Whole Genome Cytogenetic Array
EmArry Cyto
Emory Genetics Laboratory (EGL) is a worldwide leader with more than 35 years of expertise in comprehensive genetic diagnostic testing. Our innovation and strength in studying rare genetic conditions foster our dedication to providing the medical community with state-of-the-art tests, informative test reports and quality customer service. Our laboratory directors, genetics counselors and medical geneticists, recognized as leaders in their areas of interest, are available to discuss key issues related to diagnosis, interpretation and medical management for the conditions in our growing test menu. By integrating cutting-edge genetic testing technologies with clinical expertise, Emory Genetics Laboratory provides the quality laboratory services needed to enhance the clinical care you provide to your patients.

**EmArray Cyto**

Whole genome cytogenetic array analysis has revolutionized the diagnostic yield of cytogenetic testing. In our laboratory, ~20% of individuals referred for developmental delay, mental retardation, multiple congenital anomalies, and/or autism have a clinically relevant cytogenetic imbalance detected. EmArray Cyto consists of approximately 60,000 oligos, spaced at a minimum of 75kb across the genome, with high-density coverage of clinically relevant regions including all telomeres, centromeres, and known microdeletion/microduplication syndrome loci (Baldwin et al, 2008). All imbalances are confirmed by a second methodology (usually FISH analysis).

**WHY CHOOSE EMORY GENETICS FOR YOUR ARRAY TESTING NEEDS?**

- As the founding member of the ISCA Consortium, Emory Genetics Laboratory has extensive expertise in array analytics and copy number changes. By using EGL’s EmArray Cyto, your patient’s results are supported by the Consortium with standardization in design and data interpretation from more than 100 labs worldwide.

- We offer first-rate results interpretation. Many companies offer array services, but Emory Genetics Laboratory distinguishes itself by having over 35 years of experience in cytogenetic testing. Our laboratory is supported by an experienced team of cytogenetic and molecular laboratory directors, clinical geneticists and trained genetic counselors who are always available to address your needs and questions. Over the years, through their innovative research and rapid translation to clinical practice, Dr. David Ledbetter and Dr. Christa Lese-Martin have delivered novel tests, including telomere testing by FISH and the first whole genome oligo microarrays, to the clinical genetics community. These tests and the research involved in developing them have changed the clinical approach to cytogenetic testing.

- Alternative Specimen Collection Options: Dried Blood Spots
  - Less invasive for hard-to-draw patients
  - No blood draw required
  - Highly stable and doesn’t require special handling or shipping
  - As reliable as whole blood samples

- Turn Around Time of 4-7 days for the EmArray Cyto.
Case 1 - The Importance of FISH Follow-up

Cytogenetic array analysis was ordered on an 8 year old patient due to a clinical presentation of: multiple congenital anomalies, mental retardation, sensorineural hearing loss and microcephaly. As shown in Figure 1, array analysis identified a pathogenic 1.69 Mb interstitial deletion of 9q34.3. This deletion resulted in the loss of 60 genes, including EHMT1, which causes the chromosome 9q deletion syndrome. FISH analysis confirmed the deletion (indicated by the arrow in Figure 2).

Parental studies using metaphase FISH were performed to determine whether the finding in the proband was de novo or inherited. Interestingly, as shown in Figure 3, the mother of this patient was found to carry a balanced insertional translocation involving chromosomes 7 and 9. This balanced rearrangement results in a derivative 7 chromosome with material from distal 9q and a deleted chromosome 9. This mother is therefore at increased risk to have unbalanced offspring with either the same deletion as the proband or a duplication of 9q if the derivative 7 is inherited.

Some labs perform parental follow-up by molecular methods, such as qPCR (quantitative PCR) or MLPA (multiplex ligation-dependent probe amplification). These methods will not detect balanced rearrangements in a parent. Because this information is crucial to providing accurate recurrence risk counseling, EGL performs all parental follow-up by FISH. This approach allows for maximum detection of clinically significant cytogenetic findings that will impact your patients’ care.

Case 2 - Characterization of Atypical Microdeletions

Cytogenetic array analysis was performed on a 10 year old with a clinical diagnosis of Williams syndrome confirmed by FISH analysis. Previous G-banding analysis was normal. Although the patient’s history included many of the typical features of Williams syndrome, he had no language and a severe seizure disorder. Suspicious of an additional diagnosis, the clinician ordered array analysis.

The array results (Figure 4) revealed that the deletion on chromosome 7q was 10.87 Mb in size, much larger than the typical Williams syndrome deletion. Determination of the true breakpoints of this deletion explained the additional phenotypic features in this child, providing better genotype/phenotype correlations. This case also demonstrates that even large deletions can be missed by G-banding, due to the location on the chromosome or subtlety of the change, providing further evidence for array analysis as a first-line cytogenetic diagnostic test.
Case 3 - Autism

Autism spectrum disorders have a large genetic component and cytogenetic imbalances contribute significantly to their etiology. At EGL, we find pathogenic imbalances in ~8-10% of individuals with autism. As described in the examples below, these imbalances include recurrent deletions and duplications known to be associated with autism, as well as novel cytogenetic aberrations.

A sample from a 5 year old patient with autistic features and speech delay was sent for array analysis. As shown in Figure 5, a 600 kb deletion of 16p11.2 was identified.

Several recent publications have demonstrated that deletions of this region cause autism in ~50% of patients with this deletion (Kumar et al., 2008; Weiss et al., 2008; Marshall et al., 2008). Deletions of this region have also been reported in association with mild dysmorphic features, hypotonia, weight problems, seizures, and mild mental retardation.

Another sample was received for cytogenetic array analysis from an 8 year old male referred with autism. A 17 kb deletion of part of the FMR1 gene was identified, as shown in Figure 6. Mutations in the FMR1 gene cause Fragile X syndrome and this small deletion was detected due to the increased probe coverage included on our custom array for this targeted gene. The genome browser view (Figure 7) shows the extent of this deletion.

The increased sensitivity provided by cytogenetic array analysis for such predictive copy number changes allows for earlier diagnosis and earlier, more effective interventions in autism spectrum disorders.

HOW DO YOU ORDER THE EmArray Cyto?

Please contact our friendly Client Service representatives for more information at 800-366-1502, or visit our website at http://geneticslab.emory.edu.