ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

FOR IMMEDIATE RELEASE

Kathy Moran, MBA
kmoran@acmg.net

The Application of Noninvasive Prenatal Screening Using Cell-free DNA in General Risk Pregnancies – The American College of Medical Genetics and Genomics Publishes its Highly Anticipated Evidence-based Review

BETHESDA, MD – May 24, 2022 | The American College of Medical Genetics and Genomics (ACMG) has released its second, highly anticipated systematic evidence-based review (SER): "The Application of Noninvasive Prenatal Screening Using Cell-free DNA in General Risk Pregnancies."

Noninvasive prenatal screening with cell-free DNA (cfDNA), also referred to as NIPS, was developed more than a decade ago and has quickly become integrated into routine prenatal care in many parts of the world. NIPS is a simple blood test that is very accurate in the detection of Down syndrome and several other chromosomal disorders. It is performed at any time after 10 weeks of pregnancy. It identifies fragments of the placenta that circulate in maternal blood. These fragments originate from the new pregnancy and, therefore, identify the fetal chromosomal makeup. This test is used worldwide but, in the United States, there are limitations of insurance coverage on who is eligible to receive this test as a covered benefit. Many insurers cover only those at higher risk, such as patients of advanced maternal age.

"We are pleased to report this systematic evidence review on cell-free DNA screening in pregnancy in a predominantly general risk population to consolidate the available recent data on various types of aneuploidies, twin gestations, maternal conditions and cost considerations regarding this test," said co-author Nancy C. Rose, MD, FACMG. "We hope that this report will inform public health policies in this area of care."

To determine if scientific evidence would support a recommendation to offer NIPS in general-risk pregnancies, the ACMG performed a systematic evidence review. (An SER focuses on a specific scientific question and then identifies, analyses and summarizes the findings of relevant studies.) Clinical and laboratory geneticists, a genetic counselor, and ACMG methodologists developed research questions to guide the research. These questions included determining the test performance of NIPS in screening for the most common chromosomal disorders (Down syndrome (Trisomy 21), Edwards syndrome (Trisomy 18), and Patau syndrome (Trisomy 13)) in singleton and twin pregnancies. In addition, the researchers wanted to determine

-more-

how well NIPS worked in screening for sex chromosome abnormalities, copy-number variant disorders like DiGeorge syndrome, or other rare chromosome trisomies. Additional questions considered the impact of genetic counseling, the economic impacts associated with NIPS, and the ability of NIPS to detect maternal conditions, such as cancer.

Eighty-seven studies were included in this systematic evidence review. NIPS was highly accurate in identifying sex chromosome abnormalities (>99%) and the most common trisomies in singleton and twin pregnancies.

This systematic evidence review found that NIPS' accuracy, positive and negative predictive values, and overall test performance is extremely high for Trisomies 13, 18, and 21—higher than the most commonly used prenatal screening options—and is not limited to specific timing windows during the pregnancy.

Though NIPS test performance varied for other conditions, its high accuracy for the most common disorders mean fewer pregnant individuals may be mislabeled as high risk and have to undergo confirmatory testing. Overall, the results of this evidence review demonstrate that the test performance of NIPS is higher than those reported for traditionally used screening methods. This information can be used to set new standards for clinical care in the US.

Co-author Marco L. Leung, PhD, FACMG said, "This SER validates the high sensitivity and specificity of NIPS in the detection of common trisomies, as well as the variable performance in rare autosomal trisomies and copy number variants. This SER may serve as a valuable resource for laboratories that are optimizing their NIPS assays, and for clinicians who are evaluating the utilization of this technology in their medical practices."

The SER concludes that using cell-free DNA is the most effective screening test for the autosomal trisomies 21, 18 and 13 in singleton and twin gestations, with both high detection and low false positive rates. Although less accurate for sex chromosome aneuploidies, rare autosomal trisomies and copy number variants, it is the only laboratory-based prenatal screen that can identify these at all at this time. Despite its accuracy, NIPS by cfDNA is a screening for which confirmation of a screen positive test with a diagnostic procedure remains indicated.

"In addition to providing the evidentiary foundation for an upcoming guideline from ACMG, this systematic evidence review is a remarkably comprehensive study that stands on its own merits," said ACMG's CEO Max Muenke, MD, MBA, FACMG.

-more-

ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

About the American College of Medical Genetics and Genomics (ACMG) and ACMG Foundation

Founded in 1991, the American College of Medical Genetics and Genomics (ACMG) is the only nationally recognized medical professional organization solely dedicated to improving health through the practice of medical genetics and genomics, and the only medical specialty society in the US that represents the full spectrum of medical genetics disciplines in a single organization. The ACMG is the largest membership organization specifically for medical geneticists, providing education, resources and a voice for more than 2,500 clinical and laboratory geneticists, genetic counselors and other healthcare professionals, nearly 80% of whom are board certified in the medical genetics specialties. ACMG's mission is to improve health through the clinical and laboratory practice of medical genetics as well as through advocacy, education and clinical research, and to guide the safe and effective integration of genetics and genomics into all of medicine and healthcare, resulting in improved personal and public health. Four overarching strategies guide ACMG's work: 1) to reinforce and expand ACMG's position as the leader and prominent authority in the field of medical genetics and genomics, including clinical research, while educating the medical community on the significant role that genetics and genomics will continue to play in understanding, preventing, treating and curing disease; 2) to secure and expand the professional workforce for medical genetics and genomics; 3) to advocate for the specialty; and 4) to provide best-in-class education to members and nonmembers. *Genetics in Medicine*, published monthly, is the official ACMG journal. ACMG's website, www.acmg.net offers resources including policy statements, practice guidelines, educational programs and a 'Find a Genetic Service' tool. The educational and public health programs of the ACMG are dependent upon charitable gifts from corporations, foundations and individuals through the ACMG Foundation for Genetic and Genomic Medicine.

-end-