ALBERTA PRECISION LABORATORIES
Leaders in Laboratory Medicine

Chromosomal Microarray (CMA): Information for Ordering Physicians

Chromosomal Microarray (CMA)

CMA is a chromosome testing technique that detects chromosome imbalances (missing or extra genetic material). Compared to other technologies, such as karyotype, CMA has a higher resolution and can detect smaller imbalances. Non-urgent results may take up to 4 weeks.

Indications

- Autism
- Dysmorphic features
- Intellectual disability
- Multiple congenital anomalies
- Isolated congenital heart defect
- Isolated cleft lip and/or palate
- Features consistent with a microdeletion/duplication syndrome

Potential Benefits

- Provide an explanation for the patient's health/developmental problems
- Guide treatment and care of the patient
- Provide recurrence risks for the family

Considerations

- Identification of a copy number variant (CNV) that cannot be interpreted (variant of uncertain significance)
- Identification of a CNV that is not related to the patient's current health/development problems and may cause other health concerns in the future for the patient and/or their relatives (incidental finding)
- Parental testing may be required to assist in interpretation, establish the pattern of inheritance and clarify clinical implications

Limitations

- A normal CMA does not exclude all genetic causes of disease
- Low levels of mosaicism, polyploidy or balanced chromosome rearrangements cannot reliably be detected
- Cannot detect CNVs in areas of the genome that are not covered by the CMA platform

Absence of Heterozygosity (AOH)

- CMA will detect the absence of heterozygosity (AOH), also called regions of homozygosity (ROH)
- AOH limited to one chromosome may be suggestive of uniparental disomy (UPD) and follow-up testing may be required
- AOH detected on multiple chromosomes can be associated with parental consanguinity or ancestry from an isolated population. This result is not diagnostic but raises the possibility of a recessive disorder due to a homozygous variant within a region. This information is included in the report for clinical interpretation by the referring clinician.
- If AOH results are consistent with a second degree or closer relationship between parents, the laboratory will inform the referring physician as it raises concern of maternal safety. It is the physician's responsibility to assess whether the mother may be at risk.

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Types of CMA Results

Result	Interpretation
Normal	No abnormality identified. The cause of the patient's health and/or developmental problems remains unexplained (can still be a genetic condition due to a gene variant).
Pathogenic Copy Number Variant (CNV)	A CNV that is associated with a specific pattern of health and/or developmental problem is identified. An additional blood sample from the parents may be required to investigate the origin of the CNV.
Variant of Uncertain Significance (VUS)	A CNV of uncertain significance is identified. This variant may or may not be related to the reason for testing. Testing of the parents may be recommended to assist with the interpretation.
Incidental Finding	A CNV is identified that is unrelated to the reason for testing but may cause other health problems in the future for the patient and/or their relatives.
Absence of heterozygosity (AOH)	AOH suggestive of UPD will require follow-up testing. AOH of multiple chromosome regions will be reported for clinical interpretation by the referring physician.

Ordering CMA

Please refer to the APL Test Directory (http://ahsweb.ca/lab/apl-td-lab-test-directory) for ordering instructions.

- Any Specialist may order CMA after discussing the above benefits and limitations with the family
- **Samples with incomplete requisitions will not be tested until all the required information is received.**

Contact Information

Genetic Counsellors, Genetics & Genomics
Edmonton: 780-407-1015
Calgary: 403-955-3097

Requisition forms, contact information and other resources can be found at:
http://ahsweb.ca/lab/if-lab-genetics-and-genomics