Table S2. Genetically modified large animal models of human diseases over the past five years

Diseases type	Application	Gene	Species	Modification	Gene editing systems	Phenotypes	Gene information	Ref
Nervous system diseases	PD	*PINK/DJ-1*	monkey	Mutation	AAV9-CRISPR/ Cas9	Classic PD symptoms and key pathological hallmarks of PD	PINK：PTEN induced kinase 1. It plays roles in protecting cells from stress-induced mitochondrial dysfunction. DJ-1：parkinsonism associated deglycase. It protects neurons against oxidative stress and cell death.	(1)
	PD	*PINK1*	monkey	Knockout	CRISPR/ Cas9	Robust early-onset neurodegeneration	PTEN induced kinase 1. It is thought to protect cells from stress-induced mitochondrial dysfunction.	(2)
	PD	*PINK1*	monkey	Knockout	CRISPR/Cas9 & AAV9	PINK1 kinase selectively expression and neurodegeneration		(3)
	PD	*SCNA*	pig	Mutation	CRISPR/Cas9 & SCNT	Can’t detect PD-specific pathological changes at three months	Sodium voltage-gated channel alpha subunit 1. It regulates sodium exchange between intracellular and extracellular spaces and is essential for the generation and propagation of action potentials in muscle cells and neurons.	(4)
	AD	*hAPP/hTau/ hPS1*	pig	Mutation	multi-cistronic vector & SCNT	Expressed transgenes high in brain along with high level Aβ-40/42, total Tau, and GFAP	APP: amyloid beta precursor protein, a cell surface receptor and transmembrane precursor protein. After cleaved by secretases, the products could promote transcriptional activation. Tau: microtubule-associated protein tau.	(5)

							PS1: presenilin 1. Its mutations result in increased production of the longer form of amyloid-beta.	
	HD	*HTT*	pig	Knock-in	CRISPR/Cas9 & SCNT	Striking and selective degeneration of striatal medium spiny neurons, behavioral abnormalities, and early death	Huntingtin. A disease gene linked to Huntington's disease.	(6)
	LS	*SURF1*	pig	Knockout	TALENs and CRISPR/Cas9 & SCNT	No obvious COX deficiency in SURF1$^{-/-}$ tissues; delayed central nervous system development in newborn SURF1$^{-/-}$ piglets	SURF1 cytochrome C oxidase assembly factor. It is considered to be involved in the biogenesis of the cytochrome c oxidase complex.	(7)
	CLN1	*PPT1*	sheep	Mutation	CRISPR/Cas9 & zygote injection	Reduced PPT1 enzyme activity, behavioral and motor deficits and complete loss of vision as well as increased ventricular volume	Palmitoyl-Protein thioesterase 1. It involved in the catabolism of lipid-modified proteins during lysosomal degradation.	(8)
	ASD	*SHANK3*	monkey	Mutation	CRISPR/Cas9 & embryo injection	Sleep disturbances, motor deficits, increased repetitive behaviors, and social and learning impairments	SH3 and multiple ankyrin repeat domains 3. It is a multidomain scaffold protein of the postsynaptic that connect neurot density ransmitter receptors, ion channels, and other membrane proteins to the actin cytoskeleton and G-protein-coupled signaling pathways.	(9)
	ASD	*SHANK3*	monkey	Mutation	CRISPR/Cas9	Delayed vocalization, significant stereotypic and anxiety-like behaviors, impaired social interaction, reduced eye contact and brain activity		(10)
	ASD	*giant ANK2*	monkey	Knockout	CRISPR/Cas9	No typical ASDs-like behaviors but drastic brain structural	Ankyrin 2. It links the integral membrane proteins to the underlying spectrin-actin	(11)

						alteration	cytoskeleton.	
	RTT	*MECP2*	monkey	Mutation	TALEN	Physiological, behavioral, and structural abnormalities	Methyl-CpG binding protein 2. It has a binding ability specifically to methylated DNA.	(12)
	behavior abnormality	*TPH2*	pig	Knockout	CRISPR/Cas9 & SCNT	Impaired survival and growth rates were before weaning	Trypterin-dependent aromatic acid hydroxylase. It catalyzes the first step and also acts as a rate limiting step in the biosynthesis of serotonin, an important hormone and neurotransmitter.	(13)
	TSC	*TSC1*	pig	Mutation	CRISPR/Cas9 & SCNT	Cardiac rhabdomyoma and subependymal nodules	Growth inhibitory protein hamartin encoding protein. It works as a tumor suppressor gene that encodes the growth inhibitory protein hamartin.	(14)
	STXBP1-E	*STXBP1*	monkey	Mutation	Base editing	focal epilepsy	Syntaxin Binding Protein 1. It functions in releasing of neurotransmitters via regulation of syntaxin, a transmembrane attachment protein receptor.	(15)
	Genetic Ataxia Telangiectasia	*ATM*	pig	Knockout	Vector & SCNT	Infertile $ATM^{-/-}$ females, abnormal thymus structure and altered immune system in all pigs	ATM serine/threonine kinase. It is an important cell cycle checkpoint kinase.	(16)
Cardiovascular and metabolic diseases	CHD	*SAP130*	pig	Mutation	CRISPR–Cas9	Tricuspid dysplasia with tricuspid atresia	A subunit of the histone deacetylase.	(17)
	HCM	*MYH7*	pig	Mutation	TALEN & SCNT	Died within 24h post partem and mild myocyte disarray, malformed nuclei, and	Myosin heavy chain 7. beta (or slow) heavy chain subunit of cardiac myosin encoding protein.	(18)

						MYH7-overexpression		
	HB	*F9*	pig	Knockout Knock-in	CRISPR/Cas9 & SCNT	Multiple spontaneous joint bleeding episodes, improved bleeding after carrying human coagulation factor IX	Coagulation factor IX, an inactive zymogen. The activated factor IX in the blood coagulation cascade is to activate factor X to its active form through interactions with Ca^{+2} ions, membrane phospholipids, and factor VIII.	(19)
	cardiomyopathy	SGCD	pig	Knockout	TALEN	systolic dysfunction, myocardial tissue degeneration, and sudden death	Sarcoglycan delta, a subcomplex of the dystrophin-glycoprotein complex (DGC) encoding protein, which forms a link between the F-actin cytoskeleton and the extracellular matrix.	(20)
	Congenital hypothyroidism	*DUOX2*	pig	Mutation	ENU	Overt goiters; dysplastic thyroid glands	Dual oxidase 2, a glycoprotein and a member of the NADPH oxidase family encoding protein.	(21)
	Diabetes mellitus	*INS*	pig	Knockout	CRISPR/Cas9 & SCNT	High blood glucose levels and the expression of insulin in the pancreas was absent	Insulin, a peptide hormone that plays a vital role in the regulation of carbohydrate and lipid metabolism.	(22)
	Pancreatic Endocrine	*NGN3*	pig	Knockout	CRISPR/Cas9 & SCNT	Lost expression of insulin, glucagon, and somatostatin	Neurogenin 3, a basic helix-loop-helix (bHLH) transcription factor involved in neurogenesis.	(23)
	T2DM	*hIAPP*	pig	Knock-in	CRISPR/Cas9 & SCNT	Hyperglycemia, decreased glucose utilization and increased insulin tolerance	Islet amyloid polypeptide, it regulates blood glucose levels and acts as a satiation signal.	(24)
	PNDM	*GCK*	dog	Mutation	BE3	High blood glucose levels	Glucokinase, it produces glucose-6-phosphate	(25)

	CVD	*ASGR1*	pig	Knockout	CRISPR/Cas9	Decreased synthesis of hepatic de novo cholesterol, lower non-HDL-C level and less atherosclerotic lesions	Asialoglycoprotein receptor 1, and plays a critical role in serum glycoprotein homeostasis.	(26)
	atherosclerosis	*ApoE*	pig	Knockout	CRISPR/Cas9	Severe hypercholesterolemia and atherosclerotic lesions in the aorta and coronary arteries after feeding on HFHC diet for 6 months	Apolipoprotein E, a major apoprotein of the chylomicron encoding protein, is essential for the normal catabolism of triglyceride-rich lipoprotein constituents.	(27)
	cardiovascular disease	*ApoE* *LDLR*	pig	Knockout	CRISPR/Cas9	Elevated levels of LDL-C, total cholesterol (TC) and ApoB	ApoE: Apolipoprotein E, a major apoprotein of the chylomicron encoding protein, is essential for the normal catabolism of triglyceride-rich lipoprotein constituents. LDLR: Low density lipoprotein receptor, binds low density lipoprotein/cholesterol and is taken into the cell.	(28)
	Hypercholesterolaemia	*OSBPL2*	pig	Mutation	CRISPR/Cas9 & SCNT	Progressive hearing loss (HL) with degeneration of cochlea hair cells and hypercholesterolaemia.	Oxysterol binding protein like 2, can bind strongly to phosphatic acid and weakly to phosphatidylinositol 3-phosphate.	(29)
	atherosclerosis	*ApoE*	dog	Knockout	CRISPR/Cas9 & SCNT	Hypercholesterolemia and severe atherosclerosis, stroke and gangrene	Apolipoprotein E, a major apoprotein of the chylomicron encoding protein, is essential for the normal catabolism of triglyceride-rich lipoprotein constituents.	(30)
	MC3R-KO	*MC3R*	pig	Knockout	CRISPR/Cas9 & SCNT	Increased body weight and body fat	Melanocortin 3 receptor, plays a role in the regulation of energy homeostasis.	(31)
	metaflamma	*GIPR*^{dn}	pig	Knock-in	CRISPR/Cas9	Activated CD8+ T cell function in	GIPR: Gastric inhibitory polypeptide	(32)

	tion	*/hIAPP/PNPLA3^{I148M}*				liver and visceral adipose under short-term diet intervention	receptor, it stimulates insulin release in the presence of elevated glucose. IAPP: islet amyloid polypeptide, it regulates blood glucose levels and acts as a satiation signal. PNPLA3: patatin like phospholipase domain containing 3, it mediates triacylglycerol hydrolysis in adipocytes.	
	Vascular health	*UCP1*	pig	Knock-in	CRISPR/Cas9 & SCNT	Less severe DMHC-induced arterial narrowing and atherosclerotic lesions	Uncoupling protein 1, it separates oxidative phosphorylation from ATP synthesis with energy dissipated as heat.	(33)
	tyrosinemia type 1	*FAH/HPD*	pig	Mutation	CRISPR/Cas9 & cytoplasmic microinjection	Reprogrammed tyrosine metabolism pathway and decreased LLI	FAH: fumarylacetoacetate hydrolase, last enzyme in the tyrosine catabolism pathway. HPD: 4-hydroxyphenylpyruvate dioxygenase, an enzyme in the catabolic pathway of tyrosine.	(34)
	phenylketonuria	*PAH*	pig	Knockout	CRISPR/Cas9	Classical PKU, juvenile growth retardation, hypopigmentation, ventriculomegaly, and decreased brain gray matter volume	Phenylalanine hydroxylase, the encoded phenylalanine hydroxylase enzyme hydroxylates phenylalanine to tyrosine and is the rate-limiting step in phenylalanine catabolism.	(35)
	phenylketonuria	*PAH*	pig	Mutation	TALEN	Hypopigmented and low birthweight, no detectable enzymatic activity		(36)
Immune system	systemic lupus	*leptin*	pig	Transgenic	Transgenic	Anemia, leukopenia, and thrombocytopenia as well as	Leptin, plays a major role in the regulation of energy homeostasis,	(37)

diseases	erythematosus					kidney and liver impairment	activates downstream signaling pathways that inhibit feeding and promote energy expenditure.	
	C3-KO pigs	*C3*	pig	Knockout	CRISPR/Cas9	Undetectable plasma C3 protein and the hemolytic complement activity	C3: complement C3, involving in the activation of complement system.	(38)
	CAPS	*NLRP3*	pig	Mutation	CRISPR/Cpf1 & SCNT	Early mortality, poor growth, and spontaneous systemic inflammation symptoms	NLRP3: NLR family pyrin domain containing 3, interacting with the apoptosis-associated speck-like protein and it is a member of the NLRP3 inflammasome complex, an upstream activator of NF-κB signaling and plays role in the regulation of inflammation	(39)
	Acne inversa	*NCSTN*	pig	Mutation	SCNT	Thickness of the epidermis and elevated inflammatory cytokines	Nicastrin, cleaves integral membrane proteins, including Notch receptors and beta-amyloid precursor protein, and may be a stabilizing cofactor required for gamma-secretase complex assembly.	(40)
	HEV infection	J_H	pig	Knockout	CRISPR/Cas9	Lower B lymphocytes and decreased HEV replication，HEV-infected $J_H^{-/-}$ pigs had enlarged livers	J_H: Ig heavy chain	(41)
	SARS-COV-2	*ACE2*	pig	Knock-in	CRISPR/Cas9 & SCNT	Similar expression patterns of hACE2 in the lung, kidney, testis, and intestine in hACE2-pigs to human	Angiotensin converting enzyme 2, catalyzes the cleavage of angiotensin I into angiotensin 1-9, and angiotensin II into the vasodilator angiotensin 1-7; may	(42)

							play a role in the regulation of cardiovascular and renal function, as well as fertility.	
Xenotransplantation	quadruple modified pigs	*CMAHKO/GTKO/shTNFRI-Fc/HO-1*	pig	Knockout	TALEN & SCNT	Decreased expression of Neu5Gc in piglets, reduced immuno-reactivity	CMAHP: Cytidine Monophospho-N-Acetylneuraminic acid hydroxylase, pseudogene. Involving in ligand-receptor, cell-cell, and cell-pathogen interactions. GGTA1: glycoprotein Alpha-galactosyltransferase 1 (inactive); aberrant expression of the GGTA1 protein in man can lead to autoimmune diseases and sometimes germ cell tumors. TNFR1: TNF Receptor Superfamily Member 1A; it plays a role in cell survival, apoptosis, and inflammation. HMOX1: heme oxygenase 1; it cleaves heme to form biliverdin.	(43)
	pig-to-rhesus renal xenograft	*GGTA1/B4GALNT2*	pig	Knockout	CRISPR/Cas9	Still existed CDC and flow cross-match, IgM antibody-mediated rejection in early-stage, IgG antibody-mediated rejection in 435-day graft loss	GGTA1: glycoprotein Alpha-galactosyltransferase 1 (inactive); aberrant expression of the GGTA1 protein in man can lead to autoimmune diseases and sometimes germ cell tumors. B4GALNT2: Beta-1,4-N-Acetyl-galactosaminyltransferase 2; catalyzing the last step in the	(44)

							biosynthesis of the human Sd(a) antigen	
	pig-to-rhesus kidney xenograft	*GGTA1KO/CD55*	pig	Knockout Transgenic	none	Dominated by CD4+ cell infiltration in early xenograft rejection and in late phase showing signs of chronic antibody rejection	GGTA1: glycoprotein Alpha-galactosyltransferase 1 (inactive); aberrant expression of the GGTA1 protein in man can lead to autoimmune diseases and sometimes germ cell tumors. CD55: CD55 molecule (cromer blood group); a glycoprotein involved in the regulation of the complement cascade.	(45)
	pig-to-mice skin xenograft	*GGTA1 /β2M/CIITA*	pig	Knockout	CRISPR/Cas9	Peripheral blood mononuclear cells less effective in inducing human T-cell activation and proliferation and prolonged organ survival of skin grafts form GBC-3KO pigs into mice	GGTA1: glycoprotein Alpha-galactosyltransferase 1 (inactive); aberrant expression of the GGTA1 protein in man can lead to autoimmune diseases and sometimes germ cell tumors. β 2M: Beta-2-microglobulin; a serum protein that MHC class I heavy chain on the surface of nearly all nucleated cells CIITA: class II major histocompatibility complex transactivator; a positive regulator of class II MHC gene transcription, and binds GTP and uses GTP binding to facilitate its own transport into the nucleus	(46)
	xenograft survival and function	*GTKO/HLA-G1*	pig	Knockout Knock-in	CRISPR/Cas9 & SCNT	Modulated the immune response by lowering IFN-g production by T cells and proliferation of CD4+	GGTA1: glycoprotein Alpha-galactosyltransferase 1 (inactive); aberrant expression of the GGTA1	(47)

						and CD8+ T cells, B cells and NK cells, as well as by augmenting SHP-2	protein in man can lead to autoimmune diseases and sometimes germ cell tumors. HLA-G1: major histocompatibility complex, class I, G. HLA class I heavy chain paralogues.	
	pigs-to-baboons lung xenograft	*GalTKO/hCD47*	pig	Knockout Transgenic	Transgenic	Lung xenografts successfully transplant into baboons, first certified durable macrochimerism beyond 8 weeks	GGTA1: glycoprotein Alpha-galactosyltransferase 1 (inactive); aberrant expression of the GGTA1 protein in man can lead to autoimmune diseases and sometimes germ cell tumors. CD47: CD47 molecule; it is involved in the increase in intracellular calcium concentration that occurs upon cell adhesion to extracellular matrix.	(48)
	Pig-to-human kidney xenograft	*GGTA*	pig	Knockout	-	Kidney xenografts viable and functioning in brain-dead human recipients for 54 hours, without signs of hyperacute rejection	Glycoprotein Alpha-galactosyltransferase 1 (inactive); aberrant expression of the GGTA1 protein in man can lead to autoimmune diseases and sometimes germ cell tumors.	(49)
	xenoorgan overgrowth	*GHR-KO/GGTA1KO/hCD46/hTHBD*	pig	Knockout	CRISPR/Cas9 & SCNT	Reduced body weight and heart weight of	GHR: growth hormone receptor, a transmembrane GGTA1: glycoprotein Alpha-galactosyltransferase 1 (inactive); aberrant expression of the GGTA1 protein in man can lead to autoimmune diseases and sometimes germ cell tumors.	(50)

							CD46: a type I membrane protein and a regulatory part of the complement system THBD: thrombomodulin; an endothelial-specific type I membrane receptor.	
	SCID pigs	*RAG2*	pig	Knockout	TALEN	Less gene expression of T/B cell or matured-NK cell in Rag-2 SCID pigs than Rag-2 SCID mice	Recombination activating 2; it plays roles in the initiation of V(D)J recombination during B and T cell development.	(51)
	immunodeficient	*RAG2/FAH*	pig	Knockout	CRISPR/Cas9	Can receive infusions of human liver cells, but the NK cell was a barrier to expand hepatocytes	RAG2: recombination activating 2; it plays roles in the initiation of V(D)J recombination during B and T cell development. FAH: fumarylacetoacetate hydrolase, the last enzyme in the tyrosine catabolism pathway.	(52)
	immune disorder	*IL2RG*	pig	Knockout	CRISPR/Cas9	Grow faster human melanoma-derived tumor	Interleukin 2 receptor subunit gamma; an important signaling component of many interleukin receptors.	(53)
	deficient pig	*RAG2/IL2RG*	pig	Knockout	CRISPR/Cas9	Human pancreatic adenocarcinoma to growth	RAG2: recombination activating 2; it plays roles in the initiation of V(D)J recombination during B and T cell development. IL2RG: Interleukin 2 receptor subunit gamma; an important signaling component of many interleukin receptors.	(54)
	PERV	*PERV*	pig	Knockout	CRISPR/Cas9 &	~100% PERV inactivation at the	porcine endogenous retrovirus	(55)

					SCNT	genomic DNA level		
Reproductive system and Embryonic development	folliculogenesis	*BMP15*	pig	Knockout	CRISPR/Cas9	Infertile gilts, streaky ovaries, absent obvious estrous cycles	BMP15: bone morphogenetic protein 15; it binds various TGF-beta receptors leading to recruitment and activation of SMAD family transcription factors that regulate gene expression. Important in oocyte maturation and follicular development.	(56)
	sex-reversal	*SRY*	pig	Knockout	CRISPR/Cas9	Genetically male (XY) pigs owing complete external and internal female genitalia	Sex determining region Y; a transcription factor, it initiates male sex determination	(57)
	sex-reversal	*SRY*	bovine	Knock-in	TALEN & SCNT	Only one ovary and was sterile		(58)
	embryonic development	*PDHA1*	pig	knockdown	CRISPR/Cas9	Blocked early embryonic development, decreased targeted nuclear histone acetylation and several zygotic genes	Pyruvate dehydrogenase E1 subunit Alpha 1; it catalyzes the overall conversion of pyruvate to acetyl-CoA and CO, and provides the primary link between glycolysis and the tricarboxylic acid (TCA) cycle.	(59)
	embryonic development	*OCT4 (POU5F1)*	bovine	Knockout	CRISPR/Cas9 & SCNT	Important roles of OCT4 in early development maternal and absent NANOG in later phase	POU class 5 homeobox 1; a transcription factor containing a POU homeodomain that plays a key role in embryonic development and stem cell pluripotency. Tumorigenesis.	(60)
	embryonic development		bovine	Knockout	CRISPR/Cas9	Prevented blastocyst formation and aberrant CDX2 expression		(61)
Other diseases	HGPS	*LMNA*	pig	Mutation	CRISPR/Cas9	Growth retardation, lipodystrophy, skin, bone	Lamin A/C; it is part of the nuclear lamina, a two-dimensional matrix of	(62)

						alterations, cardiovascular disease and die around puberty	proteins located next to the inner nuclear membrane; involving in nuclear stability, chromatin structure and gene expression.	
	HGPS	*LMNA*	monkey	Mutation	BEs & CRISPR/Cas9	Growth retardation, bone alterations, and vascular abnormalities		(63)
	perinatal lethality	*SIRT6*	monkey	Knockout	CRISPR/Cas9	Died hours after birth and exhibit severe prenatal developmental retardation	Sirtuin 6; exhibits ADP-ribosyl transferase and histone deacetylase activities, and it plays a role in DNA repair, maintenance of telomeric chromatin, inflammation, lipid and glucose metabolism.	(64)
	ADPKD	*PKD1*	monkey	Knockout	CRISPR/Cas9	Severe cyst formation primarily in collecting ducts or distal tubules, can survive after cyst formation, and cysts progress with age	Polycystin 1, Transient Receptor Potential Channel Interacting; functions as a regulator of calcium permeable cation channels and intracellular calcium homoeostasis. It is also involved in cell-cell/matrix interactions and may modulate G-protein-coupled signal-transduction pathways. It plays a role in renal tubular development, and mutations in this gene cause autosomal dominant polycystic kidney disease type 1 (ADPKD1).	(65)
	DMD	*DMD*	dog	therapy	AAV-CRISPR	The dystrophin in skeletal muscle and cardiac muscle all restored	Dystrophin. The encoded protein forms a component of the dystrophin-glycoprotein complex (DGC),	(66)
	DMD	*DMD*	pig	therapy	AAV-CRISPR	Improved skeletal muscle		(67)

						function in DMDΔ52 pig models	which bridges the inner cytoskeleton and the extracellular matrix.	
	DMD	*FSI-I-I*	pig	Knock-in	CRISPR/Cas9 & SCNT	larger myofiber sizes	Follistatin; a single-chain gonadal protein; it specifically inhibits follicle-stimulating hormone release. It also acts as a regulator of skeletal muscle development.	(68)
	DMD	*DMD*	dog	therapy	AAV-CRISPR	Restored dystrophin expression but occurred Cas9-specific immune response	Dystrophin. The encoded protein forms a component of the dystrophin-glycoprotein complex (DGC), which bridges the inner cytoskeleton and the extracellular matrix.	(69)
	Hair	*HR*	pig	Knockout	CRISPR/Cas9 & SCNT	Lack of hair on the eyelids, abnormalities in the thymus and peripheral blood	HR lysine demethylase and nuclear receptor corepressor; hair growth	(70)
	Hair	*FGF5*	sheep	Knockout	CRISPR/Cas9	Fast hair growth and actived hair-follicle density	Fibroblast growth factor 5; the fibroblast growth factor (FGF) family; it possesses broad mitogenic and cell survival activities, and is involved in a variety of biological processes	(71)
	Hair	*EDAR*	goat	Mutation	CRISPR/Cas9	Abnormal primary hair follicles	Ectodysplasin A receptor; it can activate the nuclear factor-kappaB, JNK, and caspase-independent cell death pathways. It is required for the development of hair, teeth, and other ectodermal derivatives.	(72)
	Hair	*VEGF*	goat	Knock-in	CRISPR/Cas9	Improved fibre length of this	Vascular endothelial growth factor A; it	(73)

						gene-edited goat was	induces proliferation and migration of vascular endothelial cells, and is essential for both physiological and pathological angiogenesis.	
	ED–9	*HOXC13*	pig	Knockout	CRISPR/Cas9	Abnormal hair follicles phenotypes, including reduced number of follicles, disarrayed hair follicle cable with abnormal hair all over the body	Homeobox C13; it may play a role in the development of hair, nail, and filiform papilla.	(74)
	harlequin ichthyosis	*ABCA12*	pig	Mutation	ENU	Hyperkeratotic skin. Prolonged life span after applied systemic retinoid treatment	ATP binding cassette subfamily A member 12; it acts as a ransport various molecules across extra- and intracellular membranes.	(75)
	AMS and OCA1	*TWIST2/TYR*	pig	Mutation	BE3 & SCNT	Ablepharon macrostomia syndrome and oculocutaneous albinism type 1, respectively.	TWIST2: twist family β HLH transcription factor 2; it may inhibit osteoblast maturation and maintain cells in a preosteoblast phenotype during osteoblast development and may be upregulated in certain cancers. TYR: Tyrosinase; catalyzes the first 2 steps, and at least 1 subsequent step, in the conversion of tyrosine to melanin.	(76)
	skeletal dysplasia	*COL2A1*	pig	Mutation	CRISPR/Cas9 & SCNT	Shortened long bones, abnormal vertebrae, depressed nasal bridge, cleft palate	Collagen type II alpha 1 chain; a fibrillar collagen.	(77)
	Anephrogen	*SALL1*	pig	Knockout	injecting	Nephrogenic defects	Spalt like transcription factor 1; a zinc	(78)

	ic phenotype						finger transcriptional repressor; it may be part of the NuRD histone deacetylase complex (HDAC)	
	HPP	*ALPL*	sheep	Mutation	CRISPR/Cas9	Reduced serum alkaline phosphatase activity, decreased tail vertebral bone size, and metaphyseal faring	Alkaline phosphatase, biomineralization associated; the alkaline phosphatase family of proteins.	(79)
	lung	*FGFR2-IIIb*	pig	Transgenic	Vector & SCNT	Smaller lobes and retardation of alveolarization	Fibroblast growth factor receptor 2; the extracellular portion of the protein interacts with fibroblast growth factors, setting in motion a cascade of downstream signals, ultimately influencing mitogenesis and differentiation.	(80)
	WS2A	*MITF*	pig	Mutation	ENU	HL and hypopigmentation, stria vascularis (SV), fused hair cells, the absence of endocochlear potential	Melanocyte inducing transcription factor; it regulates melanocyte development and is responsible for pigment cell-specific transcription of the melanogenesis enzyme genes	(81)
	WS2A	*MITF*	pig	therapy	CRISPR/Cas9	Rescued symptoms of WS2A, including anophthalmia and hearing loss		(82)
	MVID	*MYO5B*	pig	Mutation	TALEN	Villus blunting, as well as liver alterations, likely cholestasis formation	Myosin VB; together with other proteins, it may be involved in plasma membrane recycling.	(83)

Note: the gene information is quoted from GENECARD website.

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