

Supplemental Table S13. Functional candidate genes under breed-specific selection in Rongchang (nine fat deposition genes), Jinhua pigs (six fat deposition genes) and Tibetan wild boar (16 high-altitude adaptation genes).

Chr.	Start	End	FDR	Gene symbol	Gene name	Associated phenotypes	Functional description
Rongchang (9 genes)							
6	65,800,001	65,830,000	7.96E-03	<i>NPPA</i>	Natriuretic peptide A		<i>NPPA</i> encoding the precursor of atrial natriuretic peptide, may serve as a part of the extended endocrine network that regulates cardiovascular and metabolic homeostasis ⁴⁶ , and is associated with hypertension ⁴⁷ , stroke, heart failure ⁴⁸ , type II diabetes and obesity ⁴⁹ .
8	55,220,001	55,360,000	0.00E+00	<i>NPY1R</i>	Neuropeptide Y receptor Y1	Feed intake and energy homeostasis	Hypothalamus plays a key role in energy homeostasis and a number of hypothalamic neuropeptides are involved in physiological control of feeding regulation and energy homeostasis ^{50,51} . <i>NPY1R</i> and <i>NPY5R</i> are two transmembrane proteins being abundantly expressed in the hypothalamus and mediate the function of neuropeptide Y (NPY) ⁵² . Both <i>NPY5R</i> and <i>NPY1R</i> are implicated in the orexigenic effects of NPY ⁵³ , and are positively correlated with energy intake and weight gain ^{54,55} .
8	55,220,001	55,360,000	0.00E+00	<i>NPY5R</i>	Neuropeptide Y receptor Y5		See functional description for <i>NYP1R</i> .
8	1,820,001	1,850,000	1.99E-02	<i>LRPAP1</i>	Low density lipoprotein receptor-related protein-associated protein 1	Lipid metabolism	As a lipid metabolizing gene, <i>LRPAP1</i> interacts with the low density lipoprotein (LDL) receptor-related protein and facilitates its proper folding and localization by preventing the binding of ligands ⁵⁶ . The polymorphisms of <i>LPRAP1</i> have been associated with body mass index in human ^{57,58} and carcass composition traits in chicken ⁵⁹ .
11	70,680,001	70,720,000	1.04E-03	<i>ABCC4</i>	ATP-binding cassette sub-family C member 4		<i>ABCC4</i> , also known as the multidrug resistance-associated protein 4 (<i>MRP4</i>) or multi-specific organic anion transporter B, is a basolateral efflux transporter that pumps various endogenous and exogenous chemicals from hepatocytes to blood ^{60,61} . The expression of <i>ABCC4</i> in liver was associated with residual feed intake (a measure of feed efficiency) in beef cattle ⁶² , and fat mass in mouse ⁶³ .
8	1,240,001	1,290,000	4.70E-04	<i>ADD1</i>	Adducin α	Obesity-induced	<i>ADD1</i> , a family of cytoskeleton proteins, is known to increase renal sodium reabsorption and may be involved in the

						hypertension, inflammatory signaling and insulin resistance	pathophysiology of essential hypertension, which is a common comorbidity of obesity ⁶⁴⁻⁶⁶ .
13	1,410,001	1,480,000	0.00E+00	<i>PIK3R4</i>	Phosphoinositide-3-kinase, regulatory subunit 4		<i>PIK3R4</i> plays a regulatory role in the phosphoinositide 3 kinase complex ⁶⁷ , are is involved in cellular response to glucose starvation ⁶⁸ and insulin receptor signaling pathway ⁶⁹ .
15	112,470,001	112,530,000	0.00E+00	<i>HSPD1</i>	Heat shock 60kDa protein 1		<i>HSPD1</i> , also known as <i>HSP60</i> , exerts autocrine/paracrine effects on adipocytes characterized by an increased release of proinflammatory adipokines ⁷⁰ , increased obesity-related inflammatory signaling ⁷¹ and insulin resistance ⁷² .
17	64,900,001	64,930,000	6.86E-03	<i>RAE1</i>	Ribonucleic acid export 1		<i>RAE1</i> , a high affinity ligand of the natural killer group 2, member D (<i>NKG2D</i>) receptor, is highly expressed under stressful environments ⁷³ . The activating receptor <i>NKG2D</i> is thought to be directly involved in the progression of type I diabetes ⁷⁴ . The delivered therapeutic <i>RAE1</i> plasmid showed a delay in the incidence of diabetes without a sharp decline of body weight and survival rate in mouse model ⁷⁵ .
Jinhua (6 genes)							
2	132,180,001	132,240,000	8.93E-06	<i>CEP120</i>	Centrosomal protein of 120 kDa	Feed intake and energy homeostasis	<i>CEP120</i> , a centrosomal protein, is preferentially expressed in neural progenitors, is involved in controlling interkinetic nuclear migration ⁷⁶ , and is also essential for centriole assembly ^{77,78} .
8	38,180,001	38,220,000	1.73E-03	<i>GABRA2</i>	γ -amino butyric acid α 2 receptor subunit		<i>GABRA2</i> , a major inhibitory neurotransmitter in the mammalian brain, is a predictor for alcoholism ^{79,80} , and associated with elevated body mass index regardless of the presence/absence of obesity and impulsiveness ⁸¹ .
15	42,760,001	42,830,000	0.00E+00	<i>ANGPT2</i>	Angiopoietin-2		<i>ANGPT2</i> , a marker of endothelial cell activation ⁸² , is crucial for controlling adipose vascular function, which is part of an adaptation to increased adipose tissue metabolism ^{83,84} .
18	6,110,001	6,150,000	9.25E-04	<i>PRKAG2</i>	AMP-activated, γ -2 non-catalytic subunit	Lipid metabolism	<i>PRKAG2</i> , a member of the AMP-activated protein kinase (AMPK) γ subunit family ⁸⁵ . AMPK is a metabolic regulator that monitors cellular energy status and functions by inactivating key enzymes involved in regulating <i>de novo</i> biosynthesis of fatty acid and cholesterol ^{86,87} , making it a key gene in the molecular regulation of feed efficiency ^{88,89} .
2	88,180,001	88,220,000	5.27E-04	<i>TBCA</i>	Tubulin-specific chaperone A	Obesity-induced hypertension, inflammatory signaling and insulin resistance	<i>TBCA</i> interacts with β tubulin and is involved in the folding and dimerization of new tubulin heterodimers, the building blocks of microtubules ⁹⁰ . The deletion variations of <i>TBCA</i> has been shown to contribute to genetic susceptibility of common childhood obesity ^{91,92} .
6	27,500,001	27,530,000	3.10E-02	<i>MMP2</i>	Matrix metalloproteinase 2		<i>MMP2</i> is suggested to be involved in the development of various clinical factors of metabolic syndrome, which plays an important

role in adipose tissue development by cleave insulin-like growth factor-binding proteins and release insulin-like growth factors⁹³. Additionally, tissue degradation by *MMP2* is pivotal to inflammation⁹⁴ and obesity is associated with low grade inflammation⁹⁵⁻⁹⁷.

Tibetan wild boar (16 genes)

2	75,150,001	75,190,000	7.43E-03	<i>MAP2K2</i>	Mitogen-activated protein kinase kinase 2	Hypoxic response	<i>MAP2K2</i> , also known as <i>MEK2</i> , activates the ERK1 and ERK2 MAP kinases ⁹⁸ . In the MAPK pathway ⁹⁹ , <i>MAP2K2</i> has been shown to be down-regulated in the hypoxia condition ¹⁰⁰ .
2	82,690,001	82,730,000	7.43E-03	<i>UNC5A</i>	Unc-5 netrin receptor A		<i>UNC5A</i> belongs to a family of netrin-1 receptors ¹⁰¹ , which could promote neuronal apoptosis during spinal cord development ¹⁰² . The neuronal guidance molecule netrin 1 could be induced by hypoxia-inducible factor 1 α (<i>HIF-1α</i>) under the hypoxic condition ¹⁰³ .
8	9,990,001	10,010,000	6.56E-01	<i>CPEB2</i>	Cytoplasmic polyadenylation element binding protein 2		<i>CPEB2</i> encodes an RNA-binding protein that participates in translational control ¹⁰⁴ , which interacts with eukaryotic elongation factor 2 to modulate the translation of <i>HIF-1α</i> (a master regulator of oxygen homeostasis) by bind to <i>HIF-1α</i> mRNA 3'-UTR ^{105 106} .
13	32,160,001	32,190,000	1.64E-02	<i>CXCR6</i>	Chemokine (C-X-C motif) receptor 6		<i>CXCR6</i> encodes a member of chemokine receptor families, could facilitate immune responses via cell-cell contact, and guide the trafficking of T-cells ^{107,108} . <i>CXCR6</i> has important roles in tumorigenesis ¹⁰⁹ and contributes significantly to cell migration during hypoxia by regulated expression of the <i>HIF-1α</i> ¹¹⁰ .
13	32,580,001	32,610,000	1.64E-02	<i>LTF</i>	Lactotransferrin		Lactotransferrin, also known as lactoferrin, is the cationic transferrin of exocrine secretions (milk, lacrimal fluid, saliva, etc.) and a key component of innate immune defense ^{111,112} . Lactoferrin plays crucial roles in hypoxic pulmonary hypertension and vascular remodeling ¹¹³ . Apo-form of lactoferrin performs as a normoxic mimetic of hypoxia, capable of stabilizing <i>HIF-1α</i> ¹¹⁴ .
6	112,290,001	112,360,000	0.00E+00	<i>RPRD1A</i>	Regulation of nuclear pre-mRNA domain containing 1A		Content of hemoglobin
17	39,120,001	39,150,000	2.21E-02	<i>SLC52A3</i>	Solute carrier family 52 (riboflavin	<i>SLC52A3</i> encodes a vitamin B2 transporter protein that plays a role in intestinal absorption of vitamin B2 ^{118,119} . Mutations in <i>SLC52A3</i> are associated with increased mean corpuscular	

					transporter), member 3		hemoglobin concentration (Mouse Genome Informatics, Supplemental URLs), which probably contribute to the metabolically active form of vitamin B2, aids in the synthesis of hemoglobin and enhances oxygen binding ¹²⁰ .
12	23,250,001	23,300,000	2.57E-03	<i>CDK12</i>	Cyclin-dependent kinase 12	Maintaining genomic stability against solar UV	<i>CDK12</i> , a member of cyclin-dependent kinase, acts as a key regulator of transcription via phosphorylating the C-terminal domain of the large subunit of RNA polymerase II ¹²¹ . <i>CDK12</i> promotes homologous recombination repair ¹²² and maintains genomic stability via regulation of expression of DNA damage response genes ^{123,124} .
3	55,770,001	55,800,000	4.06E-02	<i>TBC1D8</i>	TBC1 domain family, member 8	Hair follicle maturation	<i>TBC1D8</i> acts as a GTPase-activating protein for Rab family proteins ¹²⁵ and is involved in hair follicle maturation ³⁶ .
15	104,080,001	104,150,000	5.78E-06	<i>COL3A1</i>	Collagen, type III, α 1	Assembly of collagen in skin	<i>COL3A1</i> and <i>COL5A</i> encode two fibrillar collagens that are found in extensible connective tissues such as skin, lung, uterus, intestine and the vascular system ¹²⁶ . Mutations in <i>COL3A1</i> are associated with Ehlers-Danlos syndrome (EDS) type IV characterized by thin, pale and translucent skin and fragile blood vessels ^{127,128} . Mutations in <i>COL5A2</i> are associated with EDS types I and II characterized by severe skin involvement for type 1 and mild to moderate skin involvement for type 2 ^{129,130} .
15	104,080,001	104,150,000	5.78E-06	<i>COL5A2</i>	Collagen, type V, α 2		See functional description for <i>COL3A1</i> .
1	6,400,001	6,430,000	1.77E-02	<i>QKI</i>	KH domain containing, RNA binding		<i>QKI</i> belongs to the family of highly conserved RNA binding proteins ¹³¹ , which regulate circRNA formation during epithelial-mesenchymal transition ¹³² ; and is a critical regulator of vascular smooth muscle cell phenotype ^{133,134} .
3	7,310,001	7,350,000	1.89E-03	<i>STAG3</i>	Stromal antigen 3	Development of cardiovascular system	<i>STAG3</i> encodes a subunit of cohesin, a large protein complex that is essential for proper pairing and segregation of chromosomes during meiosis ¹³⁵ , and is associated with female infertility ¹³⁶ and Williams–Beuren syndrome characterized by supravalvular aortic stenosis, multiple peripheral pulmonary arterial stenoses, 'elfin face', mental and statural deficiency ¹³⁷ .
9	13,070,001	13,110,000	2.43E-03	<i>PAK1</i>	P21 protein (Cdc42/Rac)-activated kinase 1		<i>PAK1</i> encodes a family member of serine/threonine p21-activating kinases, is a critical effector that link RhoGTPases to cytoskeleton reorganization and nuclear signaling ¹³⁸ . <i>PAK1</i> is essential for protective physiological cardiac remodeling by maintaining ventricular Ca^{2+} homeostasis and electrophysiological stability under hypertrophic stress condition ¹³⁹⁻¹⁴¹ .
12	23,250,001	23,300,000	2.57E-03	<i>MED1</i>	Mediator complex subunit 1		<i>MED1</i> , a key subunit of the mediator complex, interacts with nuclear receptors to target gene-specific transcription ¹⁴² , which

is critical for postnatal cardiac growth and development^{143,144}. Mutations in *MED1* of mouse have been associated with abnormal heart morphology (Mouse Genome Informatics, Supplemental URLs).

15	96,990,001	97,030,000	3.00E-03	<i>PDE1A</i>	Phosphodiesterase 1A
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PDE1A, a member of the PDE1 family, is a Ca²⁺/calmodulin-dependent phosphodiesterase that plays a role in signal transduction by regulating intracellular cyclic nucleotide concentrations¹⁴⁵ and is involved in aging-related loss of vasodilator function, vascular smooth muscle cells senescence, increased blood pressure and vascular hypertrophy^{146,147}.
