Running title: Signatures of selection for cattle behavior

DETECTION OF SELECTION SIGNATURES FOR AGONISTIC BEHAVIOR IN CATTLE

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Abstract

The identification of genomic regions including signatures of selection produced by domestication and its subsequent artificial selection processes allow the understanding of the evolution of bovine breeds. Although several studies describe the genomic variability among meat or milk production cattle breeds, there are limited publications (analysis?) orientated towards bovine behavioral features. The current study is focused on mapping genomic signatures of selection which may provide insights of differentiation between neutral and selected polymorphisms. Their effects are studied in the Lidia cattle traditionally selected for agonistic behavior compared to Spanish breeds showing tamed behavior. Two different approaches, Bayescan and SelEstim, were applied using genotypic 50K SNP Beadchip data.

Both procedures detected two genomic regions bearing genes previously related to behavioral traits. The frequencies of the selected allele in these two regions in Lidia breed were opposite to those found in the tamed breeds. In these genomic regions several putative genes associated to enriched metabolic pathways related to the behavioral development were identified, as Neurochondrin gene (NCDN) or Glutamate Ionotropic Receptor Kainate Type Subunit 3 (*GRIK3*) both located at BTA3 or Leucine Rich Repeat and Ig Domain Containing 2 (LINGO2) and Phospholipase A2 Activating Protein (PLAA) at BTA8.

Keywords selective sweep, aggressive behavior, Lidia breed, Spanish cattle

Introduction

Since their domestication (~10,000 years ago), cattle populations have been subjected to natural and artificial selection processes (Ajmone-Marsan et al., 2010).

Currently most domesticated bovine breeds are specialized in milk and meat traits, and on a smaller scale in other economic traits of interest, such as leather or draft among others (Felius et al., 2014).

An early prerequisite of the domestication process in all the farm animals was probably to reduce their fear to humans (Belyaev et al., 1985). Thus, as a consequence of domestication, humans have modified the wild nature and social behavior of bovines (Jensen, 2006).

Different studies have analyzed genomic changes produced by the long-term selection in most commercial bovine breeds (Pritchard et al., 2010; Randhawa, 2016). As a consequence, several strong genomic signatures or hard-sweeps belonging to traditional selected morphological traits (muscular hypertrophy, coat color, presence/absence horns) have been reported (Druet et al., 2013; Ramey et al., 2013, González-Rodriguez et al., 2017). But so far, studies of selection signatures focused on behavioral features are limited. The Lidia bovine breed has been selected for centuries for its agonistic- aggressive behavior by means of a series of traits registered by the breeders on a categorical scale that classifies their aggression and fighting capacity (Silva et al., 2006). Furthermore, these traits have evidenced significant heritability values, which make them suitable to genetic selection (Silva et al., 2006; Menéndez-Buxadera et al., 2017,). Unlike other bovine breeds in which aggression is an undesirable trait, it is likely that the aggressiveness selection process in the Lidia bovine breed has left detectable genomic signatures (Ackey et al., 2002).

The detection of selective sweeps in quantitative traits still presents some limitations because many of the characters of interest, such as behavioral traits, are polygenic. In this case, the response to selection would be generated by modest allele

frequency shifts at many loci, detection of which can be difficult to accomplish (Pritchard et al., 2010).

The imputation of genotypes using high-density genotyping platforms has favored the identification of genomic selection signatures using demographic models, selections models or a combination of both (Ma et al., 2015). Under selection pressure, a new genetic variant at the genomic level may show one or more of the following features: extreme allele frequencies, excess of homozygotes, high frequency of long haplotypes and/or a higher genetic differentiation among populations (Qanbari and Simianer, 2014; Randhawa, 2016).

Several selection signature detection methods are based on allele frequencies differences among populations that may simply be identified in the extreme tails of the F_{ST} estimates distribution. Theoretically, loci under selection pressure or balancing selection are expected to evidence high and low levels of differentiation among populations respectively. Foll and Gaggiotti (2008) extended this approach and directly estimate the probability that each locus is subject to selection using a Bayesian method that evidenced their robustness under different demographic scenarios. However, one criticism of this kind of methodologies is that they do not quantify the intensity of selection. Recently Vitalis et al. (2014) developed a Bayesian method which allows distinguishing between selected and nearly neutral polymorphisms and estimate the intensity of selection under a genetic model that assumes the subdivision of a population into sub-populations that may exchange migrants.

In the present study, information provided by a panel of SNPs was used to analyze three groups of the Lidia bovine breed traditionally selected for agonistic related traits, and two non-specialized tamed Spanish breeds (Asturiana de los Valles

and Morenas Gallegas) as a reference to locate genomic regions associated with agonistic traits. A marginal second objective was to identify putative candidate genes mapping within these genomic regions in order to understand the evolutionary mechanisms of the Lidia breed.

Material

A total of 213 (48 from Mexico and 165 from Spain) Lidia bovine breed individuals were genotyped using the Bovine 50 K SNP BeadChip (http://www.illumina.com). According to Silva et al (2006) who evidenced differences among the three main behavior characteristics that are traditionally scored in the Lidia breed (aggressiveness, ferocity and mobility), 100 samples belonging to those Spanish lineages with higher agonist behavior (SPA+) and 65 with the lower ones (SPA-) were selected to be genotyped. Those lineages with the higher and lower behavior scores also evidenced the higher genetic differentiation among the Lidia breed lineages (Cañón et al., 2008).In addition, animals from Asturiana de los Valles and from Morenas Gallegas bovine breeds were genotyped as reference group in which agonist behavior is not desirable: 60 unrelated (based on genealogical information) Asturiana de los Valles breed individuals (35 genotyped with the 50k BeadChip and 25 with the 777k BeadChip) and 30 individuals from the Morenas Gallegas breed genotyped with the 50k BeadChip.

The SNPs in common between the 50 K and 777 K chips were identified (Nicolazzi et al., 2015). Then, the datasets of the five groups were combined using PLINK v. 1.07 (Purcell et al., 2009) and the following SNP edits were applied including

the removal of individuals with a call rate <80%, non-autosomal SNPs and SNPs with minor allele frequency < 0.01. After edits, 38,577 SNPs on 303 individuals remained.

Methods

SelEstim procedure proposed by Vitalis et al. (2014) is a hierarchical Bayesian method whose model is a diffusion approximation for the distribution of allele frequency in a population subdivided into a number of groups that exchange migrants with a rate equal to *m*. This procedure provides two parameters of differentiation between groups: σ is an average effect of selection and is a hyper-parameter that summarizes the strength of dispersion among groups at each specific locus, and the Kullback-Leiber divergence (KLD) which is a non-symmetric measure of difference between two probability distributions calculating the distance of the posterior distribution of σ of the centering distribution. The KLD parameter represents the neutral demographic history of the groups and, KLD values are strong correlated with FST estimates. Also, an estimate of the migration rate among the breeds is provided, this parameter is scaled by the effective size (i.e.$Mj = 4Njmj$) where *Mj* is the scaled migration parameter in the j^{th} population, *N* is the number of diploid individuals, and receives immigrants for the whole population at a rate *m.*

A first computation is performed on the whole-dataset to estimate the posterior distribution of the parameters, obtaining a “pseudo-observed” dataset; in order to provide a criterion to discriminate between neutral and selected markers, the calibration computation was then performed to achieve the thresholds (0.95, 0.99,

0.995 and 0.9999) quantiles of a "centering" Kullback-Leibler divergence (KLD) empirical distribution computed from the pseudo-observed dataset.

Identification of genomic regions with selection signatures

Assuming that behavioral traits are polygenic, low influence of many loci is expected. Hence, a slide window of ~10 MB that contains each of the SNP with KLD higher than 99.99% was selected to identify *genomic regions with selection signatures*. Furthermore, the previously defined SNPs with KLD higher than 95% in the 10 Mb windows were counted and used to define regions of genomic selection signatures. Gene annotation was performed by exploiting the knowledge on UMD3.1 locations of genes from the NCBI (ftp://ftp.ncbi.nih.gov/genomes/Bos_taurus/mapview/seq_gene.md.gz), and as annotation of the bovine genome is still incomplete, BioMart from Ensembl archive release 90 (www.ensembl.org/biomart) was used to determine the orthologous human gene ID for each gene detected.

BayeScan software (Foll and Gaggiotti, 2008) was also used to detect signatures of selection, with the difference that this methodology detects divergence selection from Bayesian binomial frameworks identifying loci under selection when they show F_{ST} coefficients that are significantly different to that expected under neutrality.

With BayeScan, F_{ST} coefficients are split into a population-specific component (β), common to all loci, and a locus-specific component (α) shared by all the populations using a logistic regression. Allele frequencies are assumed to follow a Dirichlet distribution. Selection is detected when α is significantly different to zero *i.e.* the locus-specific component is necessary to explain the observed pattern of diversity.

When α > 0 it is assumed that directional selection is acting on the locus under analysis, while α < 0 suggests balancing or purifying selection (Foll, 2012).

Identification of genomic regions with selection signatures

The standard PLINK files were converted to BayeScan format with the PGDSpider v 2.0.7.3 software (Lischer and Excoffier, 2012) and used the same parameters set with SelEstim to perform the analyses. A first filter was applied to the results, setting a significance threshold of 5% False Discovery Rate (Randhawa et al., 2016), and then, selecting the SNPs with alpha (α) values higher than 1, as it indicates strong evidence of diversifying selection according to Jeffrey´s interpretation (Foll, 2012).

Results

SelEstim

A total number of 19,287 SNPs had KLD estimates over the 50% quantile: 3,857 (90%), 1,918 (95%), 386 (99%), 194 (99.5%) and 5 (99.99%). The genomic regions of positive selection containing at least one SNP in the last percentile and the remaining in the 95% are described in Table 1. The migration rates (M_j) ranged from 20.92 in the Asturiana de los Valles breed to 2.52 in the Mexican Lidia group (Table 2).

Bayescan

A total of 249 outlier loci displayed strong signals of positive selection, α>1 and q value 5% (Supplementary Table 2). A q-value of 5% means that it is expected that 5% of the outlier markers (those with a q-value > 5%) are false positives (Foll, 2012) and therefore were discarded.

Positional coincidences with SelEstim and Bayescan were identified in chromosome 3 and 8 (Table 3, Figure S1). Furthermore, these selective sweeps with genomic signals of positive selection were analyzed more thoroughly in order to identify candidate genes that could have been modified by selection.

Selection signature at BTA3

The pattern of the average values of selected alleles (κ_{ij}) shown in Figure 1 evidenced that most of the polymorphisms are positively selected in the bovine populations. However, all the groups show an outlier allele at nucleotide BTA3:110,766,510 with the highest KLD value (Table 1). At this locus the intensity of selection (σ) estimated, which allows for the identification of the strongest selection coefficients, had the same selection direction in the Lidia breed sub-populations and the opposite in the tamed Morenas Gallegas bovine breed. This genomic region contains several genes related to different pathways, such as the serotonergic and dopaminergic signaling pathways, which contribute in the process of differentiation in a selection oriented for behavioral related traits.

This SNP with the highest KDL value is located proximate to the Neurochondrin gene (*NCDN*) (BTA3: 110,784,499-110,793,283). This gene is highly expressed in the central nervous system (Supplementary Table 3) and works as a negative regulator of the Ca2+/calmodulin-dependent protein kinase II (*CaMKII*), a key enzyme present in the early stages of memory formation and involved also in the hippocampal synaptic plasticity (Shinozaki et al., 1997; Dateki et al., 2005). This gene is highly associated with the serotonergic signaling pathway in modulating the acquisition and consolidation of memory (Moyano et al., 2004).

The Glutamate Ionotropic Receptor Kainate Type Subunit 3 (*GRIK3*) gene is located close to the *NCDN* gene and has been identified previously by Qanabari and Simianer (2014) as candidate gene for signatures of selection in cattle. The *GRIK3* gene is highly expressed in the central nervous system and is included in a QTL described in the reward-related processes underlying learning and memory (Minelli et al., 2009). Furthermore, the Disc Large Associated Protein 3 (*DLGAP3*) gene located within the same region is also associated in learning processes (Kähne et al., 2016).

Besides, Thyroid Hormone Receptor Associated Protein 3 (*THRAP3*) and Splicing Factor Proline and Glutamine Rich (*SFPQ*) genes, also located within the frame of this genomic region, are linked to the circadian cycle. Other genes are associated in processes implicated in domestication-related changes like sensory perception (*GJB4, SAG* and *TRPM8*), brain development and neurobehavioral functioning *(POU3F1),* muscle contraction (*FHL3*) and pigmentation (*NCDN*) (Xing et al. 2006; Ryu et al. 2007) (Supplementary Table 3).

Selection signature at BTA8

The pattern of the average values of the selected alleles (κ_{ij}) revealed opposite direction of selection intensity (σ) in the Lidia breed sub-populations compared to Asturiana de los Valles and Morenas Gallegas tamed breeds (Figure 2). Also it should be noted that the SNP with the strongest intensity of selection is present in the Lidia with higher agonist behavior (SPA+) group. Several genes are located in this genomic region, however the Leucine Rich Repeat And Ig Domain Containing 2 (*LINGO2)* and Phospholipase A2 Activating Protein (*PLAA*) genes are related with extreme

neurobehavioral phenotypes and psychiatric disorders and probably with behavior characteristics (Supplementary Table 3).

Discussion

In the present study two Bayesian approaches that are able to detect both recent and old selection events, Bayescan and SelEstim, were applied to identify genome-wide signatures of selection in three bovine breeds traditionally selected for opposite behavior characteristics.

Additionally, SelEstim procedure also estimates intensity and direction of the selection at each locus for each population and the migration rate (M_i) reflecting the relative admixture of each group with respect to all the groups .The relative genetic proximity of the Asturiana de los Valles breed respect to the rest of cattle populations analyzed (Table 2) is noteworthy. A similar result for the Asturiana de los Valles breed was also obtained by González Rodríguez et al. (2017) using seven Spanish bovine beef breeds, suggesting that this breed has been used as terminal sire line and crossbred individuals are introduced into the receptor populations. However, it is difficult to embrace this argument in our case taking into account the presence of the Lidia breed, which is extremely isolated and with low effective population sizes (Cortés et al., 2014).

A curious appreciation is the need to decrease the threshold of KLD to 90% to identify genomic regions under selection that are known to be under positive selection, such as the one bearing MSTN or myostatin gene (Supplementary Table 4). This threshold identified 3,857 SNPs, so this large amount of polymorphisms may be related to polygenic selection or adaptation processes (Pritchard et al., 2010), involving

several genes or polymorphisms with minor effects. However, when the most restrictive threshold (99.99%) was applied, the number of selected polymorphisms was reduced to only five (Table 1).

The difficulty to detect selective sweeps with statistical significance in polygenic traits, in which many loci shift their frequency moderately (Pritchard et al., 2010), could explain that only two genomic regions were shared with both methodologies. Other reasons may be the limitations of the 50K chip and the sample size of the analysis.

Furthermore, a high rate of false positives is expected due to the divergence in allelic frequencies between breeds (and groups within the Lidia breed and Morenas Gallegas) as a consequence of the genetic drift and founder effects; this is particularly important during the development of the cattle breeds´ (Petersen et al., 2013). These factors can bias the footprints left in the genome by selection and hamper the identification of selective sweeps.

The results of the present study suggest that the methods employed are able to detect signals of selection generated by recent selection events within populations. Furthermore, the absence of regions with strong signals of selection may be hidden considering that, i) artificial selection processes do not always leave relevant signatures of selection, ii) the polygenic nature of the behavioral traits (Kemper et al., 2014) and iii) the limitations of the bovine genomic resources of the SNP Beadchip already mentioned. However both methodologies detected genomic signatures of selection in BTA3 and BTA8 regions, where genes whose higher expression is detected mainly in the prefrontal cortex of the brain, where the reactions of violence and social aggression takes place (Grafman et al., 1996; Lotze et al., 2007) (Table S3).

Besides, the candidate genes *NCDN, GRIK3, DLGAP3*, *THRAP3* and *SFPQ* located in the selective sweep at chromosome 3 are involved in the serotonergic signaling pathway involved with the development of personality and behavioral traits (Minelli et al., 2009) and also in the development of different aggressive behavior manifestations, such as fear-induced aggression (Popova et al., 2005), inter-male aggression (Kulikov and Popova, 1996; Kulikov et al., 2005;), predatory aggression (Nikulina and Popova, 1988) and maternal aggression (da Veiga et al.,2011). However, the candidate-gene approach has mainly been conducted using rats, albeit with limited success. Studies involving putative behavioral genes such like those involved on serotonergic, catecholaminergic and glutamatergic pathways have failed to find variants of significance, mainly because of a small number of study subjects and a lack of functional assays (Spady and Ostrander, 2008).

In conclusion, the present study identifies two genomic regions associated with agonistic related traits in cattle. The direction of selection of both regions differed between the aggressive Lidia breed and the tamed Asturiana de los Valles and Morenas gallegas breeds that were used for comparative purposes. These findings corroborate that intensive targeted selection for different goal traits have left detectable imprints in the genome.

Conflict of interest statement

All authors declare that they have no conflict of interest.

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References

Ajmone-Marsan P., Garcia J. F., & Lenstra J. A. (2010). On the origin of cattle: how aurochs became cattle and colonized the world*. Evol. Anthropol*., **19**(4), 148-157.

Akey J. M., Zhang G., Zhang K., Jin, L., & Shriver M. D. (2002). Interrogating a high-density SNP map for signatures of natural selection. *Gen. Res*., **12**(12), 1805-1814.

Belyaev D.K., Plyusnina I.Z. & Trut .LN. (1985) Domestication in the silver fox (Vulpes fulvus Desm): Changes in physiological boundaries of the sensitive period of primary socialization*. Appl. Anim. Behav. Sci*., **13**:359–370.

Cañón J., Tupac-Yupanqui I., García-Atance M. A., Cortés O., García D., Fernández J., & Dunner S. (2008). Genetic variation within the Lidia bovine breed. *Anim. Genet.*, **39**(4), 439-445.

Cortés, O., Sevane, N., Baro, J.A., Cañón, J., (2014). Pedigree analysis of a highly fragmented population, the Lidia cattle breed. *Livest. Sci.,* **167**:1-8.

Dateki M., Horii T., Kasuya Y., Mochizuk, R., Nagao Y., Ishida J., Sugiyama F., Tanimoto K., Yagami K., Imai Hi. & Fukamizu, A. (2005). Neurochondrin negatively regulates CaMKII phosphorylation, and nervous system-specific gene disruption results in epileptic seizure. *J. Biol. Chem*., **280**(21), 20503-20508.

da Veiga C.P., Miczek K.A., Lucion A.B. & de Almeida RM (2011) Social instigation and aggression in postpartum female rats: role of 5-Ht1A and 5-Ht1B receptors in the dorsal raphe nucleus and prefrontal cortex*. Psychopharmacology* **213**:475–487.

Druet, T., Pérez-Pardal, L., Charlier, C., & Gautier, M. (2013). Identification of large selective sweeps associated with major genes in cattle. *Anim. Genet.*, 44(6), 758-762.

Eusebi P.G., Cortés O., Dunner S. and Cañón J. (2017) Genomic diversity and population structure of Mexican and Spanish bovine Lidia breed. *Anim.Genet., **48**(6), 682-685.*

Felius M., Beerling M. L., Buchanan D. S., Theunissen B., Koolmees P. A., Lenstra J. A. (2014) On the history of cattle genetic resources. *Diversity*, **6**(4), 705-750.

Foll M. & Gaggiotti O. E. (2008) A genome scan method to identify selected loci appropriate for both dominant and codominant markers: A Bayesian perspective. *Genetics,* **180**, 977–93.

Foll M. (2012). BayeScan v2. 1 user manual. Ecology, **20**, 1450-1462.

González-Rodríguez A., Munilla S., Mouresan E. F., Cañas-Álvarez J. J., Día, C., Piedrafita J., Altarriba J., Baro J.A., Molina A. & Varona, L. (2016). On the performance of tests for the detection of signatures of selection: a case study with the Spanish autochthonous beef cattle populations. *Gen. Sel. Evol*., **48**(1), 81.

González-Rodríguez A., Munilla S., Mouresan E. F., Cañas-Álvarez J. J., Baro J. A., Molina A., & Varona L. (2017). Genomic differentiation between Asturiana de los Valles, Avileña-Negra Ibérica, Bruna dels Pirineus, Morucha, Pirenaica, Retinta and Rubia Gallega cattle breeds. *Animal*, 1-13.

Grafman J., Schwab K., Warden D., Pridgen A., Brown H. R. & Salazar A. M. (1996). Frontal lobe injuries, violence, and aggression a report of the vietnam head injury study. *Neurology*, **46**(5), 1231-1231.

Jensen, P. (2006). Domestication—from behavior to genes and back again. *Applied Anim.l Behav. Sci.* **97**(1), 3-15.

Kähne T., Richter S., Kolodziej A., Smalla K. H., Pielo, R., Engler A., Ohl F.W.,. Dieterich D.C., Tischmeyer W., Naumann M., & Naumann M. (2016). Proteome rearrangements after auditory learning: high-resolution profiling of synapse-enriched protein fractions from mouse brain. *J. Neuroch*, **138**(1), 124-138.

Kemper K.E., Saxton S.J., Bolormaa S., Hayes B.J. & Goddard M.E. (2014) Selection for complex traits leaves little or no classic signatures of selection. *BMC Genomics.*,**15**:246.

Kulikov A.V. & Popova N.K. (1996) Association between intermale aggression and genetically defined tryptophan hydroxylase activity in the mouse brain. *Aggressive Behavior.,* **22**:111–117.

Kulikov A.V., Osipova D.V., Naumenko V.S. & Popova N.K. (2005) Association between Tph2 gene polymorphism, brain tryptophan hydroxylase activity and aggressiveness in mouse strains. *Genes. Brain. Behav*., **4**:482–485.

Lischer H. E. L. & Excoffier, L. (2012).PGDSpider: An automated data conversion tool for connecting population genetics and genomics programs. *Bioinformatics*, **28**, 298–99.

Lotze M., Veit R., Anders S. & Birbaumer, N. (2007). Evidence for a different role of the ventral and dorsal medial prefrontal cortex for social reactive aggression: An interactive fMRI study. *Neuroimage*, **34**(1), 470-478.

Ma Y., Ding X., Qanbari S., Weigend S., Zhang Q., & Simianer H. (2015). Properties of different selection signature statistics and a new strategy for combining them. *Heredity*., **115**(5), 426.

Makina S. O., Muchadeyi F. C., Marle-Köster E., Taylor J. F., Makgahlela M. L., & Maiwashe A. (2015). Genome-wide scan for selection signatures in six cattle breeds in South Africa. *Gen. Sel. Evol.*, ***47***(1), 92.

Menéndez-Buxadera A., Cortés O., & Cañon J. (2017). Genetic (co) variance and plasticity of behavioural traits in Lidia bovine breed. *Ital. J. Anim. Sci.*, 1-9.

Minelli A., Scassellati C., Bonvicin, C., Perez J., & Gennarelli M. (2009). An association of GRIK3 Ser310Ala functional polymorphism with personality traits. *Neuropsychobiology*, **59**(1), 28-33.

Moyano S., Del Río J. & Frechilla, D. (2004). Role of hippocampal CaMKII in serotonin 5-HT1A receptor-mediated learning deficit in rats. *Neuropsychopharmacology*, **29**(12), 2216.

Nicolazzi E. L., Caprera A., Nazzicari N., Cozzi P., Strozzi F., Lawley C.. Pirani A., Chandrasen S., Brew F., Jorjani H., & Evans, G. (2015). SNPchiMp v. 3: integrating and standardizing single nucleotide polymorphism data for livestock species. *BMC genomics.*, ***16***(1), 1.

Nikulina E.M. & Popova N.K. (1988) Predatory aggression in the mink (*Mustela vison*): roles of serotonin and food satiation. *Aggressive Behavior* **14**:77–84.

Petersen J. L., Mickelson J. R., Rendahl A. K., Valberg S. J., Andersson L. S., Axelsson J.,Bailey E., Bannasch D., Binns M.M., Borges A.S. & Brama, P. (2013). Genome-wide analysis reveals selection for important traits in domestic horse breeds. *PLoS genetics*, **9**(1), e1003211.

Popova N.K., Naumenko V.S., Plyusnina I.Z. & Kulikov A.V. (2005) Reduction in 5-HT1A receptor density, 5-HT1A mRNA expression, and functional correlates for 5-HT1A receptors in genetically defined aggressive rats*. J. Neurosci. Res*. **80**:286–292.

Pritchard J. K., Pickrell J. K., & Coop G. (2010). The genetics of human adaptation: hard sweeps, soft sweeps, and polygenic adaptation*. Curr. Biol*., **20**(4), R208-R215.

Purcell, S., Neale, B., Todd-Brown et al. (2007). PLINK: a tool set for whole-genome association and population-based linkage analyses.*Am. J. Hum. Genet*., **81(**3), 559-575.

Qanbari, S., & Simianer, H. (2014). Mapping signatures of positive selection in the genome of livestock. *Livest. Sci*., **166**, 133-143.

Ramey H. R., Decker J. E., McKay S. D., Rolf M. M., Schnabel R. D., & Taylor J. F. (2013). Detection of selective sweeps in cattle using genome-wide SNP data. *BMC genomics*., **14**(1), 382.

Shinozaki K., Maruyama K., Kume H., Kuzume H. & Obata K. (1997). A novel brain gene, norbin, induced by treatment of tetraethylammonium in rat hippocampal slice and accompanied with neurite-outgrowth in neuro 2a cells. *Biochem.Biophys. Res. Commun.*, **240**(3), 766-771.

Silva B., Gonzalo A., & Cañón J. (2006). Genetic parameters of aggressiveness, ferocity and mobility in the fighting bull breed. *Anim. Res.*, **55(**1), 65-70.

Spady T. C., & Ostrander E. A. (2008). Canine behavioral genetics: pointing out the phenotypes and herding up the genes. *Am. J. of Hum. Genet*., **82**(1), 10-18.

Vitalis R., Gautie, M., Dawson K. J., & Beaumont M. A. (2013). Detecting and measuring selection from gene frequency data. *Genetics*, genetics-113.

Xing H., Ling J., Chen M., & Gu, J. G. (2006). Chemical and cold sensitivity of two distinct populations of TRPM8-expressing somatosensory neurons. *J.Neurophysiol.*, **95**(2), 1221-1230.

Zhang C. (2010). Gap junctions in olfactory neurons modulate olfactory sensitivity. *BMC Neurosci.*, **11**(1), 108.

Supporting information

Supplementary Table 1 Classification of the Spanish lineages selected according to their extreme divergence in origins. (N) Number of individuals *per* lineage.

Supplementary Table 2 Selection signatures identified with the BayeScan software, with a threshold set on a 5% false discovery rate (FDR) and alpha (α) values <1. Chromosome number (Chr), Base Pair position (bp).

Supplementary Table 3 Candidate genes identified within the putative selective sweeps in the chromosome number (Chr) and at the Base pair position (bp).

Supplementary Table 4 Positional concordance between the SNPs detected at the 90% KLD quantile of SelEstim and other studies. Regions were constructed under the same selection criteria, using 10Mb sliding window spans. Chr: chromosome, Reg: region in Mb, N SNP: number of markers with the higher value of KLD, and its positional concordance with previously reported regions detected on Spanish cattle breeds.

Supplementary Figure 1 Whole-genome scan of the Kullback–Leiber divergence (KLD) and the locus specific component (alpha) results obtained with the SelEstim, and Bayescan software's respectively. The gray lines indicate the thresholds of significance for each approach. Genomic coordinates and statistical significance are plotted in the x- and y- axis, respectively.

Tables

Table 1 Putative selective sweeps identified with SelEstim. Chr: chromosome, N SNP: number of SNPs included in the genomic region with KLD over 95% and at least one SNP over 99.99%, Mb: Mega base pairs, and the higher value of the Kullback-Leibler Divergence (KLD) of the SNPs included in the selective sweep. .

Selective sweep	Chr	N SNP	Mb Start	Mb End	Higher KLD
1	3	9	109.49	119.08	1.92
2	8	8	14.89	27.98	1.92
3	11	11	15.07	24.92	2.55
4	13	5	26.52	31.82	1.98
5	18	12	47.83	54.86	2.22

Table 2 Estimate of the migration (M_j) parameters for the five groups, mean values and standard deviations (Std. Dev.).

Group	Mean	Std. Dev.
Asturiana de los Valles	20.92	0.24
Morenas Gallegas	9.14	0.09
Lidia Mexico	2.52	0.02
Lidia Spain(+)	12.81	0.13
Lidia Spain(-)	4.68	0.04

Table 3 Genomic concordance of the selective sweeps identified with Bayescan and SelEstim approaches. Chr: chromosome, N SNP: number of markers, Mb: mega base pairs.

Chr	SelEstim				Bayescan	
	N SNPS	Mb Start	Mb End	Higher KLD	Mb	Higher α
3	9	109.49	119.08	1.92	116.8	1.02
8	8	14.89	27.98	1.92	19.9	1.16
					22.3	1.28

Figure legends

Figure 1 Plot of the putative selective sweep localized in BTA3 between 106 and 119 Mb. The left boxplot are the mean selection coefficient (σ) per group and in right boxplot the mean values of the allele selected (κ_{ij}) for each group, where RAV= Asturiana de los Valles, MG= Morenas gallegas, Mex= Lidia from Mexico, Spanish(-)= Spanish Lidia less aggressive group and Spanish(+)= Spanish Lidia more aggressive group.

Figure 2 Plot of the putative selective sweep localized in BTA8 between the 13 and 24 Mb. The left boxplot are the mean selection coefficient (σ) per group and in right

boxplot the mean values of the allele selected (κ_{ij}) for each group, where AST= Asturiana de los Valles, MG= Morenas gallegas, Mex= Lidia from Mexico, Spanish(-)= Spanish Lidia less aggressive group and Spanish(+)= Spanish Lidia more aggressive group.

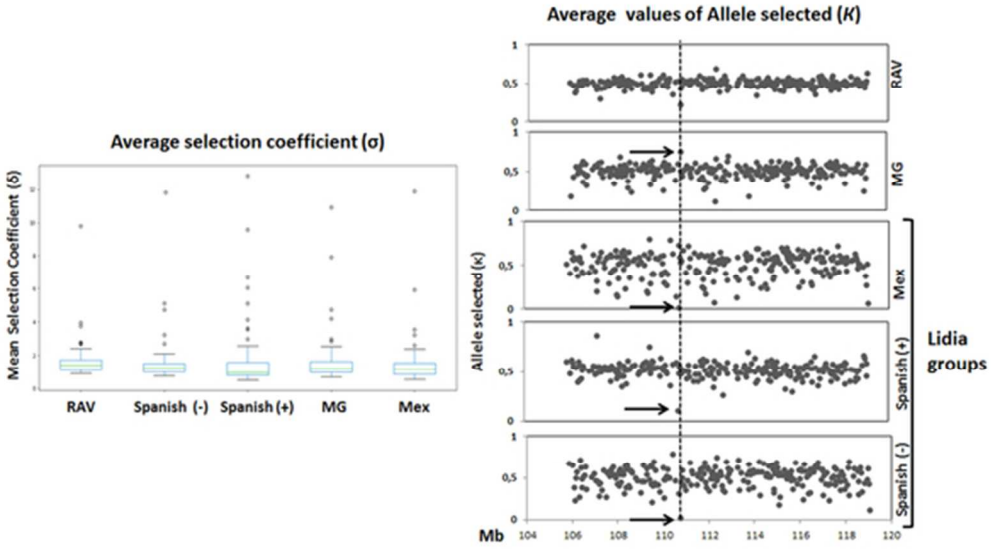

Figure 1. Plot of the putative selective sweep localized in BTA3 between 106 and 119 Mb. The left boxplot are the mean selection coefficient (σ) per group and in right boxplot the mean values of the allele selected (κij) for each group, where RAV= Asturianas de los Valles, MG= Morenas gallegas, Mex= Lidia from Mexico, Spanish(-)= Spanish Lidia less aggressive and Spanish(+)= Spanish Lidia more aggressive group.

49x28mm (300 x 300 DPI)

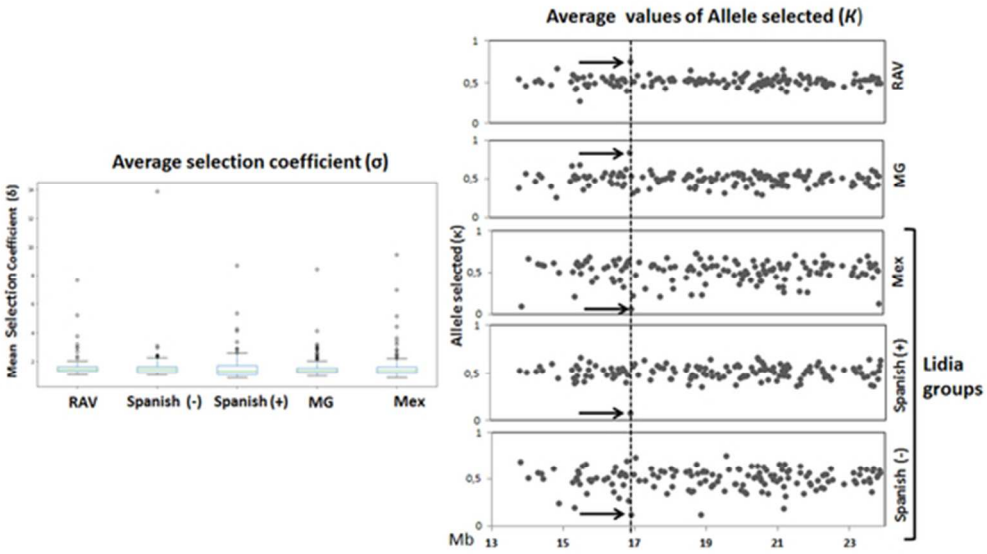

Figure 2. Plot of the putative selective sweep localized in BTA8 between the 13 and 24 Mb. The left boxplot are the mean selection coefficient (σ) per group and in right boxplot the mean values of the allele selected (κij) for each group, where RAV= Asturianas de los Valles, MG= Morenas gallegas, Mex= Lidia from Mexico, Spanish(-)= Spanish Lidia less aggressive and Spanish(+)= Spanish Lidia more aggressive group.

49x28mm (300 x 300 DPI)

Supplementary Table 1 Classification of the Spanish lineages selected according to their extreme divergence in origins. (N) Number of individuals *per* lineage.

Most agonistic behavior		Less agonistic behavior	
Name	**N**	**Name**	**N**
Albaserrada	15	Atanasio Fernández	14
Santa Coloma	36	Baltasar Ibán	12
Saltillo	15	Conde de la Corte	10
Miura	9	Domecq	29
Vega-Villar	17		
Pablo Romero	9		

Supplementary Table 2 Selection signatures identified with the BayeScan software, with a threshold set on a 5% false discovery rate (FDR) and alpha (α) values <1. Chromosome number (Chr), Base Pair position (bp).

Chr	Marker	BP	q-value	α
1	ARS-BFGL-BAC-14930	1782724	0.012	1.27
1	ARS-BFGL-NGS-11433	1851399	0.005	1.33
1	ARS-BFGL-BAC-7317	1983902	0.047	1.03
1	ARS-BFGL-NGS-65157	4348137	0.036	1.07
1	BTB-01225182	15109714	0.032	1.00
1	Hapmap54262-rs29018839	47102513	0.049	1.02
1	ARS-BFGL-NGS-25522	79324497	0.017	1.17
1	BTB-00034221	79591551	0.002	1.24
1	Hapmap47824-BTA-107197	82147822	0.046	1.04
1	Hapmap55716-rs29015966	155654021	0.011	1.25
2	ARS-BFGL-NGS-39978	5757355	0.001	1.32
2	**ARS-BFGL-NGS-93854**	**5877768**	**0.000**	**1.79**
2	ARS-BFGL-NGS-112454	6675045	0.000	1.36
2	Hapmap54028-rs29023584	6792631	0.000	1.55
2	BTB-00862033	8884527	0.004	1.20
2	BTB-00862061	8933349	0.026	1.02
2	BTB-02094616	8955989	0.025	1.05
2	ARS-BFGL-NGS-111530	9202511	0.000	1.77
2	Hapmap51202-BTA-28358	10216677	0.019	1.11
2	BTB-00084343	22644664	0.010	1.31
2	Hapmap58509-rs29024139	37635484	0.046	1.03
2	ARS-BFGL-NGS-3108	38636687	0.032	1.09
2	Hapmap48631-BTA-117251	47084459	0.013	1.21
2	BTB-01165311	55283216	0.008	1.14
2	ARS-BFGL-NGS-114696	72609348	0.010	1.22
2	ARS-BFGL-NGS-112489	72632052	0.014	1.19
2	Hapmap51113-BTA-100127	89444485	0.001	1.39
2	ARS-BFGL-NGS-118468	89707126	0.002	1.35
2	ARS-BFGL-NGS-26540	89752875	0.016	1.18
2	ARS-BFGL-NGS-3488	92715999	0.028	1.34
2	ARS-BFGL-NGS-55602	93600676	0.014	1.21

2	ARS-BFGL-NGS-117120	104800752	0.000	1.40
2	BTA-48930-no-rs	109219004	0.007	1.40
2	ARS-BFGL-NGS-29666	109295005	0.005	1.42
2	Hapmap42518-BTA-34464	111962847	0.033	1.07
2	ARS-BFGL-NGS-15508	119595498	0.031	1.16
2	ARS-BFGL-NGS-33757	123463996	0.003	1.44
2	ARS-BFGL-BAC-27911	125497767	0.030	1.02
3	Hapmap53344-ss46526153	14139949	0.010	1.31
3	ARS-BFGL-NGS-20167	16557950	0.007	1.14
3	ARS-BFGL-NGS-62323	21371931	0.006	1.25
3	Hapmap59143-ss46526687	21489190	0.011	1.20
3	ARS-BFGL-NGS-114827	49888628	0.011	1.31
3	Hapmap54928-ss46526596	67827369	0.004	1.30
3	BTB-01071906	73895121	0.005	1.51
3	BTA-107777-no-rs	73921609	0.005	1.51
3	Hapmap41332-BTA-68635	89675602	0.048	1.06
3	**Hapmap48857-BTA-69699**	**116801749**	**0.028**	**1.02**
4	ARS-BFGL-NGS-118723	4931375	0.038	1.06
4	Hapmap55272-rs29026835	15208171	0.011	1.21
4	BTB-01108314	19510899	0.044	1.02
4	Hapmap50203-BTA-107053	25646689	0.003	1.35
4	BTB-00178966	41583591	0.027	1.22
4	ARS-BFGL-NGS-110957	44792807	0.024	1.12
4	BTB-00367018	87059911	0.010	1.33
4	BTB-00202180	92436001	0.001	1.26
4	BTB-01295144	92557035	0.001	1.27
4	Hapmap52502-rs29022385	96551087	0.015	1.08
4	ARS-BFGL-NGS-95780	96754893	0.001	1.51
4	Hapmap28499-BTA-142459	96861591	0.022	1.13
4	BTA-98250-no-rs	117913533	0.050	1.00
4	BTB-00164261	119552457	0.041	1.18
5	Hapmap34360-BES2_Contig202_1418	1854424	0.034	1.09
5	BTB-00214224	2236004	0.039	1.18
5	Hapmap54917-rs29023586	7733715	0.040	1.04
5	BTB-00221495	10138236	0.028	1.11
5	BTA-27444-no-rs	50229041	0.005	1.21
5	Hapmap57248-rs29018609	54933394	0.020	1.23
5	Hapmap49515-BTA-18233	63983082	0.005	1.31
5	BTA-85562-no-rs	66083568	0.007	1.24
5	ARS-BFGL-NGS-104108	66480185	0.000	1.70
5	Hapmap43928-BTA-74110	77116302	0.009	1.33
5	BTA-74479-no-rs	84613929	0.016	1.31
5	ARS-BFGL-NGS-27066	107946258	0.029	1.19
5	ARS-BFGL-NGS-15922	113874131	0.018	1.19
6	BTB-01545399	12203460	0.003	1.45
6	Hapmap59328-rs29016355	12703601	0.030	1.10

6	Hapmap49292-BTA-75698	31570212	0.020	1.26
6	Hapmap27887-BTA-156628	35456685	0.009	1.21
6	Hapmap50194-BTA-105136	35577199	0.024	1.11
6	ARS-BFGL-NGS-110738	37252345	0.034	1.05
6	Hapmap23854-BTC-062412	37610880	0.001	1.38
6	Hapmap24039-BTC-031958	37704254	0.003	1.27
6	Hapmap30134-BTC-034283	38464203	0.000	1.47
6	Hapmap33170-BTC-071249	39371150	0.039	1.01
6	Hapmap31624-BTC-046805	41443081	0.002	1.32
6	ARS-BFGL-NGS-95035	46788536	0.000	1.39
6	BTB-01899352	72969608	0.007	1.17
6	BTB-00262807	73032896	0.007	1.16
6	Hapmap53308-rs29024839	73057109	0.018	1.06
6	Hapmap23494-BTC-046433	103307689	0.023	1.12
6	Hapmap47732-BTA-77644	103796957	0.019	1.15
6	ARS-BFGL-NGS-30562	104896770	0.011	1.27
6	ARS-BFGL-NGS-31881	104922823	0.013	1.21
6	BTB-00283603	109719477	0.038	1.06
6	BTB-00280923	110745167	0.021	1.12
7	BTB-01172167	8078251	0.026	1.13
7	BTB-01398686	22996615	0.004	1.27
7	ARS-BFGL-NGS-35201	26494064	0.043	1.26
7	BTB-01562090	39737588	0.001	1.48
7	ARS-BFGL-NGS-88233	41718041	0.000	1.41
7	ARS-BFGL-NGS-69727	41742027	0.007	1.25
7	ARS-BFGL-NGS-3154	84520981	0.037	1.13
7	Hapmap60894-rs29027443	90080630	0.000	1.46
7	Hapmap38913-BTA-80438	102342232	0.025	1.03
7	BTA-80441-no-rs	103779001	0.003	1.34
7	BTB-01548437	107770283	0.000	1.31
8	ARS-BFGL-NGS-10448	1305820	0.044	1.03
8	ARS-BFGL-NGS-113904	3617253	0.013	1.19
8	Hapmap48586-BTA-106838	5036995	0.011	1.32
8	**ARS-BFGL-NGS-22169**	**14299239**	**0.019**	**1.08**
8	**BTB-01369338**	**19967642**	**0.037**	**1.16**
8	Hapmap41606-BTA-64576	22362375	0.017	1.28
8	Hapmap39528-BTA-03210	63220492	0.021	1.18
8	Hapmap57206-rs29025935	64068111	0.041	1.16
8	Hapmap34874-BES3_Contig415_1312	79559282	0.022	1.04
8	ARS-BFGL-NGS-11101	81108363	0.035	1.29
8	ARS-BFGL-NGS-97157	90539222	0.023	1.11
8	ARS-BFGL-NGS-62416	104484489	0.025	1.34
9	ARS-BFGL-NGS-14862	58044059	0.008	1.27
10	Hapmap35793-SCAFFOLD311748_23298	8204943	0.000	1.46
10	Hapmap23512-BTA-125084	8232496	0.002	1.25
10	ARS-BFGL-NGS-97105	8255705	0.014	1.18

10	Hapmap41308-BTA-60333	21008360	0.041	1.13
10	ARS-BFGL-NGS-42815	26054054	0.000	1.58
10	ARS-BFGL-NGS-118433	26079224	0.000	1.57
10	Hapmap41316-BTA-62253	26885064	0.018	1.13
10	Hapmap49275-BTA-69259	52086383	0.017	1.17
10	Hapmap59000-rs29026853	53560658	0.006	1.26
10	ARS-BFGL-NGS-55539	58488593	0.016	1.18
10	BTB-01361971	59615280	0.024	1.15
10	BTB-01361928	59667969	0.035	1.09
10	Hapmap47084-BTA-72369	62081998	0.015	1.10
10	ARS-BFGL-NGS-105361	65212580	0.008	1.24
11	ARS-BFGL-NGS-35518	30128818	0.001	1.33
11	ARS-BFGL-BAC-12994	41854251	0.012	1.34
11	ARS-BFGL-NGS-116708	79051605	0.003	1.22
11	ARS-BFGL-NGS-88133	82409810	0.006	1.28
11	ARS-BFGL-NGS-38003	98219856	0.036	1.06
12	ARS-BFGL-NGS-14399	36335510	0.001	1.48
12	BTA-92165-no-rs	51128057	0.015	1.11
12	BTA-115591-no-rs	79224151	0.043	1.17
12	ARS-BFGL-NGS-8073	81119950	0.027	1.19
13	ARS-BFGL-NGS-21967	18762878	0.016	1.09
13	Hapmap42181-BTA-31908	25323323	0.031	1.09
13	ARS-BFGL-NGS-116062	46510476	0.003	1.25
13	ARS-BFGL-NGS-19009	57446360	0.012	1.31
13	ARS-BFGL-NGS-21649	71271729	0.012	1.20
14	Hapmap24767-BTC-058058	9964138	0.025	1.03
14	Hapmap25450-BTC-055819	10424817	0.033	1.10
14	ARS-BFGL-NGS-103654	17109001	0.045	1.14
14	UA-IFASA-7441	28053009	0.013	1.11
14	BTA-107905-no-rs	38440957	0.039	1.06
14	ARS-BFGL-NGS-84700	41809705	0.043	1.03
14	BTB-01708641	44291954	0.006	1.20
14	Hapmap31256-BTC-012280	55910671	0.014	1.31
14	BTB-00573962	59577845	0.003	1.56
15	Hapmap40697-BTA-24633	12476540	0.033	1.07
15	BTB-01786632	12520480	0.033	1.08
15	ARS-BFGL-NGS-117317	12567793	0.034	1.07
15	ARS-BFGL-NGS-37606	26291524	0.016	1.17
15	ARS-BFGL-NGS-115927	39469268	0.020	1.13
15	ARS-BFGL-NGS-54901	40356568	0.005	1.33
15	Hapmap52590-rs29020878	41383202	0.030	1.22
15	ARS-BFGL-NGS-80386	43496588	0.022	1.13
15	BTB-00596838	43883527	0.002	1.34
15	ARS-BFGL-NGS-108402	44066727	0.009	1.32
15	ARS-BFGL-NGS-59463	51853820	0.003	1.42
15	BTB-00604291	52026483	0.002	1.42

15	ARS-BFGL-NGS-112293	62823352	0.004	1.27
15	BTB-00611237	66082534	0.019	1.22
15	ARS-BFGL-NGS-3375	76729776	0.023	1.12
15	BTA-16481-no-rs	81335502	0.000	1.63
15	ARS-BFGL-NGS-5434	81869228	0.013	1.16
16	ARS-BFGL-NGS-75856	4138735	0.018	1.25
16	Hapmap39562-BTA-40351	20358990	0.005	1.20
16	Hapmap49591-BTA-38802	38830470	0.004	1.39
16	BTB-02030954	55752131	0.042	1.04
16	ARS-BFGL-NGS-31253	74481728	0.017	1.17
17	Hapmap2587-BTA-120526	10726289	0.027	1.04
17	BTA-41003-no-rs	46325733	0.004	1.31
17	ARS-BFGL-NGS-18235	47405668	0.001	1.51
17	BTB-01953505	47436239	0.002	1.32
17	ARS-BFGL-BAC-32128	48860957	0.002	1.46
17	Hapmap43749-BTA-104425	58966184	0.003	1.31
17	ARS-BFGL-NGS-111330	65700521	0.006	1.24
17	ARS-BFGL-NGS-117653	73315120	0.027	1.14
18	BTA-119338-no-rs	9403168	0.000	1.56
18	ARS-BFGL-NGS-111796	9606800	0.039	1.05
18	Hapmap48757-BTA-42449	12988265	0.006	1.35
18	Hapmap58715-rs29021176	13109858	0.002	1.42
18	ARS-BFGL-NGS-23632	13974114	0.000	1.55
18	ARS-BFGL-NGS-28825	14058919	0.002	1.23
18	ARS-BFGL-NGS-10007	15483066	0.008	1.17
18	ARS-BFGL-NGS-106191	18997878	0.001	1.61
18	ARS-BFGL-NGS-106722	19196022	0.013	1.21
18	ARS-BFGL-NGS-107813	34379769	0.000	1.46
19	Hapmap57045-rs29017091	24070908	0.031	1.09
19	Hapmap35748-SCAFFOLD151511_3373	31757498	0.010	1.46
19	ARS-BFGL-NGS-75816	36674728	0.006	1.24
19	ARS-BFGL-NGS-111365	43068079	0.042	1.05
20	ARS-BFGL-NGS-54785	28148900	0.049	1.08
20	Hapmap53513-rs29024419	28244515	0.008	1.26
20	Hapmap59121-rs29022980	31085834	0.021	1.12
20	Hapmap54258-rs29018641	31151035	0.008	1.24
20	BTB-01748945	52011466	0.046	1.04
21	BTA-21042-no-rs	4240549	0.001	1.25
21	ARS-BFGL-NGS-10533	6692583	0.010	1.20
21	ARS-BFGL-NGS-100241	8955497	0.010	1.33
21	Hapmap51253-BTA-53448	12970324	0.040	1.18
21	BTB-01769597	17712351	0.000	1.59
21	Hapmap50229-BTA-113939	40681426	0.008	1.14
21	BTB-01172066	51556381	0.012	1.24
21	ARS-BFGL-BAC-34585	62245543	0.021	1.23
21	Hapmap59281-rs29027629	67904403	0.000	1.57

22	ARS-BFGL-NGS-113315	59204394	0.001	1.27
22	ARS-BFGL-NGS-77507	59237587	0.007	1.17
23	UA-IFASA-4515	8289524	0.000	1.79
23	ARS-BFGL-BAC-30064	12548841	0.032	1.30
23	ARS-BFGL-NGS-60100	28598059	0.006	1.31
24	Hapmap41146-BTA-108100	5504370	0.029	1.24
24	BTB-01970944	11645293	0.044	1.04
24	ARS-BFGL-NGS-14250	12916861	0.017	1.41
24	Hapmap57973-rs29024513	13837820	0.004	1.52
24	ARS-BFGL-NGS-100146	36464131	0.009	1.17
24	ARS-BFGL-NGS-1521	41579956	0.008	1.23
24	ARS-BFGL-NGS-117929	41603109	0.010	1.30
24	ARS-BFGL-NGS-62539	46537819	0.015	1.22
24	ARS-BFGL-NGS-13255	50266999	0.004	1.28
24	ARS-BFGL-NGS-111274	50306117	0.005	1.27
24	ARS-BFGL-NGS-117573	58081600	0.045	1.05
25	ARS-BFGL-NGS-40549	23777990	0.001	1.48
25	ARS-BFGL-NGS-57317	32823036	0.026	1.02
25	ARS-BFGL-NGS-20432	36309252	0.015	1.32
25	ARS-BFGL-NGS-105741	39286957	0.011	1.21
26	ARS-BFGL-NGS-53115	11528933	0.048	1.06
26	Hapmap57957-rs29017349	26841116	0.047	1.11
26	ARS-BFGL-NGS-15144	42933219	0.004	1.28
26	Hapmap41566-BTA-52258	44181047	0.019	1.20
26	ARS-BFGL-NGS-14909	44238995	0.009	1.30
26	ARS-BFGL-NGS-109807	49918587	0.002	1.34
27	UA-IFASA-7203	22500067	0.009	1.28
27	Hapmap27965-BTA-148364	29300595	0.016	1.17
27	ARS-BFGL-NGS-112047	30945497	0.014	1.18
27	Hapmap57132-rs29011225	40916876	0.012	1.20
29	BTB-02050030	18592194	0.028	1.11
29	BTB-02082594	21125373	0.022	1.25
29	ARS-BFGL-NGS-94949	26697399	0.000	1.42

Supplementary table 3 Candidate genes identified within the putative selective sweeps in the chromosome number (Chr) and at the Base pair position (bp).

Chr	Position (bp)1	Gene	Function/association	Major expression tissue (RNA-seq*)
3	109,293,456	***GRIK3***	Reward-related learning	Cortex, brain, tibial nerve
3	111,388,593	***DLGAP3***	Neuronal signing and learning	Cortex, brain, cerebellum
3	110,172,233	***THRAP3***	Circadian cycle and behavior	Brain, retina, cerebellum, cortex
3	111,148,711	***SFPQ***	Circadian cycle and behavior	Brain, cortex, skin, thyroid
3	110,788,891	***NCDN***	Learning and pigmentation	Cortex, brain,

				cerebellum
3	111,521,856	***GJB4***	Olfactory neurophysiology	Skin, salivary gland
3	113,649,002	***SAG***	Visual stimulus neurophysiology	Retina
3	114,238,014	***TRPM8***	Thermoception	Liver, prostate
3	108,509,996	***POU3F1***	Neurogenesis	Tibial nerve, skin, cortex, brain
3	108,551,386	***FHL3***	Muscle contraction	Skeletal muscle, tibial nerve, cortex
8	15,681,923	***LINGO2***	Neuronal disorders	Brain, cortex, thyroid, uterus, testis
8	17,292,409	***PLAA***	Neurodegenerative diseases	Brain, cortex, thyroid, skin, testis

* mRNA expression in normal human tissues from GTEx, Illumina Body map

Supplementary table 4 Positional concordance between the SNPs detected at the 90%KLD quantile of SelEstim and previous studies. Regions were constructed under the same selection criteria, using 10Mb sliding window spans. Chr: chromosome, Reg (Mb): region in Mb, N SNP: number of markers with the higher value of KLD, and its positional concordance with previously reported regions detected on Spanish cattle breeds.

Chr	Reg (Mb)	N SNP	Higher KLD	González-Rodriguez *et al.2016*	González-Rodriguez *et al.2017*
2	0.24-7.24*	9	0.52	1.04-11.89 Mb	5.57-10.15 Mb
6	29.55-37.74	6	1.11	37.85-41.16 Mb	37.85-39.44 Mb
7	42.62-51.57	15	0.49	47.27-47.75 Mb	47.40-47.50Mb
11	65.25-74.35	7	0.52	65.07-72.20 Mb	67.05-67.08Mb
13	56.53-66.18	13	0.71	57.43-57.75 Mb	57.58 Mb
18	4.90-13.45	14	1	12.68-16.20 Mb	13.34-15.24

*The MSTN gene (myostatin) is located within this region 6.213.566..6.220.196 bp

Supplementary figure 1 Whole-genome scan of the Kullback–Leiber divergence (KLD) and the locus specific component (alpha) results obtained with the SelEstim, and Bayescan software's respectively. The gray lines indicate the thresholds of significance for each approach. Genomic coordinates and statistical significance are plotted in the x- and y-axis, respectively.