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Functional expression and impact of testis-specific gene antigen 10 in breast cancer: a combined in vitro and in silico analysis

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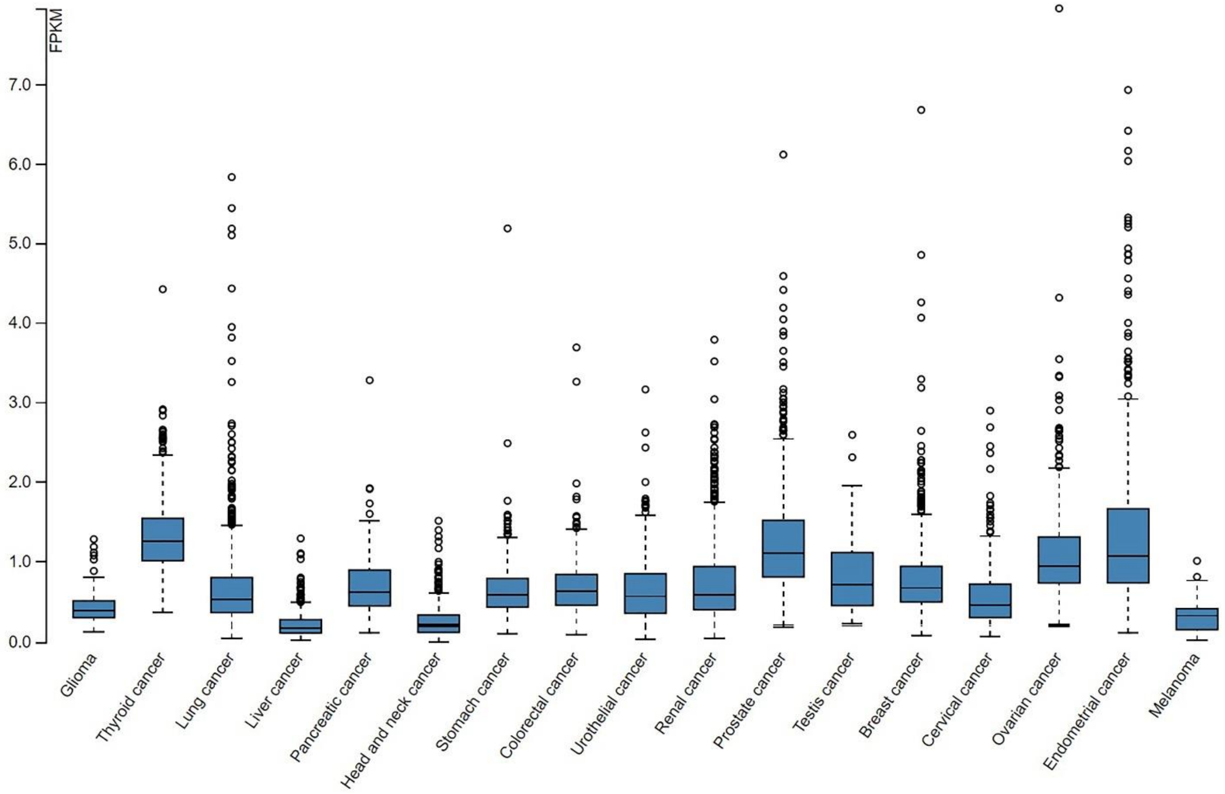

Fig. S1. RNA expression profile of TSGA10 protein based on the mRNA expression levels. In this overview plot the expression levels of TSGA10 in 17 different cancer tissues are represented. Data retrieved from the "The Cancer Genome Atlas" (TCGA).

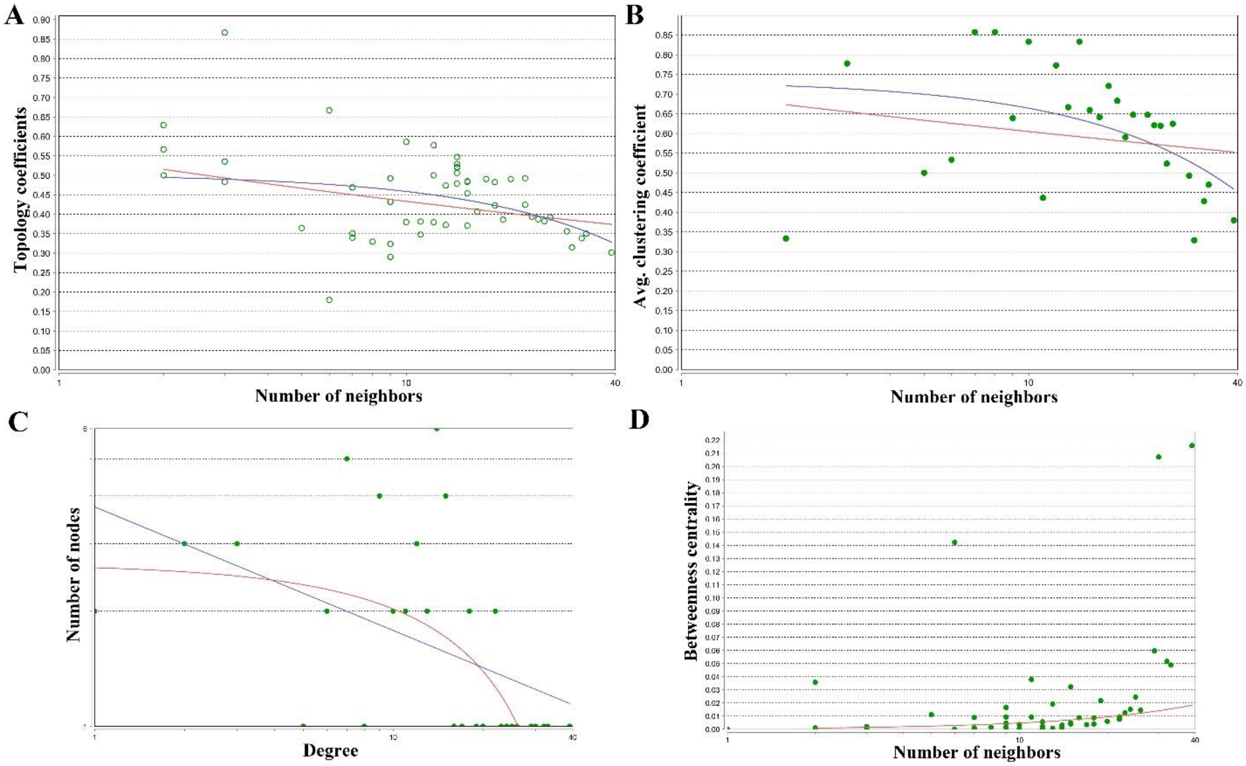

Fig. S2. **Topological characteristics of the PPI network. (A)** Topological coefficients plot. **(B)** Average clustering coefficient distribution. **(C)** Node degree distribution. **(D)** Betweenness centrality. The plots were generated by using the Network Analyzer of Cytoscape.

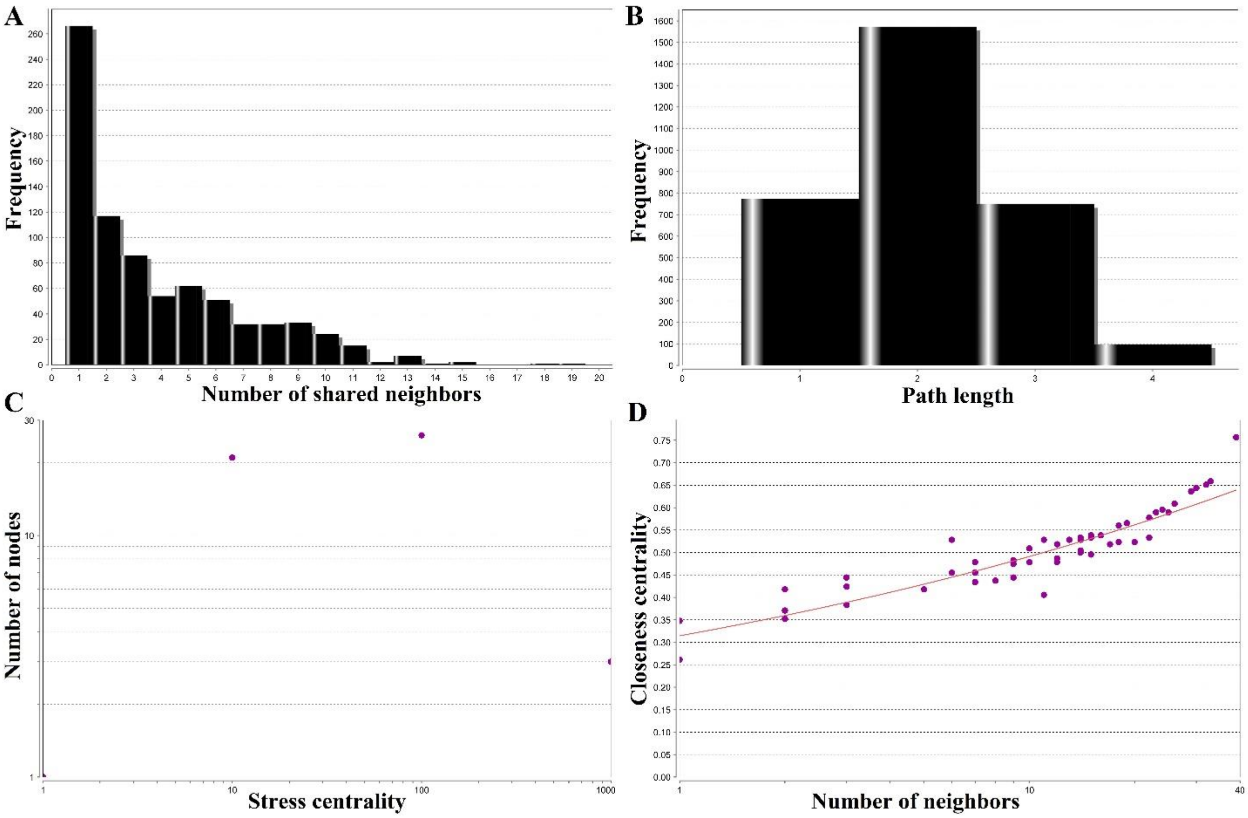

Fig. S3. Topological characteristics of the PPI network. (A) The distribution of shared neighbors. **(B)** Shortest path length distribution. **(C)** Stress centrality distribution. **(D)** closeness centrality. The plots were generated by using the Network Analyzer of Cytoscape.

Table S1. The cellular component (CC) ontology for the functional large modules.

ID	Name	GOTERM_CC_DIRECT
		Module 1
BACE1	Beta secretase 1	Endosome, Late endosome, Multi-vesicular body, Endoplasmic reticulum lumen, Golgi apparatus, trans-Golgi network, plasma membrane, Integral component of plasma membrane, Cell surface, Endosome membrane, Integral component of membrane, Axon, Cytoplasmic vesicle membrane, Cytoplasmic vesicle, Membrane raft, Golgi-associated vesicle lumen
LOC81691	Exonuclease NEF-Sp	Nucleolus, Extracellular exosome,
GGA3	Golgi associated, Gamma adaptin ear-containing, ARF binding protein 3	Trans-Golgi network, Endosome membrane, Clathrin adaptor complex
HIF1A	Hypoxia inducible factor 1 alpha Subunit	Nucleus, Nucleoplasm, Nuclear speck, Cytoplasm, Transcription factor complex , RNA polymerase II transcription factor complex, Axon cytoplasm, Motile cilium
SPAG16	Sperm associated antigen 16	Nucleus, Cytoplasm, Axoneme, Axonemal central apparatus, Motile cilium
SPAG6	Sperm associated antigen 6	Nucleus, Cytoplasm, Microtubule, Axoneme, Microtubule cytoskeleton, Motile cilium
TEKT3	Tektin 3	Nucleus, Acrosomal membrane, Microtubule, Extracellular exosome, Sperm flagellum
TSGA10	Testis specific 10	Nuclear membrane, Cytoplasm, Neuron projection, Motile cilium
TUBA3C	Tubulin Alpha 3c	Nucleus, Cytoplasm, Microtubule
TUBB1	Tubulin Beta 1 Class VI	Cytoplasm, Microtubule, Extracellular exosome
TUBB2A	Tubulin Beta 2A Class II A	Nucleus, Cytoplasm, Microtubule, Extracellular exosome, Extracellular vesicle
TUBB2B	Tubulin Beta 2B Class II B	Nucleus, Cytoplasm, Microtubule
TUBB3	Tubulin Beta 3 Class III	Nucleus, Cytoplasm, Microtubule, Axon, Dendrite, Neuronal cell body, Extracellular exosome, Cell periphery
TUBB4A	Tubulin Beta 4A Class IV A	Nucleus, Cytosol, Microtubule, Internode region of axon, Neuronal cell body, Myelin sheath, Extracellular exosome, Cilium
TUBB4B	Tubulin Beta 4B Class IV B	Nucleus, Cytosol, Cytoskeleton, Microtubule, Extracellular matrix, Myelin sheath, Extracellular exosome, Extracellular vesicle
TUBB6	Tubulin Beta 6 Class V	Nucleus, Cytoplasm, Microtubule, Extracellular exosome
TUBB	Tubulin Beta Class I	Nucleus, Extracellular region, Nuclear envelope lumen, Cytoplasm, Cytoskeleton, Microtubule, Extracellular matrix, Cytoplasmic ribonucleoprotein granule, Protein Complex, Cell body, Extracellular exosome
ID	**Name**	**Module 2***
AKT1	AKT serine/threonine kinase 1	Nucleus, Nucleoplasm, Cytoplasm, Cytosol, Mitochondrion, Spindle, Plasma membrane, cell-cell junction, Microtubule cytoskeleton, Vesicle, Ciliary basal body, Protein complex, Post-synapse
VEGFA	Vascular endothelial growth factor A	Cytoplasm, Extracellular region, Proteinaceous extracellular matrix, Extracellular space, Cell surface, Membrane, Secretory granule, Platelet alpha granule lumen

ARNT	Aryl hydrocarbon receptor nuclear translocator	Nucleus, Nucleoplasm, Cytoplasm, transcription factor complex, RNA polymerase II transcription factor complex
OS9	OS9, endoplasmic reticulum lectin	Hrd1p ubiquitin ligase complex, Endoplasmic reticulum lumen, Endoplasmic reticulum membrane, Endoplasmic reticulum quality control compartment
CUL2	Cullin 2	Nucleoplasm, Nucleolus, Cytosol, VCB complex, Cullin-RING ubiquitin ligase complex, Cul2-RING ubiquitin ligase complex,
EGLN3	EGL-9 family hypoxia inducible factor 3	Nucleus, Nucleoplasm, Cytoplasm, Cytosol
HSP90AA1	Heat shock protein 90 alpha family class A member 1	Nucleus, Nucleoplasm, Cytoplasm, Cytosol, Extracellular region, Plasma membrane,Cell surface, Membrane, Basolateral plasma membrane, Apical plasma membrane, Extracellular matrix, Brush border membrane, Ruffle membrane, Melanosome, Neuron projection, Neuronal cell body, Lysosomal lumen, Myelin sheath, Protein complex, Perinuclear region of cytoplasm, Extracellular exosome, Endocytic vesicle lumen, Sperm mitochondrial sheath, Sperm plasma membrane
TCEB1	transcription elongation factor B subunit 1	Nucleoplasm, Cytosol, VCB complex, Elongin complex
TCEB2	transcription elongation factor B subunit 2	Nucleoplasm, Cytosol, VCB complex, Elongin complex, Cul2-RING ubiquitin ligase complex, Cul5-RING ubiquitin ligase complex, Extracellular exosome
ID	**Name**	**Module 3***
FURIN	Furin, paired basic amino acid cleaving enzyme	Golgi membrane, Extracellular space, Endoplasmic reticulum, Golgi lumen, Trans-Golgi network, Plasma membrane, Cell surface, Membrane, Integral component of membrane, Trans-Golgi network transport vesicle, Membrane raft, Extracellular exosome
PKM	Pyruvate kinase, muscle	Nucleus, Cytoplasm, Mitochondrion, Cytosol, Plasma membrane, Cell-cell adherens junction, Cilium, Extracellular matrix, Vesicle, Myelin sheath, Extracellular exosome, Extracellular vesicle
NOTCH1	Notch 1	Nucleus, Nucleoplasm, Cytosol, Golgi membrane, Acrosomal vesicle, MAML1-RBP-Jkappa- ICN1 complex, Extracellular region, Endoplasmic reticulum membrane, Plasma membrane, Adherens junction, Cell surface, Integral component of membrane, Apical plasma membrane, Receptor complex
APP	Amyloid beta precursor protein	Nuclear envelope lumen, Cytoplasm, Cytosol, Extracellular region, Extracellular space, Endosome, Smooth endoplasmic reticulum, Rough endoplasmic reticulum, Golgi apparatus, Plasma membrane, Integral component of plasma membrane, Clathrin-coated pit, Cell-cell junction, Cell surface, Integral component of membrane, ER to Golgi transport vesicle, Axon, Platelet alpha granule lumen, Neuromuscular junction, Endosome lumen, Trans-Golgi network membrane, Ciliary rootlet, Terminal bouton, Dendritic spine, Dendritic shaft, Intracellular membrane-bounded organelle, Receptor complex, Main axon, Membrane raft, Apical part of cell, Synapse, Perinuclear region of cytoplasm, Spindle midzone, Extracellular exosome, Astrocyte projection, Growth cone lamellipodium, Growth cone filopodium

CXCL12	C-X-C motif chemokine ligand 12	Extracellular region, Extracellular space, External side of plasma membrane, Extracellular exosome
CXCR4	C-X-C motif chemokine receptor 4	Cytoplasm, lysosome, early endosome, Late endosome, Plasma membrane, Cell surface, Integral component of membrane, Cytoplasmic, Membrane-bounded vesicle, Cell junction, Cell leading edge, Cytoplasmic vesicle, Extracellular exosome
EPO	Erythropoietin	Extracellular region, Extracellular space, Cell surface, Cell body
GNB2L1[ɸ]	–	–
EGLN1	egl-9 family hypoxia inducible factor 1	Nucleus, Cytoplasm, Cytosol, Cell
HIF1AN	hypoxia inducible factor 1 alpha subunit inhibitor	Nucleus, Nucleoplasm, Cytoplasm, Cytosol, Perinuclear region of cytoplasm
VHL	von Hippel-Lindau tumor suppressor	Nucleus, Nucleoplasm, Cytosol, VCB complex, Mitochondrion, Endoplasmic reticulum, Membrane
JUN	Jun proto-oncogene, AP-1 transcription factor subunit	Nucleus, Nucleoplasm, Nuclear chromosome, Nuclear euchromatin, Cytosol, Transcription factor complex, Transcriptional repressor complex

***** The common genes between these 3 large modules were not repeated into the other ones. [ɸ] not found any CC ontology data in DAVID database for *H. sapiens*.

Table S2. The molecular function (MF) ontology for the functional large modules.

ID	**Name**	**GOTERM_MF_DIRECT**
		Module 1
BACE1	Beta secretase 1	beta-amyloid binding, aspartic-type endopeptidase activity, protein binding, peptidase activity, beta-aspartyl-peptidase activity, enzyme binding
LOC81691	Exonuclease NEF-Sp	nucleotide binding, nucleic acid binding, RNA binding, exonuclease activity
GGA3	Golgi associated, Gamma adaptin ear-containing, ARF binding protein 3	Protein binding, ADP-ribosylation factor binding
HIF1A	Hypoxia inducible factor 1 alpha Subunit	transcription factor activity, transcription factor binding, transcription factor activity, RNA polymerase II transcription factor binding, transcriptional activator activity, RNA polymerase II core promoter proximal region sequence-specific binding, transcriptional activator activity, RNA polymerase II transcription regulatory region sequence-specific binding, transcription factor activity, sequence-specific DNA binding, transcription factor activity, RNA polymerase II distal enhancer sequence-specific binding, protein binding, transcription factor binding, enzyme binding, protein kinase binding, ubiquitin protein ligase binding, histone acetyltransferase binding, nuclear hormone receptor binding, histone deacetylase binding, sequence-specific DNA binding, protein heterodimerization activity, Hsp90 protein binding,
SPAG16[ψ]	Sperm associated antigen 16	protein binding, protein kinase binding
SPAG6[Ŧ]	Sperm associated antigen 6	–
TEKT3	Tektin 3	protein binding

TSGA10	Testis specific 10	protein binding
TUBA3C	Tubulin Alpha 3c	GTPase activity, structural constituent of cytoskeleton, protein binding, GTP binding
TUBB1	Tubulin Beta 1 Class VI	GTPase activity, structural constituent of cytoskeleton, GTP binding
TUBB2A	Tubulin Beta 2A Class II A	GTPase activity, structural constituent of cytoskeleton, protein binding, GTP binding
TUBB2B	Tubulin Beta 2B Class II B	GTPase activity, structural constituent of cytoskeleton, protein binding, GTP binding
TUBB3	Tubulin Beta 3 Class III	GTPase activity, structural constituent of cytoskeleton, protein binding, GTP binding, peptide binding
TUBB4A	Tubulin Beta 4A Class IV A	GTPase activity, structural constituent of cytoskeleton, protein binding, GTP binding
TUBB4B	Tubulin Beta 4B Class IV B	double-stranded RNA binding, GTPase activity, structural constituent of cytoskeleton, GTP binding, MHC class I protein binding, unfolded protein binding
TUBB6	Tubulin Beta 6 Class V	GTPase activity, structural constituent of cytoskeleton, GTP binding
TUBB	Tubulin Beta Class I	GTPase activity, structural molecule activity, structural constituent of cytoskeleton, protein binding, GTP binding, protein domain specific binding, ubiquitin protein ligase binding, protein complex binding, GTPase activating protein binding, MHC class I protein binding

ID	**Name**	**Module 2***
AKT1	AKT serine/threonine kinase 1	Protein kinase activity, protein serine/threonine kinase activity, protein serine/threonine/tyrosine kinase activity, protein kinase C binding, protein binding, ATP binding, phosphatidylinositol-3,4,5-trisphosphate binding, kinase activity, enzyme binding, nitric-oxide synthase regulator activity, GTPase activating protein binding, identical protein binding, phosphatidylinositol-3,4-bisphosphate binding, protein phosphatase 2A binding, 14-3-3 protein binding
VEGFA	Vascular endothelial growth factor A	Fibronectin binding, cytokine activity, platelet-derived growth factor receptor binding, vascular endothelial growth factor receptor binding, protein binding, growth factor activity, heparin binding, neuropilin binding, chemoattractant activity, identical protein binding, protein homodimerization activity, vascular endothelial growth factor receptor 1 binding, vascular endothelial growth factor receptor 2 binding, protein heterodimerization activity, receptor agonist activity, extracellular matrix binding
ARNT	Aryl hydrocarbon receptor nuclear translocator	DNA binding, transcription factor activity, sequence-specific DNA binding, transcription factor activity, RNA polymerase II distal enhancer sequence-specific binding, transcription coactivator activity, aryl hydrocarbon receptor activity, protein binding, transcription factor binding, aryl hydrocarbon receptor binding, enhancer binding, sequence-specific DNA binding, protein heterodimerization activity
OS9	OS9, endoplasmic reticulum lectin	glycoprotein binding, protease binding, protein binding, carbohydrate binding
CUL2	Cullin 2	protein binding, ubiquitin protein ligase binding, protein complex binding, ubiquitin protein ligase activity
EGLN3	EGL-9 family hypoxia inducible factor 3	iron ion binding, protein binding, oxidoreductase activity, oxidoreductase activity, acting on paired donors, with incorporation or reduction of

		molecular oxygen, oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, 2-oxoglutarate as one donor, and incorporation of one atom each of oxygen into both donors, L-ascorbic acid binding, peptidyl-proline 4-dioxygenase activity
HSP90AA1	Heat shock protein 90 alpha family class A member 1	nucleotide binding, glycoprotein binding, UTP binding, CTP binding, mRNA binding, protein tyrosine kinase activity, protein binding, ATP binding, GTP binding, ATPase activity, sulfonylurea receptor binding, protein phosphatase binding, MHC class II protein complex binding, nitric-oxide synthase regulator activity, TPR domain binding, dATP binding, identical protein binding, protein homodimerization activity, histone deacetylase binding, ion channel binding, poly(A) RNA binding, tau protein binding, GTPase binding, Rho GDP-dissociation inhibitor binding, unfolded protein binding, protein tyrosine kinase binding
TCEB1	transcription elongation factor B subunit 1	translation elongation factor activity, ubiquitin-protein transferase activity, protein binding, protein complex binding
TCEB2	transcription elongation factor B subunit 2	translation elongation factor activity, protein binding, ubiquitin protein ligase binding
ID	**Name**	**Module 3***
FURIN	Furin, paired basic amino acid cleaving enzyme	protease binding, endopeptidase activity, serine-type endopeptidase activity, serine-type endopeptidase inhibitor activity, protein binding, peptidase activity, peptide binding, metal ion binding, nerve growth factor binding
PKM	Pyruvate kinase, muscle	Magnesium ion binding, pyruvate kinase activity, protein binding, ATP binding, kinase activity, MHC class II protein complex binding, potassium ion binding, ADP binding, poly(A) RNA binding, cadherin binding involved in cell-cell adhesion
NOTCH1	Notch 1	core promoter binding, transcriptional activator activity, RNA polymerase II transcription factor binding, transcription factor activity, sequence-specific DNA binding, enzyme inhibitor activity, receptor activity, Notch binding, calcium ion binding, protein binding, enzyme binding, chromatin DNA binding, sequence-specific DNA binding, protein heterodimerization activity
APP	Amyloid beta precursor protein	DNA binding, serine-type endopeptidase inhibitor activity, receptor binding, protein binding, heparin binding, peptidase activity, peptidase activator activity, enzyme binding, acetylcholine receptor binding, identical protein binding, transition metal ion binding, PTB domain binding, growth factor receptor binding
CXCL12	C-X-C motif chemokine ligand 12	Receptor binding, chemokine activity, growth factor activity, chemoattractant activity, chemokine receptor binding, CXCR chemokine receptor binding
CXCR4	C-X-C motif chemokine receptor 4	Virus receptor activity, actin binding, G-protein coupled receptor activity, protein binding, co-receptor activity, C-X-C chemokine receptor activity, cytokine binding, ubiquitin protein ligase binding, myosin light chain binding, ubiquitin binding
EPO	Erythropoietin	Erythropoietin receptor binding, hormone activity, protein binding, protein kinase activator activity

GNB2L1[Ŧ]	guanine nucleotide binding protein (G protein), beta polypeptide 2-like 1	–
EGLN1	egl-9 family hypoxia inducible factor 1	Iron ion binding, protein binding, oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, 2-oxoglutarate as one donor, and incorporation of one atom each of oxygen into both donors, enzyme binding, L-ascorbic acid binding, peptidyl-proline dioxygenase activity, peptidyl-proline 4-dioxygenase activity
HIF1AN	hypoxia inducible factor 1 alpha subunit inhibitor	Sulfonate dioxygenase activity, Notch binding, iron ion binding, protein binding, zinc ion binding, oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, 2-oxoglutarate as one donor, and incorporation of one atom each of oxygen into both donors, 2,4-dichlorophenoxyacetate alpha-ketoglutarate dioxygenase activity, procollagen-proline dioxygenase activity, oxygen sensor activity, carboxylic acid binding, hypophosphite dioxygenase activity, peptidyl-histidine dioxygenase activity, peptidyl-asparagine 3-dioxygenase activity, protein homodimerization activity, DNA-N1-methyladenine dioxygenase activity, cofactor binding, NF-kappa B binding, C-19 gibberellin 2-beta-dioxygenase activity, C-20 gibberellin 2-beta-dioxygenase activity, ankyrin repeat binding
VHL	von Hippel-Lindau tumor suppressor	Ubiquitin-protein transferase activity, protein binding, transcription factor binding, enzyme binding, ubiquitin protein ligase activity
JUN	Jun proto-oncogene, AP-1 transcription factor subunit	RNA polymerase II core promoter proximal region sequence-specific DNA binding, RNA polymerase II distal enhancer sequence-specific DNA binding, RNA polymerase II transcription factor activity, sequence-specific DNA binding, transcription factor activity, RNA polymerase II core promoter proximal region sequence-specific binding, transcriptional activator activity, RNA polymerase II core promoter proximal region sequence-specific binding, RNA polymerase II activating transcription factor binding, transcriptional activator activity, RNA polymerase II transcription factor binding, DNA binding, chromatin binding, transcription factor activity, sequence-specific DNA binding, transcription factor activity, RNA polymerase II distal enhancer sequence-specific binding, transcription coactivator activity, GTPase activator activity, protein binding, transcription factor binding, enzyme binding, cAMP response element binding, identical protein binding, protein homodimerization activity, sequence-specific DNA binding, transcription regulatory region DNA binding, poly(A) RNA binding, protein heterodimerization activity, R-SMAD binding, HMG box domain binding

***** The common genes between these 3 large modules were not repeated into the other ones. [ψ] Molecular function ontology for SPAG16 is annotated based on *Mus musculus* species. [Ŧ] There is no any data in DAVID database for MF ontology of SPAG6 and GNB2L1 genes.

Table S3. List of genes The biological process (BP) ontology for the functional large modules.

ID	Name	GOTERM_BP_DIRECT
		Module 1
BACE1	Beta secretase 1	Proteolysis, membrane protein ecto-domain proteolysis, protein catabolic process, cellular protein metabolic process, beta-amyloid metabolic process
LOC81691	Exonuclease NEF-Sp	Nucleic acid phosphodiester bond hydrolysis
GGA3	Golgi associated, Gamma adaptin ear-containing, ARF binding protein 3	Intracellular protein transport, vesicle-mediated transport, cellular protein metabolic process, positive regulation of protein catabolic process
HIF1A	Hypoxia inducible factor 1 alpha Subunit	Angiogenesis, response to hypoxia, neural crest cell migration, epithelial to mesenchymal transition, embryonic placenta development, B-1 B cell homeostasis, positive regulation of endothelial cell proliferation, heart looping, positive regulation of neuroblast proliferation, connective tissue replacement involved in inflammatory response wound healing, outflow tract morphogenesis, cardiac ventricle morphogenesis, lactate metabolic process, transcription, DNA-templated, regulation of transcription, DNA-templated, transcription from RNA polymerase II promoter, cellular iron ion homeostasis, signal transduction, lactation, visual learning, regulation of gene expression, vascular endothelial growth factor production, positive regulation of vascular endothelial growth factor production, positive regulation of gene expression, positive regulation of epithelial cell migration, positive regulation of receptor biosynthetic process, response to muscle activity, positive regulation of macroautophagy, axonal transport of mitochondrion, neural fold elevation formation, cerebral cortex development, negative regulation of bone mineralization, positive regulation of vascular endothelial growth factor receptor signaling pathway, negative regulation of TOR signaling, oxygen homeostasis, positive regulation of chemokine production, regulation of transforming growth factor beta2 production, collagen metabolic process, embryonic hemopoiesis, positive regulation of insulin secretion involved in cellular response to glucose stimulus, hemoglobin biosynthetic process, glucose homeostasis, mRNA transcription from RNA polymerase II promoter, regulation of transcription from RNA polymerase II promoter in response to oxidative stress, positive regulation of erythrocyte differentiation, positive regulation of angiogenesis, positive regulation of glycolytic process, positive regulation of transcription, DNA-templated, negative regulation of growth, positive regulation of transcription from RNA polymerase II promoter, muscle cell cellular homeostasis, positive regulation of hormone biosynthetic process, digestive tract morphogenesis, positive regulation of nitric-oxide synthase activity, cartilage development, elastin metabolic process, intestinal epithelial cell maturation, epithelial cell differentiation involved in mammary gland alveolus development, iris morphogenesis, retina

		vasculature development in camera-type eye, regulation of transcription from RNA polymerase II promoter in response to hypoxia, positive regulation of transcription from RNA polymerase II promoter in response to hypoxia, positive regulation of chemokine-mediated signaling pathway, negative regulation of thymocyte apoptotic process, cellular response to interleukin-1, cellular response to hypoxia, dopaminergic neuron differentiation, hypoxia-inducible factor-1alpha signaling pathway, positive regulation of pri-miRNA transcription from RNA polymerase II promoter, negative regulation of oxidative stress-induced neuron intrinsic apoptotic signaling pathway, positive regulation of mitophagy, regulation of aerobic respiration, negative regulation of reactive oxygen species metabolic process, negative regulation of mesenchymal cell apoptotic process
SPAG16	Sperm associated antigen 16	Sperm axoneme assembly, axoneme assembly, cilium assembly, microtubule sliding, cilium morphogenesis, cilium movement involved in cell motility, cell motility in response to calcium ion
SPAG6	Sperm associated antigen 6	Spermatid development, cell projection organization
TEKT3	Tektin 3	Sperm motility, cilium morphogenesis, regulation of fertilization
TSGA10	Testis specific 10	Spermatogenesis, cell projection assembly
TUBA3C	Tubulin Alpha 3c	Cytoskeleton organization, microtubule-based process
TUBB1	Tubulin Beta 1 Class VI	Spindle assembly
TUBB2A	Tubulin Beta 2A Class II A	Cytoskeleton organization, microtubule-based process
TUBB2B	Tubulin Beta 2B Class II B	Neuron migration, cytoskeleton organization, microtubule-based process
TUBB3	Tubulin Beta 3 Class III	Cytoskeleton organization, microtubule-based process, mitotic nuclear division, axon guidance
TUBB4A	Tubulin Beta 4A Class IV A	G2/M transition of mitotic cell cycle, cytoskeleton organization, microtubule-based process
TUBB4B	Tubulin Beta 4B Class IV B	G2/M transition of mitotic cell cycle, movement of cell or subcellular component, cytoskeleton organization, microtubule-based process, natural killer cell mediated cytotoxicity
TUBB6	Tubulin Beta 6 Class V	Cytoskeleton organization, microtubule-based process
TUBB	Tubulin Beta Class I	G2/M transition of mitotic cell cycle, movement of cell or subcellular component, microtubule-based process, cellular process, cytoskeleton-dependent intracellular transport, natural killer cell mediated cytotoxicity, spindle assembly, cell division
ID	**Name**	**Module 2***
AKT1	AKT serine/threonine kinase 1	protein import into nucleus, translocation, osteoblast differentiation, maternal placenta development, positive regulation of protein phosphorylation, positive regulation of endothelial cell proliferation, glycogen biosynthetic process, regulation of glycogen biosynthetic process, glucose metabolic process, translation, regulation of translation, cellular protein modification process, protein phosphorylation, negative regulation of protein kinase activity, nitric oxide biosynthetic process, activation-induced cell death of T cells, inflammatory response, cellular response to DNA damage stimulus, response to oxidative stress, signal transduction, G-protein coupled receptor signaling pathway, germ cell development, aging, cell proliferation, insulin receptor signaling pathway, apoptotic mitochondrial changes, response to heat, negative regulation of autophagy, negative regulation of gene expression, negative regulation of plasma membrane long-chain fatty acid transport, positive regulation of fibroblast migration, positive

		regulation of sodium ion transport, positive regulation of glucose metabolic process, negative regulation of endopeptidase activity, regulation of neuron projection development, regulation of phosphatidylinositol 3-kinase signaling, glucose transport, phosphorylation, protein ubiquitination, peptidyl-serine phosphorylation, peptidyl-threonine phosphorylation, spinal cord development, cell projection organization, cell differentiation, protein catabolic process, platelet activation, hyaluronan metabolic process, positive regulation of cell growth, regulation of cell migration, endocrine pancreas development, T cell costimulation, regulation of myelination, positive regulation of cyclin-dependent protein serine/threonine kinase activity involved in G1/S transition of mitotic cell cycle, lipopolysaccharide-mediated signaling pathway, negative regulation of fatty acid beta-oxidation, positive regulation of endodeoxyribonuclease activity, response to food, positive regulation of cellular protein metabolic process, peripheral nervous system myelin maintenance, positive regulation of proteasomal ubiquitin-dependent protein catabolic process, cellular response to insulin stimulus, regulation of protein localization, positive regulation of peptidyl-serine phosphorylation, response to fluid shear stress, intracellular signal transduction, interleukin-18-mediated signaling pathway, cellular response to vascular endothelial growth factor stimulus, ERBB2 signaling pathway, glucose homeostasis, positive regulation of apoptotic process, negative regulation of apoptotic process, negative regulation of cysteine-type endopeptidase activity involved in apoptotic process, regulation of mRNA stability, protein kinase B signaling, positive regulation of blood vessel endothelial cell migration, positive regulation of nitric oxide biosynthetic process, positive regulation of fat cell differentiation, positive regulation of glycogen biosynthetic process, positive regulation of epidermal growth factor receptor signaling pathway, negative regulation of cell size, negative regulation of proteolysis, positive regulation of vasoconstriction, positive regulation of transcription from RNA polymerase II promoter, positive regulation of glucose import, negative regulation of JNK cascade, protein autophosphorylation, positive regulation of lipid biosynthetic process, insulin-like growth factor receptor signaling pathway, phosphatidylinositol-mediated signaling, positive regulation of smooth muscle cell proliferation, regulation of nitric-oxide synthase activity, positive regulation of nitric-oxide synthase activity, positive regulation of sequence-specific DNA binding transcription factor activity, striated muscle cell differentiation, response to growth hormone, mammary gland epithelial cell differentiation, glycogen cell differentiation involved in embryonic placenta development, labyrinthine layer blood vessel development, response to UV-A, cellular response to mechanical stimulus, cellular response to epidermal growth factor stimulus, cellular response to prostaglandin E stimulus, cellular response to organic cyclic compound, cellular response to hypoxia, establishment of protein localization to mitochondrion, maintenance of protein location in mitochondrion, positive regulation of establishment of protein localization to plasma membrane, negative regulation of release of cytochrome c from mitochondria, cellular response to granulocyte macrophage colony-stimulating factor stimulus, execution phase of apoptosis, chemical synaptic transmission, postsynaptic, negative regulation of protein kinase activity by protein phosphorylation, positive regulation of protein localization to nucleus, negative regulation of neuron death, regulation of signal transduction by p53 class mediator, regulation of cell cycle checkpoint, negative regulation of oxidative stress-induced intrinsic apoptotic signaling pathway, cellular response to nerve growth factor stimulus, response to insulin-like growth factor stimulus, negative regulation of extrinsic apoptotic signaling pathway in absence of ligand
VEGFA	Vascular endothelial growth factor A	Negative regulation of transcription from RNA polymerase II promoter, angiogenesis, ovarian follicle development, patterning of blood vessels, vasculogenesis, response to hypoxia, in utero embryonic development, kidney development, positive regulation of protein phosphorylation, positive regulation of endothelial cell proliferation, cell migration involved in sprouting angiogenesis, positive regulation of neuroblast proliferation, positive regulation of mesenchymal cell proliferation, positive regulation of receptor internalization, basophil chemotaxis,

	platelet degranulation, positive regulation of leukocyte migration, heart morphogenesis, outflow tract morphogenesis, coronary vein morphogenesis, regulation of transcription from RNA polymerase II promoter, nervous system development, mesoderm development, lactation, positive regulation of cell proliferation, regulation of cell shape, positive regulation of endothelial cell migration, positive regulation of gene expression, monocyte differentiation, macrophage differentiation, lung development, positive regulation of cell migration, regulation of cGMP metabolic process, epithelial cell differentiation, positive regulation of vascular endothelial growth factor receptor signaling pathway, post-embryonic camera-type eye development, positive regulation of protein complex assembly, positive regulation of protein autophosphorylation, activation of protein kinase activity, positive regulation of CREB transcription factor activity, positive regulation of peptidyl-serine phosphorylation, tube formation, endothelial cell chemotaxis, cellular response to vascular endothelial growth factor stimulus, lymph vessel morphogenesis, positive regulation of endothelial cell chemotaxis by VEGF-activated vascular endothelial growth factor receptor signaling pathway, vascular endothelial growth factor signaling pathway, positive regulation of cell proliferation by VEGF-activated platelet derived growth factor receptor signaling pathway, VEGF-activated neuropilin signaling pathway, growth, eye photoreceptor cell development, positive regulation of tyrosine phosphorylation of Stat3 protein, negative regulation of apoptotic process, positive regulation of vascular permeability, surfactant homeostasis, negative regulation of cysteine-type endopeptidase activity involved in apoptotic process, positive regulation of MAP kinase activity, positive regulation of blood vessel endothelial cell migration, positive regulation of angiogenesis, positive regulation of cell adhesion, positive regulation of transcription from RNA polymerase II promoter, vascular endothelial growth factor receptor signaling pathway, cell maturation, camera-type eye morphogenesis, cardiac muscle fiber development, branching morphogenesis of an epithelial tube, positive regulation of axon extension involved in axon guidance, artery morphogenesis, positive regulation of epithelial cell proliferation, positive regulation of peptidyl-tyrosine phosphorylation, positive chemotaxis, positive regulation of positive chemotaxis, induction of positive chemotaxis, positive regulation of cellular component movement, positive regulation of cell division, positive regulation of focal adhesion assembly, primitive erythrocyte differentiation, mammary gland alveolus development, positive regulation of mast cell chemotaxis, cardiac vascular smooth muscle cell development, coronary artery morphogenesis, regulation of transcription from RNA polymerase II promoter in response to hypoxia, positive regulation of transcription from RNA polymerase II promoter in response to hypoxia, positive regulation of ERK1 and ERK2 cascade, cellular response to hypoxia, dopaminergic neuron differentiation, commissural neuron axon guidance, positive regulation of protein kinase C signaling, positive regulation of cell migration involved in sprouting angiogenesis, positive regulation of branching involved in ureteric bud morphogenesis, regulation of retinal ganglion cell axon guidance, positive regulation of peptidyl-tyrosine autophosphorylation, positive regulation of p38MAPK cascade, positive regulation of histone deacetylase activity, positive regulation of retinal ganglion cell axon guidance, positive regulation of protein localization to early endosome, positive regulation of protein kinase D signaling

ARNT	Aryl hydrocarbon receptor nuclear translocator	response to hypoxia, embryonic placenta development, positive regulation of endothelial cell proliferation, transcription, DNA-templated, positive regulation of vascular endothelial growth factor production, cell differentiation, intracellular receptor signaling pathway, positive regulation of vascular endothelial growth factor receptor signaling pathway, positive regulation of protein sumoylation, mRNA transcription from RNA polymerase II promoter, regulation of transcription from RNA polymerase II promoter in response to oxidative stress, positive regulation of erythrocyte differentiation, positive regulation of glycolytic process, positive regulation of transcription, DNA-templated, positive regulation of transcription from RNA polymerase II promoter, positive regulation of hormone biosynthetic process, regulation of transcription from RNA polymerase II promoter in response to hypoxia
OS9	OS9, endoplasmic reticulum lectin	protein targeting, protein retention in ER lumen, protein ubiquitination, ER-associated ubiquitin-dependent protein catabolic process, response to endoplasmic reticulum stress, protein ubiquitination involved in ubiquitin-dependent protein catabolic process, negative regulation of retrograde protein transport, ER to cytosol, endoplasmic reticulum mannose trimming
CUL2	Cullin 2	G1/S transition of mitotic cell cycle, ubiquitin-dependent protein catabolic process, cell cycle arrest, negative regulation of cell proliferation, viral process, protein ubiquitination involved in ubiquitin-dependent protein catabolic process, regulation of transcription from RNA polymerase II promoter in response to hypoxia, intrinsic apoptotic signaling pathway
EGLN3	EGL-9 family hypoxia inducible factor 3	Response to hypoxia, apoptotic process, activation of cysteine-type endopeptidase activity involved in apoptotic process, cellular response to DNA damage stimulus, protein hydroxylation, peptidyl-proline hydroxylation to 4-hydroxy-L-proline, regulation of cell proliferation, regulation of neuron apoptotic process, oxidation-reduction process, regulation of transcription from RNA polymerase II promoter in response to hypoxia
HSP90AA1	Heat shock protein 90 alpha family class A member 1	G2/M transition of mitotic cell cycle, neuron migration, skeletal muscle contraction, protein folding, mitochondrial transport, receptor-mediated endocytosis, response to stress, response to unfolded protein, signal transduction, response to heat, response to cold, response to salt stress, positive regulation of lamellipodium assembly, cardiac muscle cell apoptotic process, peptidyl-tyrosine phosphorylation, regulation of protein ubiquitination, positive regulation of protein import into nucleus, translocation, Fc-gamma receptor signaling pathway involved in phagocytosis, ERBB2 signaling pathway, protein refolding, response to cocaine, response to drug, regulation of protein complex assembly, protein unfolding, response to estrogen, protein import into mitochondrial outer membrane, positive regulation of nitric oxide biosynthetic process, positive regulation of cell size, response to antibiotic, vascular endothelial growth factor receptor signaling pathway, protein stabilization, regulation of nitric-oxide synthase activity, chaperone-mediated protein complex assembly, positive regulation of cardiac muscle contraction, chaperone-mediated autophagy, regulation of cellular response to heat
TCEB1	transcription elongation factor B subunit 1	Regulation of transcription from RNA polymerase II promoter, transcription from RNA polymerase II promoter, transcription elongation from RNA polymerase II promoter, ubiquitin-dependent protein catabolic process, viral process, positive regulation of transcription elongation from RNA polymerase II promoter, protein ubiquitination involved in ubiquitin-dependent protein catabolic process, regulation of transcription from RNA polymerase II promoter in response to hypoxia

TCEB2	transcription elongation factor B subunit 2	Transcription from RNA polymerase II promoter, transcription elongation from RNA polymerase II promoter, protein complex assembly, protein ubiquitination, regulation of transcription from RNA polymerase II promoter in response to hypoxia

ID	**Name**	**Module 3***
FURIN	Furin, paired basic amino acid cleaving enzyme	Signal peptide processing, transforming growth factor beta receptor signaling pathway, cell proliferation, regulation of signal transduction, negative regulation of endopeptidase activity, protein processing, peptide hormone processing, viral life cycle, viral protein processing, extracellular matrix disassembly, extracellular matrix organization, collagen catabolic process, nerve growth factor processing, negative regulation of low-density lipoprotein particle receptor catabolic process, nerve growth factor production, negative regulation of nerve growth factor production, negative regulation of transforming growth factor beta1 production, secretion by cell, regulation of protein catabolic process, peptide biosynthetic process, cellular protein metabolic process, regulation of low-density lipoprotein particle receptor biosynthetic process, positive regulation of membrane protein ectodomain proteolysis, regulation of endopeptidase activity
PKM	Pyruvate kinase, muscle	Response to hypoxia, liver development, ATP biosynthetic process, response to nutrient, response to gravity, programmed cell death, response to muscle inactivity, organ regeneration, response to insulin, pyruvate biosynthetic process, skeletal muscle tissue regeneration, canonical glycolysis, cell-cell adhesion
NOTCH1	Notch 1	Negative regulation of transcription from RNA polymerase II promoter, in utero embryonic development, cell fate specification, epithelial to mesenchymal transition, liver development, heart looping, sprouting angiogenesis, positive regulation of neuroblast proliferation, inflammatory response to antigenic stimulus, endocardium development, endocardium morphogenesis, atrioventricular node development, coronary vein morphogenesis, aortic valve morphogenesis, atrioventricular valve morphogenesis, pulmonary valve morphogenesis, mitral valve formation, epithelial to mesenchymal transition involved in endocardial cushion formation, endocardial cushion morphogenesis, cardiac chamber formation, cardiac ventricle morphogenesis, cardiac atrium morphogenesis, cardiac right atrium morphogenesis, cardiac left ventricle morphogenesis, cardiac right ventricle formation, ventricular trabecula myocardium morphogenesis, growth involved in heart morphogenesis, regulation of transcription from RNA polymerase II promoter involved in myocardial precursor cell differentiation, Notch signaling pathway involved in regulation of secondary heart field cardioblast proliferation, cell migration involved in endocardial cushion formation, pericardium morphogenesis, regulation of transcription, DNA-templated, transcription initiation from RNA polymerase II promoter, immune response, humoral immune response, Notch signaling pathway, positive regulation of transcription of Notch receptor target, multicellular organism development, spermatogenesis, determination of left/right symmetry, compartment pattern specification, axonogenesis, foregut morphogenesis, endoderm development, heart development, positive regulation of cell proliferation, negative regulation of cell proliferation, auditory receptor cell fate commitment, positive regulation of epithelial to mesenchymal transition, negative regulation of cell-substrate adhesion, negative regulation of myotube differentiation, mesenchymal cell development, regulation of somitogenesis, cell differentiation in spinal cord, neural tube development, cell differentiation, keratinocyte differentiation, negative regulation of ossification, lung development, positive regulation of cell migration, positive regulation of BMP

		signaling pathway, negative regulation of BMP signaling pathway, forebrain development, hair follicle morphogenesis, organ regeneration, response to corticosteroid, response to muramyl dipeptide, response to lipopolysaccharide, embryonic hindlimb morphogenesis, tube formation, skeletal muscle cell differentiation, cellular response to vascular endothelial growth factor stimulus, tissue regeneration, positive regulation of apoptotic process, negative regulation of catalytic activity, positive regulation of viral genome replication, positive regulation of endothelial cell differentiation, negative regulation of auditory receptor cell differentiation, positive regulation of keratinocyte differentiation, negative regulation of myoblast differentiation, negative regulation of osteoblast differentiation, positive regulation of Notch signaling pathway, negative regulation of transcription, DNA-templated, positive regulation of transcription, DNA-templated, positive regulation of transcription from RNA polymerase II promoter, negative regulation of calcium ion-dependent exocytosis, positive regulation of JAK-STAT cascade, negative regulation of photoreceptor cell differentiation, somatic stem cell division, astrocyte differentiation, oligodendrocyte differentiation, positive regulation of astrocyte differentiation, negative regulation of oligodendrocyte differentiation, branching morphogenesis of an epithelial tube, positive regulation of viral transcription, positive regulation of epithelial cell proliferation, negative regulation of neurogenesis, cardiac muscle tissue morphogenesis, cardiac muscle cell proliferation, positive regulation of cardiac muscle cell proliferation, negative regulation of glial cell proliferation, cilium morphogenesis, cardiac epithelial to mesenchymal transition, cardiac septum morphogenesis, ventricular septum morphogenesis, secretory columnal luminar epithelial cell differentiation involved in prostate glandular acinus development, prostate gland epithelium morphogenesis, regulation of epithelial cell proliferation involved in prostate gland development, arterial endothelial cell differentiation, venous endothelial cell differentiation, cardiac vascular smooth muscle cell development, endocardial cell differentiation, vasculogenesis involved in coronary vascular morphogenesis, coronary artery morphogenesis, Notch signaling involved in heart development, heart trabecula morphogenesis, positive regulation of transcription from RNA polymerase II promoter in response to hypoxia, left/right axis specification, cellular response to follicle-stimulating hormone stimulus, distal tubule development, collecting duct development, glomerular mesangial cell development, interleukin-4 secretion, negative regulation of cell migration involved in sprouting angiogenesis, negative regulation of canonical Wnt signaling pathway, neuronal stem cell population maintenance, regulation of extracellular matrix assembly, apoptotic process involved in embryonic digit morphogenesis, positive regulation of aorta morphogenesis, negative regulation of stem cell differentiation, negative regulation of anoikis, negative regulation of pro-B cell differentiation, negative regulation of endothelial cell chemotaxis
APP	Amyloid beta precursor protein	Response to yeast, suckling behavior, platelet degranulation, mRNA polyadenylation, regulation of translation, protein phosphorylation, cellular copper ion homeostasis, endocytosis, response to oxidative stress, cell adhesion, regulation of epidermal growth factor-activated receptor activity, Notch signaling pathway, nervous system development, axonogenesis, mating behavior, locomotory behavior, axo-dendritic transport, cholesterol metabolic process, adult locomotory behavior, visual learning, cellular process, response to lead ion, negative regulation of endopeptidase activity, positive regulation of peptidase activity, positive regulation

		of G2/M transition of mitotic cell cycle, axon midline choice point recognition, neuron remodeling, dendrite development, antibacterial humoral response, antifungal humoral response, extracellular matrix organization, forebrain development, neuron projection development, ionotropic glutamate receptor signaling pathway, regulation of multicellular organism growth, regulation of protein binding, cellular protein metabolic process, innate immune response, negative regulation of neuron differentiation, positive regulation of mitotic cell cycle, positive regulation of transcription from RNA polymerase II promoter, collateral sprouting in absence of injury, regulation of synapse structure or activity, defense response to Gram-negative bacterium, defense response to Gram-positive bacterium, neuromuscular process controlling balance, synaptic growth at neuromuscular junction, neuron apoptotic process, smooth endoplasmic reticulum calcium ion homeostasis, cellular response to cAMP, cellular response to norepinephrine stimulus, amyloid fibril formation, cellular response to nerve growth factor stimulus
CXCL12	C-X-C motif chemokine ligand 12	response to hypoxia, neuron migration, positive regulation of endothelial cell proliferation, cellular calcium ion homeostasis, chemotaxis, defense response, inflammatory response, immune response, cell adhesion, signal transduction, G-protein coupled receptor signaling pathway, axon guidance, blood circulation, regulation of actin polymerization or depolymerization, adult locomotory behavior, response to radiation, response to heat, response to mechanical stimulus, response to virus, telencephalon cell migration, organ regeneration, positive regulation of dopamine secretion, response to peptide hormone, positive regulation of cell adhesion, positive regulation of axon extension involved in axon guidance, positive chemotaxis, induction of positive chemotaxis, cell chemotaxis, chemokine-mediated signaling pathway, positive regulation of monocyte chemotaxis, positive regulation of calcium ion import, negative regulation of intrinsic apoptotic signaling pathway in response to DNA damage, negative regulation of leukocyte tethering or rolling, negative regulation of leukocyte apoptotic process, positive regulation of T cell migration,
CXCR4	C-X-C motif chemokine receptor 4	activation of MAPK activity, response to hypoxia, dendritic cell chemotaxis, apoptotic process, chemotaxis, inflammatory response, G-protein coupled receptor signaling pathway, positive regulation of cytosolic calcium ion concentration, response to virus, fusion of virus membrane with host plasma membrane, calcium-mediated signaling, entry into host cell, regulation of cell migration, myelin maintenance, positive regulation of oligodendrocyte differentiation, regulation of chemotaxis, chemokine-mediated signaling pathway, cellular response to cytokine stimulus
EPO	Erythropoietin	Negative regulation of transcription from RNA polymerase II promoter, response to hypoxia, regulation of transcription from RNA polymerase II promoter, apoptotic process, acute-phase response, signal transduction, embryo implantation, aging, blood circulation, positive regulation of cell proliferation, response to salt stress, negative regulation of calcium ion transport into cytosol, positive regulation of neuron projection development, peptidyl-serine phosphorylation, erythrocyte differentiation, activation of protein kinase activity, response to lipopolysaccharide, negative regulation of myeloid cell apoptotic process, response to vitamin A, response to testosterone, positive regulation of activated T cell proliferation, positive regulation of tyrosine phosphorylation of Stat5 protein, hemoglobin biosynthetic process, erythrocyte maturation, response to estrogen, positive regulation of DNA

		replication, positive regulation of transcription, DNA-templated, positive regulation of Ras protein signal transduction, response to axon injury, response to electrical stimulus, response to hyperoxia, regulation of transcription from RNA polymerase II promoter in response to hypoxia, positive regulation of ERK1 and ERK2 cascade, response to interleukin-1, cellular hyperosmotic response, response to dexamethasone, negative regulation of neuron death, negative regulation of intrinsic apoptotic signaling pathway in response to osmotic stress, negative regulation of erythrocyte apoptotic process, negative regulation of cation channel activity
GNB2L1[₸]	guanine nucleotide binding protein (G protein), beta polypeptide 2-like 1	–
EGLN1	egl-9 family hypoxia inducible factor 1	Response to hypoxia, cellular iron ion homeostasis, peptidyl-proline hydroxylation to 4-hydroxy-L-proline, negative regulation of cAMP catabolic process, oxygen homeostasis, negative regulation of sequence-specific DNA binding transcription factor activity, regulation of angiogenesis, positive regulation of transcription from RNA polymerase II promoter, negative regulation of cyclic-nucleotide phosphodiesterase activity, cardiac muscle tissue morphogenesis, oxidation-reduction process, heart trabecula formation, ventricular septum morphogenesis, labyrinthine layer development, regulation of transcription from RNA polymerase II promoter in response to hypoxia, response to nitric oxide, regulation of neuron death
HIF1AN	hypoxia inducible factor 1 alpha subunit inhibitor	Transcription, DNA-templated, peptidyl-proline hydroxylation, peptidyl-histidine hydroxylation, peptidyl-aspartic acid hydroxylation, peptidyl-asparagine hydroxylation, positive regulation of myoblast differentiation, negative regulation of Notch signaling pathway, oxidation-reduction process, regulation of transcription from RNA polymerase II promoter in response to hypoxia, negative regulation of transcription from RNA polymerase II promoter in response to hypoxia, positive regulation of vasculogenesis
VHL	Von Hippel-Lindau tumor suppressor	Negative regulation of transcription from RNA polymerase II promoter, cell morphogenesis, regulation of transcription, DNA-templated, proteolysis, negative regulation of cell proliferation, protein ubiquitination, negative regulation of apoptotic process, positive regulation of cell differentiation, positive regulation of transcription, DNA-templated, protein stabilization, regulation of transcription from RNA polymerase II promoter in response to hypoxia, negative regulation of transcription from RNA polymerase II promoter in response to hypoxia
JUN	Jun proto-oncogene, AP-1 transcription factor subunit	Angiogenesis, microglial cell activation, release of cytochrome c from mitochondria, liver development, positive regulation of endothelial cell proliferation, outflow tract morphogenesis, transcription from RNA polymerase II promoter, transforming growth factor beta receptor signaling pathway, SMAD protein import into nucleus, Ras protein signal transduction, aging, learning, circadian rhythm, negative regulation of cell proliferation, response to radiation, response to mechanical stimulus, positive regulation of epithelial cell migration, regulation of cell death, monocyte differentiation, axon regeneration, negative regulation of protein autophosphorylation, response to lipopolysaccharide, cellular response to hormone stimulus, response to cytokine, leading edge cell differentiation, response to muscle stretch, Fc-epsilon receptor signaling pathway, regulation of cell proliferation, response to drug, response to hydrogen peroxide, negative regulation of DNA binding, negative regulation of neuron apoptotic process, positive regulation of

	neuron apoptotic process, positive regulation of GTPase activity, negative regulation by host of viral transcription, positive regulation by host of viral transcription, positive regulation of cell differentiation, positive regulation of monocyte differentiation, positive regulation of DNA replication, negative regulation of transcription, DNA-templated, positive regulation of transcription, DNA-templated, positive regulation of transcription from RNA polymerase II promoter, positive regulation of fibroblast proliferation, positive regulation of smooth muscle cell proliferation, regulation of sequence-specific DNA binding transcription factor activity, cellular response to potassium ion starvation, response to cAMP, regulation of cell cycle, membrane depolarization, SMAD protein signal transduction, eyelid development in camera-type eye, positive regulation of ERK1 and ERK2 cascade, cellular response to calcium ion, positive regulation of pri-miRNA transcription from RNA polymerase II promoter, negative regulation of transcription from RNA polymerase II promoter in response to endoplasmic reticulum stress, positive regulation of DNA-templated transcription, initiation

***** The common genes between these 3 large modules were not repeated into the other ones.

Table S4. Summary of functional category of the protein-protein modules.

ID	Name	UP_Sequence_Feature
BACE1	Beta secretase 1	**Chain**: Beta-secretase 1, disulfide bond **Glycosylation site**: N-linked (GlcNAc...) **Region of interest**: Interaction with RTN3 **Topological domain**: Cytoplasmic, Extracellular, transmembrane region Signal peptide, splice variant, strand,
LOC81691	Exonuclease NEF-Sp	**Chain**: Putative RNA exonuclease NEF-sp **Domain**: Exonuclease, RRM 1, RRM 2 Splice variant
GGA3	Golgi associated, Gamma adaptin ear-containing, ARF binding protein 3	**Chain**: ADP-ribosylation factor-binding protein GGA3 **Compositionally biased region**: Poly-Pro, Poly-Ser, Poly-Val, Domain: GAE, GAT, VHS, **Region of interest**: binds to ARF1 (in long isoform), Unstructured hinge **Short sequence motif**: Autoinhibitory, Splice variant
HIF1A	Hypoxia inducible factor 1 alpha Subunit	**Chain**: Hypoxia-inducible factor 1-alph **Compositionally biased region**: Poly-Thr **Cross-link**: Glycyl lysine isopeptide (Lys-Gly) (interchain with G-Cter in SUMO), Glycyl lysine isopeptide (Lys-Gly) (interchain with G-Cter in ubiquitin) **DNA-binding region**: Basic motif, Domain: Helix-loop-helix motif, Domain: PAC, PAS 1, PAS 2 **Region of interest**: C-terminal VHL recognition site, CTAD, ID, Interaction with TSGA10, N-terminal VHL recognition site, NTAD, ODD **Short sequence motif**: Nuclear localization signal

		Splice variant
SPAG16	Sperm associated antigen 16	**Chain**: Sperm-associated antigen 16 protein **Repeat**: WD 1, WD 2, WD 3, WD 4, WD 5, WD 6, WD 7 Splice variant
SPAG6	Sperm associated antigen 6	**Chain**: Sperm-associated antigen 6 **Repeat**: ARM 1, ARM 2, ARM 3, ARM 4, ARM 5, ARM 6, ARM 7, ARM 8 Splice variant
TEKT3	Tektin 3	**Chain**: Tektin-3
TSGA10	Testis specific 10	**Chain**: Testis-specific gene 10 protein **Region of interest**: Interaction with HIF1A
TUBA3C	Tubulin alpha 3c	**Chain**: Tubulin alpha-3C/D chain **Nucleotide phosphate-binding region**: GTP, site: Involved in polymerization Splice variant
TUBB1	Tubulin beta 1 class VI	**Chain**: Tubulin beta-1 chain **Nucleotide phosphate-binding region**: GTP
TUBB2A	Tubulin beta 2A class II A	**Chain**: Tubulin beta-2A chain **Nucleotide phosphate-binding region**: GTP
TUBB2B	Tubulin beta 2B class II B	**Chain**: Tubulin beta-2 B chain **Nucleotide phosphate-binding region**: GTP
TUBB3	Tubulin beta 3 class III	**Chain**: Melanocyte-stimulating hormone receptor, Tubulin beta-3 chain **Glycosylation site**: N-linked (GlcNAc...) **Lipid moiety-binding region**: S-palmitoyl cysteine **Nucleotide phosphate-binding region**: GTP **Topological domain**: Cytoplasmic, Extracellular, transmembrane region
TUBB4A	Tubulin beta 4A class IV A	**Chain**: Tubulin beta-4 chain **Nucleotide phosphate-binding region**: GTP
TUBB4B	Tubulin beta 4B class IV B	**Chain**: Tubulin beta-2C chain **Nucleotide phosphate-binding region**: GTP
TUBB6	Tubulin beta 6 class V	**Chain**: Tubulin beta-6 chain **Nucleotide phosphate-binding region**: GTP
TUBB	Tubulin beta class I	**Chain**: Tubulin beta chain **Cross-link**: Glycyl lysine isopeptide (Lys-Gly) (interchain with G-Cter in ubiquitin) **Nucleotide phosphate-binding region**: GTP
AKT1	AKT serine/threonine kinase 1	**Active site**: Proton acceptor. **Binding site**: ATP, **Chain**: RAC-alpha serine/threonine-protein kinase, **Domain**: AGC-kinase C-terminal, PH, Protein kinase. **Nucleotide phosphate-binding region**: ATP
VEGFA	Vascular endothelial growth factor A	**Chain**: Vascular endothelial growth factor A **Glycosylation site**: N-linked (GlcNAc...) Disulfide bond, signal peptide, splice variant
ARNT	Aryl hydrocarbon receptor nuclear translocator	**Chain**: Aryl hydrocarbon receptor nuclear translocator, **Compositionally biased region**: Gln-rich, Poly-Arg, Poly-Gln, Poly-Ser, **DNA-binding region**: Basic motif.

		Domain: Helix-loop-helix motif, PAC, PAS 1, PAS 2. Splice variant
OS9	OS9, endoplasmic reticulum lectin	**Chain**: Protein OS-9, **Compositionally biased region**: Asp/Glu-rich (acidic), **Domain**: PRKCSH, **Glycosylation site**: N-linked (GlcNAc...). Signal peptide, splice variant
CUL2	Cullin 2	**Chain**: Cullin-2 **Cross-link**: Glycyl lysine isopeptide (Lys-Gly) (interchain with G-Cter in NEDD8) Modified residue
EGLN3	EGL-9 family hypoxia inducible factor 3	**Binding site**: 2-oxoglutarate **Chain**: Egl nine homolog 3, Fe2OG dioxygenase **Metal ion-binding site**: Iron
HSP90AA1	Heat shock protein 90 alpha family class A member 1	**Chain**: Heat shock protein HSP 90-alpha, Putative heat shock protein HSP90-alpha A2, **Compositionally biased region**: Glu-rich, Lys-rich,helix, Splice variant
TCEB1	transcription elongation factor B subunit 1	**Chain**: Transcription elongation factor B polypeptide 1
TCEB2	transcription elongation factor B subunit 2	**Chain**: Transcription elongation factor B polypeptide 2 **Domain**: Ubiquitin-like
FURIN	Furin, paired basic amino acid cleaving enzyme	**Active site**: Charge relay system **Chain**: Furin **Compositionally biased region**: Cys-rich **Glycosylation site**: N-linked (GlcNAc...) **Metal ion-binding site**: Calcium 1, Calcium 2 **Propeptide**: Inhibition peptide **Region of interest**: Cell surface signal **Short sequence motif**: Cell attachment site, Trans Golgi network signal, **Site**: Cleavage, first; by autolysis, site: Cleavage, second; by autolysis Signal peptide, transmembrane region, disulfide bond
PKM	Pyruvate kinase, muscle	**Binding site**: D-fructose 1,6-bisphosphate; part of allosteric site, Substrate, Substrate; via amide nitrogen **Chain**: Pyruvate kinase isozymes M1/M2 **Metal ion-binding site**: Magnesium, Potassium **Region of interest**: D-fructose 1,6-bisphosphate binding; part of allosteric site, Interaction with POU5F1, Inter-subunit contact **Site**: Transition state stabilizer, splice variant
NOTCH1	Notch 1	**Chain**: Neurogenic locus notch homolog protein 1, Notch 1 extracellular truncation, Notch 1 intracellular domain **Compositionally biased region**: Poly-Ala, Poly-Arg, Poly-Gln, Poly-Glu, Poly-Gly, Poly-Pro, Poly-Ser, Poly-Val, **Domain**: EGF-like 1,domain: EGF-like 10, domain: EGF-like 11; calcium-binding, EGF-like 12; calcium-binding, EGF-like 13; calcium-binding, EGF-like 14; calcium-binding, EGF-like 15; calcium-binding, EGF-like 16; calcium-binding, EGF-like 17; calcium-binding, EGF-like 18; calcium-binding, EGF-like 19; calcium-binding, EGF-like 2, EGF-

		like 20, EGF-like 21; calcium-binding, EGF-like 22, EGF-like 23; calcium-binding, EGF-like 24, EGF-like 25; calcium-binding, EGF-like 26, EGF-like 27, EGF-like 28, EGF-like 29, EGF-like 3, EGF-like 30, EGF-like 31; calcium-binding, EGF-like 32; calcium-binding, EGF-like 33, EGF-like 34, EGF-like 35, EGF-like 36, EGF-like 4, EGF-like 5; calcium-binding, EGF-like 6, EGF-like 7; calcium-binding, EGF-like 8; calcium-binding, EGF-like 9; calcium-binding **Glycosylation site**: N-linked (GlcNAc...) **Metal ion-binding site**: Calcium, Calcium; via carbonyl oxygen **Repeat**: ANK 1, ANK 2, ANK 3, ANK 4, ANK 5, LNR 1, LNR 2, LNR 3 Signal peptide, site: Cleavage; by furin-like protease, disulfide bond **Topological domain**: Cytoplasmic, Extracellular, transmembrane region
APP	Amyloid beta precursor protein	**Chain:** Amyloid beta A4 protein, Beta-amyloid protein 40, Beta-amyloid protein 42, C31, C80, C83, C99, Gamma-secretase C-terminal fragment 50, Gamma-secretase C-terminal fragment 57, Gamma-secretase C-terminal fragment 59, N-APP, Soluble APP-alpha, Soluble APP-beta. **Compositionally biased region**: Asp/Glu-rich (acidic), Poly-Thr. Disulfide bond, modified residue, mutagenesis site, **Domain**: BPTI/Kunitz inhibitor. **Glycosylation site**: N-linked (GlcNAc...) and O-linked (Xyl...) (chondroitin sulfate); in L-APP isoforms. **Metal ion-binding site**: Copper, Copper or zinc, **Peptide**: P3(40), P3(42). **Region of interest**: Collagen-binding, Heparin-binding, Interaction with G(o)-alpha, Zinc-binding. **Short sequence motif**: Basolateral sorting signal, NPXY motif; contains endocytosis signal, **Signal peptide**, site: Cleavage; by alpha-secretase, Cleavage; by beta-secretase, Cleavage; by caspase-6, caspase-8 or caspase-9, Cleavage; by caspase-6; when associated with variant 670-N-L-671, Cleavage; by gamma-secretase; site 1, Cleavage; by gamma-secretase; site 2, Cleavage; by gamma-secretase; site 3, Cleavage; by theta-secretase, **Site**: Implicated in free radical propagation, Reactive bond, Required for Cu^{+2} reduction, Susceptible to oxidation, Splice variant. **Topological domain**: Cytoplasmic, Extracellular, transmembrane region
CXCL12	C-X-C motif chemokine ligand 12	**Chain**: SDF-1-alpha (3-67), SDF-1-beta (3-72), Stromal cell-derived factor 1 Disulfide bond, Signal peptide, Splice variant
CXCR4	C-X-C motif chemokine receptor 4	**Chain**: C-X-C chemokine receptor type 4 Disulfide bond **Glycosylation site**: N-linked (GlcNAc...) and O-linked (Xyl...) (chondroitin sulfate) **Short sequence motif**: Important for signaling, splice variant **Topological domain**: Cytoplasmic, extracellular, transmembrane region
EPO	Erythropoietin	**Chain**: Erythropoietin **Glycosylation site**: N-linked (GlcNAc...), O-linked (GalNAc...) **Propeptide**: Removed in mature form (Partial)

		Signal peptide, disulfide bond
GNB2L1[ͳ]	guanine nucleotide binding protein (G protein), beta polypeptide 2-like 1	**Chain**: Guanine nucleotide-binding protein subunit beta-2-like 1 **Repeat**: WD 1, WD 2, WD 3, WD 4, WD 5, WD 6, WD 7
EGLN1	egl-9 family hypoxia inducible factor 1	**Binding site**: 2-oxoglutarate **Chain**: Egl nine homolog 1 **Domain**: Fe2OG dioxygenase **Metal ion-binding site**: Iron **Zinc finger region**: MYND-type Splice variant
HIF1AN	hypoxia inducible factor 1 alpha subunit inhibitor	**Binding site**: 2-oxoglutarate **Chain**: Hypoxia-inducible factor 1-alpha inhibitor **Domain**: JmjC **Metal ion-binding site**: Iron; Catalytic **Region of interest**: Interaction with HIF1A, Interaction with VHL
VHL	von Hippel-Lindau tumor suppressor	**Chain**: Von Hippel-Lindau disease tumor suppressor **Region of interest**: 8 X 5 AA tandem repeats of G-[PAVG]-E-E-[DAYSLE], Interaction with Elongin BC complex, Involved in binding to CCT complex **Repeat**:1, 2, 3, 4, 5, 6, 7, 8 Splice variant
JUN	Jun proto-oncogene, AP-1 transcription factor subunit	**Chain**: Transcription factor AP-1 **DNA-binding region**: Basic motif **Domain**: Leucine-zipper

[ͳ] The functional annotation of GNB2L1 is annotated based on *Danio rerio* species.