Infant DNA sequencing finds genetic disorders that standard testing misses

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The purpose of the study is to determine whether infants derive health benefits from having genomic information available from the very first days of life. DAVE KOTINSKY / GETTY IMAGES

Researchers have identified potentially harmful genetic diseases in infants whose DNA was sequenced at birth — illnesses that would not have been detected by blood tests routinely given to newborns.

While fewer than 90 infants have undergone the test — called “whole exome sequencing” — five were found to have genetic variants that could affect their health, said Shawn Fayer, manager of the BabySeq Project hosted by two Boston-area hospitals and Harvard Medical School. The test analyzes 1,800 genes, about 1,000 of which are known to be implicated in childhood health.

Robert Green is the lead investigator for the BabySeq Project.
GRETCHEN ERTL / PNG

Lead investigator Robert Green of Brigham and Women’s Hospital, Harvard Medical School and the Broad Institute presented his findings to the American Society of Human Genetics annual meeting Wednesday in Vancouver.

The early results suggest there may be real value in sequencing infants, even when they have no family history of genetic disease, said Fayer, a genetic counselor at Brigham and Women’s Hospital.

“You never know when you start a project what is going to happen,” he said. “But in these early days, we are getting a lot of actionable results.”

One infant was found to have partial biotinidase deficiency, a treatable metabolic disorder that would not be detected by standard blood tests widely administered in North America.

“Partial biotinidase deficiency symptoms generally arise under stress, like another illness,” said Fayer. “Symptoms would likely have appeared if the child had become sick from something else, which makes it very difficult to diagnose. Those parents were very happy to be part of the study.”

Two infants found to have genetic heart disorders were referred for cardiac care.

The project recruits newborn infants and their families from an intensive care and a well-baby nursery. Researchers take a family medical history then randomly assign infants to one of two groups. One group undergoes exome sequencing and followup counselling and the other group does not. About 170 families have been recruited to date.

The purpose of the study is to determine whether infants derive health benefits from having genomic information available from the very first days of life, said Green. The study will also measure medical benefits, harms and the costs associated with infant sequencing as well as parents’ attitudes and anxieties.

The test and its interpretation still costs several thousand dollars per patient in the research setting, but recently commercial whole genome tests have been advertised for as little as $1,000.

When genetic disorders are detected, they generally fall into one of three categories: an inherited disease that causes illness in childhood, that the child is a carrier of a genetic disease that could affect his or her offspring, or a dangerous sensitivity to medications.

The standard blood tests given to infants typically screen for about 50 disorders. The exome sequence can detect roughly 600 other childhood-onset conditions, said Fayer.

“Some of these conditions are one in a million, but a few are more common, like retinal blastoma is about one in 10,000,” he said. “Still rare, but in a (large) population you will find quite a few individuals affected.”

So far, only 15 per cent of families approached for BabySeq consent to a briefing on the project. About half of those decline to participate, citing concerns about privacy and the potential for genetic discrimination by life and health insurers.

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