Is it time to test embryos for common diseases?

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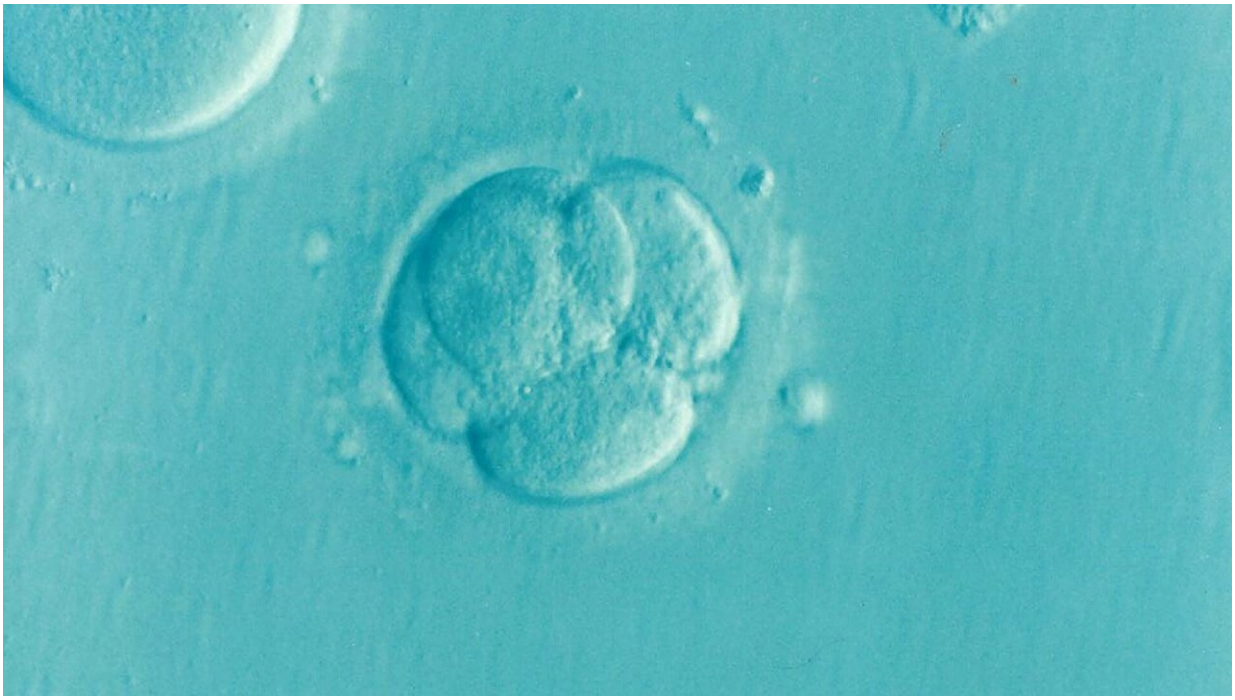

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A Silicon Valley company has designed a technique to decipher the genetic code of a tiny embryo and calculate its future risk of cancer, diabetes and 10 other common diseases—presaging a day when parents could select children with a greater chance of living a healthier life.

"Some parents are really worried about a specific disease in their

family," said pediatric medical geneticist Dr. Akash Kumar, co-founder of MyOme, a Menlo Park-based genome sequencing company. "Our hope is that by providing information relevant to the diseases that they care about, they can feel like they're more empowered."

For now, this powerful and potentially life-tinkering advance is still in the research phase and only applies to embryos conceived through in vitro fertilization (IVF), not ones naturally conceived. But if it becomes commercially available, it could relieve the burden on families and health systems, by reducing the number of people born at risk of those illnesses. Kumar's team reported its findings in the March 21 issue of the journal *Nature Medicine*.

Still, bioethicists and fertility experts warn, there is not yet a full understanding of the technique's potential benefits—or dangers.

While such testing sounds seductive, it raises an unsettling ethical question: When it is right for prospective parents to do "quality control"?

"I wouldn't do it, or recommend others do it," without proven accuracy and careful genetic counseling, said Hank Greely, director of Stanford Law School's Center for Law and the Biosciences and author of the book "The End of Sex and the Future of Human Reproduction," which explores the ethical and legal challenges posed by new reproductive technologies.

"Does it make sense to look for relatively small risks in conditions that may well happen long in the future—if at all—and to use those as the basis for selecting embryos?" he asked.

Genetic testing of embryos is usually offered only to families at risk of deadly and incurable single-gene disorders such as Huntington's or Tay-

Sachs disease. It spares parents the heartbreak of conceiving a child who will inevitably sicken.

What's new—and controversial—is the technique's ability to assess an embryo's risk for much more common, genetically complex and treatable inherited diseases, such as breast and prostate cancer. Such genetic risk prediction is being tested in adults but, until now, has not been applied to embryos.

The technique used in the study, called preimplantation genetic testing, or PGT, can only be done on embryos created using IVF, where eggs and sperm meet in a Petri dish. That alone is an emotionally and financially draining procedure—but also increasingly common, representing at least 5% of all births in metro areas such as San Francisco.

IVF embryos are already judged on general fitness, such as the number and quality of their cells. Only the best embryos are implanted; lesser embryos are stored or discarded.

The research team—a collaboration of physicians, bioinformatics experts, computer engineers and others with MyOme, the San Carlos DNA testing company Natera, and the Bay Area-wide fertility clinic Spring Fertility—is now expanding the effort, enrolling 20 couples in the Bay Area who are using IVF.

The practice would be legal in the United States because such procedures are self-regulated by the clinicians who provide them.

The researchers agree that the clinical utility of its approach remains to be proven. The exercise was strictly experimental, said the Stanford-trained Kumar.

Applying powerful computational tools to parental and embryonic DNA,

the team reconstructed the full genomes of 110 five-day-old embryos from 10 couples who had undergone in vitro fertilization. When matched against the genome of the resulting baby, it was 98% accurate. The method is much more accurate than the current approach of gene sequencing from only the embryo, they said.

Then they peered into the genome to predict the embryo's susceptibility for common diseases that may develop decades later: breast cancer, colorectal cancer, pancreatic cancer, prostate cancer, atrial fibrillation, coronary artery disease, Chron's disease, ulcerative colitis, lupus, vitiligo, and Type 1 and Type 2 diabetes.

Each embryo was assigned a "risk score," based on a calculated percentage that it would develop a specific disease. Such scores are possible because scientists have large genetic data sets of adults with these ailments.

In one example, some embryos in the study had double the risk of atrial fibrillation than others.

In another example, 13 of 20 embryos from a couple with a family history of breast cancer were found to carry the pathogenic BRCA1 mutation, which may greatly increase the chance of breast cancer and ovarian cancer.

Such testing demands a broader societal discussion before it moves beyond the research setting, said bioethicists.

By the time today's embryos are adults, there may be effective treatments for these diseases, they noted.

There are other issues. For instance, not enough is currently known about the complex genetic contributors to these diseases to create tests that are

accurate enough for embryo selection, said Art Caplan, professor of medical ethics at NYU Langone Medical Center.

Many common diseases are influenced not just by genetics, but also by the environment, such as smoking, exercise and access to healthy foods, he added.

Almost all of us have some genetic risk of these diseases, he added.

"As much as we want to believe that we can test our way to immortality, it's just not true. Everybody flunks genetic tests," he said. "We're all going to get sick from something."

If such tests are someday proven to be accurate and useful, "parents, if well counseled, should be able to make their own decisions" about its use, said Stanford's Greely. "But one can reasonably worry about just how well counseled or informed the patients will be."

But before tests are widely available to the public, the U.S. must set standards of reliability and accountability, said Caplan.

"I don't think people would be well served," he said, "by getting a printout: 'Here's your kid's profile.'"

More information: Akash Kumar et al, Whole-genome risk prediction of common diseases in human preimplantation embryos, *Nature Medicine* (2022). DOI: 10.1038/s41591-022-01735-0