For NIPT laboratories, a new proficiency test in 2018

Glenn Palomaki, PhD

September 2017—The CAP Surveys program is offering for 2018 a novel external proficiency test for laboratories that perform screening of cell-free (cf) DNA in maternal plasma for common aneuploidies.

Dr. Palomaki

Next-generation sequencing-based cfDNA testing was first offered clinically in 2011 and is now made available by a dozen or more U.S. laboratories to hundreds of thousands of pregnant women annually. The new noninvasive prenatal testing, or NIPT, Survey fills the final gap identified by laboratories, professional organizations, and others for oversight of all laboratories offering such testing.

In the United States, all clinical testing is performed using laboratory-developed tests employing at least four different methods. The optimal proficiency testing material would simulate maternal plasma with a mixture of fetal/placental and maternal cfDNA and be suitable for all laboratories offering such testing regardless of method (e.g. shotgun, targeted, SNP-based). External quality assessment schemes in China and the European Union use artificial samples for PT material. This choice may be reasonable given the large number of laboratories using approved kits for testing, while in the U.S. we are faced with a wide array of unique laboratory-developed tests. However, recent data from the collaboration of EU partners show that the artificial material distributed to 43 laboratories (excluding those using the SNP-based method) resulted in 11 percent of labs unable to report results for one or more samples. Both false-positive and false-negative results occurred. Their conclusion indicates that current artificial samples may not be adequate for this purpose.

The CAP has completed three pilot trials of proficiency testing for NIPT to optimize its PT program. Based on the data from the pilot studies, the CAP has chosen real patient samples as the optimal PT material at this time. As such, the PT program will be accuracy based rather than consensus based. This is because challenges from affected pregnancies will have been confirmed by both a clinical cfDNA test and further diagnostic testing (e.g. invasive procedure and karyotype). Having PT samples based on real patient material is uncommon and relatively expensive, but it is virtually guaranteed to be an acceptable sample for any current or future technology based on cell-free DNA in maternal plasma.

The NIPT proficiency testing program is under the auspices of the CAP/American College of Medical Genetics and Genomics Biochemical and Molecular Genetics (BCMG) Resource Committee, and a subcommittee of that group investigated for more than three years how best to offer PT. Karen Weck, MD, previous BCMG chair, was and continues to be a strong supporter of developing this PT program, saying, “Given the rapid uptake of this testing across the country and the large numbers of pregnant women affected, it is extremely important that CAP provide a PT program to ensure the quality and accuracy of testing.” Members of the CAP Next-Generation Sequencing Workgroup and the CAP Personalized Health Care Committee assisted the BCMG committee in its deliberations. To aid CAP inspections of laboratories that offer such testing, new requirements for cfDNA testing for aneuploidy were added in 2013 to the NGS section of the Laboratory Accreditation Program molecular pathology checklist. The new PT program can be found in the 2018 Surveys catalog.
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Dr. Palomaki is a member of the CAP/ACMG Biochemical and Molecular Genetics Resource Committee, and he led efforts as a member of the maternal screening subcommittee to explore how best to provide proficiency testing for NIPT. He is a professor in the Department of Pathology and Laboratory Medicine, Warren Alpert Medical School of Brown University and Women and Infants Hospital, Providence, RI.

The other members of the maternal screening subcommittee are Edward Ashwood, MD, of the University of Colorado, Denver; Robert Glen Best, PhD, of the University of South Carolina; and Philip Wyatt, MD, PhD, of Esoterix Genetic Laboratories, Santa Fe, NM. George J. Knight, PhD, of Women and Infants Hospital, is subcommittee advisor.

For more information about the NIPT PT program, visit www.cap.org, *Shop tab.*