SAMPLE REPORT

Integrated GENETICS
LabCorp Specialty Testing Group

Inheritest® Core

Patient Name:
Referring Physician:
Specimen #:
Patient ID #:

Client #:
Case #:

DOB: 00/00/0000
Sex: Female
Lab ID:
Hospital ID:
Specimen Type:

Date Collected: 00/00/0000
Date Received: 00/00/0000

Ethnicity: Caucasian
Indication: Screening

Disease *(Gene)*	Results	Interpretation
Cystic fibrosis *(CFTR)*	Negative for the mutations analyzed	These results reduce, but do not eliminate, the chance to be a carrier. For risk reductions see Information Table.
Spinal muscular atrophy *(SMN1)*	POSITIVE	*SMN1* copy number of one. Predicted to be a carrier. Genetic counseling is recommended.
Fragile X syndrome *(FMR1)*	PCR: 29 and 30 repeats.	Negative: not a carrier of a fragile X expansion mutation. This result is not associated with fragile X syndrome.

Genetic counseling services are available. To access Integrated Genetics Genetic Counselors please call (855)GC-CALLS (855-422-2557).

ADDITIONAL CLINICAL INFORMATION

Cystic fibrosis: Cystic fibrosis (CF) is an autosomal recessive disease with variable severity and age of onset. Symptoms of classic CF include elevated sweat chloride levels, progressive lung disease, pancreatic insufficiency, and male infertility. Individuals with mild CF may have pancreatic sufficiency. *CFTR*-related disorders include pancreatitis, bronchiectasis, and isolated male infertility due to congenital absence of the vas deferens. Treatment is primarily dietary and supportive. Genotype-targeted therapies may be available for some individuals. In severely affected individuals, lung transplantation may be indicated. (Moskowitz, PMID:20301428)

Spinal muscular atrophy: Spinal muscular atrophy (SMA) is an autosomal recessive disease with variable age of onset and severity caused by mutations in the *SMN1* gene. Individuals with one copy of *SMN1* are predicted to be carriers of SMA; those with two or more copies have a reduced carrier risk. Approximately 94% of affected individuals have 0 copies of *SMN1*. In individuals with 0 copies of *SMN1* an increase in the number of copies of the *SMN2* gene correlates with reduced disease severity (Feldkotter M, PMID:11791208). Clinical features of SMA include poor muscle tone, muscle weakness, absence of tendon reflexes, and delayed motor development. In severely affected individuals, abnormal fetal ultrasound findings include congenital joint contractures, polyhydramnios, and decreased fetal movement (Korinthenberg, PMID:9307259). Treatment is supportive. Genetic counseling is recommended to discuss the potential clinical and/or reproductive implications of these results, as well as recommendations for testing family members and, when applicable, this individual's partner. If this individual's reproductive partner is also a carrier the risk for an affected fetus is 25%.

Fragile X syndrome: Fragile X syndrome, also known as Martin-Bell syndrome, is an X-linked disease of intellectual disability with variable severity caused by mutations in the *FMR1* gene. 99% of mutations are expansions of CGG repeat sequences. Rare mutations include missense mutations and gene deletions. Interpretation of repeat expansion results is based on the following ranges: Negative: < 45 repeats; intermediate: 45-54 repeats; premutation: 55-200 repeats with normal methylation pattern; full mutation: >200 repeats with abnormal methylation pattern. Clinical features include mild to severe learning disabilities, autism-like behaviors, developmental delay, increased susceptibility to seizures, and macroorchidism in males. More subtle physical symptoms may include a long, narrow face with prominent ears, joint laxity, and flat feet. Treatment is supportive and focuses on educational and behavioral support and management of symptoms. (Santoro, PMID:22017584).

Under the direction of:

Testing performed at Esoterix Genetic Laboratories, LLC, 3400 Computer Drive, Westborough, MA 01581 Bernice A. Allitto, PhD, FACMG, Laboratory Director 1-800-255-7357

METHOD / LIMITATIONS:

Cystic fibrosis: *CFTR* gene regions are amplified enzymatically. 97 targeted CF mutations, listed below, are tested by multiplex allele-specific primer extension, bead array hybridization, and fluorescence detection. The test discriminates between p.F508del and three polymorphisms (p.I506V, p.I507V and p.F508C). Numbering and nomenclature follow Human Genome Variation Society recommendations. The DNA reference sequence is NG_016465.1. Legacy mutation names are available at www.integratedgenetics.com/CFplus.

c.54-5940_273+10250del21kb (p.S18fs), c.178G>T (p.E60*), c.223C>T (p.R75*), c.254G>A (p.G85E), c.262_263delTT (p.L88fs), c.273+1G>A, c.273+3A>C, c.274-1G>A, c.274G>T (p.E92*), c.313delA (p.I105fs), c.325_327delTATinsG (p.Y109fs), c.349C>T (p.R117C), c.350G>A (p.R117H), c.366T>A (p.Y122*), c.442delA (p.I148fs), c.489+1G>T, c.531delT (p.I177fs), c.532G>A (p.G178R), c.579+1G>T, c.579+5G>A, c.580-1G>T, c.617T>G (p.L206W), c.803delA (p.N268fs), c.805_806delAT (p.I269fs), c.935_937delTCT (p.F312del), c.948delT (p.F316fs), c.988G>T (p.G330*), c.1000C>T (p.R334W), c.1013C>T (p.T338I), c.1040G>A (p.R347H), c.1040G>C (p.R347P), c.1055G>A (p.R352Q), c.[1075C>A;1079C>A] (p.[Q359K;T360K]), c.1090T>C (p.S364P), c.1155_1156dupTA, c.1364C>A (p.A455E), c.1438G>T (p.G480C), c.1477C>T (p.Q493*), c.1519_1521delATC (p.I507del), c.1521_1523delCTT (p.F508del), c.1545_1546delTA (p.Y515*), c.1558G>T (p.V520F), c.1572C>A (p.C524*), c.1585-1G>A, c.1624G>T (p.G542*), c.1646G>A (p.S549N), c.1647T>G (p.S549R), c.1652G>A (p.G551D), c.1654C>T (p.Q552*), c.1657C>T (p.R553*), c.1675G>A (p.A559T), c.1679G>C (p.R560T), c.1680-1G>A, c.1721C>A (p.P574H), c.1766+1G>A, c.1766+5G>T, c.1820_1903del84 (p.M607_Q634del), c.1911delG (p.Q637fs), c.1923_1931del9insA (p.S641fs), c.1973_1985del13insAGAAA (p.R658fs), c.1976delA (p.N659fs), c.2012delT, c.2051_2052delAAinsG (p.K684fs), c.2052delA (p.K684fs), c.2052dupA (p.Q685fs), c.2125C>T (p.R709*), c.2128A>T (p.K710*), c.2175dupA (p.E726fs), c.2290C>T (p.R764*), c.2657+5G>A, c.2668C>T (p.Q890*), c.2737_2738insG (p.Y913*), c.2988G>A, c.2988+1G>A, c.3039delC (p.Y1014fs), c.3067_3072delATAGTG (p.I1023_V1024del), c.3196C>T (p.R1066C), c.3266G>A (p.W1089*), c.3276C>A (p.Y1092*), c.3276C>G (p.Y1092*), c.3302T>A (p.M1101K), c.3454G>C (p.D1152H), c.3472C>T (p.R1158*), c.3484C>T (p.R1162*), c.3528delC (p.K1177fs), c.3536_3539delCCAA (p.T1179fs), c.3587C>G (p.S1196*), c.3612G>A (p.W1204*), c.3659delC (p.T1220fs), c.3712C>T (p.Q1238*), c.3717+12191C>T, c.3744delA (p.K1250fs), c.3752G>A (p.S1251N), c.3764C>A (p.S1255*), c.3773dupT (p.L1258fs), c.3846G>A (p.W1282*), c.3889dupT, c.3909C>G (p.N1303K).

Spinal muscular atrophy: Isolated DNA is amplified by real-time polymerase chain reaction (PCR). The number of copies of exon 7 of *SMN1* is assessed relative to internal standard reference genes. A mathematical algorithm calculates 0, 1, 2 and 3 copies with statistical confidence. In samples with one copy of *SMN1*, primer and probe binding sites are sequenced to rule out variants that could interfere with copy number analysis. In samples with 0 copies of *SMN1*, *SMN2* copy number is assessed by digital PCR analysis relative to an internal standard reference gene. Copy number analysis cannot detect carriers with either 2 or, very rarely, 3 copies of *SMN1* on one chromosome and no copies of *SMN1* on the other chromosome.

Fragile X syndrome: Isolated DNA is amplified by the polymerase chain reaction (PCR) to determine the size of the CGG repeat within the *FMR1* gene. PCR products are generated using a fluorescence labeled primer and sized by capillary gel electrophoresis. If indicated, Southern blot analysis is performed by hybridizing the probe StB12.3 to EcoRI- and EagI-digested DNA. The analytical sensitivity of both Southern blot and PCR analyses is 99% for expansion mutations in the *FMR1* gene. Reported CGG repeat sizes may vary as follows: +/- one for repeats less than 60, and +/- two to four for repeats in the 60 - 120 range respectively. For repeats greater than 120, the accuracy is +/- 10%.

Limitations: False positive or false negative results may occur for reasons that include genetic variants, blood transfusions, bone marrow transplantation, somatic or tissue-specific mosaicism, mislabeled samples, or erroneous representation of family relationships.

INFORMATION TABLES

CF risk reductions for individuals with no family history			
Ethnicity	**Detection rate**	**Pre-test carrier risk**	**Post test carrier risk with negative result**
African American	81%	1 in 61	1 in 316
Ashkenazi Jewish	97%	1 in 24	1 in 767
Asian American	55%	1 in 94	1 in 208
Caucasian	93%	1 in 25	1 in 343
Hispanic	78%	1 in 58	1 in 260
Jewish, non-Ashkenazi	Varies	n/a	n/a
Mixed / other ethnic background	For counseling purposes, consider using the ethnic background with the most conservative risk estimates		

Under the direction of:

SMA risk reductions for individuals with no family history				
Ethnicity	**Detection rate**	**Pre-test carrier risk**	**Post test carrier risk with 2 copy result**	**Post test carrier risk with 3 copy result**
African American	70.5%	1 in 72	1 in 130	1 in 4,200
Ashkenazi Jewish	90.5%	1 in 67	1 in 611	1 in 5,400
Asian	93.3%	1 in 59	1 in 806	1 in 5,600
Asian Indian	90.2%	1 in 52	1 in 443	1 in 5,400
Caucasian	94.8%	1 in 47	1 in 834	1 in 5,600
Hispanic	90.0%	1 in 68	1 in 579	1 in 5,400
Mixed / other ethnic background	For counseling purposes, consider using the ethnic background with the most conservative risk estimates			

Under the direction of:

Testing performed at Esoterix Genetic Laboratories, LLC, 3400 Computer Drive, Westborough, MA 01581 Bernice A. Allitto, PhD, FACMG, Laboratory Director 1-800-255-7357