Targeted Deletion and Duplication Analysis by CGH

Genes Tested:

Please refer to www.cincinnatichildrens.org/deldup for a list of genes for which deletion and duplication analysis is currently available.

Description:

Targeted deletion/duplication analysis by comparative genomic hybridization is designed to identify gene-specific deletions or duplications, which may range in size from a single exon to the entire gene of interest. These genetic changes may be clinically relevant but are otherwise not identifiable through Sanger sequencing or next generation sequencing.

The frequency of intragenic deletions or duplications depends on the gene of interest (Boone et al. 2010). If the frequency of deletions or duplications is high in a specific gene, this test should be performed as the initial test, even before Sanger sequencing. Undergoing both sequencing and complementary deletion and duplication testing significantly improves the clinical sensitivity of molecular diagnosis in many patients.

Indications:

This test is appropriate for the following indications:

- As a reflex test for patients with a suspected autosomal dominant or X-linked disorder after full sequencing of the associated gene(s) is negative
- As a reflex test for patients with a suspected autosomal recessive disorder after full sequencing of the associated gene(s) is negative or initially identifies only one sequence change, or when one or more amplicons fail PCR amplification
- As an initial test when deletions or duplications in the gene associated with the suspected disorder are more prevalent than point mutations.

Testing Methodology:

Following DNA extraction, equivalent amounts of patient and reference DNA are labeled with two different dyes, Cy3 and Cy5, respectively. Each labeled DNA is then purified, quantified and mixed in an equimolar fashion. This mixture is hybridized on a custom array for 22 h at 65oC. Arrays are washed, scanned and only the data for the requested gene(s) are analyzed. In 3-5% of samples, hybridization patterns will not be sufficient to confirm that a deletion or duplication is present and additional PCR-based studies will be undertaken.

Sensitivity:

Clinical Sensitivity: The sensitivity of CGH for identifying deletions and duplications is variable and gene-specific.

Analytical Sensitivity: Targeted deletion/duplication analysis by comparative genomic hybridization is designed to identify gene-specific deletions or duplications, which may range in size from a single exon to the entire gene of interest. CGH may not detect deletions and duplications if present in <20% of the tested sample. In some cases, breakpoints may be difficult to determine. This assay is unable to detect genomic rearrangements, point mutations in the gene(s) of interest, or copy number changes in genes with corresponding pseudogenes.

Specimen:

At least 5 mLs whole blood in a lavender top (EDTA) tube. Saliva is also an acceptable sample type. Please call 513-636-4474 for a free saliva collection kit or for information about other specimen types.

Turn-Around Time:

42 days unless additional confirmatory testing is needed.

Billing and CPT Codes:

Please call 1-866-450-4198 for any pricing or billing questions.

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Phone: (513) 636-4474
Fax: (513) 636-4373
Email: LabGeneticCounselors@cchmc.org
www.cincinnatichildrens.org/genetics

Results:

Results will be reported to the referring physician or health care provider as specified on the requisition form.

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 by overnight Federal Express to arrive Monday through Saturday.

Ship to:

Cytogenetics and Molecular Genetics Laboratories
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229
513-636-4474

References:

Askree, S. H., E. L. Chin, et al. (2013). "Detection limit of intragenic deletions with targeted array comparative genomic hybridization." BMC Genet 14: 116.

Boone, P. M., C. A. Bacino, et al. (2010). "Detection of clinically relevant exonic copy-number changes by array CGH." Hum Mutat 31(12): 1326-1342.

Tanner, A. K., E. L. Chin, et al. (2012). "Array CGH improves detection of mutations in the GALC gene associated with Krabbe disease." Orphanet J Rare Dis 7: 38.

Tayeh, M. K., E. L. Chin, et al. (2009). "Targeted comparative genomic hybridization array for the detection of single- and multiexon gene deletions and duplications." Genet Med 11(4): 232-240.