Are you ready to explore baby's genome?

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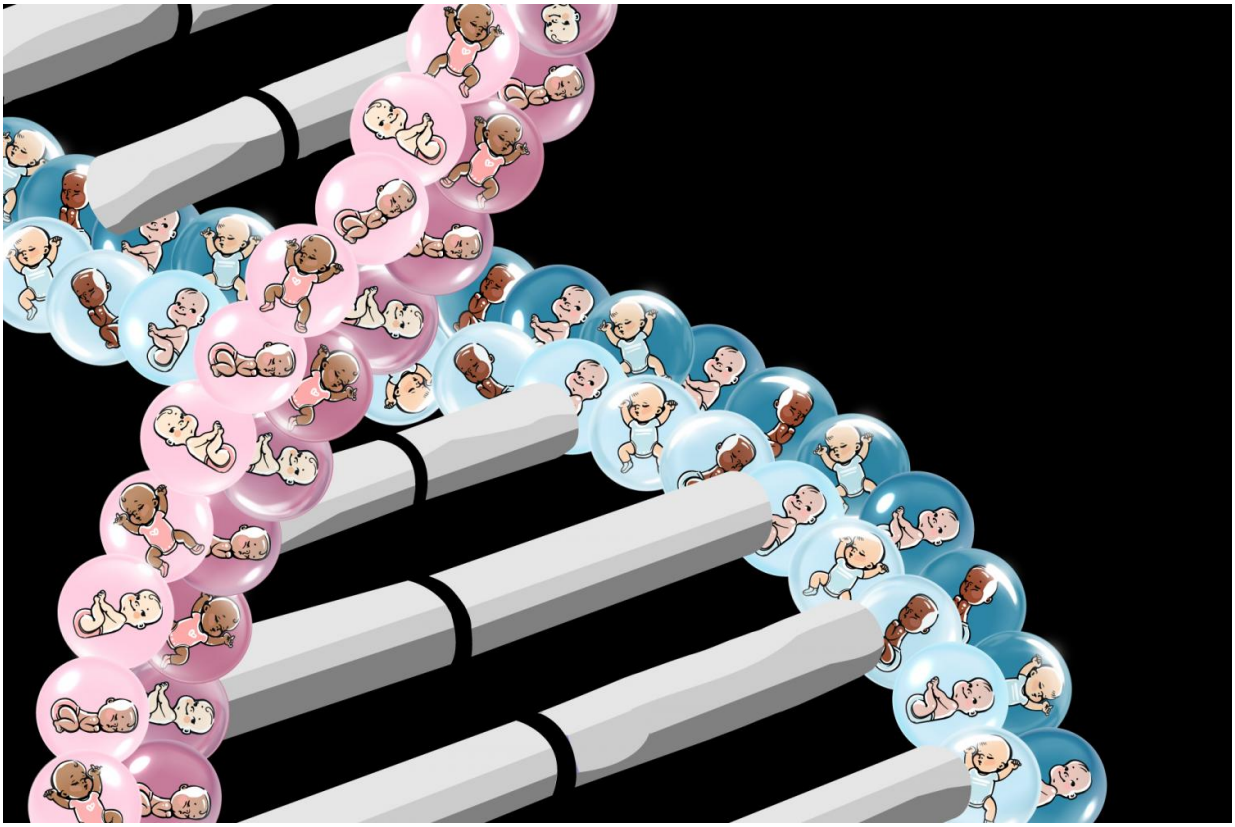


What should parents learn about their baby's genome? What shouldn't they? Credit: Christ-claude Mowandza-ndinga

When you have a baby, a nurse or a phlebotomist performs a heel stick to take a few drops of blood from your infant and sends it off to a state lab for a battery of tests. Most of the time, you never hear about the results because your child is fortunate enough to not have a rare disease,

such as cystic fibrosis or sickle cell disease or any of the dozens of conditions for which most states screen. You, as a parent, may not even remember hearing about newborn screening.

Newborn screening is mandatory in most states, unless parents refuse for religious or other reasons. Screening is generally accepted because screening is only performed for a small number of conditions where measures are available to save the baby's life or mitigate the harms of such conditions, if found early enough. However, now that scientists have developed methods for sequencing the entire genome, what would happen if states began incorporating genome sequencing to find out more about baby's health? How would that work? What should parents learn about their baby's genome? What shouldn't they?

To study these questions, through funding from the National Institutes of Health (NIH), researchers and doctors across the country have formed a consortium called NSIGHT, which includes four NIH grants spanning multiple institutions:

- University of North Carolina School of Medicine
- UC-San Francisco School of Medicine
- Brigham and Women's Hospital/ Boston Children's Hospital and Baylor College of Medicine
- UC-San Diego Rady Children's Institute for Genomic Medicine and Children's Mercy Kansas City

This consortium will work with parents and conduct genomic sequencing on newborns to develop evidence that may support guidelines for how this new technology could be effectively and appropriately incorporated into newborn screening or the care of newborns.

"Where is the boundary of parental responsibility to learn important health information about their child versus delving too far into genetic

information that could take away from that child's ability to make decisions for themselves?" said Jonathan Berg, MD, PhD, associate professor of genetics at the UNC School of Medicine and corresponding author of a paper about the consortium's work, published today in the journal *Pediatrics*. "This is one of the main bioethics questions of our time: how much should we protect a child's capacity to make decisions about what information to learn, or not to learn, about themselves when they become adults? Some people think this concern is an old, quaint notion that is being made obsolete by technology. And some people believe fervently that it could infringe on the child's autonomy or potentially even harm the child if parents learned or intervened too much."

One clear example is Huntington's disease. Is it the right of the parent to know that their child harbors the genetic lesion that underpins this terrible disease, even though manifestations are unlikely to develop until adulthood? What about an untreatable neurodegenerative disease that will present during childhood? What if early intervention might help, but the disease might not present until the child is an adult?

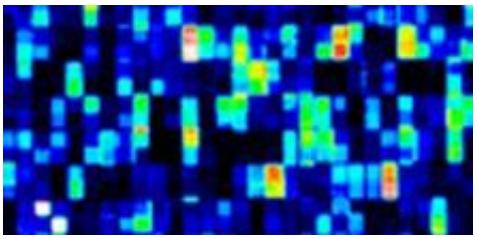
Regardless of what people might think, Berg said, "Technology is forcing this decision-making process on us." The cost of genome sequencing has plummeted in recent years, meaning the national public health system and the broader medical community need to figure out how to address these kinds of issues, and soon. Through the NIH-funded NSIGHT consortium, researchers and doctors are laying the groundwork.

The lead NSIGHT institutions are spearheading the four studies across the country to address three clinical scenarios:

- Diagnostic: using genome sequencing to find the specific genetic causes of congenital anomalies or unexplained illnesses in babies

admitted to neonatal intensive care units.

- Preventative: using genome sequencing to screen healthy newborns for preventable or treatable conditions that genetic sequencing could detect or help confirm.
- Predictive: using genome sequencing to explore the entire genome of the child, as a resource for health care throughout the course of the child's life.



Currently, NISIGHT doctors and researchers are consulting with parents and soon-to-be parents to learn about their concerns and their personal decision-making processes regarding genome sequencing for various purposes, including finding health information that could be clinically useful immediately.

"We're learning when the best time is to approach parents," Berg said. "Clearly, immediately after birth we can't just say to a new mom and dad, 'we'd like to talk to you for a few hours about your thoughts on sequencing your child's entire genome.'

"We're learning what kinds of decision aids and other resources parents need, such as genetic counseling. We're wrestling with how to implement this in practice when we already have a shortage of genetic counselors in

the United States. We can't have every single couple sit down with a genetic counselor, but we could have them go through an online decision aid."

The NSIGHT project based in Boston is co-led by Robert Green, MD, of the Division of Genetics at Brigham and Women's Hospital and Alan Beggs, PhD, of the Manton Center for Orphan Disease Research at Boston Children's Hospital and Professor of Pediatrics at Harvard Medical School, who co-authored the *Pediatrics* paper.

"Simply putting together all the pieces to design these complicated research projects is an ambitious undertaking, as described in today's article," said Green, who is also a physician-scientist at Harvard Medical School and The Broad Institute. "But it is absolutely essential that we find ways to rigorously measure the clinical utility of new technologies so that we can apply them responsibly, and that is the focus of the BabySeq Project, and of the other NSIGHT projects."

Beggs added, "Genome sequencing is a new and still enormously complex process, and oftentimes the results have uncertain implications. These studies represent some of the first organized approaches to developing the best practices for determining the right information and best ways to return it to parents and their babies' doctors."

UNC's Berg said the consortium is finding that while many parents simply aren't interested in genomic sequencing for their newborns, there's a subset of parents who want to dive into the genetic information. "Perhaps it would be appropriate to focus our genetic counseling resources on them," he said.

"The bottom line is this," Berg added. "We hope that the information we get from these studies will help us make recommendations for how to best roll out some form of newborn genomic screening in the future."

All sites are still enrolling.

Aside from the main sites, NSIGHT includes researchers and administrators from the National Institutes of Health (the National Human Genome Research Institute, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the National Center for Advancing Translational Sciences), RTI International, University of California-Berkeley, American College of Medical Genetics and Genomics, Harvard Medical School, University of Illinois-Chicago School of Public Health, California Department of Public Health, Oregon Health & Sciences University, University of Washington, and UCSF Benioff Children's Hospital San Francisco.

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