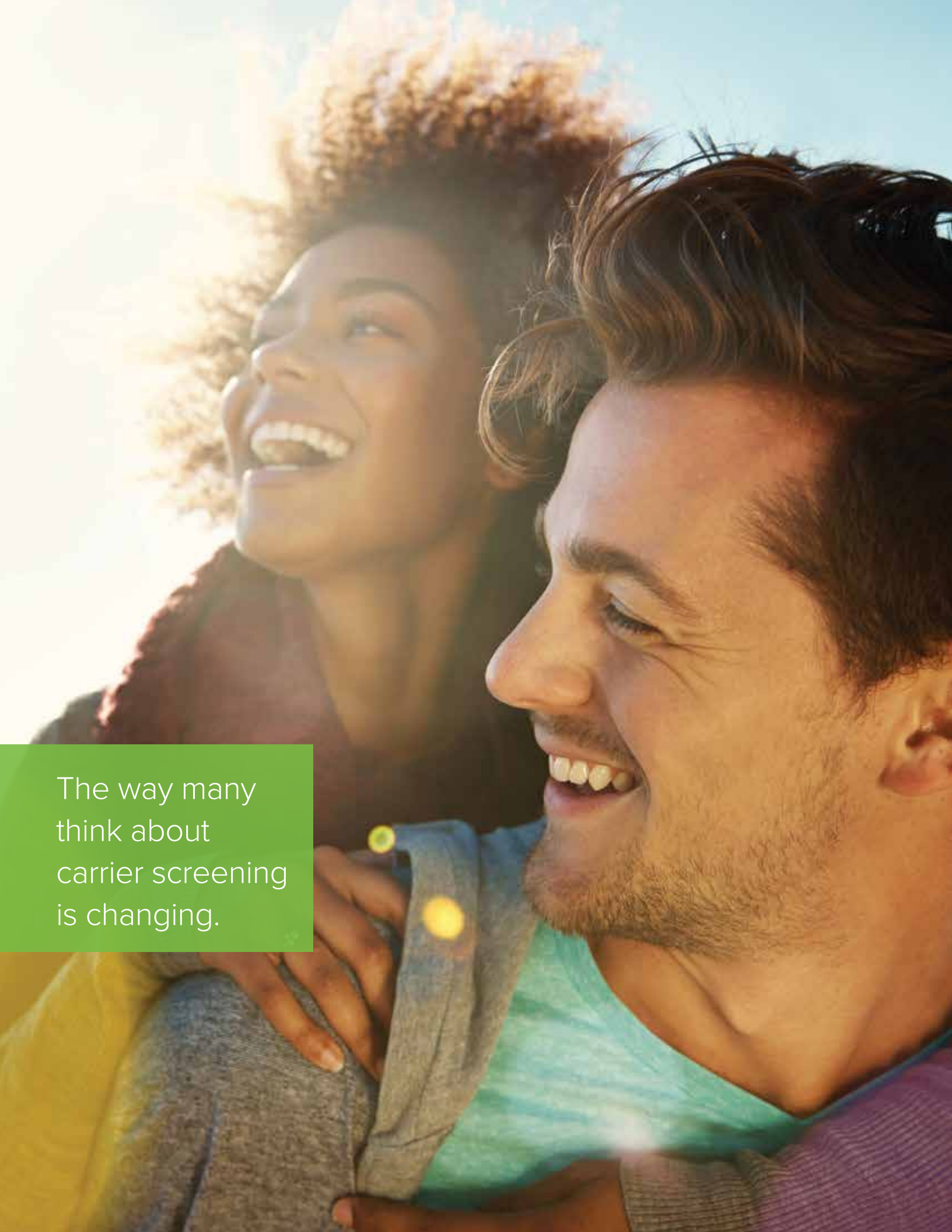
Inheritest®

CARRIER SCREEN

Genetic testing services and support, from preconception to prenatal

Integrated GENETICS

LabCorp Specialty Testing Group


The way many
think about
carrier screening
is changing.

Carrier screening, once thought to be a test primarily for specific ethnic groups, is now often recommended for every patient. The American Congress of Obstetricians and Gynecologists (ACOG) recently updated its recommendations, stating that carrier screening for spinal muscular atrophy (SMA), in addition to cystic fibrosis (CF), "should be offered to all women who are considering pregnancy or are currently pregnant."[7]



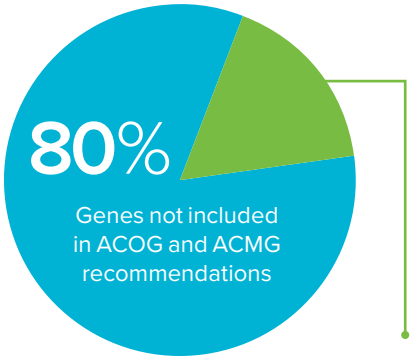


COMPREHENSIVE, VERSATILE, COVERING WHAT MATTERS

Inheritest® provides carrier screening for more than 110 severe disorders that can cause cognitive or physical impairment and/or require surgical or medical intervention. Selected to focus on severe disorders of childhood onset, and to meet ACOG and the American College of Medical Genetics and Genomics (ACMG) criteria, many of the disorders share a recommendation for early intervention.

Inheritest offers multiple panels to suit the diverse needs of your patients:

CORE PANEL **3 GENES**	Focuses on mutations for **CF**, **SMA**, and **fragile X syndrome,** with the following carrier risks: CF: as high as 1 in 24[8] (varies by ethnicity) SMA: as high as 1 in 47[9] (varies by ethnicity) Fragile X syndrome: approximately 1 in 259 females (all ethnicities)[10]
SOCIETY-GUIDED PANEL **14 GENES**	Includes mutations for **more than 13 disorders** listed in ACOG and/or ACMG recommendations
ASHKENAZI JEWISH PANEL **48 GENES**	Enhanced panel includes mutations for **more than 40 disorders** relevant to patients of Ashkenazi Jewish descent
COMPREHENSIVE PANEL **144 GENES**	Includes mutations for more than **110 disorders** across 144 different genes—includes all disorders in *Core*, *Society-guided*, and *Ashkenazi Jewish* panels



20%

Genes included in ACOG/ ACMG recommendations

Figure 1: percentage of patients who screened positive for a mutation in at least one gene in the Inheritest *Comprehensive* panel

THE CASE FOR EXPANDED CARRIER SCREENING

While some providers may only screen for CF or select screening based on ethnicity, the case for more comprehensive screening is becoming clear. According to a bulletin from the World Health Organization, the global prevalence at birth of all single-gene disorders is about 10 per 1000.[1]

Our internal laboratory data also supports the case for more comprehensive screening. In screening over a thousand patients with the *Comprehensive* panel, our data showed that focusing only on disorders listed in ACOG/ACMG recommendations can result in a significant number of missed carriers[2] *(see figure 1)*.

Of the disorders a *Comprehensive* panel can identify:*

115	can result in severe early onset, increased childhood mortality, or shortened lifespan
78	may cause intellectual disability
77	are metabolic disorders that may have treatment benefit with early medical intervention
62	may cause loss of vision/ eye problems in affected individuals—*early identification could be beneficial*
39	may cause deafness/ hearing loss—*early identification could be beneficial*
6	are X-linked, meaning only the mother has to be a carrier for the child to be at risk

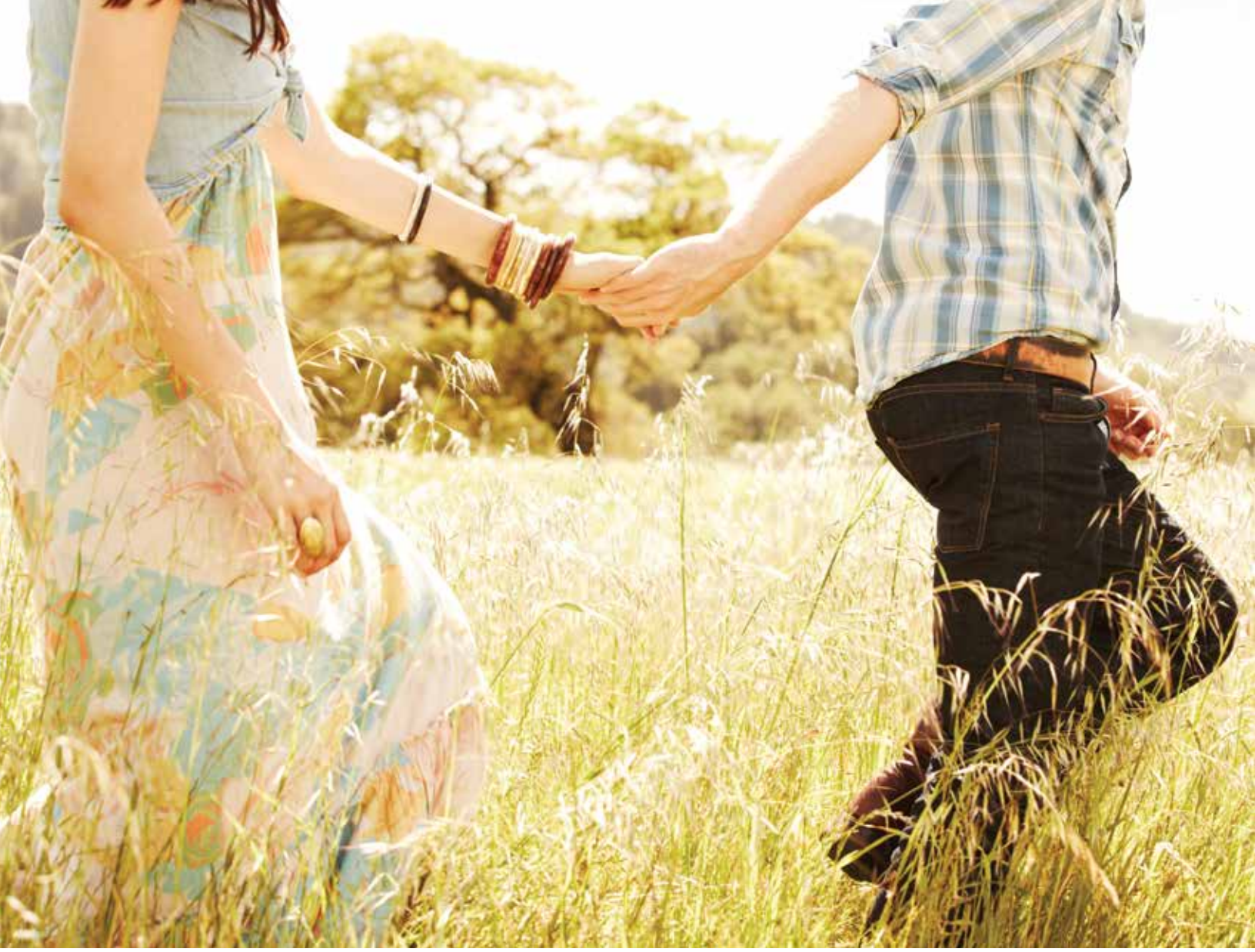
ℹ Some disorders will have characteristics of multiple categories.

ANCESTRY AND FAMILY HISTORY CAN BE A MYSTERY

An absence of disorders in a patient's family can be an insufficient guide for targeted screening. For example, more than 80% of infants with CF are born to families with no prior family history.[5] In addition, early studies estimated that each person carries three to five mutations, which, if passed along in a pregnancy, could lead to a genetic disorder.[6]

*Based on information on the relevant disorders compiled from Genetics Home Reference and GARD.[3,4]

†Next-generation sequencing is used for the Comprehensive, Ashkenazi Jewish, and Society-guided panels. PCR with reflex to Southern blot is used for fragile X syndrome analysis, quantitative PCR analysis is used for SMA analysis and deletion/duplication analysis is used for alpha-thalassemia analysis. While all panels include CF analysis, the Core panel uses a bead-based array that identifies 97 common CF mutations.



BEYOND NGS TO DELIVER GREATER ACCURACY

Inheritest Carrier Screen uses next-generation sequencing (NGS)[†] to capture a broad spectrum of mutations, including rare variants, with Sanger sequencing and other appropriate technologies to confirm positive results and deliver optimal sensitivity and specificity.

FOCUSED PARTNER TESTING

If your patient's result is positive, Integrated Genetics can offer her partner full gene sequencing for any autosomal recessive gene in the Inheritest panels (except SMA, for which we offer partners SMN1 copy number analysis).

Full gene sequencing detects disease-causing variants as well as variants of uncertain significance, to identify a greater number of potentially at-risk pregnancies.

PRENATAL DIAGNOSIS

Additionally, once an at-risk pregnancy is identified, we can perform prenatal diagnostic testing—for any of the disorders in the Inheritest panels—to deliver insights regarding the baby's condition.

Where some testing service providers are unable to offer single gene testing, VUS identification, or prenatal diagnosis—sometimes resulting in time-consuming retesting—Integrated Genetics offers a continuum of care for patients that can both save time and reduce anxiety.

Inheritest® *Core* panel

- Cystic fibrosis (97 mutations)
- Spinal muscular atrophy
- Fragile X syndrome (females only)

Inheritest® *Society-guided* panel

- NEW Alpha-thalassemia
- Beta hemoglobinopathy; includes sickle cell disease, hemoglobins C, D, E, and O, and beta thalassemias
- Bloom syndrome
- Canavan disease
- Cystic fibrosis
- Familial dysautonomia
- Fanconi anemia group C
- Fragile X syndrome (females only)
- Gaucher disease
- Mucolipidosis type IV
- Niemann-Pick disease types A and B
- Spinal muscular atrophy
- Tay-Sachs disease

Inheritest® *Ashkenazi Jewish* panel

- Abetalipoproteinemia
- NEW Alpha-thalassemia
- Alport syndrome, *COL4A3*-related
- Arthrogryposis, mental retardation, and seizures (AMRS)
- NEW Ataxia-telangiectasia
- Bardet-Biedl syndrome, *BBS2*-related
- NEW Beta hemoglobinopathy; includes sickle cell disease, hemoglobins C, D, E, and O, and beta thalassemias
- Bloom syndrome
- Canavan disease
- Carnitine palmitoyltransferase II deficiency
- Congenital amegakaryocytic thrombocytopenia
- Congenital disorder of glycosylation type 1a
- Cystic fibrosis
- NEW Cystinosis
- Dihydrolipoamide dehydrogenase deficiency
- Ehlers-Danlos syndrome type VIIC
- Familial dysautonomia
- Familial hyperinsulinism, *ABCC8*-related
- NEW Familial Mediterranean fever
- Fanconi anemia group C
- Fragile X syndrome (females only)
- Galactosemia, *GALT*-related
- Gaucher disease
- Glycogen storage disease type Ia
- NEW Glycogen storage disease type III
- Joubert syndrome 2
- Maple syrup urine disease type 1A
- Maple syrup urine disease type 1B
- NEW Metachromatic leukodystrophy
- Mucolipidosis type IV
- Multiple sulphatase deficiency
- Nemaline myopathy, *NEB*-related
- Niemann-Pick disease types A and B
- NEW Phenylalanine hydroxylase deficiency, includes phenylketonuria (PKU)
- Phosphoglycerate dehydrogenase deficiency, *PHGDH*-related
- Polycystic kidney disease, autosomal recessive
- Retinitis pigmentosa 59
- Smith-Lemli-Opitz syndrome
- Spinal muscular atrophy
- Tay-Sachs disease
- Tyrosinemia type 1
- Usher syndrome type IF
- Usher syndrome type IIIA
- Walker-Warburg syndrome, *FKTN*-related
- Wilson disease
- Zellweger spectrum disorder, *PEX2*-related
- NEW Zellweger spectrum disorder, *PEX6*-related

Inheritest® *Comprehensive* panel

- Abetalipoproteinemia
- Adenosine deaminase deficiency
- Alpha-mannosidosis
- **NEW** Alpha-thalassemia
- Alport syndrome, *COL4A3*-related
- Andermann syndrome
- Argininosuccinic aciduria
- Arthrogryposis, mental retardation, and seizures (AMRS)
- Aspartylglucosaminuria
- Ataxia with vitamin E deficiency
- Ataxia-telangiectasia
- Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS)
- Bardet-Biedl syndrome, *BBS1*-related
- Bardet-Biedl syndrome, *BBS10*-related
- Bardet-Biedl syndrome, *BBS2*-related
- Beta hemoglobinopathy, includes sickle cell disease, hemoglobins C, D, E, and O, and beta thalassemias
- Beta-mannosidosis
- Bloom syndrome
- Canavan disease
- Carbamoyl phosphate synthetase I deficiency
- Carnitine palmitoyltransferase II deficiency
- Carnitine-acylcarnitine translocase deficiency
- Cartilage-hair hypoplasia
- Citrullinemia type I
- Cobalamin C disease
- Cohen syndrome
- Congenital amegakaryocytic thrombocytopenia
- Congenital disorder of glycosylation type 1a
- Cystic fibrosis
- Cystinosis
- D-bifunctional protein deficiency
- Dihydrolipoamide dehydrogenase deficiency
- Dihydropyrimidine dehydrogenase deficiency
- **NEW** Dystrophinopathies, includes Duchenne and Becker muscular dystrophies and X-linked cardiomyopathy
- Ehlers-Danlos syndrome type VIIC
- Ethylmalonic encephalopathy
- Familial Mediterranean fever
- Familial dysautonomia
- Familial hyperinsulinism, *ABCC8*-related
- Fanconi anemia group C
- Fragile X syndrome (females only)
- Fucosidosis
- GM1 gangliosidosis and mucopolysaccharidosis type IVB
- GRACILE syndrome
- Galactosemia, *GALT*-related
- Galactosialidosis
- Gaucher disease
- Glutaric acidemia type 1
- Glutathione synthetase deficiency
- Glycine encephalopathy, *AMT*-related
- Glycine encephalopathy, *GLDC*-related
- Glycogen storage disease type III
- Glycogen storage disease type Ia
- Glycogen storage disease type Ib
- Guanidinoacetate methyltransferase deficiency
- HMG-CoA lyase deficiency
- Hereditary fructose intolerance
- Holocarboxylase synthetase deficiency
- Homocystinuria, *CBS*-related
- Hypophosphatasia, autosomal recessive
- Joubert syndrome 2
- Junctional epidermolysis bullosa, *LAMA3*-related
- Junctional epidermolysis bullosa, *LAMB3*-related
- Junctional epidermolysis bullosa, *LAMC2*-related
- Krabbe disease
- Leigh syndrome, French Canadian type
- Leigh syndrome, autosomal recessive, includes French Canadian type
- Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)
- Maple syrup urine disease type 1A
- Maple syrup urine disease type 1B
- Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)
- Metachromatic leukodystrophy
- Methylmalonic acidemia, *MMAA*-related
- Methylmalonic acidemia, *MMAB* -related
- Methylmalonic acidemia, *MUT*-related
- Mitochondrial acetoacetyl-CoA thiolase deficiency
- Mucolipidosis type II and III, *GNPTAB*-related
- Mucolipidosis type IV
- Mucopolysaccharidosis type I
- Mucopolysaccharidosis type II
- Mucopolysaccharidosis type IIIA
- Mucopolysaccharidosis type IIIB
- Mucopolysaccharidosis type IIIC
- Mucopolysaccharidosis type IIID
- Mucopolysaccharidosis type IV A
- Mucopolysaccharidosis type VI
- Mucopolysaccharidosis type VII
- Multiple sulphatase deficiency
- Nemaline myopathy, *NEB*-related
- Nephrotic syndrome, *NPHS1*-related
- Nephrotic syndrome, *NPHS2*-related
- Neuronal ceroid-lipofuscinosis, *CLN3*-related
- Neuronal ceroid-lipofuscinosis, *CLN5* -related
- Neuronal ceroid-lipofuscinosis, *CLN8*-related
- Neuronal ceroid-lipofuscinosis, *PPT1*-related
- Neuronal ceroid-lipofuscinosis, *TPP1*-related
- Niemann-Pick disease type C, *NPC1*-related
- Niemann-Pick disease type C, *NPC2*-related
- Niemann-Pick disease types A and B
- Nijmegen breakage syndrome
- Ornithine transcarbamylase deficiency
- Phenylalanine hydroxylase deficiency, includes phenylketonuria (PKU)
- Phosphoglycerate dehydrogenase deficiency, *PHGDH*-related
- Polycystic kidney disease, autosomal recessive
- Pompe disease
- Primary hyperoxaluria type 1
- Primary hyperoxaluria type 2
- Propionic acidemia, *PCCA*-related
- Propionic acidemia, *PCCB* -related
- Pyruvate dehydrogenase deficiency, *PDHA1*-related
- Retinitis pigmentosa 59
- Rhizomelic chondrodysplasia punctata type 1
- Salla disease
- Sandhoff disease
- Sialidosis
- Sjogren-Larsson syndrome
- Smith-Lemli-Opitz syndrome
- Spinal muscular atrophy
- *Sulfate transporter*-related osteochondrodysplasias, includes achondrogenesis type 1B, atelosteogenesis type 2, diastrophic dysplasia, and recessive multiple epiphyseal dysplasia
- Systemic primary carnitine deficiency
- Tay-Sachs disease
- Tyrosinemia type 1
- Usher syndrome type IF
- Usher syndrome type IIIA
- Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)
- Walker-Warburg syndrome, *FKTN*-related
- Wilson disease
- X-linked severe combined Immunodeficiency (SCID)
- Xeroderma pigmentosum, *ERCC5* -related
- Xeroderma pigmentosum, *XPA*-related
- Xeroderma pigmentosum, *XPC*-related
- Zellweger spectrum disorder, *PEX1*-related
- Zellweger spectrum disorder, *PEX10*-related
- Zellweger spectrum disorder, *PEX12*-related
- Zellweger spectrum disorder, *PEX2*-related
- Zellweger spectrum disorder, *PEX26*-related
- Zellweger spectrum disorder, *PEX6*-related

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Integrated Genetics is a brand used by Esoterix Genetic Laboratories, LLC, a wholly owned subsidiary of Laboratory Corporation of America® Holdings.

Test panel name	Test number
Core Panel	451964
Society-guided Panel	451960
Ashkenazi Jewish Panel	451920
Comprehensive Panel	451950
Gene-specific Sequencing	451910
Mutation-specific Sequencing	451382/640

10 mL whole blood in a yellow-top (ACD-A) tube or lavender-top (EDTA) tube

Integrated GENETICS
LabCorp Specialty Testing Group

A continuity of care, pioneering science, professional service

Inheritest is available through Integrated Genetics, which delivers a continuity of care for your patients, from carrier screening to noninvasive prenatal testing (NIPT, also known as cfDNA testing) to diagnostic testing.

We provide the scientific expertise you need, and the customer experience patients want.

RAPID RESULTS

Samples have a typical turnaround time of 14 calendar days after a test arrives at our lab.

EXTENSIVE MANAGED CARE CONTRACTS

Help patients maximize their benefits.

CONVENIENT BLOOD DRAWS

We have a nationwide network of patient service centers, allowing for convenient access to sample collection. Visit www.LabCorp.com to find your nearest location.

GENETIC COUNSELING

Patients with a positive test result may be offered counseling, and Integrated Genetics offers the largest national commercial network of genetic counselors to help inform and support patients. Visit our online scheduler at integratedgenetics.com or call 855.422.2557. To learn more about genetic inheritance and carrier screening for genetic disorders visit www.integratedgenetics.com/videos.

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