NTD | Eurofins Clinical Diagnostics

MM580: ACOG/ACMG Carrier Screen- Targeted Mutation Panel

Report Prepared For:

Patient:

Name: [redacted]
Date of Birth: [redacted]
IDs (Internal / External): [redacted]
Reported Gender: [redacted]
Reported Ethnicity: [redacted]

Physician/Institution Referral:

Physician Information
Institution Information
Institution Address

Sample:

Sample Collection Date: [redacted]
Sample Received Date: [redacted]
Final Report Date: [redacted]
Sample Type: [redacted]
IDs (Internal / External): [redacted]

Report Summary:

Autosomal Carrier Screening Results: **Positive Carrier**

This individual tested positive as a carrier of the following disease(s).

Cystic Fibrosis

CFTR:NM_000492.3:c.2175dupA (p.Glu726Argfs*4)

Gaucher Disease

GBA:NM_001005741.2:c.115+1G>A

Spinal Muscular Atrophy (SMA) Analysis: **Negative**

Two copies of the SMN1 gene were identified. While having 2 copies reduces the chance of being a carrier, this risk is not zero and will vary by ethnicity.

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Positive Carrier Result Details:

Cystic Fibrosis **CFTR**

Cystic fibrosis is a condition that causes the mucus in the body to thicken. This abnormal mucous is sticky and becomes hard to breakdown, clogging-up and damaging certain organs, especially the lungs, pancreas, and intestines. Breathing difficulties, poor digestion, frequent infection, infertility, and poor weight gain are all symptoms of this condition.

This condition is inherited in an autosomal recessive manner which means both parents have to be carriers to have a 1 in 4 (25%) risk to have an affected child. Being a carrier does not mean you are affected with this condition, but it can increase the risk for you to have affected children. These risks will vary depending on the carrier status of your partner, and it is recommended that you discuss these results and the available follow-up testing options with your healthcare provider. You may also wish to share your results with other family members so they can consider testing as their risks for being a carrier is also increased.

Variants Detected:

CFTR:NM_000492.3:c.2175dupA (p.Glu726Argfs*4)

Prior Reproductive Risk: 1 in 2,300 *(Specific to partners of reported ethnicity prior to testing)*

Current Reproductive Risk: <see below> *(Please see table below)*

Current Reproductive Risk:

Partner Ethnicity:	Partner Is Untested: (1)	Partner is Negative: (1, 2)	Partner is a Carrier:
African American	1 in 240	1 in 1,300	1 in 4
Asian	1 in 380	1 in 690	1 in 4
European / Caucasian	1 in 100	1 in 1,400	1 in 4
Finnish	1 in 100	1 in 1,400	1 in 4
Hispanic	1 in 230	1 in 1,000	1 in 4
Ashkenazi Jewish	1 in 96	1 in 3,100	1 in 4
Other / Mixed	1 in 96	1 in 170	1 in 4

1 - Based upon the partner's general population carrier rate for the given ethnicity (available upon request).

2 - Based upon the partner testing negative for the mutations on this carrier screen and the detection rate for the ethnicity given (available upon request).

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Positive Carrier Result Details:

Gaucher Disease **GBA**

People with Gaucher disease cannot properly breakdown certain fatty substances which then build-up and damage organs like the spleen, liver, and bone marrow. There is a range in the age and severity of different symptoms, but most people will experience bone pain or fractures, anemia, tiredness, shorter height, frequent nosebleeds, and easy bruising. Medication can be used to help lessen many of the symptoms of this condition. There are different forms of the disease with varying levels of severity.

This condition is inherited in an autosomal recessive manner which means both parents have to be carriers to have a 1 in 4 (25%) risk to have an affected child. Being a carrier does not mean you are affected with this condition, but it can increase the risk for you to have affected children. These risks will vary depending on the carrier status of your partner, and it is recommended that you discuss these results and the available follow-up testing options with your healthcare provider. You may also wish to share your results with other family members so they can consider testing as their risks for being a carrier is also increased.

Variants Detected:

GBA:NM_001005741.2:c.115+1G>A

Prior Reproductive Risk: 1 in 900 *(Specific to partners of reported ethnicity prior to testing)*

Current Reproductive Risk: <see below> *(Please see table below)*

Current Reproductive Risk:

Partner Ethnicity:	Partner Is Untested: (1)	Partner is Negative: (1, 2)	Partner is a Carrier:
African American	1 in 480	1 in 1,600	1 in 4
Asian	1 in 480	1 in 1,600	1 in 4
European / Caucasian	1 in 480	1 in 1,600	1 in 4
Finnish	1 in 480	1 in 1,600	1 in 4
Hispanic	1 in 480	1 in 1,600	1 in 4
Ashkenazi Jewish	1 in 60	1 in 1,100	1 in 4
Other / Mixed	1 in 60	1 in 190	1 in 4

1 - Based upon the partner's general population carrier rate for the given ethnicity (available upon request).

2 - Based upon the partner testing negative for the mutations on this carrier screen and the detection rate for the ethnicity given (available upon request).

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Residual Carrier Risks:

The following prior risks are based upon incidence/carrier rates published in the scientific literature, the patient's reported ethnicity, and that the patient does not have a family history of the disease. The residual risks are based upon the disease-specific detection rates and reflect remaining risk to be a carrier after a negative screening result. Residual risks in males for X-linked conditions will not be displayed as the reproductive risk falls primarily with the female partner. For more information or for calculation of reproductive risks in various partner-testing scenarios, please refer to our website at http://eglgenetics.com/pecs/.

The incidence/carrier rates are based on our current understanding of the conditions and genes on this panel. These rates may change over time as more information about the conditions and genes and their incidence in the general population becomes available.

	Carrier Risk:	
Condition (Gene):	*Prior:*	**Residual:**
Canavan Disease (ASPA)	*1 in 40*	1 in 79
Bloom Syndrome (BLM)	*1 in 100*	1 in 110
Familial Dysautonomia (ELP1)	*1 in 30*	1 in 33
Fanconi Anemia Type C (FANCC)	*1 in 89*	1 in 99
Tay Sachs Disease (a.k.a. Hexosaminidase A Deficiency) (HEXA)	*1 in 25*	1 in 61
Mucolipidosis Type IV (MCOLN1)	*1 in 120*	1 in 140
Niemann-Pick Disease Type A & B (a.k.a. Acid Sphingomyelinase Deficiency) (SMPD1)	*1 in 90*	1 in 100

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Test Methodology:

Targeted mutation analysis: In solution hybridization followed by next generation sequencing at a mean read depth of >200X of the targeted mutation regions including large indels was performed on this individual's genomic DNA. If the targeted mutation region has a pseudogene, gene specific PCR and sequence analysis was performed by Sanger sequencing. Nucleotide numbering is based on GenBank accession numbers given in the report and on the EGL Genetics website; nucleotide 1 corresponds to the A of the start codon ATG.

Spinal muscular atrophy deletion analysis: Isolated DNA from this individual was evaluated for SMN1 gene deletions using multiplex ligation polymerase chain reaction amplification (MLPA) of exons 7 and 8 according to the SALSA protocol available from MRC Holland. The gene dosage ratio was calculated relative to the average of 16 reference loci. Two copies of SMN1 most likely indicates normal (not affected) status and one copy of SMN1 most likely indicates carrier status. Note: Other pathogenic variants in SMN1, such as small pathogenic variants and fusion SMN genes, are possible in this gene but are not detected by this assay. Additionally a duplication of SMN1 on one chromosome may interfere with the detection of a deletion of SMN1 on the opposite chromosome.

Sanger sequencing: In order to avoid pseudogene sequence regions, targeted GBA mutations were analyzed by Sanger sequence analysis. The targeted mutations include: c.84dupG, c.115+1G>A, c.1226A>G (p.N409S), c.1263_1317del55, c.1297G>T (p.V433L), c.1342G>C (p.D448H), c.1343A>T (p.D448V), c.1448T>C (p.L483P), c.1504C>T (p.R502C), c.1505G>A (p.R502H) and c.1604G>A (p.R535H). PCR was used to amplify the targeted mutation regions. The PCR products were sequenced bidirectionally. Nucleotide numbering is based on GenBank accession numbers given in the report and on the EGL Genetics website; nucleotide 1 corresponds to the A of the start codon ATG.

Version NG580V01, PECS_GBA, SMACAR

Disclaimer:

These results must be interpreted in the context of this individual's clinical profile and family history. This analysis does not include testing for all mutations found in these genes. Negative results therefore reduce the risk of being a carrier but do not eliminate it. Further testing may be indicated based on family history or ethnicity, such as Tay-Sachs disease carrier analysis by enzyme. Possible diagnostic errors include sample mix-ups, genetic variants that interfere with analysis, and other sources.

For ethnicities listed as Other, Mixed, or Unknown on the referral, the residual carrier and reproductive risks were calculated using the highest carrier frequency and lowest detection rate. If more detailed risk assessment is needed, healthcare providers can contact the laboratory.

Testing was performed and results originated from EGL Genetic Diagnostics LLC (CLIA#:11D0683478; CAP#: 7181693, Lora J. H. Bean, PhD, FACMG, Director), 2460 Mountain Industrial Boulevard, Tucker, GA 30084. Pursuant to the requirements of CLIA 1988, this test was developed and its performance validated by EGL Genetic Diagnostics LLC. 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. This test is used for clinical purposes.

This case has been reviewed and electronically signed by a Laboratory Director at EGL Genetics.

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Medical Consultant
EGL Genetic Diagnostics, LLC

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Assistant Laboratory Director
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