INFANT Study Test Description and Gene List

Gene List Version: V1.2

Effective Date: May 1st, 2026

GLOSSARY OF TERMS

INHERITANCE

The way, or pattern, by which a genetic condition is passed down through families across generations. There are some genes associated with multiple different diseases and/or inheritance patterns. All conditions associated with the genes listed below have been assessed to determine if they meet the inclusion criteria for the INFANT study. In some cases, multiple conditions associated with a gene are reportable for the INFANT study, and multiple inheritance patterns may be listed below. In other cases, only one condition and/or inheritance pattern is included. Common inheritance patterns include:

Autosomal Recessive (AR)

A genetic condition that occurs only when an individual inherits two altered copies of a gene, typically one from each parent. When a person has one copy of the altered gene, they are considered a carrier, as they are not affected by the condition but their copy of the altered gene can be passed down to their offspring. Carrier status is not reported by the INFANT study.

Autosomal Dominant (AD)

A genetic condition that occurs when an individual inherits one altered copy of a gene. An affected person has a 50% chance of passing it to their children.

X-linked (XL)

A genetic condition caused by an alteration on the X chromosome. Males are more often affected because they have only one X chromosome, while females may be carriers or have milder symptoms as they have 2 copies of the X chromosome.

INFANT Study Gene List

Gene List Version: 1.2

See footnotes below for more details

Gene	Condition Name	Clinical Category	Inheritance pattern [1,2,3]
ABCC6	Generalized arterial calcification of infancy	Cardiac	AR
ABCC8	Hyperinsulinemic hypoglycemia	Endocrine	AR
ABCD1	Adrenoleukodystrophy	Metabolic	XL
ABCD4	Methylmalonic aciduria and homocystinuria	Metabolic	AR
ACADM	Medium chain acyl-CoA dehydrogenase (MCAD) deficiency	Metabolic	AR
ACADVL	Very long chain acyl-CoA dehydrogenase (VLCAD) deficiency	Metabolic	AR
ACAT1	Beta-ketothiolase deficiency	Metabolic	AR
ACVR1	Fibrodysplasia ossificans progressiva	Bone/Connective tissue	AD
ADA	Severe combined immunodeficiency	Immunology	AR
ADAMTS1	Congenital thrombotic thrombocytopenic purpura	Hematology	AR
AGL	Cori disease (GSD type 2)	Metabolic	AR
AGXT	Primary hyperoxaluria	Metabolic	AR
AKR1D1	Congenital bile acid synthesis defect	Metabolic	AR
ALDH7A1	Pyridoxine-dependent epilepsy	Metabolic	AR
ALDOB	Hereditary fructose intolerance	Metabolic	AR
ALPL	Hypophosphatasia	Metabolic	AR
AQP2	Nephrogenic diabetes insipidus	Endocrine	AD/AR
ARG1	Hyperargininemia	Metabolic	AR

ARSA	Metachromatic leukodystrophy	Metabolic	AR
ARSB	Maroteaux-Lamy syndrome (MPS type 6)	Metabolic	AR
ASL	Argininosuccinic aciduria	Metabolic	AR
ASS1	Citrullinemia	Metabolic	AR
ATM	Ataxia-telangiectasia	Neurology/Neuromuscular	AR
ATP6V0A4	Distal renal tubular acidosis	Metabolic	AR
ATP6V1B1	Distal renal tubular acidosis	Metabolic	AR
AVPR2	Nephrogenic diabetes insipidus	Endocrine	XL
BCKDHA	Maple syrup urine disease	Metabolic	AR
BCKDHB	Maple syrup urine disease	Metabolic	AR
BTD	Biotinidase deficiency	Metabolic	AR
BTK	Agammaglobulinemia	Immunology	XL
CALM1	Long QT syndrome / Catecholaminergic polymorphic ventricular tachycardia	Cardiac	AD
CALM2	Long QT syndrome / Catecholaminergic polymorphic ventricular tachycardia	Cardiac	AD
CALM3	Long QT syndrome / Catecholaminergic polymorphic ventricular tachycardia	Cardiac	AD
CASR	Neonatal hyperparathyroidism / Hypocalcemia	Endocrine	AD/AR
CBLIF	Congenital intrinsic factor deficiency	Hematology	AR
CBS	Classic homocystinuria	Metabolic	AR
CD3D	Severe combined immunodeficiency	Immunology	AR
CD3E	Severe combined immunodeficiency	Immunology	AR
CD40LG	Hyper IgM syndrome	Immunology	XL

CDH23	Usher syndrome	Syndromic hearing loss	AR
CFTR	Cystic Fibrosis	Respiratory	AR
COL4A3	Alport syndrome	Multisystem/Syndromic	AR
COL4A4	Alport syndrome	Multisystem/Syndromic	AR
COL4A5	Alport syndrome	Multisystem/Syndromic	XL
CPS1	Carbamoyl phosphate synthetase I (CPS1) deficiency	Metabolic	AR
CPT1A	Carnitine palmitoyltransferase 1A (CPT1A) deficiency	Metabolic	AR
CPT2	Carnitine palmitoyltransferase II (CPT2) deficiency	Metabolic	AR
CTNS	Cystinosis	Metabolic	AR
CYBA	Chronic granulomatous disease	Immunology	AR
CYBB	Chronic granulomatous disease	Immunology	XL
CYP11B1	Congenital adrenal hyperplasia	Endocrine	AR
CYP17A1	Congenital adrenal hyperplasia	Endocrine	AR
CYP27A1	Cerebrotendinous xanthomatosis	Metabolic	AR
CYP27B1	Vitamin D-dependent rickets	Endocrine	AR
DBT	Maple syrup urine disease	Metabolic	AR
DCLRE1C	Severe combined immunodeficiency / Omenn syndrome	Immunology	AR
DICER1	DICER1 tumour predisposition syndrome	Cancer predisposition syndrome	AD
DMD	Duchenne muscular dystrophy	Neurology/Neuromuscular	XL
DOCK8	Hyper IgE syndrome	Immunology	AR
DOK7	Congenital myasthenic syndrome	Neurology/Neuromuscular	AR

DUOXA2	Thyroid dyshormonogenesis	Endocrine	AR
ELANE	Severe congenital neutropenia	Immunology	AD
ENPP1	Generalized arterial calcification of infancy	Cardiac	AR
ETFA	Glutaric acidemia	Metabolic	AR
ETFB	Glutaric acidemia	Metabolic	AR
ETFDH	Glutaric acidemia	Metabolic	AR
F8	Hemophilia A	Hematology	XL
F9	Hemophilia B	Hematology	XL
FAH	Tyrosinemia	Metabolic	AR
FBP1	Fructose-1,6-bisphosphatase deficiency	Metabolic	AR
FOLR1	Neurodegenerative syndrome	Neurology/Neuromuscular	AR
FZD4	Exudative vitreoretinopathy	Vision loss	AD
G6PC1	Von Gierke disease (GSD type 1A)	Metabolic	AR
G6PC3	Severe congenital neutropenia / Dursun Syndrome	Immunology	AR
GAA	Pompe disease (GSD type 2)	Metabolic	AR
GALE	Galactose epimerase deficiency	Metabolic	AR
GALNS	Morquio syndrome (MPS type 4A)	Metabolic	AR
GALT	Galactosemia	Metabolic	AR
GAMT	Guanidinoacetate methyltransferase (GAMT) deficiency	Metabolic	AR
GATA3	Hypoparathyroidism, sensorineural deafness, and renal dysplasia	Syndromic hearing loss	AD
GATM	Cerebral creatine deficiency syndrome	Metabolic	AR

GCDH	Glutaric aciduria	Metabolic	AR
GCH1	GTP cyclohydrolase I (GCH1) deficiency	Neurology/Neuromuscular	AD/AR
GCK	Permanent neonatal diabetes mellitus	Endocrine	AR
GJB2	Non-syndromic genetic hearing loss	Isolated hearing loss	AR
GLUD1	Hyperinsulinism hyperammonemia	Metabolic	AD
GRHPR	Primary hyperoxaluria	Metabolic	AR
GUSB	Sly syndrome (MPS type 7)	Metabolic	AR
HADH	Short chain 3-hydroxyacyl-CoA dehydrogenase (SCHAD) deficiency	Metabolic	AR
HADHA	Long chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency	Metabolic	AR
HADHB	Mitochondrial trifunctional protein deficiency	Metabolic	AR
HAX1	Severe congenital neutropenia / Kostmann disease	Immunology	AR
HBB	Hemoglobinopathy / Sickle Cell Disease / Beta Thalassemia	Hematology	AR
HLCS	Holocarboxylase synthetase (HLCS) deficiency	Metabolic	AR
HMGCL	Hydroxymethylglutaric aciduria	Metabolic	AR
HRAS	Costello syndrome	Multisystem/Syndromic	AD
HSD11B2	Apparent mineralocorticoid excess	Endocrine	AR
HSD3B2	Congenital adrenal hyperplasia	Endocrine	AR
HSD3B7	Congenital bile acid synthesis defect	Metabolic	AR
IDS	Hunter syndrome (MPS type 2)	Metabolic	XL
IDUA	Hurler syndrome (MPS type 1)	Metabolic	AR
IFNAR2	Immunodeficiency	Immunology	AR

IGSF1	Central congenital hypothyroidism	Endocrine	XL
IL2RG	Severe combined immunodeficiency	Immunology	XL
IL7R	Severe combined immunodeficiency	Immunology	AR
INS	Permanent neonatal diabetes mellitus	Endocrine	AD
IRS4	Central congenital hypothyroidism	Endocrine	XL
IVD	Isovaleric acidemia	Metabolic	AR
JAG1	Alagille syndrome	Multisystem/Syndromic	AD
JAK3	Severe combined immunodeficiency	Immunology	AR
KCNH2	Long QT syndrome	Cardiac	AD
KCNJ11	Hyperinsulinemic hypoglycemia	Endocrine	AR
KCNQ1	Long QT syndrome / Jervell and Lange-Nielsen syndrome	Cardiac	AD/AR
LDLR	Familial hypercholesterolemia	Metabolic	AR
LHX3	Combined pituitary hormone deficiency	Endocrine	AR
LIG4	Severe combined immunodeficiency / LIG4 syndrome	Immunology	AR
LIPA	Wolman disease	Metabolic	AR
LMBRD1	Methylmalonic aciduria and homocystinuria	Metabolic	AR
LPL	Lipoprotein lipase (LPL) deficiency	Metabolic	AR
LYST	Chediak-Higashi syndrome	Multisystem/Syndromic	AR
MC2R	Glucocorticoid deficiency	Endocrine	AR
MLYCD	Malonic aciduria	Metabolic	AR
MMAA	Methylmalonic aciduria, vitamin B12-responsive	Metabolic	AR

MMAB	Methylmalonic aciduria, vitamin B12-responsive	Metabolic	AR
MMACHC	Methylmalonic aciduria and homocystinuria	Metabolic	AR
MMADHC	Methylmalonic aciduria and homocystinuria	Metabolic	AR
MMUT	Methylmalonic aciduria	Metabolic	AR
MPI	Congenital disorder of glycosylation	Metabolic	AR
MTR	Homocystinuria-megaloblastic anemia	Metabolic	AR
MTRR	Homocystinuria-megaloblastic anemia	Metabolic	AR
MYBPC3	Cardiomyopathies	Cardiac	AR
MYH7	Cardiomyopathies	Cardiac	AD/AR
MYO7A	Usher syndrome	Syndromic hearing loss	AR
NAGS	Hyperammonemia	Metabolic	AR
NCF2	Chronic granulomatous disease	Immunology	AR
NDP	Norrie disease / Exudative vitreoretinopathy	Vision loss	XL
NHEJ1	Severe combined immunodeficiency	Immunology	AR
NOTCH2[4]	Alagille syndrome	Multisystem/Syndromic	AD
NR0B1	Congenital adrenal hypoplasia	Endocrine	XL
OTC	Ornithine transcarbamylase (OTC) deficiency	Metabolic	XL
OTOF	Non-syndromic genetic hearing loss	Isolated hearing loss	AR
PAH	Classic phenylketonuria	Metabolic	AR
PAX8	Congenital hypothyroidism, dysgenesis or hypoplasia	Endocrine	AD
PCBD1	Hyperphenylalaninemia, BH4-deficient	Metabolic	AR

PCCA	Propionic acidemia	Metabolic	AR
PCCB	Propionic acidemia	Metabolic	AR
PCDH15	Usher syndrome	Syndromic hearing loss	AR
PHEX	Hypophosphatemia	Endocrine	XL
PHKB	Phosphorylase kinase b (PHKB) deficiency (GSD type 9b)	Metabolic	AR
PNPO	Neonatal epileptic encephalopathy	Neurology/Neuromuscular	AR
POU1F1	Combined or isolated pituitary hormone deficiency	Endocrine	AR
PRF1	Hemophagocytic lymphohistiocytosis	Immunology	AR
PROP1	Combined pituitary hormone deficiency	Endocrine	AR
PTPRC	Severe combined immunodeficiency	Immunology	AR
PTS	Hyperphenylalaninemia, BH4-deficient	Metabolic	AR
PYGL	Hers disease (GSD type 6)	Metabolic	AR
QDPR	Hyperphenylalaninemia, BH4-deficient	Metabolic	AR
RAG1	Severe combined immunodeficiency	Immunology	AR
RAG2	Severe combined immunodeficiency	Immunology	AR
RB1	Retinoblastoma	Cancer predisposition syndrome	AD
RET[5]	Multiple endocrine neoplasia	Cancer predisposition syndrome	AD
RFXANK	MHC class II deficiency	Immunology	AR
RPE65	Leber congenital amaurosis	Vision loss	AR
RPL11	Diamond-Blackfan anemia	Hematology	AD
RPL15	Diamond-Blackfan anemia	Hematology	AD

RPL35A	Diamond-Blackfan anemia	Hematology	AD
RPL5	Diamond-Blackfan anemia	Hematology	AD
RPS10	Diamond-Blackfan anemia	Hematology	AD
RPS17	Diamond-Blackfan anemia	Hematology	AD
RPS19	Diamond-Blackfan anemia	Hematology	AD
RPS24	Diamond-blackfan anemia	Hematology	AD
RPS26	Diamond-Blackfan anemia	Hematology	AD
RPS29	Diamond-Blackfan anemia	Hematology	AD
RPS7	Diamond-Blackfan anemia	Hematology	AD
RYR2	Catecholaminergic polymorphic ventricular tachycardia	Cardiac	AD
SCN5A	Long QT syndrome	Cardiac	AD
SCNN1A	Pseudohypoaldosteronism	Endocrine	AR
SCNN1B	Pseudohypoaldosteronism / Liddle Syndrome	Endocrine	AR
SCNN1G	Pseudohypoaldosteronism / Liddle Syndrome	Endocrine	AR
SH2D1A	Lymphoproliferative syndrome	Immunology	XL
SLC22A5	Systemic primary carnitine deficiency	Metabolic	AR
SLC25A13	Citrin deficiency	Metabolic	AR
SLC25A15	Hyperornithinemia hyperammonemia homocitrullinemia (HHH) syndrome	Metabolic	AR
SLC25A20	Carnitine-acylcarnitine translocase deficiency	Metabolic	AR
SLC26A3	Congenital secretory chloride diarrhea	Gastrointestinal	AR
SLC26A4	Pendred syndrome	Syndromic hearing loss	AR

SLC2A1	GLUT1 deficiency syndrome	Metabolic	AD/AR
SLC37A4	Glucose-6-phosphate transport defect (GSD type 1b)	Metabolic	AR
SLC39A4	Acrodermatitis enteropathica	Metabolic	AR
SLC52A2	Brown-Vialetto-Van Laere syndrome	Neurology/Neuromuscular	AR
SLC52A3	Brown-Vialetto-Van Laere syndrome	Neurology/Neuromuscular	AR
SLC5A5	Thyroid dyshormonogenesis	Endocrine	AR
SLC6A8	Cerebral creatine deficiency syndrome	Metabolic	XL
SLC7A7	Lysinuric protein intolerance	Metabolic	AR
SMARCB1	Rhabdoid tumour predisposition syndrome	Cancer predisposition syndrome	AD
SMN1[6]	Spinal muscular atrophy	Neurology/Neuromuscular	AR
SPI1	Agammaglobulinemia	Immunology	AD
SPR	Dopa-responsive dystonia	Neurology/Neuromuscular	AR
STAR	Congenital lipoid adrenal hyperplasia	Endocrine	AR
STX11	Hemophagocytic lymphohistiocytosis	Immunology	AR
STXBP2	Hemophagocytic lymphohistiocytosis	Immunology	AR
TAFAZZIN	Barth syndrome	Metabolic	XL
TAT	Tyrosinemia	Metabolic	AR
TBL1X	Central congenital hypothyroidism	Endocrine	XL
TCIRG1	Osteopetrosis	Bone/Connective tissue	AR
TCN2	Transcobalamin II deficiency	Metabolic	AR
TG	Thyroid dyshormonogenesis	Endocrine	AR

TH	Dopa-responsive dystonia	Neurology/Neuromuscular	AR
THRA	Non-goitrous congenital hypothyroidism	Endocrine	AD
TPO	Thyroid dyshormonogenesis	Endocrine	AR
TPP1	Neuronal ceroid lipofuscinosis	Neurology/Neuromuscular	AR
TRHR	Central congenital hypothyroidism	Endocrine	AR
TSHB	Central congenital hypothyroidism	Endocrine	AR
TSHR	Central congenital hypothyroidism	Endocrine	AR
TSPAN12	Exudative vitreoretinopathy	Vision loss	AD
TTPA	Ataxia with isolated vitamin E deficiency	Metabolic	AR
UNC13D	Hemophagocytic lymphohistiocytosis	Immunology	AR
USH1C	Usher syndrome	Syndromic hearing loss	AR
USH1G	Usher syndrome	Syndromic hearing loss	AR
VDR	Hypocalcemic vitamin D-resistant rickets	Endocrine	AR
WAS	Wiskott Aldrich Syndrome (WAS) / WAS-related disorders	Hematology	XL
WT1	Wilms tumor / Denys-Drash syndrome	Cancer predisposition syndrome	AD
ZAP70	Combined immunodeficiency	Immunology	AR

Total: 223 genes

IMPORTANT NOTES

[1] For most X-Linked (XL) conditions on this gene list, only pathogenic/likely pathogenic variants identified in male patients will be reported because of the expected risk of disease. The sole exception is the *PHEX* gene, condition: Hypophosphatemia, where males and females will be reported.

[2] For conditions listed as autosomal recessive (AR), only homozygous or multiple heterozygous pathogenic/likely pathogenic variants will be reported.

[3]For conditions reported as AD/AR, heterozygous, homozygous and multiple heterozygous genotypes with pathogenic/ likely pathogenic variants will be reported.

[4] Pathogenic/likely pathogenic variants in exon 34 of the *NOTCH2* gene are excluded, as they are known to cause Hajdu-Cheney Syndrome, a condition that does not meet the INFANT inclusion criteria.

[5] **Only the following variants in the *RET* gene are being reported:** c.2753T>C, p.(Met918Thr); c.1900T>C, (p.Cys634Arg); c.1900T>A, (p.Cys634Ser); c.1900T>G, (p.Cys634Gly); c.1901G>C, (p.Cys634Ser); c.1901G>A, (p.Cys634Tyr); c.1901G>T, (p.Cys634Phe); c.1902C>G, (p.Cys634Trp); c.2647_2648delinsTT, p.(Ala883Phe)

[6] The analysis of the *SMN1* gene is limited to copy number at the common *SMN1* deletion site; sequence variants and other CNVs in this gene are not assessed.

SCREEN DESCRIPTION

Whole Genome Next-Generation Sequencing: Genomic DNA is extracted from the dried blood spot using Illumina Lysis Reagent kit. DNA is prepared for sequencing using Illumina DNA PCR-Free Library Prep kit followed by sequencing on an Illumina NovaSeqX+ instrument using 10B or 25B flow cells (2x150bp paired reads).

Variant Assessment and Reporting Process: Sequencing data are analysed automatically using a custom filtering algorithm; only those cases with putative pathogenic or likely pathogenic variants in a pattern consistent with the mode of inheritance for the gene's associated INFANT condition(s) are manually reviewed. Variant curation and classification use the most recent ACMG standards and guidelines for the interpretation of sequence variants. Only variants classified as pathogenic or likely pathogenic are reported. Carrier status is not reported. All reports are reviewed and interpreted by a certified genetic counsellor and molecular laboratory director.

SCREEN LIMITATIONS

These results are generated under a research protocol and should not be used to direct treatment and/or clinical management until these findings are confirmed on a diagnostic sample in an accredited diagnostic laboratory. Familial segregation may also be required to confirm variant phasing and risk of disease.

Analysis and reporting are limited to the coding regions in the targeted gene list +/- 15 basepairs, with the inclusion of some extragenic regions with established pathogenic variants reported in Clinvar. This assay was validated and optimized to achieve an read depth >=35x with >= 90% completeness over genome, with >99.9% sensitivity and precision for SNVs and >99.5% for indels, with a minimum of 10 reads in reportable regions; however, there may be variation between genes and samples whereby reduced coverage may lead to decreased test sensitivity for some regions. A detailed report of any regions with insufficient coverage is available upon request. The detection of large copy number variants and structural rearrangements has not been fully validated, and consequently reduced sensitivity is expected for these types of variants.