Cytogenomic SNP Microarray

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Cytogenomic SNP microarray testing is used to identify genomic imbalances (deletions and duplications) and may be used to further characterize abnormalities identified by chromosome analysis, including unbalanced translocations, recombinant chromosomes, markers, and ring chromosomes. Regions of homozygosity (ROH) can also be identified. It is the recommended first-tier test for individuals with developmental delay (DD), intellectual disability (ID), multiple congenital anomalies (MCAs), and/or autism spectrum disorder (ASD)/pervasive developmental disorder (PDD).

Featured ARUP Testing

Cytogenomic SNP Microarray 2003414

Method: Genomic Microarray (Oligo-SNP Array)

- Preferred first-tier test for DD/ID, ASD, and/or MCAs
- Testing is performed on peripheral blood

Cytogenomic SNP Microarray Buccal Swab 2006267

Method: Genomic Microarray (Oligo-SNP Array)

- Same test as the Cytogenomic SNP Microarray, except testing is performed on a buccal specimen
- Requires a buccal swab using Oracollect collection kit

Disease Overview

Prevalence

- Global DD/ID: 1-3%
- ASD: 1-2%

Diagnostic Issues

- Many abnormal phenotypes are associated with chromosomal imbalances.
- Chromosome analysis has limited ability to detect small, cryptic abnormalities (<10–20 Mb).
- Genomic microarray can detect chromosomal imbalances at a much higher level of resolution than standard chromosome analysis.
- Genomic microarray can detect ROH, which may indicate an increased risk for autosomal recessive (AR) disease for genes contained within the ROH and/or the risk of an imprinting disorder due to uniparental disomy (UPD).
- Identification of specific abnormalities may be helpful in medical management and planning for special needs.

Test Interpretation

Diagnostic Yield

- 15-20% for individuals with:
  - Unexplained ID
  - ASD
  - MCAs
- The diagnostic yield varies by patient population and the presence of comorbidities

Results

- A written summary and an interpretation of the microarray findings are provided.
- Copy number variant (CNV) evaluation is performed in accordance with recommendations by the American College of Medical Genetics and Genomics (ACMG):
  - Standard five-tier classification terminology is used:
    - Pathogenic
    - Likely pathogenic
    - Variant of uncertain significance (VUS)
    - Likely benign
    - Benign
  - Variants that do not fall within these categories may be reported with descriptive language specific to that variant.
- For additional information regarding CNV classification, see the ARUP Cytogenomic Constitutional CNV Assertion Criteria.
  - Additional resources can be found on the ARUP Genetics Resources website.

Result	Description
Normal	No clinically significant CNV or ROH detected
Abnormal	One or more clinically significant CNV, ROH, or aneuploidy detected
Uncertain	One or more CNVs of uncertain clinical significance detected • Insufficient evidence for unequivocal determination of clinical significance available at the time of review • AR risk Uncertain ROH: risk for AR disease and/or imprinting disorder due to UPD • Testing may suggest relatedness between the parents of the tested individual

Reporting Criteria

- Deletions >50 kb and duplications >400 kb are generally reported, dependent on genomic content.
- Total autosomal homozygosity >3% is generally reported.
  - Only autosomal ROH >3 Mb are considered for this estimate.
- Single terminal ROH >3 Mb or single interstitial ROH >10-15 Mb are generally reported, dependent upon chromosomal location and likelihood of imprinting disorder.
- Recessive disease risk and recurrent CNVs with established reduced penetrance are generally reported.
- Known or expected pathogenic CNVs affecting genes with known clinical significance but which are unrelated to the indication for testing will generally be reported.
- CNVs classified as likely benign or benign that are devoid of relevant gene content or reported as common findings in the general population are generally not reported.

Limitations

- Does not detect:
  - CNVs below the limit of resolution of the testing platform
  - Sequence-level variants (mutations) including point mutations and small insertions/deletions
  - Balanced chromosomal rearrangements (translocations, inversions and insertions)
  - Imbalances of the mitochondrial genome
  - Low-level mosaicism (generally <20-30%)

Related Information

Testing for Genetic Syndromes Related to Developmental Delay (DD) and Intellectual Disability (ID)
Laboratory Testing for Developmental Delay, Intellectual Disability, and Autism Spectrum Disorder