

Clinical Exome Sequencing, Family Trios (with Mitochondrial Genome)

Test Code: EXMTT

Turnaround time: 6 weeks

CPT Codes: 81415 x1, 81416 x1, 81460 x1

Condition Description

What is the Medical EmExome?

The human exome is the complete coding (exonic) region of the genome. It is estimated to encompass approximately 1-2% of the genome, yet contains approximately 85% of disease-causing pathogenic variants. The Medical EmExome is expertly curated to target genes known or suspected to cause disease. The design provides >96% coverage of 19,000 genes, with a mean read depth of 100X. For the ~5,400 disease-associated genes analyzed, we typically get coverage >98%.

This testing includes sequencing of the mitochondrial genome.

Medical EmExome Trios includes the option to choose an EGL sequencing panel as an EmExome Boost. This option puts additional focus on variants in panel genes and offers fill-in coverage of the exons on the chosen panel at no additional cost.

Will a particular gene be covered on the EmExome?

The Exome Coverage Tool can be used to view typical depth of sequence coverage obtained by exome sequencing performed by EGL. To access this tool, please click [here](#). If a gene of specific interest does not have consistent (100%) coverage, please ask us about Sanger fill-in.

Will EGL release raw exome data?

Yes, upon request for data less than 3 years old.

Will EGL re-analyze data?

Yes, upon request for data less than 3 years old.

Indications

This test is indicated for individuals with a complex or ambiguous phenotype or for individuals with clinical features of a genetic disorder for whom previous testing has been non-diagnostic.

Methodology

Medical EmExome is performed on genomic DNA using in solution hybridization to enrich for the exome. These targeted regions are then sequenced using next-generation sequencing technology at an average coverage of 100X in the target regions. This sequencing typically provides >96% coverage of the ~19,100 genes in the exome at >20X. Intronic variants within 10 nucleotides from the exon/intron boundaries are analyzed, unless prohibited by the complexity of the sequence. The DNA sequence is mapped to and analyzed in comparison with the published human genome build UCSC hg19 reference sequence. The targeted coding exons and splice junctions of genes associated with disease are assessed for the depth of coverage and data quality threshold values. EGL has developed an EmExome bioinformatics analysis pipeline to compare sequence changes in the individual being tested to the reference sequence. High-quality variants which pass EGL's quality filters are not confirmed by Sanger sequencing. Reportable variants that do not pass the quality filters are confirmed using bidirectional Sanger sequence analysis.

Mitochondrial DNA sequencing: PCR was used to amplify the mitochondrial genome. Direct sequencing of the amplified region was performed using next generation short base pair read sequencing. Sequences are compared to revised Cambridge reference sequence (rCRS) NC_012920.1. Sequence analysis is limited to m.577_m.16023 region of the mitochondrial genome and excludes the highly variable control regions (m.1-m.576 and m.16024-m.16569).

Heteroplasmy: Heteroplasmy is defined as the co-presence of a reference allele and an alternate allele (variant) at a given position in the mitochondrial genome. For any given variant, the level of heteroplasmy is calculated as a percentage of the total NGS reads (at that particular position) that have the variant. In general, heteroplasmic variants detected at <10% of alleles, are not reported. Known pathogenic or likely pathogenic variants detected at <10% heteroplasmy may be reported with recommendations for additional studies, as appropriate.

Detection

Based on published studies, WES is expected to provide a diagnosis in 20-30% of the cases for rare and ultra-rare disorders.

Specimen Requirements

Type: Whole Blood (EDTA)

Specimen Requirements:

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old): 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Type: Liquid Buccal Swab

Specimen Requirements:

ORAc collect-DX (OCD-100) Assisted saliva collection kit

DNA Genotek ORAc collect-DX kit used according to manufacturer instructions.

Please contact EGL for a saliva collection kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Type: DNA, Isolated

Specimen Requirements:

Microtainer

8µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Type: Saliva

Specimen Requirements:

Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Special Instructions

Please submit medical records or clinic summary notes, and a signed consent form when ordering exome testing. Failure to receive clinic notes or a signed consent form may result in a delay in testing.