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Review points to need for public pre-natal database

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Prenatal exome sequencing can enable molecular diagnoses when standard genetic testing yields no diagnosis to families searching for answers. In their review article, Vora and Hui cover the landscape of advanced prenatal 'omics—both its promise and pitfalls. The authors cover both genomic and transcriptomic technologies, which have both revealed new insights into human development. The technologies have begun to assist in fetal diagnosis and have advanced to the point that placental function can be noninvasively sampled through maternal plasma cell-free RNA. Excitement surrounds the possibilities, but the authors point out that variant interpretation and pre- and posttest counseling remain highly challenging for clinicians. While the American College of Medical Genetics and Genomics and other professional organizations do not recommend exome sequencing for routine use in prenatal diagnosis, in select prenatal cases in which standard approaches have failed to offer an informative finding, exome sequencing can be offered as another option. When a fetus has structural abnormalities or homozygosity indicates consanguinity (or closer parental relatedness) on microarray, exome sequencing can also play a role. In addition, the technique can be more cost effective than sequencing individual genes using a targeted molecular panel. The authors argue that, given the rate of discovery, it would

be useful to the research community to have a shared prenatal database with genotype and phenotype information. A shared database would enable researchers to search for similar phenotypes and increase the confidence in pursuing novel gene discovery functional studies if there are multiple families with genotype/phenotype correlation. The review also covers transcriptomics and the use of RNA sequencing to study pre- and postimplantation embryology, stem cell biology, organogenesis, fetal maturation, and placental physiology. —Karyn Hede, News Editor

Long-term follow-up shows value of newborn screening

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When children born with metabolic disorders receive early treatment, their health outcomes are often much better than those of children who don't receive early diagnosis and treatment. But demonstrating that benefit at the population level has been a challenge for state-run newborn-screening programs. Investigators in California are now reporting five-year follow-up data for infants born between 7 July 2005 and 31 December 2009. Their long-term data reveal the success of screening for health outcomes and provide a model for other states seeking resources for their own follow-up programs. The California Department of Public Health's Genetic Disease Screening Program has tracked all newborns with initial screen-positive test results for 1 of 20 primary metabolic disorders and documented treatment received through a network of metabolic specialty care centers. The cohort reported in this issue represents an extension of the 3-year data reported in *GIM* (*Genet Med* 2014;16:484–490) in 2014. By age 5, more than half ($n = 235$; 55.2%) of the original 426 patients remained in active care compared with 82.6% ($n = 352$) in active care at age 1. Over the cumulative 5 years, 20.4% ($n = 87$) of the 426 patients were lost to follow-up, 8.7% ($n = 37$) moved out of state, 6.3% ($n = 27$) were determined to require no further follow-up, 4.7% ($n = 20$) refused follow-up, and 4.7% ($n = 20$) died, with most ($n = 13$; 65%) dying within two months of birth. The results for patients and families who stayed in active care versus those who dropped out of care were not influenced by demographic characteristics or ability to pay. Some of the data suggest that barriers to care exist for families that have transportation challenges or language barriers. The cost of collecting follow-up data is covered by revenue from the screening fees for approximately 500,000 newborns each year. The authors suggest that other states may wish to consider raising their test fees to cover collection of long-term follow-up data. —Karyn Hede, News Editor