Prenatal Chromosomal Microarray (CMA): Information for Ordering Physicians

Cytogenetic testing on amniotic fluid and chorionic villus sampling (CVS) includes:

- Rapid Aneuploidy Detection (RAD)
- Maternal cell contamination study (MCC)
- Chromosomal microarray (CMA), as indicated

RAD Testing

Once ordered, RAD testing will be performed on all prenatal samples (CVS and amniotic fluid) unless otherwise indicated or specimen is insufficient.
To order RAD ONLY, please send a sample with a completed Molecular Diagnostic Laboratory (Edmonton) or Constitutional Cytogenetic (Calgary) requisition.
RAD results will be available within 2-3 days.

RAD is used for the rapid detection of aneuploidy of chromosomes 13, 18, 21 and the sex chromosomes, or triploidy.

CMA allows for the detection of chromosome imbalances (gains or losses) that are smaller than can be detected by a standard karyotype.

Indications for Prenatal CMA

Fetal ultrasound anomalies including:

- NT ≥3.5 mm
- Intrauterine growth retardation
- Structural ultrasound abnormality
- Family chromosome imbalance detectable by CMA

If the fetus is suspected to have a single gene disorder or if there are exceptional circumstances, contact the laboratory genetic counsellors directly to discuss.

RAD is the first line test on all prenatal samples.

If RAD is normal

CMA testing will only be initiated if a completed CMA requisition form is received AND sample has at least one qualifying indication.

How do I order CMA?

- Obtain parental consent for testing then complete and submit a "Chromosomal Microarray (Array CGH) Requisition" form
- CMA requisition forms can be found under the Cytogenetics Laboratory tab at: www.albertahealthservices.ca/lab/Page8667.aspx

Maternal Cell Contamination (MCC)
Prenatal samples may be contaminated with maternal cells which prevents the interpretation of the results (nil result).

Parental Follow-up
In order to interpret the fetal results, it may be necessary to test the mother and father. Parental samples may be run for CMA in order to assist in the interpretation of the fetal CMA results.

How long will the CMA results take?

- CMA results from direct amniotic fluid may take up to 2 weeks
- CMA from cultured CVS or amniocytes may take up to 4 weeks

What are the benefits of CMA?

- CMA detects small deletions and duplications that are not visible on a karyotype
- May help guide management and care of the pregnancy

What does my patient need to know before ordering CMA?

- A normal CMA result does not exclude all genetic causes of disease
- CMA may detect a genetic imbalance unrelated to the pregnancy, but predicts future health problems that may also relate to other family members
- CMA testing may require testing of parents to help establish pattern of inheritance and clinical implications

What are the limitations and unanticipated outcomes of CMA?

- Only pathogenic or likely pathogenic imbalances will be included in the results. Benign variants or variants of uncertain clinical significance may not be reported.
- May detect the absence of heterozygosity (AOH). AOH results can be provided upon request.
    - AOH limited to one chromosome may be suggestive of uniparental disomy (UPD) and follow-up testing may be required.
    - AOH detected on multiple chromosomes suggests these regions are identical by descent. AOH results can be provided upon request.
    - 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.
- May find a genomic imbalance unrelated to the reasons for testing, but that indicates risk for other additional unanticipated health problems for family members (e.g. cancer, late onset neurological disease).
- Not all genetic conditions are detectable by CMA as some are caused by variants within a single gene or are multifactorial in nature.
- Additional descriptions of result classifications can be found in the Postnatal Chromosomal Microarray (Array CGH) Information Sheet and Discussion Guide under the Cytogenetics Laboratory tab (http://www.albertahealthservices.ca/lab/page8667.aspx).

I have array results, now what?

- If the CMA result is abnormal, it is appropriate to refer the family for genetic assessment and counselling.
- If the CMA result is normal, it does not mean that there is not a genetic cause for the ultrasound findings. In these cases, other genetic testing may be appropriate, in consultation with Clinical Genetics.

Referrals to Clinical Genetics can be sent to:

Edmonton & North: Medical Genetics Clinic
Phone: 780-407-7333 Fax: 780-407-6845

Calgary & South: R.B. Lowry Genetics Clinic
Phone: 403-955-7373 Fax: 403-955-2701

I have questions about array CMA. Who do I talk to?

Contact the laboratory genetic counsellors:
Edmonton at 780-407-1015

Calgary at 403-955-3097

It is the ordering physician's responsibility to obtain the appropriate consent and discuss the limitations and unanticipated outcomes of CMA with their patients where feasible.

Requisition forms, contact information, and other resources can be found at:
www.albertahealthservices.ca/lab/page8667.aspx