Gene Deletion/Duplication Analysis: CopyDx Quantitative PCR (qPCR) and Multiplex Ligation-Dependent Probe Amplification (MLPA)

Mendelian Inheritance in Man Number: Can be customized for any Mendelian disorder using qPCR

Clinical utility of this service:

We offer deletion/duplication analysis to detect a whole or partial gene deletion or duplication in a known gene of interest associated with a Mendelian disorder. Our deletion/duplication testing is based on the use of quantitative PCR-based technology to identify copy number changes in any gene using genomic DNA from patients. This analysis has several applications for molecular diagnosis and carrier testing and a higher resolution and sensitivity compared to FISH testing.

Gene deletion/duplication analysis can be ordered for:
1. Analysis of any gene on our current test menu in which a deletion/duplication is suspected (http://www.genedx.com/test-catalog/genes/).
2. As a second tier test on a specimen previously sequenced at GeneDx.
3. For any gene not on our test menu, GeneDx will custom design a CopyDx (qPCR) analysis for any gene in which a deletion/duplication is suspected in a patient.

Applications of deletion/duplication analysis:
1. As a complementary test or substitute for FISH and quantitative microarray analysis when a deletion or duplication syndrome (contiguous or single gene) is suspected.
2. As a confirmation test for a genomic gain or loss identified by genome-wide microarray analysis.
3. To determine the presence or absence of a specific gene within a deleted chromosomal segment (contiguous gene deletion).
4. Diagnostic testing in a Mendelian disorder due to functional loss of one allele (haploinsufficiency), in particular when sequence analysis failed to identify a causative mutation and a whole gene deletion is a possible cause (for example: STK11 deletion associated with Peutz-Jegher syndrome).
5. Carrier testing for deletion/duplication syndromes when the specific region is known in an affected relative (i.e., testing of carrier status of female relatives of an affected male with X-linked hydrocephalus due to LICAM deletion).
6. Using certain MLPA tests, contiguous gene deletion or duplication syndromes may also be detectable (i.e. WAGR syndrome can be identified with the PAX6 MLPA testing kit).

Test method:

CopyDx: For the gene of interest, the number of copies present in the patient’s sample is determined by comparative quantitative analysis. Specifically, several short genomic sequence segments (~100 bp) interspersed across the gene are probed using a fluorescent quantitative PCR-based methodology, which assures high resolution and sensitivity. The analysis is done in triplicate.

MLPA: For specific genes that are on our GeneDx testing list, Multiplex Ligation-dependent Probe Amplification (MLPA) detects partial or whole gene deletions. This quantitative assay involves
simultaneous PCR amplification, electrophoretic separation and fluorescence detection of probes that are typically placed in or near every exon of the gene being tested. For some genes, probes may also be located outside of the gene of interest because deletions of neighboring genes have been reported. Additional probes are used as internal standards in the MLPA reaction.

**Test sensitivity:**

The ability of deletion/duplication analysis to detect a partial or complete deletion or duplication of a specific gene appears to be very high. The clinical utility of deletion/duplication analysis varies according to the gene and disease. The analysis can be used for patients in whom a deletion is highly likely (e.g. RAI1 deletion in a patient with Smith-Magenis syndrome). It may also be helpful when the frequency of deletions in a gene is unknown but loss-of-function mutations are associated with the disease and sequencing fails to identify a mutation or heterozygous positions in the gene.

**Specimen Requirements and Shipping/Handling:**

- **Blood:** A single tube with 1-5 mL whole blood in EDTA. Ship overnight at ambient temperature, using a cool pack in hot weather. Specimens may be refrigerated for 7 days prior to shipping.
- **Prenatal Diagnosis:** For prenatal testing for a known deletion or duplication, please refer to the specimen requirements table on our website at: [http://www.genedx.com/test-catalog/prenatal/](http://www.genedx.com/test-catalog/prenatal/). Ship specimen overnight at ambient temperature, using a cool pack in hot weather.
- **Buccal brushes:** We cannot accept buccal brush specimens for deletion/duplication analysis.

**Required Forms:**

- Rare Disorders Requisition Form – include the payment options / institutional bill page  

For prices, CPT codes and turn-around-times, please refer to the “Deletion/Duplication Analysis” page on our website: [www.genedx.com](http://www.genedx.com).