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GENETIC TESTING THROUGH MICROARRAY

The Future Is Here

What is Chromosomal Microarray:

Human body contains genetic information that is bundled into packages called chromosomes. Any change in the genetic combinations, like addition or deletion within chromosomes or of the chromosomes, can cause medical conditions like birth defects , developmental delays , autism and other health issues. Chromosomal Microarray uses advanced technology to provide expanded genetic testing by detecting both large and small chromosomal change. Through a combination of copy number probes and SNP probes, CMA is able to detect smaller changes in chromosomes that normally goes undetected in traditional tests, which focuses on whole chromosomal structure (karyotype).

CMA in Prenatal Settings:

"The American Congress of Obstetricians and Gynecologists (ACOG) and the Society for Maternal- Fetal Medicine recommend CMA as a replacement for the fetal karyotype in patients with a pregnancy demonstrating one or more major structural abnormalities on ultrasound when undergoing invasive prenatal diagnosis"

Clinical Indications May Include Any of the Following:

- If maternal blood tests during pregnancy were abnormal, indicating an increased chance of a medical condition or birth defect
- If an abnormal finding is seen on ultrasound and other genetic testing has been normal
- If you previously had a child with a medical condition, particularly one associated with chromosomal changes
- In case of Recurrent Pregnancy Loss
- In case of advanced maternal age

Feature Test

- Chromosomal Microarray optima (315K), Prenatal, Amniotic Fluid/Chorionic Villus Sampling
- Chromosomal Microarray optima (315K), Autopsy, Products of Conception, or Stillbirth
- Chromosomal Microarray Cytosure (750K), Prenatal, Amniotic Fluid/Chorionic Villus Sampling
- Chromosomal Microarray Cytosure (750K), Autopsy, Products of Conception, or Stillbirth

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CMA in Paediatric Settings:
The American College of Medical Genetics (ACMG)[1],American Academy of Pediatrics (AAP)[2] and the American Academy of Neurology (AAN)[3] all recommend chromosomal microarray testing for individuals with one or more of the following:

- Developmental delays or intellectual disability
- Birth defects
- Unusual physical features
- Autism spectrum disorders

CMA is also an appropriate follow-up test for individuals with congenital anomalies with a previously normal conventional chromosome study.

Feature Test

- Chromosomal Microarray Cytosure (750KK, Postnatal, Peripheral Blood
- Chromosomal Microarray Optima (315K), Postnatal, Peripheral Blood

MFine Diagnostics - Chromosomal Microarray Offerings

Parameters	CytoScan HD	Cytoscan 750K	Cytoscan Optima
Where to be Used?	High-resolution analysis of CNVs constitutional postnatal samples	Analysis of gains and losses for constitutional postnatal samples	Detection of gross aneuploidies at low cost and low resolution
Probe Details	High Density coverage with > 2.6 million probes	CNV Probes = 550,000 SNP Probes = 200,000 **Total Probes = 750,000**	CNV Probes = 18,018 SNP Probes = 148,450 **Total Probes = 315,000**
Sample Types	Blood, Buccal Swabs, Saliva, fresh & frozen tissues, uncultured or cultured cells, CVS , Amniocentesis,POC, etc.	Blood, Buccal Swabs, Saliva, fresh & frozen tissues, uncultured or cultured cells, CVS, Amniocentesis, POC, etc.	Blood, Buccal Swabs, Saliva, fresh & frozen tissues, uncultured or cultured cells, CVS , Amniocentesis,POC, etc.
Analytical Claims	Gains < 10-25 Kb Losses < 10-25 kb AOH> 1mb Mocaissim > ~ 15%	Gains 200-400 kb Losses 200-400 kb AOH> 5 mb Mocaissim > ~ 15-20%	Gains 2 mb Losses 1 mb AOH> ~5 mb Mocaissim > ~ 20% 396 genes at 25m/100kb

Chromosomal Microarray Advantage :

KARYOTYPING	FISH	CHROMOSOMAL MICROARRAY
• **Low Diagnostic Yield** Only 3% of cases have a diagnosis made • **Slow Time to Results** Sample to Result – 15-21 days • **Requires live cells-** Prone to culture failure • **Miss small changes** 5MB is the smallest deletion you can detect with a microscope and a human eye • **Very specially trained people** Difficult to scale • **Subjective method** Prone to human error	• **Can only identify known aberrations** Requires prior knowledge or a suspected diagnosis to enable probe selection. Cannot be used to discover new ones • **Low Diagnostic Yield** Only 3% of cases have a diagnosis made • **Miss small changes** Resolution 80Kb-1Mb In-vitro cell culture issues	• **Diagnostic yield ~30%** More information per test/ fewer retests/reflex tests. Greater number of patients benefit from definitive diagnosis • **Quicker time to result** 8 days versus 15 -21 days Rapid turn round of samples • **Superior resolution** Whole genome / high density CN and SNP content. Increased confidence in results • **Quantitative vs subjective** Increased confidence

LC/DIA/YCMD/FLY/1118/V001

References:

1. Abnormalities in spontaneous abortions detected by G-banding and chromosomal microarray analysis (CMA) at a national reference laboratory.
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2. Improved assay performance of single nucleotide polymorphism array over conventional karyotyping in analyzing products of conception.
   Lin SB1, Xie YJ1, Chen Z2, Zhou Y1, Wu JZ1, Zhang ZQ1, Shi SS3, Chen BJ1, Fang Q4.
3. Prenatal Diagnostic Testing for Genetic Disorders (Replaces Practice Bulletin Number 88, December 2007)
   (See also Practice Bulletin Number 163, Screening for Fetal Aneuploidy)
4. The use of chromosomal microarray for prenatal diagnosis
   Society for Maternal-Fetal Medicine (SMFM); Lorraine Dugoff, MD; Mary E. Norton, MD; Jeffrey A. Kuller, MD

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