



GENOMICS

Researchers to Explore Promise, Risks Of Sequencing Newborns' DNA

Last week, U.S. human geneticists moved into perhaps their most sensitive ethical territory yet: whether it might someday make sense to sequence every newborn's genome so the information can be used in the child's medical care. That prospect raises a host of questions about what parents should be told about their baby's genes. Should they know, for example, that their child is at high risk for cancer later in life?

"We can see the potential value of looking at an infant's genome to examine all of the genes or perhaps a particularly informative subset of them," explained Alan Guttmacher, director of the National Institute of Child Health and Human Development (NICHD), in rolling out a \$25 million, 5-year federal research program to explore these issues. Genome testing could supplement the decades-old state screening programs that take a drop of blood from nearly every newborn's heel and test it for biochemical markers for several dozen rare disorders. Diagnosing a child at birth can help prevent irreversible damage, as in phenylketonuria, a metabolic disorder that can be controlled with diet.

Screening often turns up false positives, however, which genetic tests might help avoid. And genome sequencing could potentially look for all 7000 or so diseases caused by defects in single genes. Ever-cheaper sequencing is making this more feasible: An entire genome now costs \$5000,

and decoding just protein-coding DNA—the "exome"—can be done for \$1000, compared with several hundred dollars to test for a single genetic mutation.

But genome sequencing, unlike the current newborn screening tests, could potentially reveal many more unexpected genetic risks, some for untreatable diseases. Which of these results should be divulged is already controversial. Sparks are still flying over a report in March from the American College

Studies on Benefits and Risks of Newborn Genomic Sequencing

| Institution | Number of infant genomes | Objectives include |
|--|--------------------------|--|
| Brigham and Women's, Boston Children's hospitals, Boston | 120 sick, 120 healthy | Study how parents and doctors use genomic data |
| Children's Mercy Hospital, Kansas City, Missouri | 500 sick | Diagnose genetic disorders within 24 hours |
| University of California, San Francisco | ~1250 sick, ~200 healthy | Assess parent interest in drug metabolism genes |
| University of North Carolina, Chapel Hill | 200 sick, 200 healthy | Study how to share results with multicultural families |

New ground. Four projects funded at a total of \$25 million over 5 years will look at how genome testing could improve newborn screening and other questions.

of Medical Genetics and Genomics (ACMG) that listed 57 disease risk mutations that should be reported to a patient (or to a child's parents) when his or her genome is sequenced as part of routine clinical care (*Science*, 29 March, p. 1507).

To explore how sequence data from newborns might be used in medical care, as well as the related ethical, legal, and social issues, NICHD and the National Human Genome Research Institute are funding four pilot projects. All will examine whether genomic infor-

Handle with care. Genome testing could enhance newborn screening, but it raises ethical issues.

mation can improve the accuracy of newborn screening tests, but they differ in which additional genes they will test and what results they will offer parents.

One group will use sequencing for very sick newborns to help diagnose their illness quickly. Lead investigator Stephen Kingsmore at Children's Mercy Hospital in Kansas City, Missouri, wants to halve the time for his current 50-hour test, which he has used to diagnose genetic disorders in up to 50% of infants in his hospital's neonatal intensive care unit. The test homes in on a subset of genes that may explain the baby's symptoms. While his group may ask parents if they're interested in unrelated genetic results, the focus is on "a critically ill baby and a distressed family who want answers," Kingsmore says.

A team at the University of North Carolina is studying how to return results to the poor and others who might not be familiar with genomics. But it is also dividing genetic findings into three categories—mutations that should always be reported; those that parents can choose to receive, which might include risk genes for adult cancers; and a third set that should not be disclosed. That last set includes risk genes for untreatable adult-onset diseases such as Alzheimer's.

A team at Brigham and Women's Hospital in Boston and Boston Children's Hospital hopes to learn how doctors and parents will use genomic information. "We're trying to imagine a world where you have this information available, whether you're a sick child or healthy child. How will it change the way doctors care for children?" asks co-principal investigator Robert Green of Brigham and Women's, a lead author of the ACMG report on unexpected findings.

Genome sequencing might never replace existing newborn screening because of its costs and the complexity, says ethicist Jeffrey Botkin of the University of Utah in Salt Lake City. But he and others say it is important to explore these issues because wealthy, well-informed parents will soon be able to mail a sample of their baby's DNA to a company to have it sequenced—regardless of whether medical experts think that's a good idea. "There's an appetite for this. It will be filled either within the medical establishment or outside of it," Green says.

—JOCELYN KAISER