



Donor 5249

Genetic Testing Summary

Fairfax Cryobank recommends reviewing this genetic testing summary with your healthcare provider to determine suitability.

Last Updated: 08/14/18

Donor Reported Ancestry: Indian

Jewish Ancestry: No

Genetic Test*	Result	Comments/Donor's Residual Risk**
Chromosome analysis (karyotype)	Normal male karyotype	No evidence of clinically significant chromosome abnormalities
Hemoglobin evaluation	Normal hemoglobin fractionation and MCV/MCH results	Reduced risk to be a carrier for sickle cell anemia, beta thalassemia, alpha thalassemia trait (aa/-- and a-/a-) and other hemoglobinopathies
Cystic Fibrosis (CF) carrier screening	Negative by genotyping of 149 mutations in the CFTR gene	1/280
Spinal Muscular Atrophy (SMA) carrier screening	Negative for deletions of exon 7 in the SMN1 gene	1/628
Standard testing attached- 22 diseases by genotyping	Negative for mutations tested	
Special testing requests		
Combined Malonic and Methylmalonic Aciduria	Negative by sequencing in the ACSF3 gene	1/1701
Usher Syndrome Type 2 A	Negative by sequencing in the USH2A gene	1/404
Sulfate Transporter-Related Osteochondrodysplasia	Negative by sequencing in the SLC26A2 gene	1/85,200

*No single test can screen for all genetic disorders. A negative screening result significantly reduces, but cannot eliminate, the risk for these conditions in a pregnancy.**Donor residual risk is the chance the donor is still a carrier after testing negative.

Ordering Practice:

Practice Code: 1139

Fairfax Cryobank

Physician:

Report Generated: 2016-05-23

Report Updated: 2016-06-03

Donor 5249

DOB:

Gender: Male

Ethnicity: South Asian

Procedure ID: 53240

Kit Barcode:

Specimen: Blood, #56052

Specimen Collection: 2016-05-10

Specimen Received: 2016-05-11

Specimen Analyzed: 2016-05-23

Partner Not Tested

TEST INFORMATIONTest: CarrierMap^{GEN} (Genotyping)

Panel: Fairfax Cryobank Panel V2

Diseases Tested: 22

Genes Tested: 22


Mutations Tested: 451

SUMMARY OF RESULTS: NO MUTATIONS IDENTIFIED

Donor 5249 was not identified to carry any of the mutation(s) tested.

No pathogenic mutations were identified in the genes tested, reducing but not eliminating the chance to be a carrier for the associated genetic diseases. CarrierMap assesses carrier status for genetic disease via molecular methods including targeted mutation analysis and/ or next-generation sequencing; other methodologies such as CBC and hemoglobin electrophoresis for hemoglobinopathies and enzyme analysis for Tay-Sachs disease may further refine risks for these conditions. Results should be interpreted in the context of clinical findings, family history, and/or other testing. A list of all the diseases and mutations screened for is included at the end of the report. This test does not screen for every possible genetic disease.

For additional disease information, please visit recombine.com/diseases. To speak with a Genetic Counselor, call 855.OUR.GENES.

Assay performed by

Reprogenetics

CLIA ID: 31D1054821

3 Regent Street, Livingston, NJ 07039

Lab Technician: Bo Chu

Recombine CLIA # 31D2100763

Reviewed by Pere Colls, PhD, HCLD, Lab Director

ADDITIONAL RESULTS: NO INCREASED REPRODUCTIVE RISK

The following results are not associated with an increased reproductive risk.

Disease (Gene)	Donor 5249	Partner Not Tested
Spinal Muscular Atrophy: SMN1 Linked (SMN1) *	SMN1 Copy Number: 2 or more copies Method: Genotyping & dPCR	

* SMA Risk Information for Individuals with No Family History of SMA

	Detection Rate	Pre-Test Carrier Risk	Post-Test Carrier Risk (2 SMN1 copies)	Post-Test Carrier Risk (3 SMN1 copies)
European	95%	1/35	1/632	1/3,500
Ashkenazi Jewish	90%	1/41	1/350	1/4,000
Asian	93%	1/53	1/628	1/5,000
African American	71%	1/66	1/121	1/3,000
Hispanic	91%	1/117	1/1,061	1/11,000

For other unspecified ethnicities, post-test carrier risk is assumed to be <1%. For individuals with multiple ethnicities, it is recommended to use the most conservative risk estimate.

Methods and Limitations

Genotyping: Genotyping is performed using the Illumina Infinium Custom HD Genotyping assay to identify mutations in the genes tested. The assay is not validated for homozygous mutations, and it is possible that individuals affected with disease may not be accurately genotyped.

Spinal Muscular Atrophy: Carrier status for SMA is assessed via copy number analysis by dPCR and via genotyping. Some individuals with a normal number of SMN1 copies (2 copies) may carry both copies of the gene on the same allele/chromosome; this analysis is not able to detect these individuals. Thus, a normal SMN1 result significantly reduces but does not eliminate the risk of being a carrier. Additionally, SMA may be caused by non-deletion mutations in the SMN1 gene; CarrierMap tests for some, but not all, of these mutations. Some SMA cases arise as the result of de novo mutation events which will not be detected by carrier testing.

Limitations: In some cases, genetic variations other than that which is being assayed may interfere with mutation detection, resulting in false-negative or false-positive results. Additional sources of error include, but are not limited to: sample contamination, sample mix-up, bone marrow transplantation, blood transfusions, and technical errors. The test does not test for all forms of genetic disease, birth defects, and intellectual disability. All results should be interpreted in the context of family history; additional evaluation may be indicated based on a history of these conditions. Additional testing may be necessary to determine mutation phase in individuals identified to carry more than one mutation in the same gene. All mutations included within the genes assayed may not be detected, and additional testing may be appropriate for some individuals.

This test was developed and its performance determined by Recombine, Inc., and it has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary.

Diseases & Mutations Assayed

Alpha Thalassemia : Mutations (9): ♂ Genotyping | SEA deletion, c.207C>A (p.N69K), c.223G>C (p.D75G), c.2T>C (p.M1T), c.207C>G (p.N69K), c.340_351delCTCCCGCCGAG (p.L114_E117del), c.377T>C (p.L126P), c.427T>C (p.X143Qext32), c.*+94A>G

Beta Thalassemia : Mutations (82): ♂ Genotyping | c.124_127delTTCT (p.F42Lfs), c.17_18delCT, c.20delA (p.E7Gfs), c.217insA (p.S73Kfs), c.223+702_444+342del620insAAGTAGA, c.230delC, c.25_26delAA, c.315+1G>A, c.315+2T>C, c.316-197C>T, c.316-146T>G, c.315+745C>G, c.316-1G>A, c.316-1G>C, c.316-2A>G, c.316-3C>A, c.316-3C>G, c.4delG (p.V2Cfs), c.51delC (p.K18Rfs), c.93-21G>A, c.92+1G>A, c.92+5G>A, c.92+5G>C, c.92+5G>T, c.92+6T>C, c.93-1G>A, c.93-1G>T, c.-50A>C, c.-78a>g, c.-79a>g, c.-81a>g, c.52A>T (p.K18X), c.-137c>g, c.-138c>t, c.-151c>t, c.118C>T (p.Q40X), c.169G>C (p.G57R), c.295G>A (p.V99M), c.34G>A (p.V12I), c.415G>C (p.A139P), c.47G>A (p.W16X), c.48G>A (p.W16X), c.-80T>a, c.2T>C (p.M1T), c.75T>A (p.G25G), c.444+111A>G, c.-29g>a, c.68_74delAAGTTGG, c.92G>C (p.R31T), c.92+1G>T, c.93-15T>G, c.93-1G>C, c.112delT, c.113G>A (p.W38X), c.114G>A (p.W38X), c.126delC, c.444+113A>G, c.250delG, c.225delC, c.383_385delAGG (p.Q128_A129delQAinsP), c.321_322insG (p.N109fs), c.316-1G>T, c.316-2A>C, c.287_288insA (p.L97fs), c.271G>T (p.E91X), c.203_204delTG (p.V68Afs), c.154delC (p.P52fs), c.135delC (p.F46fs), c.92+2T>A, c.92+2T>C, c.90C>T (p.G30G), c.84_85insC (p.L29fs), c.59A>G (p.N20S), c.46delT (p.W16Gfs), c.45_46insG (p.L16fs), c.36delT (p.T13fs), c.2T>G (p.M1R), c.1A>G (p.M1V), c.-137c>t, c.-136c>g, c.-142c>t, c.-140c>t

Bloom Syndrome : Mutations (25): ♂ Genotyping | c.2207_2212delATCTGAinsTAGATTC (p.Y736Lfs), c.2407insT, c.557_559delCAA (p.S186X), c.1284G>A (p.W428X), c.1701G>A (p.W567X), c.1933C>T (p.Q645X), c.2528C>T (p.T843I), c.2695C>T (p.R899X), c.3107G>T (p.C1036F), c.2923delC (p.Q975K), c.3558+1G>T, c.3875-2A>G, c.2074+2T>A, c.2343_2344dupGA (p.781EfsX), c.318_319insT (p.L107fs), c.380delC (p.127Tfs), c.3564delC (p.1188Dfs), c.4008delG (p.1336Rfs), c.947C>G (p.S316X), c.2193+1_2193+9del9, c.1642C>T (p.Q548X), c.3143delA (p.1048NfsX), c.356_357delTA (p.C120Hfs), c.4076+1delG, c.3281C>A (p.S1094X)

Canavan Disease : Mutations (8): ♂ Genotyping | c.433-2A>G, c.854A>C (p.E285A), c.693C>A (p.Y231X), c.914C>A (p.A305E), c.71A>G (p.E24G), c.654C>A (p.C218X), c.2T>C (p.M1T), c.79G>A (p.G27R)

Cystic Fibrosis : Mutations (149): ♂ Genotyping | c.1029delC, 1153_1154insAT, c.1477delCA, c.1519_1521delATC (p.S07delI), c.1521_1523delCTT (p.S08delF), c.1545_1546delTA (p.Y515Xfs), c.1585-1G>A, c.164+12T>C, c.1680-886A>G, c.1680-1G>A, c.1766+1G>A, c.1766+1G>T, c.1766+5G>T, c.1818del84, c.1911delG, c.1923delCTCAAAATinsA, c.1973delGAAATCAATCTinsAGAAA, c.2052delA (p.K684fs), c.2052insA (p.Q685fs), c.2051_2052delAAinsG (p.K684SfsX38), c.2174insA, c.261delIT, c.2657+5G>A, c.273+1G>A, c.273+3A>C, c.274-1G>A, c.2988+1G>A, c.3039delC, c.3140-26A>G, c.325delTAinsG, c.3527delC, c.3535delACCA, c.3691delT, c.3717+12191C>T, c.3744delA, c.3773_3774insT (p.L1258fs), c.442delA, c.489+1G>T, c.531delT, c.579+1G>T, c.579+5G>A (IVS4+5G>A), c.803delA (p.N268fs), c.805_806delAT (p.I269fs), c.933_935delCTT (p.311delF), c.946delT, c.1645A>C (p.S549R), c.2128A>T (p.K710X), c.1000C>T (p.R334W), c.1013C>T (p.T338I), c.1364C>A (p.A455E), c.1477C>T (p.Q493X), c.1572C>A (p.C524X), c.1654C>T (p.Q552X), c.1657C>T (p.R553X), c.1721C>A (p.P574H), c.2125C>T (p.R709X), c.223C>T (p.R75X), c.2668C>T (p.Q890X), c.3196C>T (p.R1066C), c.3276C>G (p.Y1092X), c.3472C>T (p.R1158X), c.3484C>T (p.R1162X), c.349C>T (p.R117C), c.3587C>G (p.S1196X), c.3712C>T (p.Q1238X), c.3764C>A (p.S1255X), c.3909C>G (p.N1303K), c.1040G>A (p.R347H), c.1040G>C (p.R347P), c.1438G>T (p.G480C), c.1558G>T (p.V520F), c.1624G>T (p.G542X), c.1646G>A (p.S549N), c.1646G>T (p.S549I), c.1652G>A (p.G551D), c.1675G>A (p.A559T), c.1679G>C (p.R560T), c.178G>T (p.E60X), c.1865G>A (p.G622D), c.254G>A (p.G85E), c.271G>A (p.G91R), c.274G>T (p.E92X), c.3209G>A (p.R1070Q), c.3266G>A (p.W1089X), c.3454G>C (p.D1152H), c.350G>A (p.R117H), c.3611G>A (p.W1204X), c.3752G>A (p.S1251N), c.3846G>A (p.W1282X), c.3848G>T (p.R1283M), c.532G>A (p.G178R), c.988G>T (p.G330X), c.1090T>C (p.S364P), c.3302T>A (p.M1101K), c.617T>G (p.L206W), c.14C>T (p.P51), c.19G>T (p.E7X), c.171G>A (p.W57X), c.313delA (p.I105fs), c.328G>C (p.D110H), c.580-1G>T, c.1055G>A (p.R352Q), c.1075C>A (p.Q359K), c.1079C>A (p.T360K), c.1647T>G (p.S549R), c.1976delA (p.N659fs), c.2290C>T (p.R764X), c.2737_2738insG (p.Y913X), c.3067_3072delATAGTG (p.I1023_V1024delI), c.3536_3539delCCAA (p.T1179fs), c.3659delC (p.T1220fs), c.54-5940_273+10250del21080bp (p.S18fs), c.4056G>C (p.Q1352H), c.4364C>G (p.S1455X), c.4003C>T (p.L1335F), c.2538G>A (p.W846X), c.200C>T (p.P67L), c.4426C>T (p.Q1476X), c.1116+1G>A, c.1986_1989delAACT (p.T663R), c.2089_2090insA (p.R697Kfs), c.2215delG (p.V739Y), c.263T>G (p.L196X), c.3022delG (p.V1008S), c.3908dupA (p.N1303Kfs), c.658C>T (p.Q220X), c.868C>T (p.Q290X), c.1526delG (p.G509fs), c.2908+1085-3367+260del7201, c.11C>A (p.S4X), c.3700A>G (p.I1234V), c.416A>T (p.H139L), c.366T>A (p.Y122X), c.3767_3768insC (p.A1256fs), c.613C>T (p.P205S), c.293A>G (p.Q98R), c.3731G>A (p.G1244E), c.535C>A (p.Q179K), c.3368-2A>G, c.455T>G (p.M152R), c.1610_1611delAC (p.D537fs), c.3254A>G (p.H1085R), c.496A>G (p.K166E), c.1408_1417delGTGATTATGG (p.V470fs), c.1585-8G>A, c.2909G>A (p.G970D), c.653T>A (p.L218X), c.1175T>G (p.V392G), c.3139_3139+1delGG

Familial Dysautonomia : Mutations (4): ♂ Genotyping | c.2204+6T>C, c.2741C>T (p.P914L), c.2087G>C (p.R696P), c.2128C>T (p.Q710X)

Familial Hyperinsulinism: Type 1: ABCC8 Related : Mutations (10): ♂ Genotyping | c.3989-9G>A, c.4159_4161delITC (p.1387delF), c.4258C>T (p.R1420C), c.4477C>T (p.R1493W), c.2147G>T (p.G716V), c.4055G>C (p.R1352P), c.560T>A (p.V187D), c.4516G>A (p.E1506K), c.2506C>T (p.Q836X), c.579+2T>A

Fanconi Anemia: Type C : Mutations (8): ♂ Genotyping | c.456+4A>T, c.67delG, c.37C>T (p.Q13X), c.553C>T (p.R185X), c.1661T>C (p.L554P), c.1642C>T (p.R548X), c.66G>A (p.W22X), c.65G>A (p.W22X)

Gaucher Disease : Mutations (6): ♂ Genotyping | c.84_85insG, c.1226A>G (p.N409S), c.1343A>T (p.D448V), c.1504C>T (p.R502C), c.1297G>T (p.V433L), c.1604G>A (p.R535H)

Glycogen Storage Disease: Type IA : Mutations (13): ♂ Genotyping | c.376_377insTA, c.79delC, c.979_981delTTC (p.327delF), c.1039C>T (p.Q347X), c.247C>T (p.R83C), c.724C>T (p.Q242X), c.248G>A (p.R83H), c.562G>C (p.G188R), c.648G>T, c.809G>T (p.G270V), c.113A>T (p.D38V), c.975delG (p.L326fs), c.724delC

Joubert Syndrome : Mutations (2): ♂ Genotyping | c.218G>T (p.R73L), c.218G>A (p.R73H)

Maple Syrup Urine Disease: Type 1B : Mutations (6): ♂ Genotyping | c.1114G>T (p.E372X), c.548G>C (p.R183P), c.832G>A (p.G278S), c.970C>T (p.R324X), c.487G>T (p.E163X), c.853C>T (p.R285X)

Maple Syrup Urine Disease: Type 3 : Mutations (8): ♂ Genotyping | c.104_105insA, c.685G>T (p.G229C), c.214A>G (p.K72E), c.1081A>G (p.M361V), c.1123G>A (p.E375K), c.1178T>C (p.I393T), c.1463C>T (p.P488L), c.1483A>G (p.R495G)

Mucopolipidosis: Type IV : Mutations (5): ♂ Genotyping | c.-1015_788del6433, c.406-2A>G, c.1084G>T (p.D362Y), c.304C>T (p.R102X), c.244delC (p.L82fsX)

Nemaline Myopathy: NEB Related : Mutations (1): ♂ Genotyping | c.7434_7536del2502bp

Niemann-Pick Disease: Type A : Mutations (6): ♂ Genotyping | c.996delC, c.1493G>T (p.R498L), c.911T>C (p.L304P), c.1267C>T (p.H423Y), c.1734G>C (p.K578N), c.1493G>A (p.R498H)

Sickle-Cell Anemia : Mutations (1): ♂ Genotyping | c.20A>T (p.E7V)

Spinal Muscular Atrophy: SMN1 Linked : Mutations (19): ♂ Genotyping | DEL EXON 7, c.22_23insA, c.43C>T (p.Q15X), c.91_92insT, c.305G>A (p.W102X), c.400G>A (p.E134K), c.439_443delGAAGT, c.558delA, c.585_586insT, c.683T>A (p.L228X), c.734C>T (p.P245L), c.768_778dupTGCTGATGCTT, c.815A>G (p.Y272C), c.821C>T (p.T274I), c.823G>A (p.G275S), c.834+2T>G, c.835-18_835-12delCCTTTAT, c.835G>T, c.836G>T dPCR | DEL EXON 7

Tay-Sachs Disease : Mutations (76): ♂ Genotyping | c.1073+1G>A, c.1277_1278insATC, c.1421+1G>C, c.805+1G>A, c.532C>T (p.R178C), c.533G>A (p.R178H), c.805G>A (p.G269S), c.1510C>T (p.R504C), c.1496G>A (p.R499H), c.509G>A (p.R170Q), c.1003A>T (p.I335F), c.910_912delITC (p.305delF), c.749G>A (p.G250D), c.632T>C (p.F211S), c.629C>T (p.S210F), c.613delC, c.611A>G (p.H204R), c.598G>A (p.V200M), c.590A>C (p.K197T), c.571-1G>T, c.540C>G (p.Y180X), c.538T>C (p.Y180H), c.533G>T (p.R178L), c.508C>T (p.R170W), c.409C>T (p.R137X), c.380T>G (p.L127R), c.346+1G>C, c.116T>G (p.L39R), c.78G>A (p.W26X), c.1A>G (p.M1V), c.1495C>T (p.R499C), c.459+5G>A (IVS4+5G>A), c.1422-2A>G, c.535C>T (p.H179Y), c.1141delG (p.V381fs), c.796T>G (p.W266G), c.155C>A (p.S52X), c.426delIT (p.F142fs), c.413-2A>G, c.570+3A>G, c.536A>G (p.H179R), c.1146+1G>A, c.736G>A (p.A246T), c.1302C>G (p.F434L), c.778C>T (p.P260S), c.1008G>T (p.Q336H), c.1385A>T (p.E462V), c.964G>A (p.D322N), c.340G>A (p.E114K), c.1432G>A (p.G478R), c.1178G>C (p.R393P), c.805+1G>C, c.1426A>T (p.R476X), c.623A>T (p.D208V), c.1537C>T (p.Q513X), c.1511G>T (p.S201), c.1307_1308delTA (p.L436fs), c.571-8A>G, c.624_627delITCT (p.D208fs), c.1211_1212delTG (p.L404fs), c.621T>G (p.D207E), c.1511G>A (p.R504H), c.1177C>T (p.R393X), c.2T>C (p.M1T), c.1292G>A (p.W431X), c.947_948insA (p.Y316fs), c.607T>G (p.W203G), c.1061_1063delTCT (p.F354_Y355delinsX), c.615delG (p.L205fs), c.805+2T>C, c.1123delG (p.E375fs), c.1121A>G (p.Q374R), c.1043_1046delTCAA (p.F348fs), c.1510delC (p.R504fs), c.1451T>C (p.L484P), c.964G>T (p.D322Y)

Usher Syndrome: Type 1F : Mutations (7): ♂ Genotyping | c.733C>T (p.R245X), c.2067C>A (p.Y684X), c.7C>T (p.R3X), c.1942C>T (p.R648X), c.1101delT (p.A367fsX), c.2800C>T (p.R934X), c.4272delA (p.L1425fs)

Usher Syndrome: Type 3 : Mutations (5): ♂ Genotyping | c.144T>G (p.N48K), c.131T>A (p.M120K), c.300T>G (p.Y176X), c.634C>T (p.Q212X), c.221T>C (p.L74P)

Walker-Warburg Syndrome : Mutations (1): ♂ Genotyping | c.1167insA (p.F390fs)

Residual Risk Information

Detection rates are calculated from the primary literature and may not be available for all ethnic populations. The values listed below are for genotyping. Sequencing provides higher detection rates and lower residual risks for each disease. More precise values for sequencing may become available in the future.

Disease	Carrier Rate	Detection Rate	Residual Risk
Alpha Thalassemia	♂ General: 1/48	50.67%	1/97
Beta Thalassemia	♂ African American: 1/75	84.21%	1/475
	♂ Indian: 1/24	74.12%	1/93
	♂ Sardinians: 1/23	97.14%	1/804
	♂ Spaniard: 1/51	93.10%	1/739
Bloom Syndrome	♂ Ashkenazi Jewish: 1/134	96.67%	1/4,020
	♂ European: Unknown	66.22%	Unknown
	♂ Japanese: Unknown	50.00%	Unknown
Canavan Disease	♂ Ashkenazi Jewish: 1/55	98.86%	1/4,840
	♂ European: Unknown	53.23%	Unknown
Cystic Fibrosis	♂ African American: 1/62	69.99%	1/207
	♂ Ashkenazi Jewish: 1/23	96.81%	1/721
	♂ Asian: 1/94	66.40%	1/280
	♂ European: 1/25	94.96%	1/496
	♂ Hispanic American: 1/48	77.32%	1/212
	♂ Native American: 1/53	84.34%	1/338
Familial Dysautonomia	♂ Ashkenazi Jewish: 1/31	>99%	<1/3,100
Familial Hyperinsulinism: Type 1: ABCC8 Related	♂ Ashkenazi Jewish: 1/52	98.75%	1/4,160
	♂ Finnish: 1/101	45.16%	1/184
Fanconi Anemia: Type C	♂ Ashkenazi Jewish: 1/101	>99%	<1/10,100
	♂ General: Unknown	30.00%	Unknown
Gaucher Disease	♂ Ashkenazi Jewish: 1/15	87.16%	1/117
	♂ General: 1/112	31.60%	1/164
	♂ Spaniard: Unknown	44.29%	Unknown
	♂ Turkish: 1/236	59.38%	1/581
Glycogen Storage Disease: Type IA	♂ Ashkenazi Jewish: 1/71	>99%	<1/7,100
	♂ Chinese: 1/159	80.00%	1/795
	♂ European: 1/177	76.88%	1/765
	♂ Hispanic American: 1/177	27.78%	1/245
	♂ Japanese: 1/177	89.22%	1/1,641
Joubert Syndrome	♂ Ashkenazi Jewish: 1/92	>99%	<1/9,200
Maple Syrup Urine Disease: Type 1B	♂ Ashkenazi Jewish: 1/97	>99%	<1/9,700
Maple Syrup Urine Disease: Type 3	♂ Ashkenazi Jewish: 1/94	>99%	<1/9,400
	♂ General: Unknown	68.75%	Unknown
Mucopolipidosis: Type IV	♂ Ashkenazi Jewish: 1/97	96.15%	1/2,522
Nemaline Myopathy: NEB Related	♂ Ashkenazi Jewish: 1/108	>99%	<1/10,800

Disease	Carrier Rate	Detection Rate	Residual Risk
Niemann-Pick Disease: Type A	♂ Ashkenazi Jewish: 1/101	95.00%	1/2,020
Sickle-Cell Anemia	♂ African American: 1/10	>99%	<1/1,000
	♂ Hispanic American: 1/95	>99%	<1/9,500
Tay-Sachs Disease	♂ Argentinian: 1/280	82.35%	1/1,587
	♂ Ashkenazi Jewish: 1/29	99.53%	1/6,177
	♂ Cajun: 1/30	>99%	<1/3,000
	♂ European: 1/280	25.35%	1/375
	♂ General: 1/280	32.09%	1/412
	♂ Indian: Unknown	85.71%	Unknown
	♂ Iraqi Jewish: 1/140	56.25%	1/320
	♂ Japanese: 1/127	82.81%	1/739
	♂ Moroccan Jewish: 1/110	22.22%	1/141
	♂ Portuguese: 1/280	92.31%	1/3,640
	♂ Spaniard: 1/280	67.65%	1/865
	♂ United Kingdom: 1/161	71.43%	1/564
Usher Syndrome: Type 1F	♂ Ashkenazi Jewish: 1/126	93.75%	1/2,016
Usher Syndrome: Type 3	♂ Ashkenazi Jewish: 1/120	>99%	<1/12,000
	♂ Finnish: 1/134	>99%	<1/13,400
Walker-Warburg Syndrome	♂ Ashkenazi Jewish: 1/150	>99%	<1/15,000

Patient	Sample	Referring Doctor
Patient Name: Donor 5249 Date of Birth: [REDACTED] Reference #: FFAXCB-S45249 Indication: Carrier Testing Test Type: Custom Carrier Screen (ECS)	Specimen Type: Purified DNA (Semen) Lab #: [REDACTED] Date Collected: 5/22/2018 Date Received: 5/25/2018 Final Report: 6/8/2018	[REDACTED] Fairfax Cryobank, Inc. [REDACTED] [REDACTED] [REDACTED] Fax: [REDACTED]

RESULT SUMMARY

Results: No clinically significant variant(s) detected

Gene(s) analyzed: *ACSF3* and *USH2A*

Interpretation: Screening for the presence of pathogenic variants in the *ACSF3* and *USH2A* genes which are associated with combined malonic and methylmalonic aciduria and Usher syndrome, type IIA, respectively, was performed by next generation sequencing and possibly genotyping for select variants on DNA extracted from this patient's sample. No clinically significant variants were detected during this analysis. This negative result does not rule out the possibility that a pathogenic variant in the genes examined is present.

Genetic counseling is recommended.

This technology may not detect all small insertion/deletions and is not diagnostic for large duplications/deletions and structural genomic variation. The coding DNA sequence of the gene plus at least five base pairs flanking splice sites were sequenced and analyzed relative to the hg19 assembly. A mutation(s) deep in intronic sequences or in untranslated regions of the gene except a portion described above or a pathogenic variant(s) in other genes not included in this test could be present in this patient. The analytical sensitivity of this test is estimated at 99% for single base substitutions and 97% overall. All potentially pathogenic variants were subjected to Sanger sequencing or genotyping by allele specific primer extension analysis for confirmation of the result. Any benign variants identified during this analysis were not reported.

Please note that this carrier screening test masks likely benign variants and variants of uncertain significance (VUS) if there are any. Only known pathogenic variants or likely pathogenic variants which are expected to result in deleterious effects on protein function are reported. If reporting of likely benign variants and VUS is desired in this patient, please contact the laboratory (tel. 212-241-2537) to request an amended report.

Comments: This test was developed and its performance characteristics were determined by Mount Sinai Genomics, Inc. It is considered acceptable for patient testing. It has not been cleared or approved by the FDA. The FDA has determined that such clearance or approval is not necessary.

This type of mutation analysis generally provides highly accurate genotype information for point mutations and single nucleotide polymorphisms. Despite this level of accuracy, it should be kept in mind that there are many potential sources of diagnostic error, including misidentification of samples, polymorphisms, mosaicism or other rare genetic variants that interfere with analysis. In addition, families should understand the limitations of the testing and that rare diagnostic errors may occur for the reasons described.

Patient:	Donor 5249	DOB:	██████	Lab #:	██████
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For Disease Specific Standards and Guidelines:

<https://www.acmg.net/>

Additional disease-specific references available upon request.

This case has been reviewed and electronically signed by Ruth Kornreich, Ph.D., FACMG, Co-Laboratory Director

Laboratory Medical Consultant: George A. Diaz, M.D., Ph.D.

Table of Residual Risks by Ethnicity

Please note: This table displays residual risks after a negative result for each of the genes and corresponding disorders. **If a patient is reported to be a carrier of a disease, their residual risk is 1 and this table does not apply for that disease.**

Disease (Inheritance)	Gene	Ethnicity	Carrier Frequency	Detection Rate	Residual Risk	Analytical Detection Rate
Combined Malonic and Methylmalonic Aciduria (AR) NM_001127214.3	ACSF3	Worldwide	1 in 86	>95%	1 in 1701	>95%
Usher Syndrome, Type IIA (AR) NM_206933.2	USH2A	Caucasian	1 in 73	77%	1 in 314	88%
		Worldwide	1 in 126	69%	1 in 404	>95%
		Sephardic Jewish – Iraqi and Iranian	1 in 36	71%	1 in 122	75%

AR: Autosomal Recessive

Patient	Sample	Referring Doctor
Patient Name: Donor 5249 Date of Birth: [REDACTED] Reference #: FFAXCB-S45249 Indication: Carrier Testing Test Type: Unmask Additional Gene	Specimen Type: Purified DNA semen Lab #: [REDACTED] Date Collected: 5/22/2018 Date Received: 7/2/2018 Final Report: 7/16/2018	[REDACTED] Fairfax Cryobank, Inc. [REDACTED] [REDACTED] [REDACTED] Fax: [REDACTED]

Results

Negative: No clinically significant variant(s) detected

Gene(s) analyzed: *SLC26A2*

Recommendations:

Consideration of residual risk by ethnicity after a negative carrier screen is recommended, especially in the case of a positive family history for a specific disorder.

Interpretation:

Screening for the presence of pathogenic variants in the *SLC26A2* gene which is associated with sulfate transporter-related osteochondrodysplasia was performed by next generation sequencing and possibly genotyping for select variants on DNA extracted from this patient's sample. No clinically significant variants were detected during this analysis.

Please note that negative results reduce but do not eliminate the possibility that this individual is a carrier for the disorder(s) tested. Please see table of residual risks for specific detection rates and residual risk by ethnicity. With individuals of mixed ethnicity, it is recommended to use the highest residual risk estimate. Only variants determined to be pathogenic or likely pathogenic are reported in this carrier screening test.

Comments:

This carrier screening test masks likely benign variants and variants of uncertain significance (VUS) if there are any. Only known pathogenic variants or likely pathogenic variants which are expected to result in deleterious effects on protein function are reported. If reporting of likely benign variants and VUS is desired in this patient, please contact the laboratory (tel. 212-241-2537) to request an amended report.

Please note these tests were developed and their performance characteristics were determined by Mount Sinai Genomics, Inc. They have not been cleared or approved by the FDA. These analyses generally provide highly accurate information regarding the patient's carrier or affected status. Despite this high level of accuracy, it should be kept in mind that there are many potential sources of diagnostic error, including misidentification of samples, polymorphisms, or other rare genetic variants that interfere with analysis. Families should understand that rare diagnostic errors may occur for these reasons.

Patient: Donor 5249

DOB: [REDACTED]

Lab #: [REDACTED]

This case has been reviewed and electronically signed by Rebekah Zimmerman, Ph.D., FACMG, Laboratory Director

Laboratory Medical Consultant: George A. Diaz, M.D., Ph.D.

Table of Residual Risks by Ethnicity

Please note: This table displays residual risks after a negative result for each of the genes and corresponding disorders. **If a patient is reported to be a carrier of a disease, their residual risk is 1 and this table does not apply for that disease.**

Disease (Inheritance)	Gene	Ethnicity	Carrier Frequency	Detection Rate	Residual Risk	Analytical Detection Rate
Sulfate Transporter-Related Osteochondrodysplasia (AR) NM_000112.3	SLC26A2	African	1 in 341	99%	1 in 34,000	99%
		Ashkenazi Jewish	1 in 220	99%	1 in 21,900	
		East Asian	1 in 510	83%	1 in 3,000	
		Finnish	1 in 69	99%	1 in 6,800	
		Caucasian	1 in 129	93%	1 in 1,800	
		Latino	1 in 248	98%	1 in 10,000	
		South Asian	1 in 853	99%	1 in 85,200	
		Worldwide	1 in 147	95%	1 in 3,000	

AR: Autosomal Recessive

Test Methods

Genomic DNA isolated from this patient was analyzed by one or more of the following methodologies, as applicable:

Next Generation Sequencing (NGS) (Analytical Detection Rate >95%)

NGS was performed on a panel of genes for the purpose of identifying pathogenic or likely pathogenic variants.

Agilent SureSelectTMQXT technology was used with a custom capture library to target the exonic regions and intron/exon splice junctions of the relevant genes, as well as a number of UTR, intronic or promoter regions that contain previously reported mutations. Samples were pooled and sequenced on the Illumina HiSeq 2500 platform in the Rapid Run mode or the Illumina NovaSeq platform in the Xp workflow, using 100 bp paired-end reads. The sequencing data was analyzed using a custom bioinformatics algorithm designed and validated in house.

The coding exons and splice junctions of the known protein-coding RefSeq genes were assessed for the average depth of coverage (minimum of 20X) and data quality threshold values. Most exons not meeting a minimum of >20X read depth across the exon are further analyzed by Sanger sequencing. Please note that several genomic regions present difficulties in mapping or obtaining read depth >20X. The exons contained within these regions are noted within Table 1 (as "Exceptions") and will not be reflexed to Sanger sequencing if the mapping quality or coverage is poor. Any variants identified during testing in these regions are confirmed by a second method and reported if determined to be pathogenic or likely pathogenic. However, as there is a possibility of false negative results within these regions, detection rates and residual risks for these genes have been calculated with the presumption that variants in these exons will not be detected, unless included in the MassARRAY[®] genotyping platform.

This test will detect variants within the exons and the intron-exon boundaries of the target regions. Variants outside these regions may not be detected, including, but not limited to, UTRs, promoters, and deep intronic areas, or regions that fall into the Exceptions mentioned above. This

Patient: Donor 5249

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technology may not detect all small insertion/deletions and is not diagnostic for repeat expansions and structural genomic variation. In addition, a mutation(s) in a gene not included on the panel could be present in this patient.

Variant interpretation and classification was performed based on the American College of Medical Genetics Standards and Guidelines for the Interpretation of Sequence Variants (Richards et al, 2015). All potentially pathogenic variants may be confirmed by either a specific genotyping assay or Sanger sequencing, if indicated. Any benign variants, likely benign variants or variants of uncertain significance identified during this analysis will not be reported.

Copy Number Variant Analysis (Analytical Detection Rate >95%)

Large duplications and deletions were called from the relative read depths on an exon-by-exon basis using a custom exome hidden Markov model (XHMM) algorithm. Deletions or duplications determined to be pathogenic or likely pathogenic were confirmed by either a custom arrayCGH platform, quantitative PCR, or MLPA (depending on CNV size and gene content). While this algorithm is designed to pick up deletions and duplications of 2 or more exons in length, potentially pathogenic single-exon CNVs will be confirmed and reported, if detected.

Exon Array (Confirmation method) (Accuracy >99%)

The customized oligonucleotide microarray (Oxford Gene Technology) is a highly-targeted exon-focused array capable of detecting medically relevant microdeletions and microduplications at a much higher resolution than traditional aCGH methods. Each array matrix has approximately 180,000 60-mer oligonucleotide probes that cover the entire genome. This platform is designed based on human genome NCBI Build 37 (hg19) and the CGH probes are enriched to target the exonic regions of the genes in this panel.

Quantitative PCR (Confirmation method) (Accuracy >99%)

The relative quantification PCR is utilized on a Roche Universal Library Probe (UPL) system, which relates the PCR signal of the target region in one group to another. To test for genomic imbalances, both sample DNA and reference DNA is amplified with primer/probe sets that specific to the target region and a control region with known genomic copy number. Relative genomic copy numbers are calculated based on the standard $\Delta\Delta Ct$ formula.

Long-Range PCR (Analytical Detection Rate >99%)

Long-range PCR was performed to generate locus-specific amplicons for *CYP21A2*, *HBA1* and *HBA2* and *GBA*. The PCR products were then prepared for short-read NGS sequencing and sequenced. Sequenced reads were mapped back to the original genomic locus and run through the bioinformatics pipeline. If indicated, copy number from MLPA was correlated with the sequencing output to analyze the results. For *CYP21A2*, a certain percentage of healthy individuals carry a duplication of the *CYP21A2* gene, which has no clinical consequences. In cases where two copies of a gene are located on the same chromosome in tandem, only the second copy will be amplified and assessed for potentially pathogenic variants, due to size limitations of the PCR reaction. However, because these alleles contain at least two copies of the *CYP21A2* gene in tandem, it is expected that this patient has at least one functional gene in the tandem allele and this patient is therefore less likely to be a carrier. When an individual carries both a duplication allele and a pathogenic variant, or multiple pathogenic variants, the current analysis may not be able to determine the phase (cis/trans configuration) of the *CYP21A2* alleles identified. Family studies may be required in certain scenarios where phasing is required to determine the carrier status.

Residual Risk Calculations

Carrier frequencies and detection rates for each ethnicity were calculated through the combination of internal curations of >28,000 variants and genomic frequency data from >138,000 individuals across seven ethnic groups in the gnomAD database. Additional variants in HGMD and novel deleterious variants were also incorporated into the calculation. Residual risk values are calculated using a Bayesian analysis combining the *a priori* risk of being a pathogenic mutation carrier (carrier frequency) and the detection rate. They are provided only as a guide for assessing approximate risk given a negative result, and values will vary based on the exact ethnic background of an individual. This report does not represent medical advice but should be interpreted by a genetic counselor, medical geneticist or physician skilled in genetic result interpretation and the relevant medical literature.

Sanger Sequencing (Confirmation method) (Accuracy >99%)

Sanger sequencing, as indicated, was performed using BigDye Terminator chemistry with the ABI 3730 DNA analyzer with target specific amplicons. It also may be used to supplement specific guaranteed target regions that fail NGS sequencing due to poor quality or low depth of coverage (<20 reads) or as a confirmatory method for NGS positive results. False negative results may occur if rare variants interfere with amplification or annealing.

SELECTED REFERENCES

Patient: Donor 5249

DOB: [REDACTED]

Lab #: [REDACTED]

Carrier Screening

Grody W et al. ACMG position statement on prenatal/preconception expanded carrier screening. *Genet Med.* 2013 15:482-3.

Variant Classification:

Richards S et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med.* 2015 May;17(5):405-24

Additional disease-specific references available upon request.