

# Sema4 Natalis

## Clinical significance of panel

Sema4 has designed and validated Natalis, a supplemental newborn screening panel offered for newborns, infants, and young children. This test may be offered to parents as an addition to the state mandated newborn screening that their child received at birth. This panel includes next-generation sequencing, targeting genotyping, and multiplex ligation-dependent probe amplification in a total of 166 genes to screen for 193 conditions that have onset in infancy or early childhood and for which there is treatment or medical management that, when administered early in an infant or child's life, will significantly improve the clinical outcome. Conditions included in this panel were curated based on criteria such as: inclusion on current state mandated newborn screening panels, onset of symptoms occurring <10 years of age, evidence of high penetrance (>80%), and availability of a treatment or improvement in life due to early intervention.

Sema4 has also designed and validated a pediatric pharmacogenetic (PGx) genotyping panel as an adjunct test to the Natalis assay. This panel includes 10 genes and 41 sequence variants involved in drug response variability. The genes and variants in the PGx genotyping panel inform on more than 40 medications that can be prescribed during childhood. Currently, there is evidence supporting the clinical utility of testing for certain PGx variants for which there are genotype-directed clinical practice recommendations for selected gene/drug pairs. Approximately 95% of all individuals will carry at least one clinically actionable variant in the PGx panel.

## Testing methods, sensitivity, and limitations

A cheek swab, saliva sample, or blood sample is provided by the child and a biological parent. DNA is obtained from the specimens collected. High-throughput, next-generation sequencing is performed to examine multiple genes at one time. In addition, some of the genes on the panel may be partially subjected to Sanger sequencing due to inadequate sequence coverage by next-generation sequencing and targeted pathogenic and likely pathogenic variants may be analyzed by allele specific primer extension analyses. Targeted genotyping analysis looks for the presence of specific variants in the pediatric PGx genotyping panel. Multiplex ligation-dependent probe amplification (MLPA) is used to detect copy number changes for *SMN1* and *SMN2* (spinal muscular atrophy), *HBA1* and *HBA2* (alpha thalassemia), *CYP2D6*, *CYP2C9*, *CYP2C19*, and *CYP3A5*.

All testing is >95% accurate. A negative test result for any given disease does not exclude an individual from having a disease-causing genotype that was not identified by this testing. Only variants determined to have a high likelihood of pathogenicity (pathogenic or likely pathogenic) are reported in this test. Carrier status for autosomal recessive diseases is not reported. Next-generation sequencing of the parental DNA is not performed. If indicated, only targeted testing (genotyping, Sanger sequencing, and/or copy number analysis) is performed on the parental DNA to confirm the inheritance pattern or phase of variants identified in the proband.

## Turnaround time

- 10-14 days from the receipt of the specimen

## Specimen requirements

### Cheek swab

- Pediatric: 1 cheek swab specimen collected in ORAcollect kit from DNA Genotek
- Parental: 1 cheek swab specimen collected in ORAcollect kit from DNA Genotek for each biological parent

### Saliva samples

- Pediatric: 1 saliva sample collected in ORAGENE DNA (OG-500) kits manufactured by DNA Genotek
- Parental: 1 saliva sample collected in ORAGENE DNA (OG-500) kits manufactured by DNA Genotek for each biological parent

### Blood samples

- Pediatric: One 5-10 mL EDTA tube (lavender top)
- Parental: One 5-10 mL EDTA tube (lavender top) for each biological parent

## Please include the following with each sample

- Completed and signed test requisition form and informed consent for patient and parent
- Indication for testing, patient's family history, ethnic background, and prior relevant test results

## Shipping requirements

- Ship at room temperature. Do not freeze

## Genetic counseling

- Genetic counseling is available at any time during this process and is highly recommended if there is a positive family history for any of the conditions covered by this test
- Genetic counseling is available for all parents with a child who is found to have positive/abnormal result for a genetic condition

## Cost of test

- Natalis costs \$379 out of pocket

**Table 1. Summary of genes and associated diseases included in the Sema4 Natalis panel**

MIM No.	Gene	Disease	Inheritance	Disease Category
600509	<i>ABCC8</i>	Familial Hyperinsulinism ( <i>ABCC8</i> -Related)	AR	Endocrine
300371	<i>ABCD1</i>	Adrenoleukodystrophy, X-Linked	XLR	Neurological
607008	<i>ACADM</i>	Medium Chain Acyl-CoA Dehydrogenase Deficiency	AR	Inborn errors of metabolism, Neurological
609575	<i>ACADVL</i>	Very Long Chain Acyl-CoA Dehydrogenase Deficiency	AR	Inborn errors of metabolism, Cardiovascular
607809	<i>ACAT1</i>	Beta-Ketothiolase Deficiency	AR	Inborn errors of metabolism, Mitochondrial
608958	<i>ADA</i>	Adenosine Deaminase Deficiency	AR	Immunodeficiency
610860	<i>AGL</i>	Glycogen Storage Disease, Type III	AR	Hepatic, Muscular
604285	<i>AGXT</i>	Primary Hyperoxaluria, Type 1	AR	Renal
604741	<i>AKR1D1</i>	Congenital Bile Acid Synthesis Defect ( <i>AKR1D1</i> -Related)	AR	Hepatic, Gastrointestinal
107323	<i>ALDH7A1</i>	Pyridoxine-Dependent Epilepsy	AR	Neurological
612724	<i>ALDOB</i>	Hereditary Fructose Intolerance	AR	Inborn errors of metabolism
171760	<i>ALPL</i>	Hypophosphatasia	AD/AR	Skeletal
612641	<i>ANK1</i>	Spherocytosis, Type 1	AD	Hematologic
107777	<i>AQP2</i>	Nephrogenic Diabetes Insipidus, Type II	AD/AR	Renal
608313	<i>ARG1</i>	Argininemia	AR	Inborn errors of metabolism
607574	<i>ARSA</i>	Metachromatic Leukodystrophy	AR	Neurological
611542	<i>ARSB</i>	Mucopolysaccharidosis Type VI	AR	Inborn errors of metabolism, Neurological
608310	<i>ASL</i>	Argininosuccinic Aciduria	AR	Inborn errors of metabolism
603470	<i>ASS1</i>	Citrullinemia, Type 1	AR	Inborn errors of metabolism
300538	<i>AVPR2</i>	Nephrogenic Diabetes Insipidus ( <i>AVPR2</i> -Related) / Nephrogenic Syndrome of Inappropriate Antidiuresis	XLR	Renal
608348	<i>BCKDHA</i>	Maple Syrup Urine Disease, Type 1a	AR	Inborn errors of metabolism
248611	<i>BCKDHB</i>	Maple Syrup Urine Disease, Type 1b	AR	Inborn errors of metabolism
609019	<i>BTBD</i>	Biotinidase Deficiency	AR	Inborn errors of metabolism
601199	<i>CASR</i>	Neonatal Hyperparathyroidism / Autosomal Dominant Hypocalcemia	AD/AR	Endocrine
613381	<i>CBS</i>	Homocystinuria ( <i>CBS</i> -Related)	AR	Inborn errors of metabolism, Neurological
186790	<i>CD3D</i>	Immunodeficiency 19	AR	Immunodeficiency
186830	<i>CD3E</i>	Immunodeficiency 18	AR	Immunodeficiency
151460	<i>PTPRC</i>	Severe Combined Immunodeficiency ( <i>PTPRC</i> -Related) (CD45)	AR	Immunodeficiency

MIM No.	Gene	Disease	Inheritance	Disease Category
602421	<i>CFTR</i>	Cystic Fibrosis	AR	Pulmonary
120070	<i>COL4A3</i>	Alport Syndrome ( <i>COL4A3</i> -Related)	AR	Renal
120131	<i>COL4A4</i>	Alport Syndrome ( <i>COL4A4</i> -Related)	AR	Renal
303630	<i>COL4A5</i>	Alport Syndrome ( <i>COL4A5</i> -Related)	XLD	Renal
608307	<i>CPS1</i>	Carbamoylphosphate Synthetase I Deficiency	AR	Inborn errors of metabolism
600528	<i>CPT1A</i>	Carnitine Palmitoyltransferase IA Deficiency	AR	Inborn errors of metabolism, Neurological
600650	<i>CPT2</i>	Carnitine Palmitoyltransferase II Deficiency	AR	Inborn errors of metabolism, Neurological
606272	<i>CTNS</i>	Cystinosis	AR	Inborn errors of metabolism
608508	<i>CYBA</i>	Chronic Granulomatous Disease ( <i>CYBA</i> -related)	AR	Immunodeficiency
300481	<i>CYBB</i>	Chronic Granulomatous Disease ( <i>CYBB</i> -related)	XLR	Immunodeficiency
610613	<i>CYP11B1</i>	Congenital Adrenal Hyperplasia due to 11-beta-hydroxylase deficiency	AR	Endocrine
124080	<i>CYP11B2</i>	Corticosterone Methyloxidase Deficiency	AR	Endocrine
606530	<i>CYP27A1</i>	Cerebrotendinous Xanthomatosis	AR	Neurological
248610	<i>DBT</i>	Maple Syrup Urine Disease, Type 2	AR	Inborn errors of metabolism
605988	<i>DCLRE1C</i>	Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type	AR	Immunodeficiency
238331	<i>DLD</i>	Lipoamide Dehydrogenase Deficiency	AR	Inborn errors of metabolism, Neurological
606759	<i>DUOX2</i>	Thyroid Dyshormonogenesis 6	AR	Endocrine
612772	<i>DUOXA2</i>	Thyroid Dyshormonogenesis 5	AR	Endocrine
177070	<i>EPB42</i>	Spherocytosis, Type 5	AR	Hematologic
608053	<i>ETFA</i>	Glutaric Acidemia, Type IIa	AR	Inborn errors of metabolism, Neurological
130410	<i>ETFB</i>	Glutaric Acidemia, Type IIb	AR	Inborn errors of metabolism, Neurological
231675	<i>ETFDH</i>	Glutaric Acidemia, Type IIc	AR	Inborn errors of metabolism, Neurological
608451	<i>ETHE1</i>	Ethylmalonic Encephalopathy	AR	Inborn errors of metabolism, Neurological
300746	<i>F9</i>	Factor IX Deficiency	XLR	Hematologic
613871	<i>FAH</i>	Tyrosinemia, Type I	AR	Inborn errors of metabolism
134797	<i>FBN1</i>	Marfan syndrome and other <i>FBN1</i> -related disorders	AD	Skeletal
611570	<i>FBP1</i>	Fructose-1,6-Bisphosphatase Deficiency	AR	Inborn errors of metabolism
136430	<i>FOLR1</i>	Neurodegeneration due to Cerebral Folate Transport Deficiency	AR	Neurological
613742	<i>G6PC</i>	Glycogen Storage Disease, Type Ia	AR	Hepatic
305900	<i>G6PD</i>	Hemolytic Anemia ( <i>G6PD</i> -Related)	XLR	Hematologic

<b>MIM No.</b>	<b>Gene</b>	<b>Disease</b>	<b>Inheritance</b>	<b>Disease Category</b>
606800	<i>GAA</i>	Glycogen Storage Disease, Type II	AR	Cardiovascular
606953	<i>GALE</i>	Galactose Epimerase Deficiency	AR	Inborn errors of metabolism
604313	<i>GALK1</i>	Galactokinase Deficiency	AR	Inborn errors of metabolism
612222	<i>GALNS</i>	Mucopolysaccharidosis Type IVa	AR	Inborn errors of metabolism, Neurological
606999	<i>GALT</i>	Galactosemia	AR	Inborn errors of metabolism
601240	<i>GAMT</i>	Cerebral Creatine Deficiency Syndrome 2	AR	Inborn errors of metabolism, Neurological
602360	<i>GATM</i>	Cerebral Creatine Deficiency Syndrome 3	AR	Neurological, Muscular
608801	<i>GCDH</i>	Glutaric Acidemia, Type I	AR	Inborn errors of metabolism, Neurological
600225	<i>GCH1</i>	Dopa-Responsive Dystonia / BH4-Deficient Hyperphenylalaninemia B	AD/AR	Inborn errors of metabolism
300644	<i>GLA</i>	Fabry Disease	XLR	Inborn errors of metabolism
138130	<i>GLUD1</i>	Hyperinsulinism-Hyperammonemia Syndrome	AD	Endocrine, Inborn errors of metabolism
604296	<i>GRHPR</i>	Primary Hyperoxaluria, Type 2	AR	Renal
601002	<i>GSS</i>	Glutathione Synthetase Deficiency	AR	Inborn errors of metabolism, Neurological
138571	<i>GYS2</i>	Glycogen storage disease, Type 0	AR	Hepatic
601609	<i>HADH</i>	Familial Hyperinsulinemic Hypoglycemia 4 / 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	AR	Endocrine, Inborn errors of metabolism
600890	<i>HADHA</i>	Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	AR	Inborn errors of metabolism, Cardiovascular
143450	<i>HADHB</i>	Mitochondrial Trifunctional Protein Deficiency ( <i>HADHB</i> -Related)	AR	Inborn errors of metabolism, Neurological
605998	<i>HAX1</i>	Congenital Neutropenia ( <i>HAX1</i> -Related)	AR	Immunodeficiency
141800	<i>HBA1/HBA2</i>	Alpha-Thalassemia	AR	Hematologic
141900	<i>HBB</i>	Beta-Globin-Related Hemoglobinopathies	AD/AR	Hematologic
609018	<i>HLCS</i>	Holocarboxylase Synthetase Deficiency	AR	Inborn errors of metabolism, Hepatic
613898	<i>HMGCL</i>	HMG-CoA Lyase Deficiency	AR	Inborn errors of metabolism, Neurological
600234	<i>HMGCS2</i>	HMG-CoA Synthase 2 Deficiency	AR	Inborn errors of metabolism, Hepatic
613597	<i>HOGA1</i>	Primary Hyperoxaluria, Type 3	AR	Renal

MIM No.	Gene	Disease	Inheritance	Disease Category
609695	<i>HPD</i>	Tyrosinemia, type III	AR	Inborn errors of metabolism
613890	<i>HSD3B2</i>	3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	AR	Endocrine
607764	<i>HSD3B7</i>	Congenital Bile Acid Synthesis Defect ( <i>HSD3B7</i> -Related)	AR	Hepatic, Gastrointestinal
300823	<i>IDS</i>	Mucopolysaccharidosis Type II	XLR	Inborn errors of metabolism, Neurological
252800	<i>IDUA</i>	Mucopolysaccharidosis Type I	AR	Inborn errors of metabolism, Neurological
300137	<i>IGSF1</i>	Central Hypothyroidism and Testicular Enlargement	XLR	Endocrine
308380	<i>IL2RG</i>	X-Linked Severe Combined Immunodeficiency	XLR	Immunodeficiency
146661	<i>IL7R</i>	Severe Combined Immunodeficiency ( <i>IL7R</i> -Related)	AR	Immunodeficiency
176730	<i>INS</i>	Permanent Neonatal Diabetes Mellitus ( <i>INS</i> -Related)	AD	Endocrine
607036	<i>IVD</i>	Isovaleric Acidemia	AR	Inborn errors of metabolism, Neurological
612025	<i>IYD</i>	Thyroid Dyshormonogenesis 4	AR	Endocrine
601920	<i>JAG1</i>	Alagille syndrome 1 / Tetralogy of Fallot	AD	Cardiovascular, Multiple Congenital Abnormalities
600173	<i>JAK3</i>	Severe Combined Immunodeficiency ( <i>JAK3</i> -Related)	AR	Immunodeficiency
600937	<i>KCNJ11</i>	Familial Hyperinsulinism ( <i>KCNJ11</i> -Related)	AR	Endocrine
602235	<i>KCNQ2</i>	Early Infantile Epileptic Encephalopathy 7 / Benign Neonatal Seizures 1	AD	Neurological
606945	<i>LDLR</i>	Familial Hypercholesterolemia	AR	Inborn errors of metabolism, Cardiovascular
600577	<i>LHX3</i>	Combined Pituitary Hormone Deficiency 3	AR	Endocrine
613497	<i>LIPA</i>	Wolman Disease / Cholesteryl Ester Storage Disease	AR	Endocrine, Gastrointestinal
612625	<i>LMBRD1</i>	Methylmalonic Aciduria and Homocystinuria, Cobalamin F Type	AR	Inborn errors of metabolism, Neurological
609708	<i>LPL</i>	Lipoprotein Lipase Deficiency	AR	Inborn errors of metabolism, Gastrointestinal
610550	<i>MAT1A</i>	Methionine Adenosyltransferase I/III Deficiency	AR	Inborn errors of metabolism, Neurological
609010	<i>MCCC1</i>	3-Methylcrotonyl-CoA Carboxylase Deficiency ( <i>MCCC1</i> -Related)	AR	Inborn errors of metabolism
609014	<i>MCCC2</i>	3-Methylcrotonyl-CoA Carboxylase Deficiency ( <i>MCCC2</i> -Related)	AR	Inborn errors of metabolism
608419	<i>MCEE</i>	Methylmalonyl-CoA Epimerase Deficiency	AR	Inborn errors of metabolism
606761	<i>MLYCD</i>	Malonyl-CoA Decarboxylase Deficiency	AR	Inborn errors of metabolism, Neurological

<b>MIM No.</b>	<b>Gene</b>	<b>Disease</b>	<b>Inheritance</b>	<b>Disease Category</b>
607481	<i>MMAA</i>	Methylmalonic Acidemia ( <i>MMAA</i> -Related)	AR	Inborn errors of metabolism, Neurological
607568	<i>MMAB</i>	Methylmalonic Acidemia ( <i>MMAB</i> -Related)	AR	Inborn errors of metabolism, Neurological
609831	<i>MMACHC</i>	Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type	AR	Inborn errors of metabolism, Neurological
611935	<i>MMADHC</i>	Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type	AR	Inborn errors of metabolism, Neurological
154550	<i>MPI</i>	Congenital Disorder of Glycosylation, Type Ib	AR	Inborn errors of metabolism
159530	<i>MPL</i>	Congenital Amegakaryocytic Thrombocytopenia	AR	Hematologic
156570	<i>MTR</i>	Homocystinuria-Megaloblastic Anemia, Cobalamin G Type	AR	Inborn errors of metabolism, Hematologic
602568	<i>MTRR</i>	Homocystinuria, Cobalamin E Type	AR	Inborn errors of metabolism, Neurological
157147	<i>MTTP</i>	Abetalipoproteinemia	AR	Inborn errors of metabolism
609058	<i>MUT</i>	Methylmalonic Acidemia ( <i>MUT</i> -Related)	AR	Inborn errors of metabolism, Neurological
608300	<i>NAGS</i>	N-Acetylglutamate Synthase Deficiency	AR	Inborn errors of metabolism, Neurological
613349	<i>OAT</i>	Ornithine Aminotransferase Deficiency	AR	Vision Loss, Muscular
300461	<i>OTC</i>	Ornithine Transcarbamylase Deficiency	XLR	Inborn errors of metabolism
612349	<i>PAH</i>	Phenylalanine Hydroxylase Deficiency	AR	Inborn errors of metabolism, Neurological
167415	<i>PAX8</i>	Congenital Hypothyroidism due to Thyroid Dysgenesis or Hypoplasia	AD	Endocrine
126090	<i>PCBD1</i>	BH <sub>4</sub> -deficient Hyperphenylalaninemia D	AR	Inborn errors of metabolism
232000	<i>PCCA</i>	Propionic Acidemia ( <i>PCCA</i> -Related)	AR	Inborn errors of metabolism
232050	<i>PCCB</i>	Propionic Acidemia ( <i>PCCB</i> -Related)	AR	Inborn errors of metabolism
606879	<i>PHGDH</i>	3-Phosphoglycerate Dehydrogenase Deficiency	AR	Inborn errors of metabolism
172490	<i>PHKB</i>	Glycogen Storage Disease, Type IXb	AR	Hepatic, Muscular
603287	<i>PNPO</i>	Pyridoxamine 5'-Phosphate Oxidase Deficiency	AR	Inborn errors of metabolism, Neurological
173110	<i>POU1F1</i>	Combined Pituitary Hormone Deficiency 1	AD/AR	Endocrine
601538	<i>PROP1</i>	Combined Pituitary Hormone Deficiency 2	AR	Endocrine

MIM No.	Gene	Disease	Inheritance	Disease Category
614386	<i>PRRT2</i>	Familial Infantile Convulsions with Paroxysmal Choreoathetosis	AD	Neurological
612719	<i>PTS</i>	6-Pyruvoyl-Tetrahydropterin Synthase Deficiency	AR	Inborn errors of metabolism
613741	<i>PYGL</i>	Glycogen storage disease, Type VI	AR	Hepatic
612676	<i>QDPR</i>	BH4-deficient Hyperphenylalaninemia C	AR	Inborn errors of metabolism
179615	<i>RAG1</i>	Omenn syndrome and other <i>RAG1</i> -related disorders	AR	Immunodeficiency
179616	<i>RAG2</i>	Omenn Syndrome ( <i>RAG2</i> -Related)	AR	Immunodeficiency
614041	<i>RB1</i>	Retinoblastoma	AD	Malignancy
182390	<i>SCN2A</i>	Early Infantile Epileptic Encephalopathy 11 / Benign Familial Infantile Seizures 3	AD	Neurological
600702	<i>SCN8A</i>	Early Infantile Epileptic Encephalopathy 13 / Benign Familial Infantile Seizures 5	AD	Neurological
603377	<i>SLC22A5</i>	Primary Carnitine Deficiency	AR	Cardiovascular
603859	<i>SLC25A13</i>	Citrin Deficiency	AR	Inborn errors of metabolism
603861	<i>SLC25A15</i>	Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome	AR	Inborn errors of metabolism, Neurological
613698	<i>SLC25A20</i>	Carnitine Acylcarnitine Translocase Deficiency	AR	Inborn errors of metabolism, Neurological
138140	<i>SLC2A1</i>	Glucose transporter 1 deficiency syndrome and other <i>SLC2A1</i> -related disorders	AD/AR	Neurological
607059	<i>SLC39A4</i>	Acrodermatitis Enteropathica	AR	Dermatological, Immunodeficiency
109270	<i>SLC4A1</i>	Distal Renal Tubular Acidosis and other <i>SLC4A1</i> -related disorders	AR	Renal, Hematologic
601843	<i>SLC5A5</i>	Thyroid Dyshormonogenesis 1	AR	Endocrine
603593	<i>SLC7A7</i>	Lysinuric Protein Intolerance	AR	Inborn errors of metabolism, Gastrointestinal
600354	<i>SMN1</i>	Spinal Muscular Atrophy	AR	Neurological
607608	<i>SMPD1</i>	Niemann-Pick Disease ( <i>SMPD1</i> -Related)	AR	Inborn errors of metabolism
182125	<i>SPR</i>	Sepiapterin Reductase Deficiency	AR	Inborn errors of metabolism, Neurological
600617	<i>STAR</i>	Lipoid Adrenal Hyperplasia	AR	Endocrine
613018	<i>TAT</i>	Tyrosinemia, Type II	AR	Inborn errors of metabolism
300394	<i>TAZ</i>	Barth Syndrome	XLR	Inborn errors of metabolism, Cardiovascular
604592	<i>TCIRG1</i>	Osteopetrosis 1	AR	Skeletal
188450	<i>TG</i>	Thyroid Dyshormonogenesis 3	AR	Endocrine
191290	<i>TH</i>	Segawa Syndrome	AR	Neurological
190120	<i>THRA</i>	Congenital Nongoitrous Hypothyroidism 6	AD	Endocrine
606765	<i>TPO</i>	Thyroid Dyshormonogenesis 2A	AR	Endocrine
188545	<i>TRHR</i>	Generalized Thyrotropin-Releasing Hormone Resistance	AR	Endocrine



MIM No.	Gene	Disease	Inheritance	Disease Category
610230	<i>TRMU</i>	Acute Infantile Liver Failure	AR	Hepatic
188540	<i>TSHB</i>	Congenital Nongoitrous Hypothyroidism 4	AR	Endocrine
603372	<i>TSHR</i>	Congenital Nongoitrous Hypothyroidism 1 / Nonautoimmune Hyperthyroidism	AD/AR	Endocrine
600415	<i>TTPA</i>	Ataxia with Isolated Vitamin E Deficiency	AR	Neurological
191740	<i>UGT1A1</i>	Crigler-Najjar Syndrome, Types 1 & 2 / Gilbert Syndrome	AR	Hepatic, Neurological
607102	<i>WT1</i>	Wilms tumor, type 1 and other WT1-related disorders	AD	Renal

The following genes will be unmasked and full diagnostic analysis will be performed if a child is positive on the mandated state newborn screen and physician requests the molecular results: *ACADS*, *FTCD*, *GALC*, *MTHFR*, *PRODH*. *MEFV* will be unmasked if requested by physician and there is an existing family history.

AD: Autosomal dominant; AR: Autosomal recessive; XL: X-linked

**Table 2. Summary of genes and associated medications included in the PGx panel**

Therapeutic Class	Medication	Gene	PGx Significance	PGx Recommendation
Analgesic	Celecoxib (Celebrex)	<i>CYP2C9</i>	Adverse reaction	Alternative medication, dosing
Analgesic	Hydrocodone	<i>CYP2D6</i>	Efficacy, adverse reaction	Dosing, alternative medication
Analgesic	Oxycodone	<i>CYP2D6</i>	Efficacy, adverse reaction	Dosing, alternative medication
Analgesic	Codeine	<i>CYP2D6</i>	Efficacy, adverse reaction	Alternative medication
Analgesic	Tramadol (Ultram)	<i>CYP2D6</i>	Efficacy, adverse reaction	Dosing
Antibacterial	Amikacin	<i>MT-RNR1</i>	Adverse reaction	Alternative medication
Antibacterial	Gentamicin	<i>MT-RNR1</i>	Adverse reaction	Alternative medication
Antibacterial	Neomycin	<i>MT-RNR1</i>	Adverse reaction	Alternative medication
Antibacterial	Paramomycin	<i>MT-RNR1</i>	Adverse reaction	Alternative medication
Antibacterial	Streptomycin	<i>MT-RNR1</i>	Adverse reaction	Alternative medication
Antibacterial	Tobramycin	<i>MT-RNR1</i>	Adverse reaction	Alternative medication
Anticoagulant	Warfarin	<i>CYP2C9</i> , <i>VKORC1</i>	Adverse reaction	Dosing, alternative medication
Anticonvulsant	Fosphenytoin (Cerebyx)	<i>CYP2C9</i>	Adverse reaction	Dosing
Anticonvulsant	Phenytoin	<i>CYP2C9</i>	Adverse reaction	Dosing
Antidepressant	Amitriptyline (Elavil)	<i>CYP2C19</i> , <i>CYP2D6</i>	Efficacy, adverse reaction	Alternative medication, dosing
Antidepressant	Citalopram (Celexa)	<i>CYP2C19</i>	Efficacy, adverse reaction	Alternative medication, dosing
Antidepressant	Clomipramine (Anafranil)	<i>CYP2C19</i> , <i>CYP2D6</i>	Efficacy, adverse reaction	Alternative medication, dosing
Antidepressant	Desipramine (Norpramin)	<i>CYP2D6</i>	Efficacy, adverse reaction	Alternative medication, dosing
Antidepressant	Doxepin (Silenor)	<i>CYP2C19</i> , <i>CYP2D6</i>	Efficacy, adverse reaction	Alternative medication, dosing
Antidepressant	Escitalopram (Lexapro)	<i>CYP2C19</i>	Efficacy, adverse reaction	Alternative medication, dosing

Therapeutic Class	Medication	Gene	PGx Significance	PGx Recommendation
Antidepressant	Fluoxetine (Prozac)	CYP2D6	Adverse reaction	Dosing
Antidepressant	Fluvoxamine (Luvox)	CYP2D6	Adverse reaction	Dosing
Antidepressant	Imipramine (Tofranil)	CYP2C19, CYP2D6	Efficacy, adverse reaction	Alternative medication, dosing
Antidepressant	Nortriptyline (Pamelor)	CYP2D6	Efficacy, adverse reaction	Alternative medication, dosing
Antidepressant	Paroxetine (Paxil)	CYP2D6	Efficacy, adverse reaction	Dosing, alternative medication
Antidepressant	Sertraline (Zoloft)	CYP2C19	Adverse reaction	Alternative medication, dosing
Antidepressant	Trimipramine (Surmontil)	CYP2C19, CYP2D6	Efficacy, adverse reaction	Alternative medication, dosing
Antiemetic	Ondansetron	CYP2D6	Efficacy	Alternative medication
Antifungal	Voriconazole	CYP2C19	Efficacy, adverse reaction	Alternative medication
Antilipemic agent	Simvastatin (Zocor)	SLCO1B1	Adverse reaction	Alternative medication, dosing
Antineoplastic	Capecitabine (Xeloda)	DPYD	Adverse reaction	Alternative medication, dosing
Antineoplastic	Fluorouracil	DPYD	Adverse reaction	Alternative medication, dosing
Antineoplastic	Mercaptopurine	TPMT	Adverse reaction	Dosing
Antineoplastic	Thioguanine	TPMT	Adverse reaction	Dosing
Antiplatelet agent	Clopidogrel (Plavix)	CYP2C19	Efficacy, adverse reaction	Alternative medication
Antipsychotic	Aripiprazole (Aricept)	CYP2D6	Adverse reaction	Dosing
Antipsychotic	Iloperidone (Fanapt)	CYP2D6	Efficacy, adverse reaction	Dosing
Antipsychotic	Pimozide (Orap)	CYP2D6	Efficacy, adverse reaction	Dosing
Antiretroviral	Atazanavir (Reyataz)	UGT1A1	Adverse reaction	Alternative medication
Endocrine-metabolic agents	Eliglustat (Cerdelga)	CYP2D6	Efficacy, adverse reaction	Dosing
Immunosuppressant	Azathioprine	TPMT	Adverse reaction	Dosing
Immunosuppressant	Tacrolimus	CYP3A5	Efficacy	Dosing
Psychotropic	Atomoxetine (Strattera)	CYP2D6	Adverse reaction	Dosing

Sema4 developed this test and determined its performance characteristics. This test has not been cleared or approved by the FDA. The FDA has determined that such clearance or approval is not necessary. This type of analysis generally provides highly accurate information for microdeletions and microduplications. Despite this level of accuracy, it should be kept in mind that there are many potential sources of diagnostic error, including misidentification of samples, rare polymorphisms, or other rare genetic variants that interfere with analysis. References provided upon request.



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