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SNP-based genetic signatures revealed breeding effects in indigenous Livni compared with Landrace and Large White breeds

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Abstract:
Livni is one of the Russian local pig breeds. We previously reported that this breed was more distinct from Duroc breed than from Landrace and the Large White breeds, which participated in the Livni breed creation. The aim of the study was to determine the SNP-based genetic signatures in fat-type Livni breed shared with commercial Landrace and the Large White breeds, and ones that are affected by putative selection.
The genome-wide SNP genotyping was carried out using the Porcine GGP HD BeadChip, which contains ~ 80 000 SNPs.
Obtained breed relationship and admixture results indicated the insignificant participation of the Landrace and the Large White breeds in the formation of the modern allelofund of Livni pigs. 238 candidate genes were found in the genomic regions with selection signatures, 182 genes with described functions were identified. In the Livni and Landrace breeds, 35 common genes were detected which formed one cluster with enrichment coefficient = 4.94 and predominant *HOXD* genes. In the Livni and Large White breeds, the largest amounts of common genes were detected (62 in average), which formed two clusters. Cluster 1, with enrichment coefficient = 2.11, was characterized with genes involved in glucose metabolism. Cluster 2, with enrichment coefficient = 1.60, demonstrated helicase genes. Annotated clusters were not determined for the Livni breed. However, 50 candidate genes were specific to Livni pigs and associated with various growth, carcass and reproductive traits, essential for thermoregulation.
Results revealed common SNP-based genetic signatures and breeding effects in indigenous Livni compared with Landrace and Large White breeds.

Keywords: Livni breed, animal genetic resources, SNPs, pig, carcass, traits

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INTRODUCTION

The pig is a major livestock species, and the global pork production primarily relies on the use of a limited number of international commercial breeds, specifically Duroc, Large White, and Landrace [1]. Intensive implementation of commercial hybrid breeds characterized by high production standards led to an impoverishment of genetic resources which in the past had a fair distribution [2]. However, recently a strong attention has been attracted to local breeds for improving genetic diversity and conservation of genetic resources. Local breeds are valued not only by adaptive traits, but also by the unique functional characteristics and intensively studied in Asia, Europe, Africa, as well as North and Latin America [3–14].

Twenty-two local breeds were recorded in the Soviet Union in 1980, which were generated by crossing of native breeds adapted to the local climate and having appropriate constitution and disease resistance with highly-productive improved European breeds [15, 16]. As a result of the interbreeding of the imported breeds and crossing them with the native animals, many pig breeds were created during 1920–1990. For example, Ukranian White Steppe was created in Askania Nova and approved in 1932; North Siberian – in Novosibirsk and approved in 1942, Urzgum – in the Kirov region

and approved in 1957 – by crossing native pigs with the Large White boars. Breeds, as Kemerovo (approved in 1961), Breitov (approved in 1948), Latvian White and Lithuanian White (both approved in 1967), Semirechensk (1978), Mirgorod (1940), Tsivilsk (a cross of native Chuvash pigs with Large White boars, the breed is not approved), Mangalitsa, Altai (approved in 2015), and others were created by multiple crossbreeding procedures. [15]. According to the Department of Livestock and Breeding of the Ministry of Agriculture of the Russian Federation data, 98% of the total pig purebred population in 2020 included four breeds – Large White (66%), Landrace (15%), Yorkshire (13%) and Duroc (4%) [17]. Other breeds' share was about 2%. Pavlova *et al.* consider 0.56% of the total pig population in the RF are of the local breeds – Livni, Altai, Tsivilsk, as of January 1, 2022. Four breeds make 99.46% of the RF pig herd, namely 56.9% Large White, 18.52% – Yorkshire, 18.18% – Landrace, and 5.83% – Duroc breed [18]. The dramatically reduction of local pig breeds during last 30 years finally led to remaining only Livni, Altai Meat-type, Short-Eared White, and Tsivislk. The authentic Kemerovo breed has also been mentioned for a number of years. However, according to the Yearbook on breeding work in pig husbandry in establishment of the Russian Federation for 2021, the last time a breeding farm certificate for the Kemerovo purebred was issued in 2019 [19]. It should be noted, that the certificate for the Tsivislk breed was last issued in 2021.

Livni is one of the Russian local pig breeds approved in 1949. Pigs of the Livni breed are large, white, black-mottled, black and red. At present, only a small population of Livni pigs is kept in a single farm in the Oryol region [20]. According to the Yearbook on breeding work, in pig husbandry in establishment of the Russian Federation for 2021 one certificate is issued annually for the Livni purebred, but the total number of the Livni pigs is steadily declining. At the beginning of 2022, 547 heads were purebreds, including 348 sows with the share in the total livestock of 0.24% [19]. For comparison, in 1949 the Livni livestock was 6757 purebreds (1334 sows), while in 1980 it was 27 200 purebreds (5500 sows) [21]. It is noteworthy that at the age of 6 months, Livni correspond to the bacon (meat) type. Then the active accumulation of fat begins and at the age of 10 months Livni pigs are already belong to meat-and-fat type, and with further fattening lead to fat type [21].

We previously reported that Livni breed is characterized the highest level of genetic diversity compared with commercial breeds. The neighbor-joining tree showed that this breed was the most distinct from Duroc breeds, but formed the knot bounding the branches corresponding to the Landrace and the Large White breeds. This observation confirmed the participation of these two breeds in the Livni breed creation. The aim of our study was to determine the SNP-based genetic signatures in Livni breed common with Landrace and the Large White breeds, and ones that are affected by putative selection in the genome of Livni breed and could be associated with fatty tissue formation and breed specificity.

STUDY OBJECTS AND METHODS

Samples and genotyping. For the study, we used samples (ear tissue) of Livni pigs (n = 35). Only purebred animals registered in Russian swine herdbook were selected, the origin of which is confirmed by both the pedigree data and DNA analysis. For genotyping, we selected the most unrelated individuals. Samples of all breeds were sent to the Ernst Federal Research Center for Animal Husbandry. A parentage and breed assignment of those breeds were confirmed based on the microsatellites in the laboratory of the Ernst Federal Research Center for Animal Husbandry, which has a certificate of 2020–2021 ISAG Pig STR Comparison Test (2020–2021) and has a special license issued by the Russian Ministry of Agriculture. Commercial breeding farms and the Ernst Federal Research Center for Animal Husbandry collaborate based on the contracts. In the contract, a clause states the consent of the owners (breeding farms) to use the samples with research purpose.

Moreover, the study did not involve any endangered or protected animal and all procedures were conducted according to the ethical guidelines of the L.K. Ernst Federal Science Center for Animal Husbandry. The Commission on the Ethics of Animal Experiments of the L.K. Ernst Federal Science Center for Animal Husbandry approved the protocol No. 6 of May 10, 2021. The ear tissues were collected by trained personnel under strict veterinary rules in accordance with the rules for conducting laboratory research (tests) in the implementation of the veterinary control (supervision) approved by Council Decision Eurasian Economic Commission № 80 (November 10, 2017).

Genomic DNA was extracted using the DNA Extran 2 kit (ZAO Sintol, Moscow, Russia) according to the manufacturer's instructions. Concentrations of dsDNA solutions were determined using a Qubit 1.0 fluorometer (Invitrogen, Life Technologies, Waltham, Massachusetts, USA). The OD260/280 ratio was determined using NanoDrop 2000 (Thermo Fisher Scientific, Waltham, Massachusetts, USA).

The genome-wide SNP genotyping was carried out using an iScan microarray scanner (Illumina Inc., Singapore) using the Porcine GGP HD BeadChip (Illumina Inc., San Diego, CA, USA), which contains ~ 80 000 SNPs. In our study, we used all the capital equipment required for SNP genotyping by Illumina SNP arrays. The equipment belongs to the Center for Collective Use "Bioresources and Bioengineering of Agricultural Animals" of the Ernst Federal Research Center for Animal Husbandry (https://www.vij.ru/infrastruktura/ckp, accessed on 10 May 2021). The SNPs genotypes of Large White (n = 53) and Landrace (n = 50) breeds were included in the data set and obtained from Center for Collective Use "Bioresources and Bioengineering of

Agricultural Animals" of the Ernst Federal Research Center for Animal Husbandry.

Quality control. Using PLINK 1.9 software, the SNP quality control was performed [22, 23]. All samples were subjected to filtering for genotyping efficiency (--mind 0.2). The SNPs genotyped in less than 90% of the samples (--geno), minor allele frequencies below 0.01 (--maf 0.01), and *p*-values below 10^{-6} for Hardy-Weinberg equilibrium were excluded from the analysis. The final data set used for analysis included 51 912 autosomal SNPs. Additional filters for linkage disequilibrium (LD) with r2 every 50kb (--indep-pairwise) were performed, amount of SNP passes LD-filtration amounted 24 861.

Genetic diversity, PCA, Neighbor-Net and Admixture. To assess the within-population genetic diversity, the observed (H_O) and unbiased expected ($_UH_E$) heterozygosity, the rarefied allelic richness (A_R), and the unbiased in-breeding coefficient ($_UF_{IS}$) were estimated using the R package, diveRsity [24]. Additionally, we computed the genomic inbreeding coefficient based on runs of homozygosity (ROH, F_{ROH}) as the ratio of the sum of the length of all ROHs per animal to the total autosomal SNP coverage; for ROH estimation, see the "*Runs of Homozygosity Estimation*" Section below). PCA was performed using PLINK v1.9 software. An R package, ggplot2, was used to visualize the results [25]. Pairwise FST values were calculated in the R package, diveRsity, and used for the construction of the Neighbor-Net tree in SplitsTree software (version 4.14.5) [24, 26, 27]. Admixture software (version 1.3.0) was employed for genetic admixture analysis and an R package, pophelper, was used for plotting the results [28, 29]. A cross-validation (CV) procedure was used to calculate the number of ancestral populations (k) from one to five using Admixture software (version 1.3.0).

Selection signature analysis. Three different statistics were used for detecting the signatures of selection in the genome of pigs: the calculation of F_{ST} values for each SNP when comparing pairs of breeds, the estimation of the ROH islands, which were overlapped among different animals within each breed, and hapFLK analysis.

F_{ST} analysis. F_{ST} values for all SNPs were estimated for pairs of breeds using PLINK 1.9 [24]. Minor allele frequencies were below 5% (--maf 0.05) [30]. The top SNPs corresponding to 0.1% of F_{ST} values were used to represent a selection signature, according to Kijas *et al.* and Zhao *et al.* [31, 32].

Runs of homozygosity estimation. Runs of homozygosity were detected according to the window-free method for consecutive SNP-based detection using the R package, detectRUNS [33]. One SNP with a missing genotype and up to one possible heterozygous genotype in one run were allowed to avoid the underestimation of the number of ROHs that were longer than 8 Mb [34]. The minimum ROH length was set to 500 kb to exclude the common ROHs. To minimize false-positive results, the minimum number of SNPs was calculated as it was proposed by Lencz *et al.* and later modified by Purfield *et al.* [35, 36].

Putative ROH islands were defined as overlapping homozygous regions in analyzed individuals within each breed. A threshold of 50% (the minimum proportion of animals within the breed in which overlapping ROH were detected) was selected, as this was suggested in other studies [37, 38]. We applied the threshold of 0.1 Mb for the minimal overlapping length size and 5 SNP for minimum number in ROH island.

HapFLK analysis. In this study, a hapFLK analysis was performed to detect the selection signatures through haplotype differentiation among the studied breeds using hapFLK software (version 1.4.) [39]. The number of haplotype clusters per chromosome was calculated in fast-PHASE by using cross-validation and was set to 35 [40]. For detailed analyses, the hapFLK regions containing at least one SNP with a *p*-value threshold of 0.01 ($-\log10(p) > 2$) were selected.

Identification of candidate genes. For candidate gene mining in the genomic regions under putative selection, the genomic localization of the regions as detected by three different statistics was used, i.e., the FST, ROH, and hapFLK methods. Regions that were overlapped and revealed by at least two different techniques were prioritized. Borders of these regions according to the 10.2 genome assembly were converted to genome assembly 11.1. Genes located on the selected regions were obtained from the Ensembl Genes Release 103 database based on the *Sus scrofa* gene sequence assembly [41].

Functional enrichment analysis. To understand the biological functions of the candidate genes, the Database for Annotation, Visualization, and Integrated Discovery (DAVID) was used for enrichment analysis [42]. Significant annotation clusters of enriched Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways and Gene Ontology were selected using an enrichment score of more than 1.3 and a *p*-value of < 0.05. To learn the biological functions of annotated genes and genes not included in clusters, a comprehensive literature search including information from other species was carried out.

RESULTS AND DISCUSSION

Genetic diversity. The Livni pigs were characterized by higher level of genetic diversity assessed by the levels of observed heterozygosity, unbiased expected heterozygosity, and allelic richness as compared to the Landrace and Large White breeds. The negative value of the inbreeding coefficient $_UF_{IS}$ indicates an excess of heterozygotes from the Hardy–Weinberg equilibrium in all the breeds (Table 1). In commercial breeds, the excess of heterozygotes was more significant compared to the Livni breed.

Breed relationship and admixture. The PCA-plot (Fig. 1a), the neighbor-joining tree (Fig. 1b) and cluster structure (Fig. 1c) showed the breed-specific distribution of individuals for all of the studied breeds. Obtained distribution indicated the insignificant participation of

Table 1 Summary of genetic diversity statistics calculated in studied pig breeds

Breed	*n**	H_O (M ± SE)	${}_UH_E$ (M ± SE)	${}_UF_{IS}$ [CI 95%]	A_R (M ± SE)
Livni	35	0.416 ± 0.001	0.411 ± 0.001	–0.011 [–0.013; –0.009]	1.998 ± 0
Landrace	50	0.373 ± 0.001	0.360 ± 0.001	–0.032 [–0.034; –0.030]	1.969 ± 0.001
Large White	53	0.351 ± 0.001	0.339 ± 0.001	–0.032 [–0.034; –0.030]	1.941 ± 0.001

* n – number of individuals; H_O – observed heterozygosity; M – mean value; SE – standard error; ${}_UH_E$ – unbiased expected heterozygosity; A_R – rarefied allelic richness; ${}_UF_{IS}$ – unbiased inbreeding coefficient [CI 95%, range variation of ${}_UF_{IS}$ coefficient at a confidence interval of 95%]

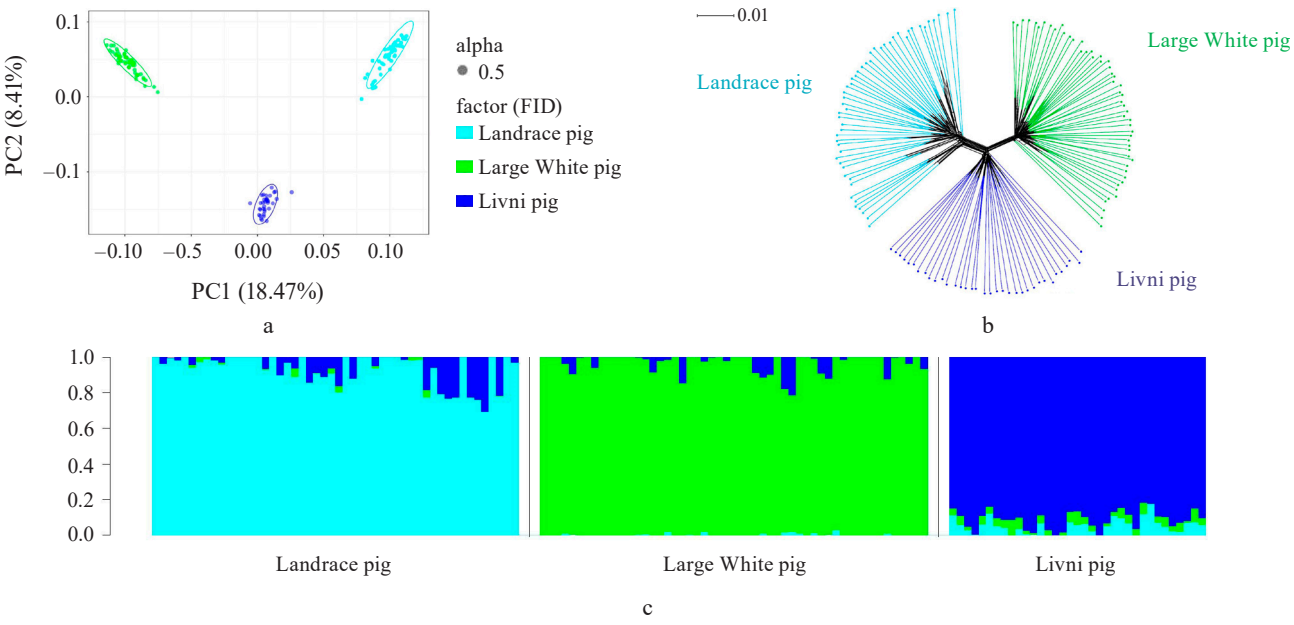

Figure 1 Genetic relationships between Landrace, Large White and Livni pig populations: (a) Principal component analysis (PCA) plot showing the distribution of Landrace, Large White and Livni individuals in two-dimensional coordinate system, i.e., the first (PC1; X-axis) and second (PC2; Y-axis) principal components, with percentage of total genetic variability, which can be explained by each of the two components, being indicated within the parentheses; (b) Neighbor-Net tree constructed based on the IBS-distances among the studied populations; (c) Admixture plot representing cluster structure of the studied populations if the number of clusters K = 3

the Landrace and Large White breeds in the formation of the modern allelofund of Livni pigs and demonstrated that sampling is suitable for searching for loci under selection pressure in the studied pig breeds and their subsequent structural annotation.

Selection signature detection. SNPs with F_{ST}-values beyond the cut-off (top 0.1%) were distributed among all autosomes, excepting SSA18. Most of these SNPs were specific to breed pairs. Six SNPs were found in SSA4 (1 SNP), SSA6 (2 SNP), and SSA11 (3 SNP), which were common for Livni – Landrace and Landrace – Large White, and seven SNPs on SSA5 (5 SNP), SSA8 (1 SNP), and SSA12 (1 SNP), for Livni – Large White and Landrace – Large White (Fig. 2).

The distribution of ROH island number and length in chromosomes is presented in Table 2. Forty-two ROH islands were detected in the Livni breed, which covered 34.415 Mb of the genome, while for Landrace and Large White, 126 and 224 ROH islands covered 161.792 and 282.402 Mb of the genome, respectively. The average length of the ROH island in Livni breed was significantly lower than that of pigs of commercial breeds: 2.868 ± 0.822 Mb versus 8.988 ± 2.185 (Landrace) and 15.689 ± 2.770 Mb (Large White), respectively ($p < 0.001$).

Eighteen common ROH islands were detected in the Large White and Landrace breeds, which were identified in ten autosomes: SSA1 (4 ROH islands), SSA4 (3 ROH islands), SSA5, SSA6 (3 ROH islands), SSA8, SSA9, SSA11, SSA13, SSA14, SSA16, and SSA17. Eight common ROH islands were detected in the Livni and Large White breeds, which were identified in six autosomes, namely SSA1, SSA2, SSA7, SSA12, SSA14 (3 ROH islands), and SSA15. Eight common ROH islands were detected in the Livni and Landrace breeds, which were identified in five autosomes: SSA1, SSA3 (2 ROH islands), SSA4, SSA6, SSA11 (2 ROH islands), and SSA15. Five ROH islands detected in SSA1, SSA6, SSA11, SSA14, and SSA15 were common for three breeds (Table 3).

The hapFLK analysis resulted in the identification of 13 putative regions affected by the selection (Fig. 3). These regions were distributed among 10 autosomes, including regions on SSA1, SSA3, SSA14, and SSA13 with

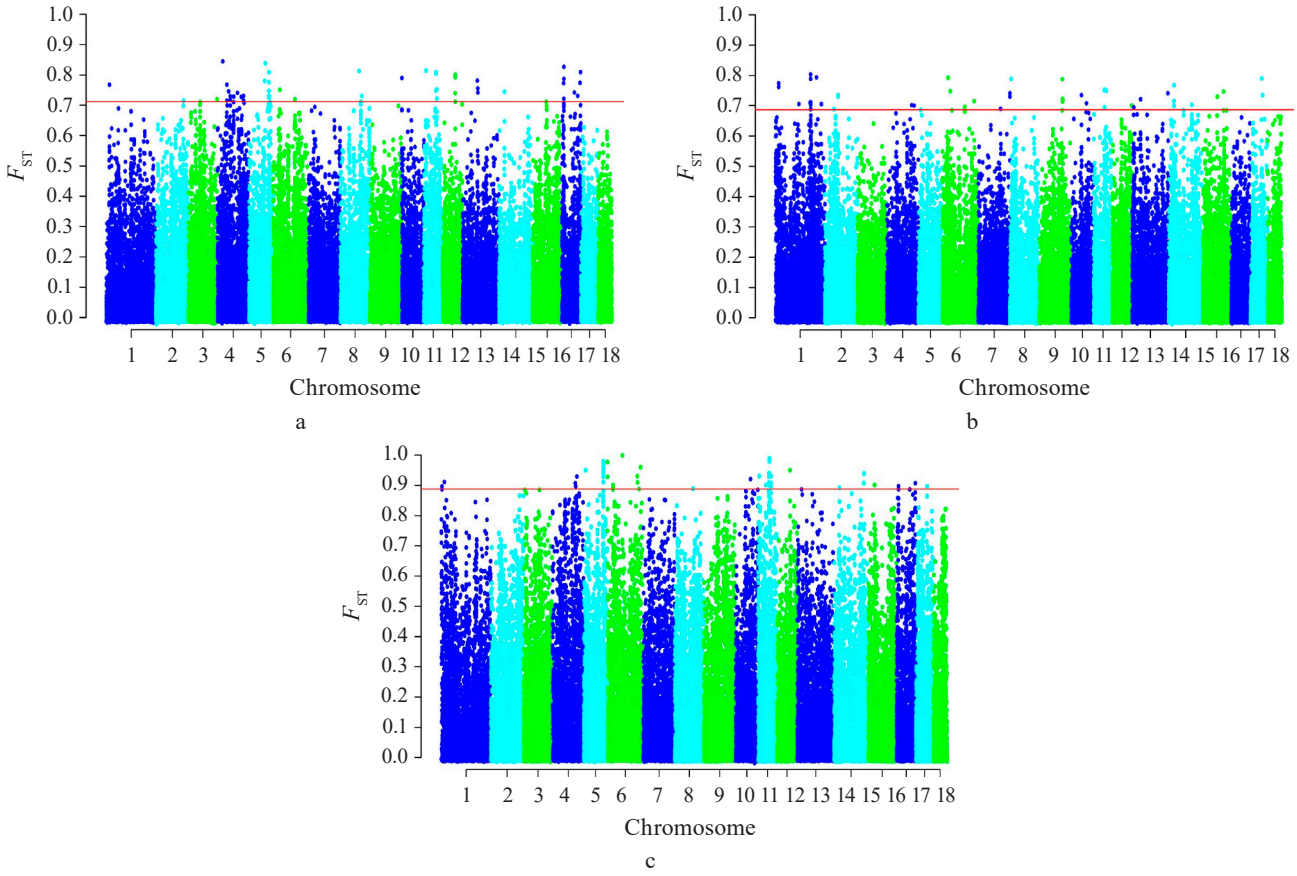

Figure 2 Genomic distribution of F_{ST} values estimated between the breeds: (a) Livni – Landrace; (b) Livni – Large White; (c) Landrace – Large White. Values for the X-axis are pig autosomes (the breadth of autosomes corresponds to their length); and those for the Y-axis are F_{ST} values. SNPs were plotted relative to their positions within each autosome. The threshold, which was estimated as the top 0.1% for F_{ST} values, is indicated by a horizontal line

Table 2 The distribution of ROH island number and length in chromosomes

SSA*	Livni breed				Landrace breed				Large White breed			
	50%		70%		50%		70%		50%		70%	
	n#	Length, Mb	n	Length, Mb	n	Length, Mb	n	Length, Mb	n	Length, Mb	n	Length, Mb
1	8	6.027			13	40.348	4	3.574	25	35.475	2	2.942
2	3	3.596	1	0.181	1	1.991			12	13.752	4	1.387
3	4	1.748			7	5.025			13	25.441	2	3.136
4	1	0.611			11	11.232			30	44.178	5	9.820
5					3	4.004	1	1.907	14	13.519	2	1.819
6	2	1.322	1	0.700	14	12.401	1	0.497	21	31.490	6	5.046
7	1	0.365			6	4.943	1	0.618	12	12.894	1	0.681
8	1	0.706			4	5.273			10	10.570	2	2.155
9					13	18.110	1	0.127	14	15.720	2	0.846
10					5	4.054			6	3.227	1	0.494
11	5	6.298	1	4.116	5	10.478	3	4.824	7	11.946	4	5.088
12	1	0.562			3	1.115			6	2.886		
13	3	1.478			10	8.386	1	0.485	11	13.026		
14	9	9.187	2	1.748	15	17.094			13	18.220	7	8.033
15	4	2.516	2	1.183	5	7.820	3	4.719	13	17.427	4	3.230
16					5	3.429			8	6.952	1	0.777
17					4	2.838	1	0.607	6	3.558		45.455
18					2	3.251			3	2.120		3.247 ± 0.762
SUM	42	34.415	7	7.928	126	161.792	16	17.358	224	282.402	43	45.455
Average		2.868 ± 0.822		1.586 ± 0.684		8.988 ± 2.185		1.929 ± 0.643		15.689 ± 2.770		3.247 ± 0.762

* SSA – *Sus scrofa* autosomes; # *n* – number of SSA

a statistical significance of $p < 0.001$. Four regions were Large White-specific, three – Landrace-specific, three – Large White and Landrace-specific, three – Livni and Large White-specific (Table 4).

Comparing the genomic localization of the regions under putative selection detected by three different statistics (F_{ST}, ROHs, and hapFLK) revealed the presence of 13 overlapping regions, which were identified by at least two different methods (Table 5); 7 regions corresponded to the Large White breed, 2 corresponded to the Landrace breed, 2 were common to Large White and Landrace breeds, and 2 were common to Large White and Livni breeds. Additionally, in the list of genes for structural and functional annotation, we included ROH islands identified only in Livni pigs, as well as common ROH islands identified in the Livni and one or two compared breeds. Thus, 16 Livni-specific regions, and 39 regions, which are common for both two and more breeds were selected for the structural and functional annotation.

Candidate gene determination and functional enrichment determination. The structural annotation of these regions revealed the presence of 238 candidate genes: 50 genes were specific to Livni pigs, 62 to Livni

Table 3 Common ROH islands identified in genome of two or three studied breeds

SSA*	Livni breed			Landrace breed			Large White breed		
	SNP#	Position&	Mb	SNP	Position	Mb	SNP	Position	Mb
1	17	65.16–65.97	0.811				20	65.10–65.97	0.868
				15	82.43–83.14	0.709	14	82.43–83.12	0.687
	22	83.26–84.22	0.964	17	83.23–84.06	0.827			
				18	94.66–96.30	1.647	22	94.37–96.30	1.936
				34 (31)	216.94–222.84 (218.18–222.84)	5.901 (4.657)	38 (20)	215.75–221.94 (219.60–221.43)	6.190 (1.833)
	19	241.90 242.96	1.052	219 (180)	223.97–245.52 (228.65–245.52)	21.551 (16.864)	22 (21)	241.90–243.21 (241.90–243.01)	1.303 (1.109)
				24	265.78–266.65	0.873	25	265.78–266.71	0.928
2	41 (5)	44.46–46.37 (45.09–45.27)	1.909 (0.181)				21	44.46–45.27	0.804
3	19	28.95–29.45	0.493	8	29.18–29.62	0.441			
	9	111.31–111.65	0.340	13	111.31–111.81	0.499			
4				20	13.87–14.59	0.715	20	13.87–14.59	0.715
				37	49.18–52.60	3.428	98 (48)	48.13–61.32 (48.38–53.11)	13.189 (4.735)
				20	84.63–85.69	1.065	6	85.11–85.40	0.291
	10	107.67–108.28	0.611	33	107.09–108.28	1.194			
5				21	67.31–67.88	0.570	45	66.43–67.68	1.251
6				24 (18)	14.62–15.26 (14.65–15.14)	0.635 (0.497)	74	14.18–16.13	1.947
				16	18.83–19.35	0.525	25	18.39–19.00	0.615
				20	19.66–20.42	0.761	38	19.11–20.64	1.526
	18	71.44–72.06	0.622	13	71.88–72.48	0.601			
	19 (18)	88.24–88.94 (88.24–88.94)	0.700 (0.700)	13	88.24–88.62	0.373	63 (19)	88.05–91.08 (88.24–88.94)	3.026 (0.700)
7	9	36.20–36.57	0.365				30	35.88 37.26	1.380
8				23	34.62 35.34	0.715	15	34.81 35.22	0.405
9				18	83.56 84.66	1.099	30	83.40 85.15	1.751
11	6	7.81–8.06	0.249	19 (10)	7.55–8.45 (7.55–8.06)	0.900 (0.504)	75 (64)	6.48–10.17 (6.48–9.59)	3.686 (3.112)
	29 (23)	34.82–39.79 (35.23–39.35)	4.966 (4.116)	45 (23) (16)	34.72–40.9 (34.72–37.40) (38.52–40.16)	6.246 (2.683 (1.637)			
	6	45.77–46.05	0.284	20	45.77–46.69	0.920			
	11	46.24–46.64	0.407						
				24	59.35–61.04	1.684	32	59.82–62.09	2.270
12	20	1.56–2.12	0.562				24	1.56–2.25	0.694
13				8	95.33–96.75	1.421	18	94.50–97.50	3.004
14				30	47.72–48.97	1.255	64	47.65–50.41	2.752
		51	49.26–51.17		1.911				

Continuation of Table 3

SSA*	Livni breed			Landrace breed			Large White breed		
	SNP#	Position&	Mb	SNP	Position	Mb	SNP	Position	Mb
14	40	71.65–73.67	2.023				58 (40)	70.89–74.21 (71.65–73.67)	3.325 (2.023)
	37 (20)	75.38–76.74 (75.38–76.01)	1.354 (0.624)				82 (36)	75.38–78.86 (75.45–76.74)	3.474 (1.291)
	34 (25)	76.89–78.43 (77.05–78.17)	1.545 (1.124)				31	76.89–78.22	(1.325)
	7	78.49–78.69	0.199						
	7	94.10–94.94	0.846				29	93.46 95.28	1.818
	6	95.18–95.40	0.226						
	24	98.02–99.36	1.341	24	98.02–99.36	1.341	28 (14)	97.62–98.92 (98.02–98.73)	1.300 (0.707)
15	5	84.30–84.56	0.262				55 (18)	84.37–87.85 (84.70–85.83)	3.476 (1.135)
	19 (5)	90.46–91.44 (91.14–91.44)	0.983 (0.297)	11	90.76–91.44	0.675			
	24 (19)	92.81–93.87 (92.86–93.75)	1.059 (0.886)	33 (26)	92.40–93.87 (92.69–93.87)	1.469 (1.180)	21	92.86–93.77	0.902
16				5	5.85–6.00	0.151	44	5.43–6.42	0.990
17				30	8.32–9.16	0.839	6	8.63–8.78	0.153

* SSA – *Sus scrofa* autosomes; # SNP – number of SNP in ROH island; & position – start and end of ROH island in accordance with genome assembly 10.2, information about ROH islands detected in more than 70% of animals is presented in brackets

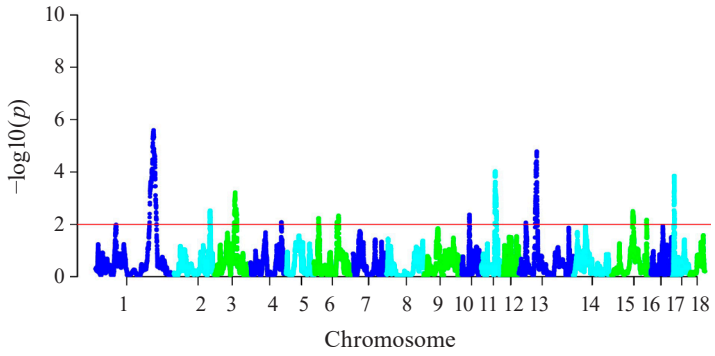

Figure 3 Signatures of selection in the genomes of the studied breeds based on the hapFLK statistics. Values for the *X*-axis are pig autosomes, and those for the *Y*-axis are values of statistical significance (−log10 *p*-values). The red line indicates the threshold of significance at $p < 0.01$ (i.e., $-\log10(p) > 2$)

Table 4 HapFLK regions identified in the genome of the studied breeds

SSA*	Breed	Position of Region		Amount of SNP in Region	Length, Mb	The Most Significant SNP	*p*-Value
		Start	End				
1	Landrace	216 939 236	244 858 851	245	27.92	232 953 425	2.44E-06
2	Large White	143 991 472	146 088 237	78	2.10	144 881 039	2.99E-03
3	Large White	79 798 323	89 895 102	92	10.10	83 233 266	5.92E-04
4	Large White	124 675 286	124 955 662	10	0.28	124 832 207	8.14E-03
6	Landrace, Large White	18 888 120	20 189 159	38	1.30	19 601 974	5.73E-03
6	Livni, Large White	92 938 033	100 318 389	20	7.38	99 706 201	4.56E-03
10	Landrace	30 140 466	31 750 116	36	1.61	31 038 967	4.14E-03
11	Landrace, Large White	54 362 880	61 415 073	110	7.05	56 397 482	9.27E-05
13	Landrace	27 775 922	27 893 903	7	0.12	27 823 032	8.43E-03
13	Livni, Large White	64 933 643	74 382 805	122	9.45	71 775 121	1.62E-05
15	Livni, Large White	84 301 944	88 728 150	80	4.43	85 769 904	3.14E-03
15	Large White	140 660 077	141 264 578	30	0.60	140 897 463	6.65E-03
17	Landrace, Large White	6 263 548	8 746 763	71	2.48	7 572 534	1.40E-04

* SSA – *Sus scrofa* autosomes

Table 5 Overlapped genomic regions and/or SNPs under putative selection identified by at least two different statistics in the Duroc and Livni breeds

SSA*	F_{ST} [a]		ROH[b]		hapFLK[c]	
	Breed	Position	Breed	Position	Breed	Position
1	Landrace/Livni	9 951 603	Landrace	9.87–10.52		
		10 051 445				
		10 070 322				
1	Landrace/Livni	226 429 888–226 458 237	Landrace	216.94–222.84	Landrace	216.94–244.86
		230 057 074		218.18–515.22		
		231 262 134–231 476 049		223.97–245.52		
		232 259 626		228.65–245.52		
1	Livni/Large White	145 137 405	Large White	143.69–145.62	Large White	143.99–146.09
				144.50–144.81		
3			Large White	78.28–91.19	Large White	79.80–89.90
				80.19–81.59		
4	Livni/Large White	31 519 009–31 637 170	Large White	30.71–33.25		
5	Landrace/Large White	94 308 964–94 995 044	Large White	94.26–95.05		
	Livni/Large White	94 408 638–94 822 437				
6			Large White	19.11–20.64	Landrace, Large White	18.89–20.19
			Landrace	19.66–20.42		
6			Large White	94.45–96.28	Large White	92.94–100.32
11	Landrace/Large White	54 595 810	Large White	54.83–57.35	Large White	54.36–61.42
		54 768 013				
		54 829 740		56.40–56.90		
		55 413 895				
		56 258 459–56 663 342				
13	Livni/Large White	68 207 174	Large White	71.91–72.12	Livni, Large White	64.93–74.38
		71 946 567				
		72 118 478				
15	Livni/Large White	84 696 087	Livni	84.30–84.56	Livni, Large White	84.30–88.73
			Large White	84.37–87.85		
				84.70–85.83		
15			Large White	140.12–142.04	Large White	140.66–141.26
17			Large White	6.68–7.82	Landrace, Large White	6.26–8.75
			Landrace	8.32–9.16		
			Large White	8.63–8.78		

* SSA – *Sus scrofa* autosomes. Methods used for defining the signatures of selection: [a]F_{ST} – top 0.1% SNPs by the F_{ST} value at pairwise population comparison; [b]ROH – ROH segments distributed in more than 70% of animals; and [c]hapFLK – regions identified by hapFLK analysis at $p < 0.001$

and Large White pigs, 35 to Livni and Landrace pigs, 36 to all studied breeds, and 55 were specific to Large White and Landrace pigs (Table 6).

Using the DAVID web tool and a list of 238 candidate genes found in the genomic regions with selection signatures, 182 genes with described functions were identified. The significant clusters are shown in Table 7. Annotated clusters with an enrichment coefficient – log10(p) > 1.3 (corresponds to $p < 0.05$) were not determined for the Livni breed and all three studied breeds (Livni, Large White and Landrace). Two reliably annotated clusters were identified for the Livni and Large White, Large White and Landrace breeds, and one annotated cluster for Livni and Landrace. For the list of Livni and Large White genes, the presence of two annotated clusters was revealed. Cluster 1 (enrichment coefficient = 2.11) included *G6PC2*, *HKDC1*, *HK1* genes involved in carbohydrate metabolism. Cluster 2 (enrichment coefficient = 1.60) included *SUPV3L1*, *SLC25A16*, *HKDC1*, *DDX21*, *PIK3C2A*, *MAP3K7*, *DDX50*, and *HK1* genes involved in the processes of DNA replition and repair. For Livni and Landrace one reliable cluster (enrichment coefficient = 4.49) was determined, including the genes *CIART*, *HORMAD1*, *HOXD3*, *HOXD4*, *HOXD8*, *HOXD9*, *HOXD10*, *HOXD12*, *HOXD13*, *EVX2*, *NR2E1*, and *PLEKHO1*. Genes under selection pressure in commercial pig breeds (Large White and Landrace) were combined into two reliable clusters. Cluster 1 (enrichment co-efficient = 1.74) combined the genes *KCNA1*, *KCNA6*, *KV1.5*, and *SLC30A9* involved in the regulation of ion transmembrane transport, mainly potassium. The *IBTK*, *KCNA1*, *KCNA6*, and *ZBTB10* genes regulating transcription repression and interaction with components of histone deacetylase co-repressor complexes were localized in cluster 2 (enrichment coefficient = 1.54).

Specific and overlapping sites in the genome of Livni, Large White and Landrace breeds that are under

Table 6 Genes within the overlapped genomic regions affected by putative selection

SSA	Region (Mb)			Genes[a]
	Livni	Landrace	Large White	
1	4.31–4.80			*PDE10A*, *C6orf118*
1	71.81–72.72			*FHL5*, *GPR63*, *NDUFAF4*, *KLHL32*
1	87.60–87.85			*U6*, *WISP3*, *TUBE1*, *FAM229B*
1	204.60–205.65			*WDHD1*, *SOCS4*, *MAPK1IP1L*, *LGALS3*, *DLGAP5*, *ATG14*, *TBPL2*, *U4*, *KTN1*
1	299.94–300.44			*U5*, *PBX3*
2	98.53–99.63			*7SK*, *ssc-mir-9-2*, *MEF2C*
2	118.05–118.64			–
3	29.62–30.60*			*PARN*, *BFAR*, *ssc-mir-365-1*, *CCDC12*, *ERCC4*
8	102.43–103.14			*C4orf33*, *JADE1*
11	42.95–43.35			–
13	36.28–36.92			*MAPKAPK3*, *CISH_TV2*, *DOCK3*, *SNORD22*, *RBM15B*, *MANF*, *VPRBP*
13	60.38–61.29*			*PDZRN3*
14	74.80–75.20			–
14	94.10–95.53**			*WAPAL*, *OPN4*, *LDB3*, *C14H10orf116*, *SNCG*, *BMPR1A*, *GLUD1*
14	100.10–101.35			*ZNF239*, *ZNF32*, *TFAM*, *RPL37A*
15	91.54–91.76			–
1	65.16–65.97		65.10–65.97	*MAP3K7*
2	44.46–46.37		44.46–45.27	*MYOD1*, *OTOG*, *SNORD89*, *USH1C*, *ABCC8*, *KCNJ11*, *NUCB2*, *PIK3C2A*, *RPS13*, *SNORD14*, *U1*, *PLEKHA7*, *C11orf58*
7	36.20–36.57		35.88–37.26	*DEF6*, *ZNF76*, *FKBP5*, *ARMC12*, *CLPSL2*, *CLPS*, *LHFPL5*
12	1.56–2.12		1.56–2.25	*CHMP6*, *NPTX*, *RNF213*
14	71.65–73.67		70.89–74.21	*NRBF2*, *JMJD1C*, *ssc-mir-1296*, *REEP3*
14	75.38–78.69**		75.38–78.86	*LRRTM3*, *DNAJC12*, *SIRT1*, *HERC4*, *MYPN*, *ATOH7*, *PBLD*, *HNRNPH3*, *RUFY2*, *SLC25A16*, *CCAR1*, *STOX1*, *SNORA70*, *DDX50*, *DDX21*, *KIAA1279*, *SRGN*, *VPS26A*, *SUPV3L1*, *HKDC1*, *TACR2*, *HK1*, *COL13A1*
14	94.10–95.40*		93.46–95.28	*WAPAL*, *OPN4*, *LDB3*, *U3*, *C14H10orf116*, *SNCG*, *BMPR1A*
15	84.30–84.56		84.37–87.85	*NOSTRIN*, *SPC25*, *G6PC2*, *ABCB11*
1	83.26–84.22	83.23–84.06		*SEC63*, *GL*, *NR2E1*, *SNX3*, *FOXO3A*
3	28.95–29.45	29.18–29.62		*ABCC1*, *U6*, *SNORA70*, *CPPED1*
3	111.31–111.65	111.31–111.81		–
4	107.67–108.28	107.09–108.28		*HORMAD1*, *GOLPH3L*, *ENSA*, *MCL1*, *ADAMTSL4*, *ECM1*, *TARS2*, *RPRD2*, *PRPF3*, *CIART*, *PLEKHO1*, *VPS45*
6	71.44–72.06	71.88–72.48		*MINOS1*, *HTR6*, *TMCO4*
11	34.82–39.79	34.72–40.96		*SNORA31*
11	45.77–46.64*	45.77–46.69		*KLHL1*
15	90.46–91.75*	90.76–91.44		*EVX2*, *HOXD13*, *HOXD12*, *HOXD10*, *HOXD9*, *HOXD8*, *ssc-mir-10b*, *HOXD4*, *HOXD3*
1	241.90–242.96	223.97–245.52	241.90–243.21	*MLANA*, *ERMP1*, *RIC1*, *U6*, *SNORA19*, *PDL1*, *PLGRKT*, *RLN*, *INSL6*, *JAK2*
6	88.24–88.94	88.24–88.62	88.05–91.08	*PABPC4*, *SNORA55*, *U6*, *HEYL*, *NT5C1A*, *HPCAL4*
11	7.81–8.06	7.55–8.45	6.48–10.17	*HSPH1*, *U6*, *B3GALTL*
14	98.02–99.36	98.02–99.36	97.62–98.92	*CHAT*, *C10orf53*, *OGDHL*, *PARG*, *NCOA4*, *MSMB*, *ZFAND4*, *MARCH8*, *ALOX5*, *ZNF22*, *C10orf10*
15	92.81–93.87	92.40–93.87	92.86–93.77	*RBM45*, *U1*, *SNORD112*, *OSBPL6*, *PRKRA*, *DFNB59*, *FKBP7*, *PLEKHA3*
1		82.43–83.14	82.43–83.12	*SOBP*
1		94.66–96.30	94.37–96.30	*TPBG*, *IBTK*, *SNORD112*, *FAM46A*
1		216.94–222.84	215.75–221.94	*TEK*, *IFT74*, *LRRC19*, *PLAA*, *CAAP1*, *U6*, *TUSC1*, *IZUMO3*, *ELAVL2*
1		265.78–266.65	265.78–266.71	*ZCCHC7*, *GRHPR*, *POLR1E*, *U6*, *FRMPD1*, *TRMT10B*, *EXOSC3*, *DCAF10*
4		13.87–14.59	13.87–14.59	*FAM84B*, *U6*, *5S_rRNA*
4		49.18–52.60 60.52–61.40	48.13–61.32	*OTUD6B*, *TMEM55A*, *NECAB1*, *CALB1*, *DECR1*, *NBN*, *OSGIN2*, *CU607036.1*, *RIPK2*, *5S_rRNA*, *PAG1*, *ZNF704*, *ZBTB10*
4		84.63–85.69	85.11–85.40	*ST18*, *PCMTD1*

Continuation of Table 6

SSA	Region (Mb)			Genes[a]
	Livni	Landrace	Large White	
5		67.31–67.88	66.43–67.68	*KV1.5*, *KCNA1*, *KCNA6*
6		14.62–15.26	14.18–16.13	*HP*, *ZFHX3*
6		18.83–19.35	18.39–19.00	–
6		19.66–20.42	19.11–20.64	–
8		34.62–35.34	34.81–35.22	*TMEM33*, *SLC30A9*, *BEND4*, *U6*
9		83.56–84.66	83.40–85.15	*SDHAF3*
11		59.35–61.04	59.82–62.09	*SLITRK1*
13		95.33–96.75	94.50–97.50	*7SK*, *ZIC1*, *ZIC4*
14		47.72–1.17*	47.65–50.41	*MN1*, *PITPNB*, *TTC28*, *U1*
16		5.85–6.00	5.43–6.42	–
17		8.32–9.16	8.63–8.78	–

[a] Candidate genes. *2 closely located ROH islands, **3 closely located ROH islands

selection pressure have been identified. Positional candidate genes were identified and their annotation was performed. In the current study, three pig breeds were examined and compared. We previously reported that Livni breed is characterized the highest level of genetic diversity compared with commercial breeds. The neighbor-joining tree showed that this breed was the most distinct from Duroc but formed the knot bounding the branches corresponding to the Landrace and the Large White breeds. This observation confirmed the participation of these two breeds in the formation of the Livni breed during it artificial selection. We observed the highest level of genetic diversity in Livni pigs compared to commercial breeds (Table 1), which may be a consequence of the participation of various breeds in the development of the Livni breed, including Large White and Landrace. However, results of breed relationship and admixture revealed distribution indicated the insignificant participation of the Landrace and Large White breeds in the formation of the modern allelofund of the Livni pigs.

Using three different statistics (top 0.1 F_{ST} at pairwise breed comparison, ROH islands and hapFLK analysis), we selected 13 overlapping regions, which were identified by at least two different methods (Table 2); 7 regions corresponded to the Large White breed, 2 corresponded to the Landrace breed, 2 were common to Large White and Landrace breeds, and 2 were common to Large White and Livni breeds. Among 238 candidate genes, which were localized within selected genomic regions (Table 3), 182 genes had the described functions in GO-terms; among them, 50 genes were specific to Livni pigs, 62 were specific to Livni and Large White pigs, 35 were specific to Livni and Landrace pigs, 36 were specific to all studied breeds, and 55 were specific to Large White and Landrace pigs (Table 3).

Among common genes for three studied breeds, *MLANA* and *JAK2* were previously observed in Livni and Duroc breeds and involved in adipogenesis [20, 43]. It was reported that *FKBP7* is highly expressed in subcutaneous adipose tissue of mature Erhualian pig, while *CHAT* is essential for macrophages as a source of acetylcholine for the regulation of adaptive thermogenesis [44, 45]. *HSPH1* is a known marker of both human and mouse brown adipocytes and was upregulated in young and old brown adipocytes after acute cold exposure [46]. *HSPA1L* were found to be differently expressed between the low and high drip loss groups in the Duroc pigs [47]. *NCOA4* may play a role in early events of adipocyte differentiation and were found in Pudong White pigs [48, 49]. *PLGRKT* coordinately regulates multiple aspects of adipose function and was found to be related to obesity [50, 51]. According to Gene Ontology terms, *ALOX5* is strongly associated with immunity, lipid metabolism and fat cell differentiation, insulin secretion, and oxidative stress. Interestingly, this gene was also very highly significantly associated with feet and leg structure soundness traits in pigs [52]. *OSBPL6* linked with lipid and sterol transport and encoded by *miR-33*, which may also regulate adaptive thermogenesis [53]. *PLEKHA3* is also associated with lipid metabolism, and mutations were identified for this gene in the Puławska pig breed, which is characterized by thicker backfat and better meat quality values [54]. *PARG* is linked with carbohydrate metabolic process and could be involved in lipid metabolism [55]. According to Gene Ontology terms, *ERMP1* involved incellular response to oxidative stress, *HEYL* – in skeletal muscle cell differentiation. *INSL6* was linked with male fertility in Enshi pigs and reproduction in Anhui pigs [56, 57]. *MSMB* was closely related to body weight, body height, abdominal circumference, and chest depth in Xiangsu hybrid pigs [58]. *OGDHL* was up-regulated in the liver in pigs with higher backfat thickness of Songliao black female pig population [59]. Although *PRKRA* is strongly associated with immune response, including piglets, this gene plays unexpected role in the regulation of mitochondrial biogenesis and energetics in cells and brown adipocytes [60, 61]. *ZFAND4* gene encodes stress proteins and was detected in Pudong White pigs, as well as *ZNF22* [49, 62]. *C10orf10* is involved in adipose tissue thermogenesis and was observed in heavy Iberian

Table 7 Functional Gene Ontology terms enriched with candidate genes

Claster	Category	Term	P	Genes
Livni and Large White				
Cluster 1, enrichment coefficient = 2.11	KEGG_PATHWAY	ssc00052: galactose metabolism	0.002	*G6PC2*, *HKDC1*, *HK1*
		ssc00500: starch and sucrose metabolism	0.003	
		ssc04973: glucose digestion and absorption	0.005	
		ssc00010: glycolysis/gluconeogenesis	0.009	
		ssc04910: insulin signaling pathways	0.040	
Cluster 2, enrichment coefficient = 1.60	UP_KW_MOLECULAR_FUNCTION	KW-0347 ~ helicase	0.002	*SUPV3L1*, *SLC25A16*, *DDX21*, *DDX50*
	GOTERM_MF_DIRECT	GO:0003724 ~ activity of RNA helicase	0.009	*SUPV3L1*, *DDX21*, *DDX50*
	UP_KW_LIGAND	KW-0067 ~ ATP binding	0.010	*SUPV3L1*, *SLC25A16*, *HKDC1*, *DDX21*, *PIK3C2A*, *MAP3K7*, *DDX50*, *HK1*
		KW-0547 ~ nucleotide binding	0.013	
	UP_SEQ_FEATURE	DOMAIN: C-terminal helicase	0.025	*SUPV3L1*, *DDX21*, *DDX50*
	INTERPRO	IPR001650: C-terminal helicase	0.029	
	SMART	SM00490: HELICc	0.043	
Livni and Landrace				
Cluster 1, enrichment coefficient = 4.94	GOTERM_MF_DIRECT	GO:0000981 ~ transcription factor activity of RNA polymerase II, sequence-specific DNA binding	0.001	*HOXD13*, *HOXD4*, *HOXD12*, *HOXD3*, *EVX2*, *HOXD10*, *HOXD8*
		GO:0000978 ~ sequence-specific DNA binding of the proximal promoter region of RNA polymerase II	0.001	*HOXD13*, *HOXD4*, *NR2E1*, *HOXD3*, *EVX2*, *HOXD10*, *HOXD9*
		GO:0001228 ~ transcription activator activity, sequence-specific binding of the transcriptional regulatory region of RNA polymerase II	0.002	*HOXD13*, *HOXD4*, *NR2E1*, *HOXD10*, *HOXD8*
		GO:0005634 ~ nucleus	0.028	*PLEKHO1*, *HOXD4*, *HORMAD1*, *NR2E1*, *HOXD12*, *HOXD3*, *EVX2*, *HOXD10*, *HOXD9*, *HOXD8*, *CIART*
Large White and Landrace				
Cluster 1, enrichment coefficient = 1.74	UP_KW_MOLECULAR_FUNCTION	KW-0631 ~ potassium channel	0.003	*KV1.5*, *KCNA1*, *KCNA6*
		KW-0851 ~ voltage-controlled ion channels	0.007	
	UP_KW_BIOLOGICAL_PROCESS	KW-0633 ~ potassium transport	0.007	
	UP_SEQ_FEATURE	DOMAIN: ion transport	0.007	
	GOTERM_MF_DIRECT	GO:0005249 ~ activity of the voltage-controlled potassium channel	0.008	
		GO:0008076 ~ voltage-controlled complex of potassium channels	0.008	
		GO:0034765 ~ regulation of ion transmembrane transport	0.025	
	INTERPRO	IPR005821: ion transport domain	0.020	
	UP_KW_BIOLOGICAL_PROCESS	KW-0406 ~ ion transport	0.030	*SLC30A9*, *KV1.5*, *KCNA1*, *KCNA6*
	UP_KW_LIGAND	KW-0630 ~ potassium	0.032	*KV1.5*, *KCNA1*, *KCNA6*
Cluster 2, enrichment coefficient = 1.54	UP_SEQ_FEATURE	DOMAIN: BTB	0.005	*IBTK*, *KCNA1*, *KCNA6*
	INTERPRO	IPR000210: BTB/POZ-like	0.046	*IBTK*, *KCNA1*, *ZBTB10*

Pigs [63, 64]. *PDL1* was determined as candidate biomarkers for predicting residual feed intake in Yorkshire pigs, as well as *U1* [65, 66]. *RLN* is a candidate gene for reproductive traits in pigs and was found to regulate adipose tissue development through stimulating adipogenesis and modulating adipocyte metabolism [67–69]. *SNORA19* could be involved in body temperature regulation [70]. *U6* was associated with litter traits in Yorkshire and Landrace pigs and was a selection signature gene in Meishan population [71, 72].

In the Livni and Landrace breeds, 35 common genes were detected, which formed one cluster with enrichment coefficient = 4.94 and predominant *HOXD* genes. According to Gene Ontology terms, *HOXD10* and *HOXD9* are involved in various developmental processes, such as single fertilization, skeletal muscle tissue development, adult locomotory behavior, embryonic skeletal system morphogenesis, peripheral nervous system neuron development, neuromuscular process, etc. *HOXD10* is required systemically for secretory activation in lactation [73]. Expression level of *HOXD10* was increased in animals with high marbling [74]. *HOXD9* and *HOXD10* are associated with such traits as growth, body weight and composition, abdominal fat, organogenesis, and feed intake and consumption [75]. They also play an active role in chondrogenesis and the development of adipose depots [76, 77]. *HOXD3*, *HOXD8*, *HOXD12*, and *HOXD13* are also associated with skeletal system development. *HOXD12* is differently expressed between large and small piglet size [78]. *HOXD3* is also associated with nervous system development, considered as predictors for feed efficiency traits [79, 80]. It was reported that *HOXD4* and *HOXD8* are up-regulated in differentiated adipocytes [81]. *HOXD8* gene is involved in patterning the lower thoracic and lumbar vertebrae, in the urogenital tract development, also of mesoderm origin [82, 83]. *HTR6*, associated with nervous system, was identified as interesting candidate genes involved in axonogenesis and synapsis in Iberian breed [84]. *ADAMTSL4* was found to evolve under positive selection and exhibited significant down-regulated mRNA expression in the Tibetan pigs [85]. *ABCC1* is expressed in adipose and skeletal muscle, up-regulated in obesity, and involved in the embryo development of pig; it was also detected in Northeast wild boar [86–89]. *HORMAD1* is linked with embryo development and productivity. Z. Zeng *et al.* noted *HORMAD1* to belong to growth-related Meishan pig genes [90]. *HORMAD1* was under heavy selection based on runs of homozygosity in a Large White pig population and associated with obesity [91]. *SEC63* was determined as candidate genes for estimated breeding values feed conversion ratio in Maxgro boars [92]. It was found an association between the *CIART* genotype and backfat thickness in Duroc pigs, and its expression is affected by food intake [93, 94]. According to Gene Ontology terms, *ENSA* is associated with regulation of insulin secretion and related to adipocyte development [95]. *ECM1* is involved in immunity and bone development. It was reported to be an important gene highly expressed in subcutaneous white adipose tissue (sWAT) as compared to brown adipocytes, and was determined in Korean Wild Boar, up-regulated in Congjiang Xiang pigs with large litter size and in testis tissue from Duroc boars [96–99]. *KLHL1* could be linked with Landrace and Yorkshire pig backfat thickness in Korea and involved in environmental adaptation [100, 101]. *NR2E1* is involved in developmental processes and linked with environmental adaptation concerning behavioral defense response in Xiang pigs [102]. It showed significant associations with feed conversion efficiency and growth rate in pigs [92]. *PRPF3* gene is differentially expressed in the *Longissimus dorsi* muscle being more abundant in Large White than in Wujin pigs [103]. *VPS45* could be linked with growth trait [104]. *FOXO3A* promotes metabolic adaptation and stress resistance in hypoxia, associated with carcass length, backfat thickness and drip loss, related to muscle development in Iberian pigs [105–107]. *FOXO3A* could promote lipid accumulation as well [108]. *Ssc-mir-10b* was downregulated in Tibetan pigs, related to hypoxia adaptation, play important roles in fat-related processes in adipose tissue, had been frequently reported highly expressed in skeletal muscle during porcine prenatal and postnatal developmental stages and abundantly expressed in subcutaneous adipose tissue in pigs [109–113].

In the Livni and Large White breeds the largest amount of common genes was detected and averaged 62, which formed two clusters. Cluster 1, with enrichment coefficient = 2.1, was characterized with genes involved in glucose metabolism. Among them, *G6PC2*, *HKDC1* and *HK1* are critical for glucose homeostasis. *HK1* effects on growth and meat quality in Polish Landrace [114]. It is important for sperm motility in Duroc, enriched in brown adipocytes of aged mice, up-regulated by severe cold and essential for brown adipocytes thermogenesis [115–118]. Cluster 2, with enrichment coefficient = 1.60, demonstrated helicase genes. *DDX21* is associated with immunity and belongs to the top 4 lymphocyte associated genes in pigs [119]. *SUPV3L1* is important for the maintenance of the skin barrier and related to percentage of certain fiber types [120, 121]. *MAP3K7* is also linked with immunity and strongly associated with neuropsychiatric processes [122]. It was reported to be associated with growth traits and adipocyte differentiation [100, 123]. *PIK3C2A* gene is related to hepatic insulin resistance and steatosis, average daily gain and lean meat percentage, intramuscular fat and backfat thickness in two Duroc populations, being under positive selection in all high-altitude species [124–127]. According to Gene Ontology terms, *ABCB11* is associated with fatty and bile acid metabolic process and could be involved in gene networks for intramuscular fatty acid composition in porcine [128, 129]. *ABCC8* was reported to be selection region for intramuscular fat and backfat thickness in two Duroc populations, and the most down-regulated genes in the group with higher backfat thickness in Yimeng black pigs [126, 130]. *DEF6*

is linked with average backfat thickness [131]. *FKBP5* is associated with immunity, backfat thickness and leaf fat weight, significantly contributed to residual feed intake [79, 131–133]. Expression of this gene is inversely associated with the expression of lipolytic, lipogenic and adipogenic genes [134]. According to Gene Ontology terms, *LDB3* is associated with heart development and muscle structure development, related to muscle growth traits in pig and may have potential roles in environmental adaptation [135, 136]. *ARMC12* regulates spatiotemporal mitochondrial dynamics during spermiogenesis and is required for male fertility [137]. *BMPR1A* is associated with numerous developmental processes, identified as a novel candidate gene affecting the number of thoracic vertebrae in pigs, and regulates the development of hypothalamic circuits that are critical to the feeding behavior [138, 139]. Additionally, *BMPR1A* is important in brown fat development and involved in browning of white adipose tissue [140, 141]. *CCAR1* positively regulates adipocyte differentiation [142]. *CLPSL2* and *CLPS* are linked with digestion, lipid catabolic process, and response to food. *CLPSL2* could be involved in the regulation of acrosomal integrity, spermatozoa motility, and male fertility, while *CLPS* demonstrated effect on some characteristics connected with lean content of the carcass and fat content and affected intramuscular fat content [143–145]. It may be associated with former selection toward reduced fat content in carcass [114]. According to Gene Ontology terms, *COL13A1* is associated with skeletal system development, was under significant positive selection Yorkshire pigs and associated with fat deposition, as well as *HNRNPH3* [146–148]. *JMJD1C* is potentially associated with cold adaptation [149, 150]. It demonstrates the positive selection in regulation of various reproductive traits in pigs [151–154]. *JMJD1C* was identified in Tibetan pigs that are well adapted to the high altitude [155]. On the other hand, this gene have been associated with white blood cells in Large White pigs, identified as a novel regulator of adipogenesis and contributed to browning [156–158]. According to Gene Ontology terms, *MYOD1* and *MYPN* are strongly involved in skeletal muscle tissue development. It was reported about potential role of *MYOD1* in body-fat distribution regulation [159]. Mutations in the *MYOD1* gene show a significant effect on the pork meat quality and single nucleotide polymorphisms in the porcine *MYOD1* affected on meat quality traits and carcass traits in heavy pigs [160–162]. *MYPN* is related to body composition and can be considered as candidate for meat and carcass traits in pigs [163–165]. *NRBF2* is linked with energy metabolism and was specific selective for Tibetan pig [155]. *NUCB2* is expressed in fat depots of the pig and that level of expression is sensitive to stimulation of appetite-regulating pathways in the hypothalamus [166]. It plays an important role in whole-body energy homeostasis and body weight at puberty by regulation of appetite of Jinhua Pigs [126]. *NUCB2* is also involved in cold adaptation, indicating that central nesfatin-1 regulates thermogenesis [167, 168]. *REEP3* mediates adipogenic differentiation [169]. According to Gene Ontology terms, *SIRT1* is linked with regulation of lipid storage, white and brown fat cell differentiation, adipose tissue development, etc. It is implied in the browning of white adipose tissue, promotes lipid metabolism and mitochondrial biogenesis in adipocytes and coordinates abiogenesis by targeting key enzymatic pathways [170, 171]. Apart from that, it negatively correlates with intramuscular fat content and demonstrates protective role in skeletal muscle's adaptation to cold stress [172, 173]. *SNCG* controls metabolic functions in fat cells and belongs to white adipose tissue-selective genes [174, 175]. *ZNF76* is very close to peroxisome proliferative activated receptor delta (PPARD) at 35 Mb, which is a positional and physiological candidate for affecting backfat thickness [176]. *RNF213* is involved in adipogenesis and emerged as a link between obesity, inflammation, and insulin resistance [177, 178]. *SNORD14* were more expressed in Large White heavy pigs with high intramuscular fat content [179]. *U3* was identified as a promising candidate gene for average backfat thickness in multiple pig breeds and populations [180].

Annotated clusters with an enrichment coefficient $-\log10(p) > 1.3$ (corresponds to $p < 0.05$) were not determined for the Livni breed. However, 50 candidate genes were specific to Livni pigs. *DLGAP5* is a stillbirth associated gene involved in lipid deposition-related pathways and significantly associated with intramuscular fat content [181–183]. *ERCC4* is also associated with intramuscular fat content, presented in Tibetan wild boar and related to "response to UV" [151, 184, 185]. *GPR63* has been identified as a receptor for intercellular lipid messengers and associated with reproduction traits [186, 187]. According to Gene Ontology terms, *LDB3* is involved in heart and muscle structure development, while *PBX3* – in various important developmental processes. *PDZRN3* and *ATG14* could affect intramuscular fat content in Suhuai pigs [183, 184]. They are involved in adipocyte differentiation, demonstrating negatively influence [188, 189]. *RBM15B* is linked with average daily gain in Italian Large White pigs, while *TBPL2* – with fertility [190, 191]. *WDHD1* is associated with stillbirth in Large White sows and residual feed intake [79, 181]. According to Gene Ontology terms, *BMPR1A* is associated with immunity, bone, lung and heart development. *BMPR1A* is reported to be associated with obesity and important for brown adipocytes, candidate gene affecting the number of thoracic vertebrae in a Large White × Minzhu intercross pigs [138, 192–194]. *DOCK3* is linked with fatness and growth in Huainan pigs [195]. *LGALS3* is linked with immunity, sensitive to cold exposure, associated with stillbirth, and involved in adipogenesis [181, 196–198]. *GLUD1* is an important gene for metabolic process, increased by cold exposure and essential for brown adipocytes [199, 200]. *MANF* positively regulates thermogenesis, resists obesity, as well as regulates hypothalamic control of food intake and body weight [201–203]. *MAPK1IP1L* and *SOCS4*

are likely candidate genes for stillborn [181, 204]. According to Gene Ontology terms, *MEF2C* is involved in numerous developmental processes, may be a key gene in insulin-induced adipocyte differentiation, involved in fat deposition in pigs, important for foetal developmental, and associated with total number born and number born alive [205–207]. *WISP3* is linked with sketetal and muscular development [208]. *PDE10A* is associated with chest circumference in Yorkshire Pigs, back fat thickness at 100 kg in Landrace pigs, and contributes to the regulation of energy homeostasis [209–211]. *PARN* was identified as candidate genes associated with age at 100 kg in Large White pigs [212]. *TFAM* promotes mitochondrial DNA content, which necessary for increased fusion during cold adaptation [213]. Its amount significantly elevated after cold exposure and essential for thermoregulation [214, 215]. Mutation in the *TFAM* gene effects on fattening and carcass traits in commercial pig populations [216]. *TFAM* gene expression abundance in particular tissues such as liver and *L. dorsi* revealed some strong correlations with carcass and meat quality traits including marbling [217]. *SNORD22* is associated with trimmed thigh weight in Italian crossbred pigs [218]. *U4* and *ssc-mir-9-2* were previously determined in pigs [219, 220]. Genes associated with reproductive, meat and fat quality, carcass, and immunity traits in pigs were found in genomic regions affected by putative selection. Along with fatting genes, ones linked with thermogenesis were unexpectedly detected which oppositely should led to fat reduction. However, pigs could not have brown adipocytes but could have beige ones, which are very important for maintaining alternative mechanisms of thermoregulation in pigs that possibly avoid fat reduction [221–224].

CONCLUSION

The dramatic reduction of local pig breeds during last 30 years finally led to 0.56% of the total pig population in the RF, mainly Livni, Altai, and Tsivilsk breeds. There are several reasons for the reduction of local pig breeds: a trend to the reduction the total amount of fat on pork carcass and in meat and the aggressive implementation of the Western commercial breeds. Commercial breeds were bred without taking into account Russia environment, the quality and composition of feed and drinking water. Local pigs bred in the USSR are characterized by unpretentiousness to feed, stress and cold resistance, as well as precocity and high productivity. Livni is one of the Russian local pig breeds. Landrace and the Large White breeds participated in creation of the Livni breed, but obtained breed relationship and admixture results indicated the insignificant participation of these breeds in the formation of the modern allelofund of Livni pigs. The largest amount of common genes was detected between the Livni and Large White breeds. Genes involved in glucose metabolism, namely *G6PC2*, *HKDC1*, and *HK1* are critical for glucose homeostasis, which could effect on the growth and meat quality traits, as well as on thermogenesis. Other genes were associated with immunity, related to percentage of certain fiber types, growth traits, average daily gain and lean meat percentage, intramuscular fat and backfat thickness, etc. Among 35 common genes of the Livni and Landrace breeds, enrichment with *HOXD* genes was observed. *HOXD* genes are involved in various developmental processes, such as single fertilization, skeletal muscle tissue development, adult locomotory behaviour, embryonic skeletal system morphogenesis, lipid metabolism, etc., and are associated with traits such as growth, body weight and composition, fat development, organogenesis and feed intake, etc. Candidate genes associated with various growth, carcass and reproductive traits and essential for thermoregulation were specific to Livni pigs. Livni breed belongs to the meat-and-fat type, but during development pigs could be also meat and fat types. The analysis of genetic architecture confirmed the unique structure of local breed that was bred using commercial Landrace and the Large White breeds. During formation own allelofund, the Livni breed fixed important traits, including flexibility during growing and feeding.

CONTRIBUTION

I.M. Chernukha conceived and designed the study. I.M. Chernukha, L.V. Fedulova and E.A. Kotenkova designed the methodology. L.V. Fedulova and E.A. Kotenkova analysed and described the results. I.M. Chernukha and E.A. Kotenkova wrote the manuscript. All authors contributed to data interpretation.

CONFLICT OF INTEREST

The authors declared no conflict of interest regarding the publication of this article.

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