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Cell-free DNA screening study reveals range of chromosomal abnormalities

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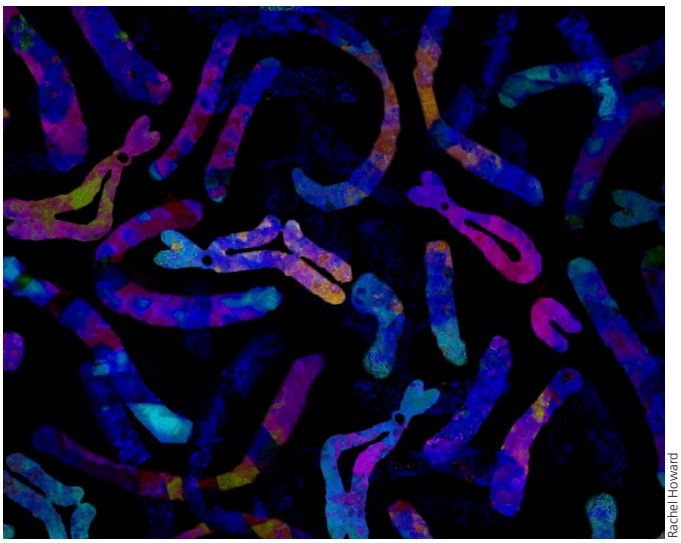
A comprehensive study of at-risk pregnant women in the Netherlands has revealed a wider range of chromosome aberrations than the common aneuploidies typically targeted by noninvasive prenatal screening (NIPS). Investigators leading the TRIDENT study (Trial by Dutch laboratories for Evaluation of Non-Invasive Prenatal Testing) report that about one-third of chromosomal aberrations detected over one year of screening were different from trisomy 21, 18, and 13. The study included 2,527 cases of women at elevated risk who elected noninvasive prenatal screening (NIPS) rather than invasive testing. Trisomy 21, 18, or 13 was subsequently diagnosed in 78 (3.1%) of the cases. Another 41 (1.6%) had other chromosome aberrations. Follow-up testing confirmed fetal, placental, or maternal origin of the chromosome aberration in, respectively, 25%, 55%, and 2% of the abnormal cases. All of the detected fetal chromosome anomalies were clinically significant and relevant for pregnancy management. Recently, the American College of Medical Genetics and Genomics did not recommend screening for autosomal aneuploidies other than those involving chromosomes 21, 18, and 13. But the new study reveals that "rare" fetal chromosome anomalies, when combined, are actually more frequent than trisomy 13 and almost as frequent as trisomy 18. The authors make an argument that there is clinical utility in performing genome-wide NIPS beyond the currently recommended autosomal aneuploidies of chromosomes 21, 18, and 13. —*Karyn Hede, News Editor*



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Population screening for *BRCA1/2* yields early cancer diagnoses

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Women with no known family history of breast cancer or those who don't know their family history are unlikely to undergo a genetic test for breast cancer–associated genes. The use of such tests as a screening tool could enable early cancer diagnoses, but its clinical utility has not been demonstrated. As a first step in that direction, investigators at Geisinger Health System in Pennsylvania used data gathered as part of a community whole-exome sequencing project to show that population screening can lead to early cancer diagnoses. The initiative encompasses 76 genes with potentially medically actionable variants. Between 2014 and April 2017, 55 participants and their doctors were notified of a clinically confirmed pathogenic/likely pathogenic *BRCA1/2* variant and followed for at least 12 months. Of the 26 (79%; 15 women, 11 men) who acted on the information, three were diagnosed via these procedures with an early-stage, *BRCA1/2*-associated cancer, a subclinical phenotype revealed through evaluation. These cancers were found in individuals lacking a family history, suggesting that genomic screening programs for *BRCA1/2* variants could help identify at-risk individuals who would not otherwise realize their elevated risk. The authors suggest two important factors in making a similar screening program work in other health-care settings: "(i) an *integrated* health-care system capable of managing cases from genome-scale testing through evaluation and risk management and (ii) a *learning* health-care system committed to studying the outcomes of clinical interventions."—*Karyn Hede, News Editor*