

Women's Health

APRIL 2021 | A NEWSLETTER FOR MEDICAL PROFESSIONALS

Chromosomal Testing for Formalin-Fixed Paraffin-Embedded (FFPE) Products of Conception

In the general reproductive population, 10-15% of clinically recognized pregnancies result in miscarriage prior to 20 weeks gestation.¹ It is estimated that approximately 50% of first trimester pregnancy losses have an underlying chromosomal abnormality, the most common being trisomy, polyploidy and monosomy X.¹ Therefore, chromosome studies may provide useful information about the cause of pregnancy loss.

Formalin-fixation and paraffin-embedding of tissues preserves the morphology and cellular details of tissue samples, thus it has become a standard preservation procedure in pathology.² Formalin-fixation and paraffin-embedding of products of conception (POC) allows for long-term storage and clinical follow-up of these specimens. This is also more cost effective than storage of fresh POC samples via freezing or refrigeration. The use of FFPE specimens for genetic analysis can be informative, but challenging as standard chromosome analysis is not possible due to the lack of viable dividing cells for tissue culture. Chromosomal microarray analysis, however, does not require actively dividing cells and has become a popular methodology for detecting copy number and copy neutral changes across the genome.

In the past, FFPE POC samples were not good candidates for chromosomal microarray analysis, yielding more degraded DNA from small amounts of tissue. With the advent of the OncoScan™ FFPE assay samples that previously may not have had reportable results on the Cytoscan® microarray platform can now be analyzed and reported to providers, allowing patients to better understand the underlying causes of a pregnancy loss and recurrence risk for future pregnancies.

The OncoScan™ platform requires a smaller footprint of intact DNA for microarray analysis, which is useful for FFPE specimens that often have highly fragmented DNA. OncoScan™ Assay utilizes the Molecular Inversion Probe (MIP) assay technology which has been used for detection of focal insertions and deletions and larger copy number

alterations. This assay, although it has fewer probes than Cytoscan is positioned by the manufacturer as a robust solution for degraded FFPE sample analysis.

The Oncoscan™ FFPE assay can detect whole chromosomal aneuploidies in POC samples with greater than 10% fetal DNA as well as copy number variants (CNVs) of 25 kb or greater in clinically significant regions. Copy number losses of greater than 1 MB and copy number gains of greater than 2 MB outside of known clinically significant regions with at least one OMIM gene are also reported. Microarray also allows for detection of complete or partial molar pregnancies, possible uniparental isodisomy, as well as percent and location of regions of homozygosity, including the degree of identity by descent.^{3,4} Given the higher rate of maternal cell contamination (MCC) in POC specimens, MCC studies can also be ordered on FFPE specimens concurrently with a microarray. Paraffin blocks or ten 10-micron thick section slides can be sent for analysis along with a copy of the pathology report and an H&E slide. Samples may be deemed insufficient for microarray analysis if pathology determines that only a small amount of the sample is found to have fetal tissue.

Summary

Labcorp has analyzed over 1,600 microarrays on FFPE POC samples to date. We have an extensive database of copy number variants (CNVs) detected by microarray analysis, which provides an exceptional reference to support interpretation of clinically relevant results. Reveal® Microarray - FFPE POC makes it possible for older preserved specimens to be tested, which may be beneficial to patients who have had a prior pregnancy loss or recurrent losses that were not previously tested for chromosome anomalies.

For any questions related to Reveal® FFPE microarray analysis, please call **800.345.4363** and ask to speak to a cytogenetic laboratory counselor.

April Health Awareness Calendar

- World Autism Awareness Day (April 2)
- World Health Day (April 7)
- Medical Laboratory Professionals Week (week of April 20th)
- National Infertility Awareness Week (April 21-27)
- World Immunization Week (April 22-28)
- Parkinson's Awareness Month



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References

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3. American College of Obstetricians and Gynecologists. The Use of Chromosomal Microarray Analysis in Prenatal Diagnosis. Committee Opinion No. 581 (2013). *Obstet Gynecol.* doi: 10.1097/01.AOG.0000438962.16108.d1.
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