Legacy Laboratory Services brings cytogenetics into the new genomic era

By Yassmine Akkari, Ph.D., FACMG

The ability to visualize the genome has undergone a dramatic change over the last half of the century. It began with the elucidation of the number of chromosomes in human cells, and continued with the identification of chromosomes, recognition of specific chromosomal bands and the introduction of fluorescence in situ hybridization (FISH). The latest advance in genome analysis, namely chromosomal microarray analysis (CMA), has enabled health professionals to view the hereditary material at a much higher resolution.

Since this revolution in genome analysis, we have been able to describe multiple disease entities based on specific phenotypes and accurate correlation with a genotypic change. Having the ability to examine increasingly larger proportions of a patient’s genome has revolutionized the field of cytogenetics.

Legacy Cytogenetics Laboratory offers CMA testing in prenatal diagnosis, and as first-line testing for all cases referred for mental retardation of unknown etiology, autism spectrum disorders and developmental delay.

CMA testing in prenatal diagnosis, the first of its kind in Oregon, uses an algorithm that serves our patients both medically and economically. The use of CMA in prenatal diagnosis is supported by data from the National Institutes of Health (NIH). In prenatal CMA trial studies, the NIH showed that 6 percent of cases referred for prenatal diagnosis through an amniocentesis or chorionic villi sampling revealed a clinically relevant abnormality using CMA. This occurred when a structural abnormality was found by ultrasound and when classical cytogenetic analysis revealed a normal karyotype (data presented at the Society for Maternal Fetal Medicine and American College of Medical Genetics 2012 annual meetings).

This is a significant percentage given that little is known about the actual phenotype of the fetus after birth. To better serve our patients financially, CMA testing is initiated only if abnormalities are not found with conventional preliminary tests. In short, once a structural abnormality is found on ultrasound, a preliminary study is initiated. This study
is a FISH screening test looking for common aneuploidy in the case of amniocentesis or a direct preparation following chorionic villi sampling. If the results from this preliminary study are abnormal, CMA becomes unnecessary and the long-term cultures are analyzed with classical cytogenetics. If the preliminary results are normal, CMA is initiated from amniotic fluid or villi. A back-up of the results from this preliminary study are abnormal, chromosomal microarrays as a first-line test in the initial postnatal evaluation of individuals with nonsyndromic developmental delay/intellectual disability, autism spectrum disorders and multiple congenital anomalies.

Although truly balanced rearrangements, such as reciprocal translocations and inversions, are not detected by arrays, these are relatively infrequent causes of abnormal phenotypes in this population (<1 percent). Therefore, available evidence in the literature strongly supports the use of CMA in place of G-banded conventional karyotyping as the first-tier cytogenetic diagnostic test for patients with the above described phenotypes. G-banded karyotype analysis should continue to be reserved for patients with obvious chromosomal abnormalities (such as common aneuploidies), a family history of chromosome rearrangement or a history of multiple miscarriages.

Legacy Cytogenetics has offered CMA for all cases referred for mental retardation of unknown etiology, autism spectrum disorders and developmental delay since 2010. Although routine conventional karyotyping has been the standard of care, the diagnostic yield does not exceed 5–10 percent. The American College of Medical Genetics has issued a practice guideline (Manning M. and Hudgins L., 2010), recommending the use of chromosome testing and personal interaction with referring clinicians and genetic counselors to assure patients have the best information available when making decisions during an emotional and vulnerable time.

New comprehensive respiratory virus panel
Legacy Laboratory Services is now offering a comprehensive respiratory virus panel, FilmArray RP, targeting Adenovirus, Coronavirus HKU-1, Coronavirus NL63, Influenza A (including targets for H1, H3, and H1N1), Influenza B, Rhinovirus, Human Metapneumovirus, Respiratory Syncytial Virus, ParaInfluenza 1, ParaInfluenza 2, ParaInfluenza 3, and ParaInfluenza 4. FilmArray RP, manufactured by BioFire Diagnostics (formerly Idaho Technology, Inc.) utilizes nested multiplexed polymerase chain reaction technology to amplify and simultaneously detect multiple viral targets.

Testing will be performed in the Legacy Central Microbiology Laboratory, and turn-around time is up to 24 hours, dependent on time of specimen receipt. Sample types accepted include nasopharyngeal swabs, nasal washes and bronchial washes. The FilmArray RP is recommended for inpatients being served by infectious disease specialists, pulmonologists, pediatricians and ICU specialists.

We use sophisticated microscopes equipped with high-resolution cameras, advanced chromosome analysis software and tissue culture technology. Advanced technology in tissue culture and automatic harvesting enables consistent high-quality and efficient testing strategies. Each specimen is processed with care and expertise, and the patient story remains personal. We follow patients from prenatal testing through delivery and from diagnosis through treatment. Referring physicians personally interact with patients, providing both continuity of care and proper follow-up during an emotional and vulnerable time.

Our ability to offer our patients the best available genetic testing will help them make decisions about their pregnancies that best suit their needs. We now can also allow for equal treatment and management of the emotions and vulnerability of those needing CMA for mental retardation and autism diagnoses.
Celebrating 20 years together

Serving patients, physicians, hospitals and employers since 1992, Legacy Laboratory Services remains committed to quality, service and innovation. Thank you for your continued support.