High Density SNP Microarray
also known as: Copy Number + SNP Array

TEST DESCRIPTION: Our postnatal microarray is a high density single nucleotide polymorphism (SNP) platform designed to interrogate the whole genome at resolution much higher than is possible using traditional karyotyping or fluorescence *in situ* hybridization (FISH) methodologies. Our High Density SNP array contains a total of 2.6 million markers distributed throughout the genome for the detection of both genomic dosage anomalies (deletions and duplications) and regions of homozygosity (ROH; regions lacking typical amounts of genetic variation). This marker density provides a global resolution of 10 Kb to 20 Kb for copy number changes and 5 Mb resolution for ROH. Due to the increased diagnostic yield of microarray, the American College of Medical Genetics (ACMG) recommends microarray as a first tier test for individuals with intellectual disabilities, autism spectrum disorders, and/or multiple congenital anomalies.1

TEST DETAILS and COMPLEMENTARY TESTING:
- Recommendations for additional testing differ based on the disorder suspected; contact a laboratory genetic counselor to discuss which testing options are most useful for your patient.
- If trisomy 13, 18, or 21 (Down syndrome) is suspected, Chromosome Analysis is recommended.
- If an imprinting disorder, such as Angelman syndrome is suspected, additional testing such as Methylation Analysis may be indicated.

ADVANTAGES:
- Evaluates hundreds of different genetic conditions across the genome with one test
- Detects aneuploidy (including trisomy and sex chromosome abnormalities) and triploidy
- Identifies large and small deletions and duplications, many of which are undetectable by traditional chromosome analysis
- Detects ROH, which cannot be identified using other testing methodologies
- Allows for enhanced breakpoint detection and refinement in patients with a structural chromosome anomaly
- Offers a more comprehensive and cost-effective approach to testing for microdeletion or microduplication syndromes than ordering multiple FISH tests
- Allows for testing on limited amounts of specimen, including DNA extracted from non-invasive buccal swabs

LIMITATIONS:
- Cannot identify all genetic conditions or the cause of all congenital defects
- Does not detect changes in the DNA sequence of genes
- Cannot detect balanced chromosome rearrangements, such as translocations (a complementary test such as Postnatal Chromosome Analysis should be performed to detect balanced chromosome rearrangements)
- Unable to reliably detect all cases of low-level mosaicism
- Despite dense marker distribution throughout the genome, this assay is limited in its detection of genetic aberrations by the probe density at a given locus.
INDICATIONS FOR TESTING:
Due to the increased diagnostic yield of microarray, this assay is recommended as a first tier test for individuals with:
- Intellectual disabilities
- Autism spectrum disorder (syndromic and non-syndromic) [GeneReviews](http://www.ncbi.nlm.nih.gov/books/NBK1442/)
- Multiple congenital anomalies

In addition, the High Density SNP Array can be helpful in the identification of an underlying genetic etiology for patients with other significant concerns:
- Seizure disorders
- Vision/hearing problems
- Low muscle tone
- Neurodevelopmental and neuromuscular disorders
- Suspension of well-known microdeletion/microduplication syndromes, such as:
  - 22q11.2 deletion [GeneReviews](http://www.ncbi.nlm.nih.gov/books/NBK1523/)
  - Williams syndrome [GeneReviews](http://www.ncbi.nlm.nih.gov/books/NBK1249/)
- Abnormal unbalanced karyotypes, particularly those with supernumerary marker chromosomes, or mosaic karyotypes
- Imprinting associated disorders, such as:
  - Angelman syndrome (AS) [GeneReviews](http://www.ncbi.nlm.nih.gov/books/NBK1144/)
  - Prader-Willi syndrome (PWS) [GeneReviews](http://www.ncbi.nlm.nih.gov/books/NBK1330/)
  - Beckwith-Weidemann syndrome (BWS) [GeneReviews](http://www.ncbi.nlm.nih.gov/books/NBK1394/)
  - Russel-Silver syndrome (RSS) [GeneReviews](http://www.ncbi.nlm.nih.gov/books/NBK1324/)
- Suspicion of consanguinity
- A family history of a structural chromosome abnormality or rearrangement
- Certain cytogenetic cases with abnormal ‘apparently balanced’ karyotypes including Robertsonian translocations, inversions, and isochromosomes

SPECIMEN COLLECTION & TRANSPORT:
Complimentary test kits are available upon request, but are not required.

SAMPLE TYPE and REQUIREMENTS:
- blood: 2-5 ml whole blood in an EDTA tube (purple top)
- newborn minimum requirement: 1-3 ml
- buccal swab: 2 swabs
- extracted DNA: 70 ng/µg with a total yield of 7-10 µg (in TE) in a DNA microcentrifuge tube
  * When submitting extracted DNA for genetic testing, nucleic isolation must have occurred in a CLIA-certified laboratory or a laboratory meeting equivalent requirements as determined by the CAP and/or CMS.
- tissue / skin: > 5 mm³ tissue from biopsy or skin punch (transport at room temperature in tissue culture media)

SHIPPING:
- Maintain and ship samples at room temperature.
- Coordinate transport for sample to be received in our laboratory within 24-48 hours of collection.
  - LOCAL: Call 402-559-5070 (option 1)
  - OUT OF AREA: Prior to shipment, please fax the completed test request form to 402-559-7248, including the FedEx® airbill tracking number.
    - Saturday delivery MUST be checked when sending FedEx® on Friday.
    - Please include Internal Billing Reference # 3155070600 on the FedEx® airbill.
    - Ship To: Human Genetics Laboratory – Zip 5440
      UNMC Shipping & Receiving Dock
      601 S. Saddle Creek Road
      Omaha, NE 68106

FORMS FOR TESTING: The following form can be downloaded via our website.
- Required: Postnatal Test Request Form
- Optional: Informed Consent for Genetic Testing
POTENTIAL TEST RESULTS:

NORMAL:
- A normal result indicates no clinically-significant chromosome abnormalities were identified.
  - arr[hg19](1-22,X)x2 (female)
  - arr[hg19](1-22)x2,(XY)x1 (male)

ABNORMAL:
- Results are reported by location in the genome, including chromosome and size.
- Deletion: Part of a chromosome (genetic material) is missing. Some may be very small and only include one gene and others are bigger and may involve numerous genes.
- Duplication: Extra chromosome material is present in the patient’s DNA.
- An abnormal result indicates that a chromosome abnormality was identified that likely provides an explanation for the indications.
  - Pathogenic – Reported when a copy number variant (CNV) is:
    1) associated with a known microdeletion/microduplication syndrome,
    2) cytogenetically visible or > 3 Mb,
    3) documented in multiple peer-reviewed publications.
  - Uncertain Clinical Significance (UCS) – In some circumstances, the clinical significance of a finding may not be well understood. Uncertain variants may also be classified as “Likely Pathogenic” or “Likely Benign” based on the ACMG recommendations for variant classification.
  - ROH – Reported when it represents uniparental disomy (UPD), when it represents >1.5% of the entire genome and when a segment of ROH is >3Mb.
- Parental testing (Postnatal Chromosome Analysis on maternal and/or paternal blood) may be recommended in order to clarify whether the result is de novo or familial for the purpose of recurrence risk calculation.

TURNAROUND TIMES: Results are typically available in 1-2 weeks for routine studies on all sample types; 1 week when performed on newborn blood.

BILLING: Our laboratory offers patient/self-pay, insurance (including Medicare/Medicaid), and client/institution billing options. Verifying coverage requirements or obtaining preauthorization PRIOR TO OR AT THE TIME OF SPECIMEN COLLECTION is often necessary. We provide preauthorization services upon request by calling 402-559-5070 (option 3); the following form is helpful for obtaining the information required by insurance providers and can be downloaded via our website.
- Insurance Preauthorization Request

In some circumstances, a test may be warranted even though insurance coverage is denied or not guaranteed. For these situations, we request the following form be signed by the patient and submitted with the sample. This helps inform patients of their potential financial responsibility, should the costs of genetic testing not be paid by their insurance provider.
- Advanced Beneficiary Notice of Noncoverage (ABN) – required when billing Medicare

CPT CODES: 81229, 88230

PRICING: For current costs contact the laboratory billing staff at 402-559-5070 (option 3).

REFERENCES:


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