Optical Genome Mapping (OGM)

Description:

A proportion of genomic diagnoses is attributable to structural variation (SV). Optical genome mapping (OGM) can detect genome-wide SVs at high resolution by labeling and mapping ultra-long DNA molecules (>150kb) in nanochannel arrays. OGM identifies most types of large structural variations (SVs) in a single assay, including copy number variations (CNVs), unbalanced and balanced SV events (inversions, insertions, and translocations), triploidies, aneuploidies, and other complex chromosomal rearrangements. For most detected duplications, OGM can determine the genomic position and orientation of the extra copy. In addition, OGM can further refine breakpoints and/or the structure of previously identified chromosomal abnormalities.

Indications:

- Global developmental delay
- Intellectual disability
- Multiple congenital anomalies
- Recurrent pregnancy loss/infertility
- Single variant in an autosomal recessive gene
- Suspicion for complex chromosomal events by prior testing
- Unsolved diagnosis after other testing

Testing Options:

- **Genome-wide comprehensive structural variant analysis**
  - Postnatal samples
- **Targeted analysis for a known variant or selected gene/condition***
  - Cultured prenatal amniotic fluid samples
  - Postnatal samples

**Please contact the lab to confirm OGM's coverage for the target region before ordering the test*

Testing Methodology:

OGM technology labels ultra-high molecular weight DNA at a specific sequence motif (CTTAAG) occurring approximately 14-16 times per 100kb in the human genome. The long fluorescently labeled DNA molecules are linearized and imaged in nanochannel arrays in a high throughput, automated manner. High-resolution images of labeled motifs are converted into single molecule contigs and assembled into whole genome de novo maps with approximately 800 gigabytes of data. Structural variant calling is based on changes in the coverage pattern or spacing of the labels. Clinically relevant SVs that pass quality control thresholds with sufficient labeling motifs will be reported.

Technical Limitations:

This assay was not validated to detect regions of homozygosity (ROH), nucleotide repeat expansion variants, and mosaic changes. OGM is a non-sequencing method and does not provide base-pair level resolution at SV breakpoints. OGM has different limits of resolution depending on the SV (>20kb for deletions; >50-70kb for duplications, insertions, inversions, and translocations). OGM cannot reliably detect SVs in regions with poor molecule coverage and/or insufficient motif labels, such as large, highly repetitive segments (e.g., heterochromatic/centromeric/telomeric and neighboring regions). Therefore, OGM is not used to detect balanced centromeric SVs, Robertsonian translocations, or single nucleotide variations. Current OGM pipelines have limited ability to detect breakpoints involving the pseudoautosomal regions (PAR1/2). Some multicopy or homologous genes may be difficult to interpret unambiguously. SVs detected by OGM may not be well-described in the literature and may be of uncertain clinical significance.

Cincinnati Children's®
changing the outcome together

Genetics and Genomics Diagnostic Laboratory
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Fax: (513) 636-4373
Email: LabGeneticCounselors@cchmc.org
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Accuracy:

The performance characteristics of this test have been developed and validated by the Genetics and Genomics Diagnostic Laboratory at Cincinnati Children's. Most constitutional structural variations (SVs) can be detected using OGM technology. However, a genetic etiology for disease cannot be ruled out based on a normal OGM result. If a specific genetic diagnosis is suspected, please contact the laboratory for additional testing.

Results:

Results will be reported to the ordering provider and/or genetic counselor as specified on the requisition form.

Turn-Around Time:

42-56 days

CPT Codes:

Optical Genome Mapping (genome-wide): **81479**
Optical Genome Mapping - Targeted Analysis: **81479**

Please call 1-866-450-4198 for current pricing, insurance preauthorization or with any billing questions.

Specimen Requirements:

- 3 mL whole blood in lavender top (EDTA) or green top (Sodium Heparin) tube
- 2-3 mL bone marrow in lavender top (EDTA) or green top (Sodium Heparin) tube
- Fresh tissue (1cm x 1cm or 2mm punch biopsy) for cell culture sent in sterile media or saline (not frozen)
- Prenatal sample: 20-25 mL amniotic fluid or two T25 flasks (80% confluent)

Shipping Instructions:

Please enclose test requisition with sample.
All information must be completed before sample can be processed.

Place samples in Styrofoam mailer and ship at room temperature for overnight delivery to arrive Monday through Saturday*. Please call the lab at 513-636-4474 with shipment tracking information when available.

Ship to:

Genetics and Genomics Diagnostic Laboratories
3333 Burnet Avenue TCHRF 1042
Cincinnati, OH 45229
513-636-4474

*For Saturday deliveries only: Please add "Dock 5" to the address and select the Saturday delivery check box on the shipping label if applicable.

References:

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Lam, E. T., Hastie, et al. (2012). Genome mapping on nanochannel arrays for structural variation analysis and sequence assembly. Nature biotechnology, 30(8), 771–776.

Levy, B., et al. (2024). Multisite Evaluation and Validation of Optical Genome Mapping for Prenatal Genetic Testing. The Journal of molecular diagnostics : JMD, 26(10), 906–916.

Mantere, T., et al. (2021). Optical genome mapping enables constitutional chromosomal aberration detection. American journal of human genetics, 108(8), 1409–1422.

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