SUPPLEMENTARY MATERIAL

Effect of Next-Generation Exome Sequencing Depth for Discovery of Diagnostic Variants

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Supplementary Table 1. List of diagnostic genes

Gene Symbol	Description	Associated diseases
ABCB11	ATP-binding cassette, sub-family B (MDR/TAP), member 11	Intrahepatic cholestasis
ABCD1	ATP-binding cassette, sub-family D (ALD), member 1	Adrenoleukodystrophy
ACVR1	Activin A receptor, type I	Fibrodysplasia ossificans progressiva
AGL	Amylo-alpha-1, 6-glucosidase, 4-alpha-glucanotransferase	Glycogen storage disease
ALB	Albumin	Analbuminaemia
APC	Adenomatous polyposis coli	Adenomatous polyposis coli
APOE	Apolipoprotein E	Apolipoprotein E deficiency
AR	Androgen receptor	Androgen insensitivity syndrome
ARG1	Arginase 1	Arginase deficiency
ASS1	Argininosuccinate synthase 1	Citrullinaemia
ATN1	Atrophin 1	Dentatorubro-pallidoluysian atroph
ATP7A	ATPase, Cu++ transporting, alpha polypeptide	Menkes syndrome
ATP7B	ATPase, Cu++ transporting, beta polypeptide	Wilson disease
ATP8B1	ATPase, aminophospholipid transporter, class I, type 8B, member 1	Intrahepatic cholestasis
ATXN1	Ataxin 1	Spinocerebellar ataxia
ATXN2	Ataxin 2	Spinocerebellar ataxia
ATXN3	Ataxin 3	Spinocerebellar ataxia
ATXN7	Ataxin 7	Spinocerebellar ataxia
BEST1	Bestrophin 1	Best macular dystrophy
BMPR2	Bone morphogenetic protein receptor, type II (serine/threonine kinase)	Pulmonary hypertension
BRAF	v-raf murine sarcoma viral oncogene homolog B	Cardio-facio-cutaneous syndrome
BRCA1	Breast Cancer 1, Early Onset	Breast and/or ovarian cancer syndrome
BRCA2	Breast Cancer 2, Early Onset	Breast and/or ovarian cancer syndrome
BTK	Bruton agammaglobulinemia tyrosine kinase	Agammaglobulinaemia
CACNA1A	Calcium channel, voltage-dependent, P/Q type, alpha 1A subunit	Episodic ataxia
CACNA1S	Calcium channel, voltage-dependent, L type, alpha 1S subunit	Hypokalaemic periodic paralysis
CCM2	Cerebral cavernous malformation 2	Cerebral cavernous malformations
CDKL5	Cyclin-dependent kinase-like 5	Rett syndrome
CDMP1(GDF5)	Growth differentiation factor 5	Brachydactyly, type C
CFTR	Cystic fibrosis transmembrane conductance regulator (ATP-binding cassette sub-family C, member 7)	Cystic fibrosis
CLCN1	Chloride channel, voltage-sensitive 1	Myotonia congenita
COL10A1	Collagen, type X, alpha 1	Metaphyseal chondrodysplasia, Schmid
COL1A1	Collagen, type I, alpha 1	Osteogenesis imperfecta
COL1A2	Collagen, type I, alpha 2	Osteogenesis imperfecta
COL2A1	Collagen, type II, alpha 1	Stickler syndrome
COL3A1	Collagen, type III, alpha 1	Ehlers-Danlos syndrome
COMP	Cartilage oligomeric matrix protein	Multiple epiphyseal dysplasia
CRB1	Crumbs family member 1, photoreceptor morphogenesis associated	Leber congenital amaurosis
CSTB	Cystatin B (stefin B)	Epilepsy, progressive myoclonus
CYP21A2	Cytochrome P450, family 21, subfamily A, polypeptide 2	Adrenal hyperplasia
CYP2C19	Cytochrome P450, family 2, subfamily C, polypeptide 19	
CYP2C9	Cytochrome P450, family 2, subfamily C, polypeptide 9	
DHCR7	7-Dehydrocholesterol reductase	Smith-Lemli-Opitz syndrome
DMD	Dystrophin	Duchenne muscular dystrophy
DMPK	Dystrophia myotonica-protein kinase	Myotonic dystrophy
EGFR	Epidermal growth factor receptor	
ELANE	Elastase, neutrophil expressed	Congenital neutropaenia
EXT1	Exostosin glycosyltransferase 1	Multiple exostoses
EXT2	Exostosin glycosyltransferase 2	Multiple exostoses
FANCA	Fanconi anemia, complementation group A	Fanconi anemia
FANCC	Fanconi anemia, complementation group C	Fanconi anemia
FANCG	Fanconi anemia, complementation group G	Fanconi anemia
FBN1	Fibrillin 1	Marfan syndrome
FGF23	Fibroblast growth factor 23	Tumoural calcinosis with hyperphosphataemia
FGFR1	Fibroblast growth factor receptor 1	Kallmann syndrome
FGFR2	Fibroblast growth factor receptor 2	Crouzon syndrome
FGFR3	Fibroblast growth factor receptor 3	Hypochondroplasia
FMR1	Fragile X mental retardation 1	Fragile X syndrome
FOXP3	Forkhead box P3	IPEX syndrome
FXN	Frataxin	Friedreich ataxia
G6PC	Glucose-6-phosphatase, catalytic subunit	Glycogen storage disease
GAA	Glucosidase, alpha; acid	Glycogen storage disease
GALC	Galactosylceramidase	Krabbe disease
GALE	UDP-galactose-4-epimerase	Galactosaemia
GALK1	Galactokinase 1	Galactosaemia
GALT	Galactose-1-phosphate uridylyltransferase	Galactosaemia
GBA	Glucosidase, beta, acid	Gaucher disease
GBE1	Glucan (1,4-alpha-), branching enzyme 1	Glycogen storage disease
GCDH	Glutaryl-CoA dehydrogenase	Glutaricacidaemia
GCH1	GTP cyclohydrolase 1	Dystonia, dopa-responsive
GJB1	Gap junction protein, beta 1, 32kDa	Charcot-Marie-Tooth disease
GJB2	Gap junction protein, beta 2, 32kDa	Deafness
GST	Glutathione S-transferase theta	
GUCY2D	Guanylate cyclase 2D, membrane (retina-specific)	Leber congenital amaurosis
HAX1	HCLS1 associated protein X-1	Kostmann disease
HBA1	Hemoglobin, alpha 1	Thalassaemia
HBA2	Hemoglobin, alpha 2	Thalassaemia
HBB	Hemoglobin, beta	Thalassaemia
HMBS	Hydroxymethylbilane synthase	Porphyria, acute intermittent
HNF1B	HNF1 homeobox B	Diabetes, MODY
HPS1	Hermansky-Pudlak syndrome 1	Hermansky-Pudlak syndrome
HRAS	Harvey rat sarcoma viral oncogene homolog	Costello syndrome
HTT	Huntingtin	Huntington disease
IDS	Iduronate 2-sulfatase	Mucopolysaccharidosis
IKBKG	Inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase gamma	Incontinentia pigmenti
INS	Insulin	Diabetes, permanent neonatal
JAG1	Jagged 1	Alagille syndrome
JPH3	Junctophilin 3	Huntington disease-like 2
KCNH2	Potassium voltage-gated channel, subfamily H (eag-related), member 2	Long QT syndrome

Gene Symbol	Description	Associated diseases
KCNJ11	Potassium inwardly-rectifying channel, subfamily J, member 11	Hyperinsulinism
KCNQ1	Potassium voltage-gated channel, KQT-like subfamily, member 1	Long QT syndrome
KRAS	Kirsten rat sarcoma viral oncogene homolog	Noonan syndrome
KRIT1	KRIT1, ankyrin repeat containing	Cerebral cavernous malformations
LAMP2	Lysosomal-associated membrane protein 2	Glycogen storage disease
LMNA	Lamin A/C	Muscular dystrophy, Emery-Dreifuss
MAPT	Microtubule-associated protein tau	Frontotemporal dementia
MATN3	Matrilin 3	Multiple epiphyseal dysplasia
MECP2	Methyl CpG binding protein 2 (Rett syndrome)	Rett syndrome
MEN1	Multiple endocrine neoplasia I	Multiple endocrine neoplasia
MFN2	Mitofusin 2	Charcot-Marie-Tooth disease
MLH1	mutL homolog 1	Colorectal cancer, non-polyposis
MPZ	Myelin protein zero	Charcot-Marie-Tooth disease
MSH2	mutS homolog 2	Colorectal cancer, non-polyposis
MYBPC3	Myosin binding protein C, cardiac	Cardiomyopathy, hypertrophic
MYH7	Myosin, heavy chain 7, cardiac muscle, beta	Cardiomyopathy, hypertrophic
MYH9	Myosin, heavy chain 9, non-muscle	May-Hegglin anomaly
NAT2	N-acetyltransferase 2 (arylamine N-acetyltransferase)	
NDP	Norrie disease (pseudoglioma	Norrie disease
NF1	Neurofibromin 1	Neurofibromatosis 1
NF2	Neurofibromin 2	Neurofibromatosis 2
NOTCH3	Notch 3	CADASIL
NPHS2	Nephrosis 2, idiopathic, steroid-resistant (podocin)	Nephrotic syndrome, steroid resistant
NRAS	Neuroblastoma RAS viral (v-ras) oncogene homolog	Noonan syndrome
NTNG1	Netrin G1	Rett syndrome
NTRK1	Neurotrophic tyrosine kinase, receptor, type 1	Pain insensitivity, congenital
OPA1	Optic atrophy 1 (autosomal dominant)	Optic atrophy
OTC	Ornithine carbamoyltransferase	Ornithine transcarbamylase deficiency
PABPN1	Poly(A) binding protein, nuclear 1	Oculopharyngeal muscular dystrophy
PANK2	Pantothenate kinase 2	Pantothenate kinase-associated neurodegeneration
PARK2	Parkin RBR E3 ubiquitin protein ligase	Parkinson disease
PAX6	Paired box 6	Aniridia
PDCD10	Programmed cell death 10	Cerebral cavernous malformation
PGD	Phosphogluconate dehydrogenase	
PKD2	Polycystic kidney disease 2 (autosomal dominant)	Polycystic kidney disease
PLP1	Proteolipid protein 1	Pelizaeus-Merzbacher disease
PMP22	Peripheral myelin protein 22	Charcot-Marie-Tooth disease
POLG	Polymerase (DNA directed), gamma	Progressive external ophthalmoplegia
PRF1	Perforin 1 (pore forming protein)	Haemophagocytic lymphohistiocytosis
PRKAG2	Protein kinase, AMP-activated, gamma 2 non-catalytic subunit	Cardiomyopathy, hypertrophic
PROC	Protein C (inactivator of coagulation factors Va and VIIIa)	Protein C deficiency
PROS1	Protein S (alpha)	Protein S deficiency
PRRT2	Proline-rich transmembrane protein 2	Episodic kinesigenic dyskinesia
PSEN1	Presenilin 1	Alzheimer disease
PTEN	Phosphatase and tensin homolog	Cowden disease
PTPN11	Protein tyrosine phosphatase, non-receptor type 11	Noonan syndrome
RB1	Retinoblastoma 1	Retinoblastoma
RET	ret proto-oncogene	Hirschsprung disease
RP1L1	Retinitis pigmentosa 1-like 1	Retinitis pigmentosa
RPE65	Retinal pigment epithelium-specific protein 65kDa	Leber congenital amaurosis
RPGRIP1	Retinitis pigmentosa GTPase regulator interacting protein 1	Leber congenital amaurosis
RS1	Retinoschisin 1	Retinoschisis
SCN4A	Sodium channel, voltage-gated, type IV, alpha subunit	Paramyotonia congenita
SCN5A	Sodium channel, voltage-gated, type V, alpha subunit	Brugada syndrome
SDHB	Succinate dehydrogenase complex, subunit B, iron sulfur (Ip)	Pheochromocytoma
SDHD	Succinate dehydrogenase complex, subunit D, integral membrane protein	Pheochromocytoma
SERPINC1	Serpin peptidase inhibitor, clade C (antithrombin), member 1	Antithrombin deficiency
SGCE	Sarcoglycan, epsilon	Limb-girdle muscular dystrophy
SLC12A3	Solute carrier family 12 (sodium/chloride transporter), member 3	Gitelman syndrome
SLC25A13	Solute carrier family 25 (aspartate/glutamate carrier), member 13	Intrahepatic cholestasis, neonatal
SLC26A4	Solute carrier family 26 (anion exchanger), member 4	Pendred syndrome
SLC7A7	Solute carrier family 7 (amino acid transporter light chain, y+L system), member 7	Lysinuric protein intolerance
SMAD4	SMAD family member 4	Juvenile polyposis syndrome
SMN1	Survival of motor neuron 1, telomeric	Spinal muscular atrophy
SOD1	Superoxide dismutase 1, soluble	Amyotrophic lateral sclerosis
SPAST	Spastin	Hereditary spastic paraplegia
SPG3A(ATL10)	Atlastin GTPase 1	Hereditary spastic paraplegia
STK11	Serine/threonine kinase 11	Peutz-Jeghers syndrome
TAZ	Tafazzin	Barth syndrome
TBP	TATA box binding protein	Ataxia
TCF1 (HNF1A)	Transcription factor 1 (T-cell specific, HMG-box)	Diabetes, MODY3
TGFBI	Transforming growth factor, beta-induced, 68kDa	Corneal dystrophy
TGFBR1	Transforming growth factor, beta receptor 1	Loeys-Dietz syndrome
TGFBR2	Transforming growth factor, beta receptor II (70/80kDa)	Loeys-Dietz syndrome
TOR1A	Torsin family 1, member A (torsin A)	Torsion dystonia
TP53	Tumor protein p53	Li-Fraumeni syndrome
TSC1	Tuberous sclerosis 1	Tuberous sclerosis
TSC2	Tuberous sclerosis 2	Tuberous sclerosis
TTR	Transthyretin	Amyloidotic polyneuropathy
UGT1A1	UDP glucuronosyltransferase 1 family, polypeptide A1	Crigler-Najjar syndrome
UNC13D	unc-13 homolog D (C. elegans)	Haemophagocytic lymphohistiocytosis
VHL	von Hippel-Lindau tumor suppressor, E3 ubiquitin protein ligase	Von Hippel-Lindau syndrome
VKORC1	vitamin K epoxide reductase complex, subunit 1	Warfarin resistance
VPS33B	vacuolar protein sorting 33 homolog B (yeast)	Arthrogryposis, renal dysfunction and cholestasis
VWF	von Willebrand factor	Von Willebrand disease
WAS	Wiskott-Aldrich syndrome	Wiskott-Aldrich syndrome