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Genetic Carrier Testing

Dr. John Doe, M.D. **Laboratory Director**

PATIENT INFORMATION		SPECIMEN INFORMATION	
PATIENT NAME:	Jane Doe	SPECIMEN TYPE:	Saliva
AMD ACCESS #:	XXX-17-12345	DATE RECEIVED:	06/12/2017
DATE OF BIRTH:	08/18/1888	INITIATION OF TESTING:	07/12/2017
GENDER:	Female	COMPLETION OF TESTING:	07/20/2017

ORDERED BY			
ORDERING PHYSICIAN'S NAME:	Dr. John Smith, M.D.	PHYSICIAN'S ADDRESS:	233 E. Erie Street Suite #506 Chicago, IL 60611
PHONE:	312-838-2400	FAX:	312-838-2404

REPORT SUMMARY

NEGATIVE RESULTS	
RESULTS:	NEGATIVE
INTERPRETATION:	The patient tested negative for all mutations analyzed, which reduces but does not eliminate the risk of being a carrier for any other deleterious variant and/or genetic diseases.

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COMPLETE LIST OF TARGETED GENES (LISTED ALPHABETICALLY)

ACTA2, AKAP9, ASPA, BCKDHA, BCKDHB, BLM, CA12, CDH23, CFTR, COL11A2, COL3A1, COL4A1, DBT, DLD, DYNCH1, FANCA, FANCC, FANCF, FANCG, FBN1, FMR1, GAA, GALT, GBA, GBE1, GJB2, GJB3, GJB6, HBA1, HBA2, HBB, HEXA, IKBKAP, KCNE1, KCNE2, KCNQ1, KCNQ4, MCOLN1, MYH11, MYLK, MYO7A, NPC1, NPC2, OTC, PAH, PCDH15, SCN5A, SCNN1A, SCNN1B, SCNN1G, SLC26A4, SLC2A10, SMAD3, SMN1, SMN2, TGFBR1, TGFBR2, UBA1, USH1C, USH2A, VAPB.

THE ABOVE GENES ARE RELATED TO THE FOLLOWING DISEASES (LISTED ALPHABETICALLY)

Alpha Thalassemia, Arterial Tortuosity Syndrome, Beta Thalassemia, Bloom Syndrome, CA12 - Cystic Fibrosis Related, Canavan Disease, Classical galactosemia, congenital aneurysms, Cystic Fibrosis, DYNC1H1, Ehlers Danlos Syndrome Type 4, Familial Dysautonomia, Familial thoracic aortic aneurysm and dissection (familial TAAD) & Loeys-Dietz syndrome type I, Familial thoracic aortic aneurysm and dissection (familial TAAD) ACTA2-related, Familial thoracic aortic aneurysm and dissection (familial TAAD) MYLK-related, Fanconi Anemia: Type A, Fanconi Anemia: Type C, Fanconi Anemia: Type F, Fanconi Anemia: Type G, Gaucher disease, Glycogen Storage Disease II - Pompe Disease, Glycogen Storage Disease IV, Jervell and Lange-Nielsen - LQT11, Jervell and Lange-Nielsen - LQT5, Loeys-Dietz syndrome type I, Loeys-Dietz syndrome type III, Long Q-T Syndrome 3, Long Q-T Syndrome 6, Long Q-T Syndrome 11, Maple Syrup Urine Type 3 (Dihydrolipoamide dehydrogenase deficiency), Maple Syrup Urine Type Ia, Maple Syrup Urine Type Ib, Maple Syrup Urine Type II, Marfan syndrome, Mucolipidosis IV, Niemann-pick Disease Type C1, Niemann-pick Disease Type C2, Nonsyndromic deafness (connexin 30), Nonsyndromic deafness GJB3-related, Nonsyndromic deafness KCNQ4-related, Nonsyndromic Hearing Loss & Deafness, Nonsyndromic Hearing Loss & Deafness: GJB2 related (connexin 26), Ornithine Transcarbamylase Deficiency, Pendred Syndrome, Phenylketonuria, SCNN1A - Cystic Fibrosis Related, SCNN1B - Cystic Fibrosis Related, SCNN1G - Cystic Fibrosis Related, Sickle Cell Disease, Spinal muscular atrophy, Spinal muscular atrophy: SMN1 linked (Werdnig-Hoffman), SMN2- Modifier of severity of spinal muscular atrophy, Tay-Sachs, Thoracic aortic aneurysms, Usher Syndrome Type 1B, Usher Syndrome Type 1C, Usher Syndrome Type 1D, Usher syndrome type 1F, Usher Syndrome Type 2A.

RESIDUAL REPRODUCTIVE RISK FOR PATIENTS WITH MUTATIONS DEEMED "NEGATIVE"

A negative test for carrier screening reduces, but does not eliminate the risk of being a carrier. "Residual risk" is the likelihood that you are a carrier even if you did not test positive for one of the mutations included in our test. Note that for some diseases, residual risk has not been determined. Please contact the Lab with requests for information about risk for a specific disease.

DISEASE	GENE	POPULATION	DETECTION RATE	CARRIER FREQUENCY	RESIDUAL RISK
Canavan Disease	ASPA	Ashkenazi Jewish	98%	1 in 55	1 in 2750
Canavan Disease	ASPA	General	50%	1 in 100	1 in 200
Maple Syrup Urine Disease Type 1A	BCKDHA	Ashkenazi Jewish	99%	1 in 80	1 in 8000
Maple Syrup Urine Disease Type 1A	BCKDHA	General	11%	1 in 321	1 in 361
Maple Syrup Urine Disease Type 1A	BCKDHA	Mennonite	99%	1 in 13	1 in 1300
Maple Syrup Urine Disease Type 1A	BCKDHA	Amish	97%	1 in 10	1 in 333
Maple Syrup Urine Disease Type 1B	BCKDHB	Ashkenazi Jewish	99%	1 in 97	1 in 9700
Bloom Syndrome	BLM	Ashkenazi Jewish	97%	1 in 134	1 in 4467
Bloom Syndrome	BLM	European	65%	Unknown	1 in 250
Bloom Syndrome	BLM	Japanese	55%	Unknown	1 in 250
Usher Syndrome 1D	CDH23	General	9%	1 in 160	1 in 176
Cystic Fibrosis	CFTR	African American	81%	1 in 61	1 in 321
Cystic Fibrosis	CFTR	Ashkenazi Jewish	97%	1 in 24	1 in 800
Cystic Fibrosis	CFTR	Asian	51%	1 in 94	1 in 192
Cystic Fibrosis	CFTR	Caucasian	93%	1 in 25	1 in 357
Cystic Fibrosis	CFTR	Hispanic	77%	1 in 58	1 in 252
Maple Syrup Disease Type III (Dihydrolipoamide dehydrogenase deficiency)	DLD	Ashkenazi Jewish	95%	1 in 80	1 in 1600

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DISEASE	GENE	POPULATION	DETECTION RATE	CARRIER FREQUENCY	RESIDUAL RISK
Maple Syrup Disease Type III (Dihydrolipoamide dehydrogenase deficiency)	DLD	General	69%	Unknown	Unknown
Fanconi Anemia Group C	FANCC	Ashkenazi Jewish	99%	1 in 100	1 in 10000
Fanconi Anemia Group C	FANCC	General	30%	Unknown	Unknown
Pompe Disease	GAA	African American	43%	1 in 60	1 in 105
Pompe Disease	GAA	Chinese	80%	1 in 110	1 in 550
Pompe Disease	GAA	Dutch	50%	1 in 100	1 in 200
Pompe Disease (Glycogen Storage Disease II)	GAA	European	50%	1 in 100	1 in 200
Galactosemia GALT-related	GALT	African American	65%	1 in 78	1 in 223
Classical galactosemia	GALT	Ashkenazi Jewish	99%	1 in 127	1 in 12700
Galactosemia GALT-related	GALT	Caucasian	81%	1 in 108	1 in 568
Classical galactosemia	GALT	Dutch	70%	1 in 91	1 in 303
Classical galactosemia	GALT	European	88%	1 in 110	1 in 917
Classical galactosemia	GALT	General	80%	1 in 125	1 in 625
Classical galactosemia	GALT	Irish Travellers	99%	1 in 14	1 in 1400
Gaucher Disease	GBA	Ashkenazi Jewish	98%	1 in 15	1 in 750
Gaucher Disease	GBA	General	32%	1 in 112	1 in 164
Nonsyndromic hearing loss and deafness: GJB2 related	GJB2	Ashkenazi Jewish	96%	1 in 20	1 in 480
Nonsyndromic hearing loss and deafness: GJB2 related	GJB2	Chinese	82%	1 in 100	1 in 564
Nonsyndromic hearing loss and deafness: GJB2 related	GJB2	European	78%	1 in 53	1 in 238
Nonsyndromic hearing loss and deafness: GJB2 related	GJB2	General Population	98%	1 in 136	1 in 6800
Nonsyndromic hearing loss and deafness: GJB2 related	GJB2	Indian	67%	Unknown	Unknown
Nonsyndromic hearing loss and deafness: GJB2 related	GJB2	Israeli	93%	1 in 16	1 in 232
Nonsyndromic hearing loss and deafness: GJB2 related	GJB2	Japanese	69%	1 in 75	1 in 245
Nonsyndromic hearing loss and deafness: GJB6 related	GJB6	General Population	10%	Rare	Unknown
Beta Thalassemia	HBB	African American	85%	1 in 75	1 in 500
Beta Thalassemia	HBB	East Asian	93%	1 in 50	1 in 714
Beta Thalassemia	HBB	Indian	64%	1 in 24	1 in 66
Beta Thalassemia	HBB	Mediterranean	97%	1 in 20	1 in 667
Beta Thalassemia	HBB	Middle Eastern	84%	1 in 30	1 in 188
Beta Thalassemia	HBB	Northern Spain (Seville)	80%	1 in 8	1 in 40
Beta Thalassemia	HBB	South Asian	95%	1 in 20	1 in 400
Sickle Cell Disease	HBB	African American	99%	1 in 10	1 in 1000
Sickle Cell Disease	HBB	Hispanic American	99%	1 in 95	1 in 9500
Tay-Sachs	HEXA	Ashkenazi Jewish	98%	1 in 27	1 in 1350
Tay-Sachs	HEXA	Cajun	99%	1 in 30	1 in 3000
Tay-Sachs	HEXA	European	25%	1 in 280	1 in 373
Tay-Sachs	HEXA	French Canadian	80%	1 in 70	1 in 350
Tay-Sachs	HEXA	General	46%	1 in 300	1 in 556
Tay-Sachs	HEXA	Iraqi Jewish	55%	1 in 140	1 in 311
Tay-Sachs	HEXA	Japanese	85%	1 in 127	1 in 847
Familial Dysautonomia	IKBKAP	Ashkenazi Jewish	99%	1 in 30	1 in 3000
Mucolipidosis, Type IV	MCOLN1	Ashkenazi Jewish	99%	1 in 96	1 in 9600
Usher Syndrome Type 1B	MYO7A	European	40%	1 in 166	1 in 277
Usher Syndrome Type 1B	MYO7A	General	14%	1 in 143	1 in 166
Niemann-Pick Disease Type C NPC1-related	NPC1	Acadian	99%	Unknown	Unknown
Niemann-Pick Disease Type C NPC1-related	NPC1	General	20%	1 in 183	1 in 229
Niemann-Pick Disease Type C NPC2-related	NPC2	General	75%	1 in 200	1 in 800
Phenylalanine Hydroxylase Deficiency AKA phenylketonuria (PKU)	PAH	Caucasian	50%	1 in 50	1 in 100

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DISEASE	GENE	POPULATION	DETECTION RATE	CARRIER FREQUENCY	RESIDUAL RISK
Phenylalanine Hydroxylase Deficiency AKA phenylketonuria (PKU)	PAH	European	20%	1 in 50	1 in 63
Phenylalanine Hydroxylase Deficiency AKA phenylketonuria (PKU)	PAH	French Canadian	27%	1 in 80	1 in 109
Phenylalanine Hydroxylase Deficiency AKA phenylketonuria (PKU)	PAH	Iraqi Jewish	58%	Unknown	Unknown
Phenylalanine Hydroxylase Deficiency AKA phenylketonuria (PKU)	PAH	Irish	68%	1 in 34	1 in 106
Phenylalanine Hydroxylase Deficiency AKA phenylketonuria (PKU)	PAH	North Irish	78%	1 in 34	1 in 152
Phenylalanine Hydroxylase Deficiency AKA phenylketonuria (PKU)	PAH	Roma	94%	1 in 4	1 in 64
Phenylalanine Hydroxylase Deficiency AKA phenylketonuria (PKU)	PAH	Serbian	63%	1 in 56	1 in 152
Phenylalanine Hydroxylase Deficiency AKA phenylketonuria (PKU)	PAH	Slovak	40%	1 in 39	1 in 65
Phenylalanine Hydroxylase Deficiency AKA phenylketonuria (PKU)	PAH	Turkish	55%	1 in 26	1 in 58
Usher Syndrome Type 1F	PCDH15	Ashkenazi Jewish	75%	1 in 140	1 in 560
Usher Syndrome Type 1F	PCDH15	Hutterite	Unknown	1 in 40	Unknown
Pendred Syndrome	SLC26A4	European	40%	1 in 58	1 in 97
Pendred Syndrome	SLC26A4	Japanese	46%	Unknown	Unknown
Pendred Syndrome	SLC26A4	Pakistani	30%	Unknown	Unknown
Usher Syndrome Type 1C	USH1C	Acadian	99%	1 in 80	1 in 7018
Usher Syndrome Type 1C	USH1C	French Canadian	83%	1 in 227	1 in 1362
Usher Syndrome Type 2A	USH2A	French Canadian	55%	1 in 125	1 in 278
Usher Syndrome Type 2A	USH2A	General	20%	1 in 125	1 in 156

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TEST METHODOLOGY

Genomic DNA from Alexis Hymen's submitted specimen was enriched for the complete coding regions and splice site junctions of the genes described in the panel. The products were sequenced on two different massive parallel sequencing platforms; Miniseq Illumina platform (clonal bridge amplification/reversible dye terminator) and Ion Torrent Platform (Ion sphere particles- Chef System/S5XL). The sequences were aligned to reference sequences based on Human Genome build GRCh37/UCSChg19. SMN-1 (survival motor neuron-1 gene) exon 7 and exon 8, deletion/duplication testing was performed by Multiple Ligation Probe Amplification (MLPA). Fragment analysis and comparative analysis were performed by Coffalyser DB software, v.140701 (MRC-Holland).

Sequencing bio-informatics pipelines were analyzed by Illumina VariantStudio v.3.0 and Torrent Suite Software v.4.0.2., respectively. Discrepancies between platforms, if any, were resolved by selective incorporation of chain-terminating dideoxynucleotides (Sanger Sequencing) targeting with specific FWD/REV primer 5' M13 tailed and HPLC purified. All sequence alterations are described according to the Human Genome Variation Society (HGVS) nomenclature guidelines. Genetic data are stored under Variant Call Format (VCF). (1)(2). AMD follows internal policies and ACMG recommendations for variants reporting (3). Benign and likely benign variants, if present, are not included in this report, but are available upon request.

(1) Bio-IT World, Davies, K. Powering Preventative Medicine. Bio-IT World 2011. (2) GenomeWeb DNA Electronics Licenses IP to Ion Torrent. August 2010.
(3) 2013 Annual Clinical Genetics Meeting. American College of Medical Genetics and Genomics. Green R, Berg JS, Grody WW et al.

RECOMMENDATIONS

It is recommended that this test result be communicated to the patient in a setting that includes appropriate genetic counseling by a licensed/certified genetic counselor. This test result should only be used in conjunction with the patient's clinical history and any previous analysis of appropriate family members.

DISCLAIMERS & TEST LIMITATIONS

The accompanying Technical Specifications summary describes the analysis, method, performance characteristics, nomenclature, and interpretive criteria of this test. This test result does not exclude the possibility of other predisposing mutations that have been reported in individuals with increased risk. This test may be considered investigational by some states. This test and its performance characteristics were determined by the laboratory. It has not been reviewed by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

Mutations may not be detected in areas of lower sequence coverage. Triplet repeats and large deletions and duplications may not be detected. Small insertions and deletions may not be as accurately determined as single nucleotide variants. Genes that have closely related pseudogenes are not well analyzed by this method.

High-throughput sequencing detects, on average, 94% of known clinically significant variants. All variants that are a recognized cause of the disease will be reported. In addition, variants that have not previously been established as a recognized cause of disease may be identified. In these cases, only variants classified as "predicted" or "likely" pathogenic are reported.

Predicted/likely pathogenic variants are described elsewhere in the report as "predicted/likely to have a negative impact on gene function". In general, predicted pathogenic variants are those which are predicted to be pathogenic based on the nature of the sequence change. Likely pathogenic variants are evaluated by reviewing reports of allele frequencies in cases and controls, functional studies, variant annotation and effect prediction, and segregation studies. Benign variants, variants of uncertain significance, and variants not directly associated with the intended disease phenotype are not reported.

List of targeted genomic nucleotide positions are available upon request.