MedicalXpress

Researchers confirm key feature of age-related miscarriages and birth defects

April 14 2011

Washington State University researchers have confirmed a critical step in cell division that results in age-related miscarriages and birth defects, including Down syndrome.

Writing in the upcoming issue of the journal Current Biology, the researchers say they recreated the conditions in which an egg cell will continue to undergo cell division without properly arranging its chromosomes, creating offspring with aneuploidy, or an abnormal number of chromosomes. Sperm cells and those from elsewhere in the body will stop dividing until chromosomes are properly lined up.

"This paper says, yes, this cell does have a different way of controlling division and that makes it inherently error prone," said Pat Hunt, a professor of molecular biosciences.

The problem is particularly acute in older women.

"We think that by the time a woman is in her 40s, about half the eggs she's ovulating are probably chromosomally abnormal," said Hunt. "And for women in their 20s, it's probably about 10 percent. So it's a huge change."

Just why age would have such a powerful effect on an egg is still unclear, says Hunt, "but it does provide us some good basic knowledge that allows us to understand why in fact the egg is so different."

Co-author graduate student So Iha Nagaoka says the finding could lead to an in-vitro fertilization "screening system" that might sort out bad eggs.

"We would also like to find the gene or genes responsible for this insensitivity, but this might be a bit of a long shot," he says.

Between 15 and 20 percent of pregnancies end in miscarriages. Most are in the first 13 weeks, and more than half of those are the result of problems with chromosomes in the fetus, according to the American College of Obstetricians and Gynecologists. Fetuses with chromosomal abnormalities are carried to term in 1 of 160 pregnancies, with Down syndrome, one of the most common aneuploid conditions, occurring in 1 in every 800 children.

The researchers set up the conditions for improper cell division using a model mouse cell. Collaborating with them were researchers from Case Western University and the University of Kansas Medical Center.

They focused on the meiotic spindle, a structure that separates and aligns chromosomes before cell division. In most cells, the so-called Spindle Assembly Checkpoint will keep a cell from dividing if all the chromosomes aren't in their place. Hunt compares it to the starting line of a race in which everyone has to be in position before the starting gun fires.

“Quite surprisingly, however, eggs seem to bend the rules, allowing the division to occur when most—but not all—chromosomes are properly positioned,” she said. “This difference in cell cycle control provides an explanation for the high error rate in human eggs.”

In an accompanying commentary, R. Scott Hawley of the Stowers Institute of Medical Research suggests that “a simple numbers game”

may make eggs more tolerant of one or two misaligned chromosomes. Males produce hundreds of millions of sperm cells at a time, so there are plenty to spare if a few cells that are trying to produce sperm are prevented from dividing.

But female mammals usually produce only one egg per cycle. A failure of that egg to divide would make fertilization impossible, but continuing with one or two misplaced chromosomes at least leaves open the possibility of a viable conception, says Hawley.

“I always say the difference is not that men don’t make mistakes in making sperm,” said Hunt. “It’s just they kill those mistakes. And women are just better with living with those mistakes.”

Provided by Washington State University