006112	BAYESB	0.09	
					BAYESC	0.11	
			18626728	ARS-BFGL-NGS-118918	EMMAX		3.44E-06
		22	33624719	BovineHD2200009696	BAYESB	0.18	
					BAYESC	0.22	
			33760924	BovineHD2200009726	BAYESB	0.15	
					BAYESC	0.14	
			29120539	Hapmap53119-rs29018	BAYESB	0.10	
					BAYESC	0.10	
	Simbrah	3	104074474	BovineHD0300029985	BAYESB	0.12	
					BAYESC	0.14	
		17	24825598	BovineHD1700007095	BAYESB	0.12	
		18	47994061	ARS-BFGL-NGS-103183	BAYESB	0.10	
					BAYESC	0.16	
	Simmental	2	28349857	ARS-BFGL-NGS-60458	BAYESB	0.23	
					BAYESC	0.18	
			56674297	BTB-01145846	BAYESB	0.13	
					BAYESC	0.11	
		17	19461407	BTB-01087937	BAYESC	0.11	
		19	59345427	BovineHD1900017112	BAYESC	0.09	
			62590391	BovineHD1900018261	BAYESC	0.09	
		20	69702259	BovineHD2000020384	BAYESB	0.49	
					BAYESC	0.54	
					EMMAX		6.62E-06
SC[e]	Joint	1	24964189	BovineHD0100007238	BAYESB	0.22	
					BAYESC	0.24	
			69664149	BovineHD0100020122	BAYESC	0.06	
		3	14395023	BovineHD0300004685	BAYESB	0.08	
					BAYESC	0.08	

		6	32965679	BovineHD0600009601	BAYESB	0.46	
					BAYESC	0.46	
		10	18541772	ARS-BFGL-NGS-74837	BAYESB	0.22	
					BAYESC	0.22	
			22308257	BovineHD1000007178	BAYESB	0.13	
					BAYESC	0.14	
					EMMAX		8.50E-06
		17	15972230	BovineHD1700004678	BAYESB	0.17	
					BAYESC	0.18	
	Simbrah	6	32965679	BovineHD0600009601	BAYESB	0.16	
					BAYESC	0.20	
		10	18541772	ARS-BFGL-NGS-74837	BAYESB	0.10	
					BAYESC	0.10	
		17	7548169	BovineHD1700002151	BAYESC	0.08	
		23	23730493	BovineHD2300006211	BAYESC	0.12	
	Simmental	10	22308257	BovineHD1000007178	BAYESB	0.55	
					BAYESC	0.57	
					EMMAX		3.29E-06
		13	73602949	BovineHD1300021455	BAYESB	0.42	
					BAYESC	0.43	
FV[f]	Joint	4		ARS-BFGL-NGS-105821	BAYESC	0.07	
			57768518	BovineHD0400015866	BAYESC	0.10	
		17	26596450	BovineHD1700007641	BAYESB	0.32	
					BAYESC	0.34	
					EMMAX		3.19E-06
		18	34260554	ARS-BFGL-NGS-107813	BAYESB	0.16	
					BAYESC	0.18	
	Simbrah	17	26596450	BovineHD1700007641	BAYESB	0.15	
					BAYESC	0.15	
					EMMAX		6.46E-06
	Simmental	4	32656334	BovineHD0400009320	BAYESC	0.13	
		21	13241858	BovineHD2100003533	BAYESB	0.25	
					BAYESC	0.28	
					EMMAX		1.07E-05
STAY[g]	Joint	21	25151974	BovineHD2100007401	BAYESC	0.07	
	Simmental	1	136386893	ARS-BFGL-BAC-14872	BAYESB	0.13	
					BAYESC	0.15	
		28	6493973	BovineHD2800001953	BAYESB	0.26	
					BAYESC	0.32	
					EMMAX		4.87E-06

[a] Chromosome; [b] Single nucleotide polymorphism; [c] Posterior probabilities; [d] Frame score; [e] Scrotal circumference; [f] Heifer fertility; [g] Stayability.

Table S3. Haplotypes associated with reproductive traits and frame score with the models BAYESB, BAYESC and EMMAX in Simmental and Simbrah cattle.

Trait	Breed	Chr[a]	Position	SNPs[b]	Model	P-value	PP[c]
FS[d]	Joint	4	59489126-59503146	BovineHD0400016239, BTB-00190917	BAYESC		0.09
		8	65744992-65802549	BTB-01847877, BovineHD0800019879, BovineHD0800019885, BovineHD0800019890	BAYESB		0.76
					BAYESC		0.79
	Simbrah	3	104074474-104081372	BovineHD0300029985, BovineHD0300029986	BAYESB		0.22
					BAYESC		0.23
					EMMAX	1.37E-05	
	Simmental	1	60895445-60899823	BovineHD0100017414, ARS-BFGL-BAC-20015	BAYESB		0.43
					BAYESC		0.41
		2	28329020-28349857	Hapmap48633-BTA-118034, BovineHD0200008314, ARS-BFGL-NGS-60458	BAYESB		0.16
					BAYESC		0.14
		4	6351817-6418053	BovineHD0400001800, BovineHD0400001811, BovineHD0400001814, ARS-BFGL-NGS-66869	BAYESB		0.27
					BAYESC		0.34
		12	50678326-50689493	BTA-23832-no-rs, BovineHD1200014038	BAYESB		0.54
					BAYESC		0.66
SC[e]	Joint	19	43058602-43162697	BovineHD1900012356, BovineHD1900012359, BovineHD1900012364, BovineHD1900012372	BAYESC		0.08
		25	27577974-27654242	BovineHD2500007771, BovineHD2500007775, Hapmap44260-BTA-597, Hapmap41591-BTA-597	BAYESB		0.29
					BAYESC		0.34
					EMMAX	1.67E-05	
	Simbrah	2	5747611-5759652	BovineHD0200001651, BovineHD0200001656	BAYESB		0.48
					BAYESC		0.47
					EMMAX	1.12E-05	
		23	23730493-23745977	BovineHD2300006211, BovineHD2300006215	BAYESB		0.15
	Simmental	2	41538841-41567719	BovineHD0200040589, ARS-BFGL-BAC-2790, BovineHD0200012088, BovineHD0200012090	BAYESB		0.26
					BAYESC		0.23
		8	38363220-38366097	BovineHD0800011512, BovineHD0800011514	BAYESB		0.16
		9	15900318-15919300	BovineHD0900004308, BovineHD0900004311, BTB-01407863	BAYESB		0.16
					BAYESC		0.34
		13	73602949-73620495	BovineHD1300021455, BovineHD1300021459	BAYESB		0.20
FV[f]	Joint	2	44292504-44317544	BovineHD0200012875, BovineHD0200012878, BovineHD0200012883, BovineHD0200012884	BAYESB		0.07
					BAYESC		0.05
					EMMAX	4.73E-06	
		4	57701711-57701711	BovineHD0400015851, ARS-BFGL-NGS-105821	BAYESC		0.10
		15	82616506-82629156	BovineHD1500024589, BovineHD1500024595, BovineHD1500024597	BAYESC		0.09
		17	26596450-26603052	BovineHD1700007641, Hapmap43860-BTA-46675	BAYESB		0.58
					BAYESC		0.58
					EMMAX	1.27E-06	
	Simbrah	2	44282846-44313656	BovineHD0200012872, BovineHD0200012875, BovineHD0200012878, BovineHD0200012883, BovineHD0200012884, BovineHD0200012888	BAYESB		0.27
					BAYESC		0.06
					EMMAX	4.32E-06	

		8	34351802-34400070	BovineHD0800010236, Hapmap55107-rs29014632, BovineHD0800010244, BovineHD0800010247	BAYESB		0.15
					EMMAX	1.29E-05	
		28	9026425-9054402	BovineHD2800002746, ARS-BFGL-NGS-114215, BovineHD2800002756	EMMAX	1.38E-05	
	Simmental	4	32641770-32656334	BTB-01476087, BovineHD0400009320	BAYESB		0.49
					BAYESC		0.54
					EMMAX	1.18E-05	
STAY[g]	Simmental	28	6480000-6493973	BovineHD2800001945, BovineHD2800001953	BAYESB		0.28
					BAYESC		0.29
					EMMAX	5.65E-06	
		3	40032182-40154599	ARS-BFGL-NGS-114492, BTA-93165-no-rs, BovineHD0300012268, BTB-01436387, BovineHD0300012278	EMMAX	1.50E-05	

[a]Chromosome; [b]Single nucleotide polymorphism; [c]Posterior probabilities; [d]Frame score; [e]Scrotal circumference; [f]Heifer fertility; [g]Stayability.