

'Genetic biopsy' of human eggs might help pick the best for IVF

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Given the stakes of in vitro fertilization, prospective parents and their doctors need the best information they can get about the eggs they will extract, attempt to fertilize, and implant. New research at Brown University and Women & Infants Hospital of Rhode Island has found a way to see which genes each egg cell is expressing without harming it. As researchers learn more about how those genes affect embryo development, the new technique could ultimately give parents and doctors a preview of which eggs are likely to make the most viable embryos.

In the research, now in press in the *Journal of Biological Chemistry*, the team of physicians and biologists were able to sequence the transcribed genetic material, or mRNA, in egg cells and, in a scientific first, in smaller structures pinched off from them called "polar bodies." By comparing the gene expression sequences in polar bodies and their host eggs, the researchers were able to determine that the polar bodies offer a faithful reflection of the eggs' genetic activity.

"We can now consider the [polar body](#) a natural cytoplasmic biopsy," said study co-author Sandra Carson, professor obstetrics and gynecology at the Warren Alpert Medical School of Brown University and director of the Center for Reproduction and Infertility at Women & Infants Hospital.

Polar bodies are where egg cells dispense with the second copies of chromosomes that, as sex cells, they don't need. But the polar bodies also

capture a microcosm of the egg's mRNA, the genetic material produced when genes have been transcribed and a cell is set to make proteins based on those genetic instructions.

Pairs of genes

Last year the team became the first to find mRNA in human polar bodies. Now they have transcribed it in 22 pairs of human eggs and their polar bodies, and confirmed that what is in the polar bodies is a good proxy for what is in the eggs.

Given how little mRNA is present in polar bodies, the task was not easy, said Gary Wessel, professor of biology, but through a combination of clever amplification and analysis techniques by lead author and graduate student Adrian Reich and second author Peter Klatsky, the team got it done.

"There's no reason this should have worked, just because there was so little material," Wessel said. "Single-cell sequencing is very challenging."

To hedge their bets the team analyzed most of their samples in two pools of 10 cells each, for instance comparing the mRNA in 10 eggs with the mRNA in the 10 related polar bodies. But to their pleasant surprise, they were also able to sequence two individual eggs and their polar bodies directly.

What they found is that more than 14,000 genes can be expressed in the eggs. Of those, more than 90 percent of the genes detected in the polar bodies were also detected in the eggs and of the 700 most abundant genes found in the polar bodies, 460 were also among the most abundant in the eggs.

Toward clinical use

"It seems that the polar body does reflect what is in the egg," Carson said. "Because the egg is the major driver of the first three days of human embryo development, what we find in the polar body may give us a clue into what is happening during that time."

But Carson and Wessel acknowledged that more research will be required to create a clinically useful tool.

Finding which genes affect embryo viability is the next major step. With the new knowledge and techniques developed in their study, the researchers said, scientists could analyze the mRNA from polar bodies of eggs that are fertilized and track the progress of the resulting embryos. Once the key genes are known, they could create fast assays to look for those [genes](#) in polar bodies so that clinicians and patients could pick the best eggs. A sufficiently developed technology could also be used for choosing which [eggs](#) to bank for later use.

"We don't quite have the answer of what those messages are doing exactly or necessarily the purpose of them in the cell function, but that's to come," Carson said. "Now we have the words, but not the sentences."

Provided by Brown University

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