

Table S4: Biological Function categories known to involve 45 well characterized genes that were affected by a high-impact SNP.

Category	Functions Annotation	Molecules
Amino Acid Metabolism	secretion of GABA	HTR2C
Auditory and Vestibular System Development and Function	sensitivity of basilar membrane	TECTA
	abnormal morphology of otolithic membrane	TECTA
	quantity of otoliths	TECTA
	abnormal morphology of enlarged otoliths	TECTA
	abnormal morphology of tectorial membrane	TECTA
Auditory Disease	childhood onset deafness DFNB8	TECTA
Behavior	Stereotypy	HTR2C
Cancer	survival of pancreatic cancer cells	XIAP
	survival of carcinoma cells	XIAP
	growth of lung tumor	XIAP
	malignant cutaneous melanoma cancer	CDC27,MLL3, TECTA
	childhood acute lymphoblastic leukemia	XIAP
	tumorigenesis of fibroblast cell lines	CAST
	Cancer	CAD,CDC27, CES1,CLTCL 1,DST,MLL3,PP2R2B,SAFB2,TECTA,TF AP2B,XIAP
	alveolar rhabdomyosarcoma	TFAP2B
Carbohydrate Metabolism	hydrolysis of inositol phosphate	HTR2C
	regulation of D-glucose	HTR2C
Cardiovascular Disease	congestive heart failure	TFAP2B,XIAP
	vascular dementia	HTR2C
	Hemopericardium	XIAP
Cell Cycle	mitotic exit of cervical cancer cell lines	MYT1
	re-entry into cell cycle progression of fibroblast cell lines	CAST
	metaphase/anaphase transition	CDC27
	mitochondrial fission	PPP2R2B

	cell cycle progression	CAST,CDC27,CLTCL1,MYT1,PPP2R2B
	cell cycle progression of colon cancer cell lines	CDC27
Cell Death and Survival	anoikis of prostate cancer cells	XIAP
	survival of pancreatic cancer cells	XIAP
	apoptosis of insect cell lines	XIAP
	survival of carcinoma cells	XIAP
	degeneration of retinal ganglion cells	XIAP
	apoptosis of ovarian surface epithelial cells	XIAP
	apoptosis of pancreatic cancer cells	XIAP
	loss of neurons	CAST,XIAP
	apoptosis of brain cells	CAST,XIAP
	apoptosis of endometrial cancer cell lines	XIAP
	apoptosis of renal tubule	TFAP2B
	apoptosis of neurons	CAST,PPP2R2B,XIAP
	apoptosis of carcinoma cell lines	TFAP2B,XIAP
	apoptosis of lung cancer cell lines	TFAP2B,XIAP
	cell death of neuroblastoma cell lines	CAST,DST
	anoikis of intestinal cell lines	XIAP
	apoptosis of leukocytes	CAST,PPP2R2B,XIAP
	apoptosis of T-cell hybrid cells	XIAP
	apoptosis of granulosa cells	XIAP
Cell Morphology	coalignment of microfilaments	DST
	coalignment of neurofilaments	DST
	polarization of Schwann cells	DST
	binucleation of fibroblasts	PCNT
	morphology of filopodia	CAST
	polarization of neutrophils	CAST
	polarization of cells	CAST,DST
	cell spreading of blood platelets	CAST
	extension of lamellipodia	CAST
	morphology of cellular protrusions	CAST,DST
	abnormal morphology of myelin sheath	DST
	formation of autophagosomes	CAST

Cell-To-Cell Signaling and Interaction	dissociation of focal adhesions	CAST
	activation of ova	CAST
	modulation of dopamine	HTR2C
	activation of dopaminergic neurons	HTR2C
	cochlear microphonics	TECTA
	concentration of dopamine	HTR2C,XIAP
	compound action potential of cochlear nerve	TECTA
	secretion of acetylcholine	HTR2C
	synaptic transmission of superior cervical ganglion neurons	CAST
Cellular Assembly and Organization	formation of phagosomes	CAST,CDC27
	coalignment of microfilaments	DST
	coalignment of neurofilaments	DST
	dissociation of focal adhesions	CAST
	formation of annulate lamellae	NUP153
	transport of axons	DST
	secretion of alpha granules	CAST
	organization of cytoplasmic microtubule	DST
	extension of lamellipodia	CAST
	shortening of telomeres	TFAP2B
	nucleation of microtubules	PCNT
	organization of mitotic spindle	PCNT
	disruption of cytoskeleton	CAST
	formation of autophagosomes	CAST
Cellular Compromise	binucleation of fibroblasts	PCNT
	neurodegeneration of CA1 neuron	XIAP
	breakdown of nuclear envelope	NUP153
	endoplasmic reticulum stress response of neuroblastoma cell lines	DST
	degeneration of retinal ganglion cells	XIAP
	disorganization of cytoskeleton	DST
	fragmentation of mitochondria	PPP2R2B
	fragmentation of Golgi apparatus	DST
	disruption of cytoskeleton	CAST
Cellular Development	osteoclastogenesis of macrophage cancer cell lines	CAST

	osteoclastogenesis of bone-marrow-derived monocyte/macrophage precursor cells	CAST
	differentiation of adipoblasts	CAST
Cellular Function and Maintenance	formation of phagosomes	CAST,CDC27
	function of gamma cells	MYT1
	endoplasmic reticulum stress response of neuroblastoma cell lines	DST
	secretion of alpha granules	CAST
	function of outer hair cells	TECTA
	organization of cytoplasmic microtubule	DST
	extension of lamellipodia	CAST
	nucleation of microtubules	PCNT
	organization of mitotic spindle	PCNT
	axonal transport	DST
	formation of autophagosomes	CAST
Cellular Movement	transport of axons	DST
	chemokinesis of neutrophils	CAST
	migration of bladder cancer cell lines	XIAP
Cellular Response to Therapeutics	sensitivity of tumor cell lines	XIAP
Connective Tissue Development and Function	re-entry into cell cycle progression of fibroblast cell lines	CAST
	osteoclastogenesis of bone-marrow-derived monocyte/macrophage precursor cells	CAST
	differentiation of adipoblasts	CAST
Connective Tissue Disorders	microcephalic osteodysplastic primordial dwarfism, type 2	PCNT
	tumorigenesis of fibroblast cell lines	CAST
Dermatological Diseases and Conditions	infection of epithelial cell lines	CAD,NUP153, XIAP
	malignant cutaneous melanoma cancer	CDC27,MLL3, TECTA
	blister	DST
Developmental Disorder	Char syndrome	TFAP2B
	microcephalic osteodysplastic primordial dwarfism, type 2	PCNT
	Seckel syndrome 4	PCNT
	postaxial polydactyly	TFAP2B

	dystrophy of neurites	CAST
	congenital anomaly of musculoskeletal system	CAST,PCNT,T FAP2B
DNA Replication, Recombination, and Repair	organization of mitotic spindle	PCNT
Drug Metabolism	hydrolysis of D-methylphenidate	CES1
	hydrolysis of cocaine	CES1
	hydrolysis of irinotecan	CES1
	modulation of dopamine	HTR2C
	concentration of dopamine	HTR2C,XIAP
Embryonic Development	ventralization of embryo	XIAP
	development of collecting tubule	TFAP2B
	osteoclastogenesis of bone-marrow-derived monocyte/macrophage precursor cells	CAST
Endocrine System Development and Function	release of corticosterone	HTR2C
	quantity of PTH in blood	TFAP2B
Endocrine System Disorders	hypocalciuria	TFAP2B
	hyperprolactinemia	HTR2C
	hypocalcemia	TFAP2B
Gastrointestinal Disease	primary sclerosing cholangitis	XIAP
Hematological Disease	hyperphosphatemia	TFAP2B
	childhood acute lymphoblastic leukemia	XIAP
	hypocalcemia	TFAP2B
Hematological System Development and Function	chemokinesis of neutrophils	CAST
	polarization of neutrophils	CAST
	osteoclastogenesis of bone-marrow-derived monocyte/macrophage precursor cells	CAST
	quantity of foam cells	CES1
	cell spreading of blood platelets	CAST
Hematopoiesis	osteoclastogenesis of bone-marrow-derived monocyte/macrophage precursor cells	CAST
Hepatic System Disease	primary sclerosing cholangitis	XIAP
Hereditary Disorder	Char syndrome	TFAP2B
	X-linked familial hemophagocytic lymphohistiocytosis	XIAP
	dystonia mysculorum deformans 2	DST

	microcephalic osteodysplastic primordial dwarfism, type 2	PCNT
	spinocerebellar ataxia 12	PPP2R2B
	spinocerebellar ataxia recessive 9	ADCK3
	Seckel syndrome 4	PCNT
	X-linked lymphoproliferative syndrome	XIAP
	childhood onset deafness DFNB8	TECTA
	spinocerebellar ataxia	ADCK3,PPP2R2B
	Schizophrenia	CAD,HTR2C,MLL3,NBPF15 (includes others)
	hebephrenic schizophrenia	HTR2C
	paranoid schizophrenia	HTR2C
	X-linked hereditary disease	CAST,XIAP
Immune Cell Trafficking	chemokinesis of neutrophils	CAST
Immunological Disease	X-linked familial hemophagocytic lymphohistiocytosis	XIAP
Immunological Disease	X-linked lymphoproliferative syndrome	XIAP
	seasonal allergic rhinitis	HTR2C
	allergic rhinoconjunctivitis	HTR2C
	childhood acute lymphoblastic leukemia	XIAP
Infectious Disease	infection of embryonic cell lines	CAD,NUP153,XIAP
	infection of epithelial cell lines	CAD,NUP153,XIAP
	infection of kidney cell lines	CAD,NUP153,XIAP
	infection of cells	CAD,CLTCL1,NUP153,XIAP
Inflammatory Disease	seasonal allergic rhinitis	HTR2C
	allergic rhinoconjunctivitis	HTR2C
	primary sclerosing cholangitis	XIAP
Inflammatory Response	chemokinesis of neutrophils	CAST
	polarization of neutrophils	CAST
	quantity of foam cells	CES1
	cell spreading of blood platelets	CAST
Lipid Metabolism	elimination of cholesterol	CES1
	synthesis of D-erythro-C16-ceramide	XIAP
	release of corticosterone	HTR2C
	secretion of GABA	HTR2C

	concentration of bile acid	MLL3
Lymphoid Tissue Structure and Development	osteoclastogenesis of bone-marrow-derived monocyte/macrophage precursor cells	CAST
Metabolic Disease	spinocerebellar ataxia recessive 9	ADCK3
	beta amyloidosis	CAST
Molecular Transport	elimination of cholesterol	CES1
	concentration of dopamine	HTR2C,XIAP
	secretion of acetylcholine	HTR2C
	release of corticosterone	HTR2C
	secretion of GABA	HTR2C
	quantity of PTH in blood	TFAP2B
	concentration of bile acid	MLL3
Nervous System Development and Function	coalignment of neurofilaments	DST
	activation of dopaminergic neurons	HTR2C
	cochlear microphonics	TECTA
	transport of axons	DST
	mechanotransduction of hair cells	TECTA
	compound action potential of cochlear nerve	TECTA
	function of outer hair cells	TECTA
	synaptic transmission of superior cervical ganglion neurons	CAST
	loss of neurons	CAST,XIAP
	abnormal morphology of myelin sheath	DST
	axonal transport	DST
Neurological Disease	dysmyelination of peripheral nervous system	DST
	dystonia musculorum deformans 2	DST
	microcephalic osteodysplastic primordial dwarfism, type 2	PCNT
	spinocerebellar ataxia 12	PPP2R2B
	spinocerebellar ataxia recessive 9	ADCK3
	childhood onset deafness DFNB8	TECTA
	neurodegeneration of CA1 neuron	XIAP
	spinocerebellar ataxia	ADCK3,PPP2R2B
	onset of amyotrophic lateral sclerosis	XIAP
	suicidal behavior	CAD

	beta amyloidosis	CAST
	microgliosis of brain	CAST
	dystrophy of neurites	CAST
	Schizophrenia	CAD,HTR2C, MLL3,NBPF15 (includes others)
	muscle spasm	TFAP2B
	tic disorder	HTR2C
	amyotrophic lateral sclerosis	HTR2C,XIAP
	Asperger syndrome	HTR2C
	tonic seizure	HTR2C
	bipolar II disorder	HTR2C
	cannabis dependence	HTR2C
	hebephrenic schizophrenia	HTR2C
	major depression	CAD,HTR2C
	paranoid schizophrenia	HTR2C
	vascular dementia	HTR2C
	anorexia	HTR2C
	psychomotor agitation	HTR2C
Nutritional Disease	anorexia	HTR2C
	adult-onset obesity	HTR2C
Ophthalmic Disease	allergic rhinoconjunctivitis	HTR2C
Organ Development	development of collecting tubule	TFAP2B
	osteoclastogenesis of bone-marrow-derived monocyte/macrophage precursor cells	CAST
Organ Morphology	sensitivity of basilar membrane	TECTA
	abnormal morphology of otolithic membrane	TECTA
	abnormal morphology of enlarged otoliths	TECTA
	abnormal morphology of dilated proximal convoluted tubule	TFAP2B
	abnormal morphology of tectorial membrane	TECTA
	opening of eyelid	MLL3
Organismal Development	ventralization of embryo	XIAP
	development of collecting tubule	TFAP2B
	osteoclastogenesis of bone-marrow-derived monocyte/macrophage precursor cells	CAST

Organismal Injury and Abnormalities	neurodegeneration of CA1 neuron	XIAP
	microgliosis of brain	CAST
	infection of embryonic cell lines	CAD,NUP153, XIAP
	hot flashes	HTR2C
	hemopericardium	XIAP
	size of lesion	CES1,XIAP
Post-Translational Modification	ubiquitination of protein	CAST,XIAP
Protein Synthesis	quantity of PTH in blood	TFAP2B
Protein Trafficking	targeting of green fluorescent protein	PPP2R2B
Psychological Disorders	suicidal behavior	CAD
	Schizophrenia	CAD,HTR2C, MLL3,NBPF15
	Asperger syndrome	HTR2C
	bipolar II disorder	HTR2C
	cannabis dependence	HTR2C
	hebephrenic schizophrenia	HTR2C
	major depression	CAD,HTR2C
	paranoid schizophrenia	HTR2C
	vascular dementia	HTR2C
	anorexia	HTR2C
Renal and Urological Disease	infection of kidney cell lines	CAD,NUP153, XIAP
Renal and Urological System Development and Function	development of collecting tubule	TFAP2B
	abnormal morphology of dilated proximal convoluted tubule	TFAP2B
Reproductive System Development and Function	activation of ova	CAST
Reproductive System Disease	hyperprolactinemia	HTR2C
Respiratory Disease	growth of lung tumor	XIAP
	seasonal allergic rhinitis	HTR2C
	allergic rhinoconjunctivitis	HTR2C
Skeletal and Muscular Disorders	microcephalic osteodysplastic primordial dwarfism, type 2	PCNT
	postaxial polydactyly	TFAP2B
	muscle spasm	TFAP2B
	congenital anomaly of musculoskeletal system	CAST,PCNT,T FAP2B
	psychomotor agitation	HTR2C

	alveolar rhabdomyosarcoma	TFAP2B
Skeletal and Muscular System Development and Function	osteoclastogenesis of macrophage cancer cell lines	CAST
	osteoclastogenesis of bone-marrow-derived monocyte/macrophage precursor cells	CAST
Small Molecule Biochemistry	biosynthesis of pyrimidine	CAD
	elimination of cholesterol	CES1
	hydrolysis of irinotecan	CES1
	modulation of dopamine	HTR2C
	hydrolysis of inositol phosphate	HTR2C
	concentration of dopamine	HTR2C,XIAP
	synthesis of D-erythro-C16-ceramide	XIAP
	secretion of acetylcholine	HTR2C
	regulation of D-glucose	HTR2C
	release of corticosterone	HTR2C
	secretion of GABA	HTR2C
	quantity of PTH in blood	TFAP2B
	concentration of bile acid	MLL3
Tissue Development	dissociation of focal adhesions	CAST
	development of collecting tubule	TFAP2B
	osteoclastogenesis of bone-marrow-derived monocyte/macrophage precursor cells	CAST
Tissue Morphology	quantity of foam cells	CES1
	size of lesion	CES1,XIAP
	abnormal morphology of myelin sheath	DST
Tumor Morphology	anoikis of prostate cancer cells	XIAP
	survival of pancreatic cancer cells	XIAP
	survival of carcinoma cells	XIAP
	apoptosis of pancreatic cancer cells	XIAP
Visual System Development and Function	opening of eyelid	MLL3