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Leaders in Laboratory Medicine

Prenatal Genetic Investigations: Information for Ordering Physicians

Genetic testing on amniotic fluid and chorionic villus sampling (CVS) may include:

- Rapid Aneuploidy Detection (RAD)
- Chromosomal Microarray (CMA)
- Maternal Cell Contamination study (MCC)
- Molecular testing such as exome/panel/single gene/targeted variant analysis

RAD provides molecular results for aneuploidy involving chromosomes 13, 18, 21, X and Y.

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

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

RAD Testing

Once analysis is ordered, RAD testing will be performed on all prenatal samples (CVS and amniotic fluid) unless otherwise indicated or specimen is insufficient.

RAD is the first line test on all prenatal samples. → If RAD is normal → Additional testing will only be initiated if a completed order is received AND sample has at least one qualifying indication.

CMA Testing

Indications

Fetal ultrasound anomalies including:

- Nuchal translucency (NT) ≥3.5 mm
- Intrauterine growth restriction
- Structural ultrasound abnormality
- Familial chromosome imbalance detectable by CMA

Potential Benefits

- May help guide management and care of the pregnancy and future pregnancies
- May provide recurrence risks for the family

Considerations

- Only pathogenic or likely pathogenic imbalances will be included in the results. Variants of uncertain clinical significance may not be reported.
- May find a genomic imbalance unrelated to the reasons for testing, but that indicates risk for other additional unanticipated health problems for the fetus or family members (e.g. cancer, late onset neurological disease).
- To interpret fetal results, it may be necessary to test the biological mother and father. CMA may be performed on parental samples to assist in the interpretation of the fetal CMA results.
- CMA may detect the absence of heterozygosity (AOH).
  - AOH results will only 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.

- 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.

Limitations

- A normal CMA result 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

When can I expect results?

RAD results will be available within 2-3 days.
CMA results from direct amniotic fluid may take up to 2 weeks.
CMA from cultured CVS or amniocytes may take up to 4 weeks.
Molecular testing turnaround times vary. Please refer to the APL Test Directory (http://ahsweb.ca/lab/apl-td-lab-test-directory), or contact the laboratory genetic counsellors.

How are results reported?

Results are sent to the ordering provider and available in Netcare and Connect Care.

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