Researchers propose model for disorders caused by improper transmission of chromosomes

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Parents of healthy newborns often remark on the miracle of life. The joining of egg and sperm to create such delightful creatures can seem dazzlingly beautiful if the chromosome information from each parent has been translated properly into the embryo and newborn.

The darker side is that when extra copies of chromosomes or fewer than the normal 46 (23 from each parent) are present, tragic birth defects can occur. Now, scientists at the University of Georgia have developed a model system for plants and animals that shows the loss of a key structural protein can lead to the premature separation of one DNA copy called a chromatid.

The new model shows for the first time that the loss of this protein can lead to aneuploidy—the name given to birth disorders caused by extra or too few chromosomes.

Disorders caused by errors in the proper transmission of chromosomes from each parent are uncommon but tragic nonetheless. Best known may be Down Syndrome, which is caused by an extra copy of chromosome 21. Many errors in chromosome transmission are so severe that miscarriages usually occur.

"As we know, human females have all the eggs they will ever have from the time of birth, and so as they age, the protein structures on chromosomes also age," said Kelly Dawe, a geneticist and plant biologist at UGA. "If an egg is fertilized late in life, the final stages of chromosome separation may not occur properly. The goal of the work, which was done in maize, is to find out which parts of the chromosomes are most sensitive to failure. We now believe that proteins in a structure called the kinetochore are among the most sensitive to degradation or mutation. That may be a clue as to why older women have more problems with these kinds of chromosomal disorders when giving birth than younger women."

The research was published today in the journal Nature Cell Biology. Co-author on the paper is former University of Georgia graduate student Xuexian Li.

Irregularities in chromosome number are usually caused during a biological event called meiosis, in which the number of chromosomes per cell is halved and, in animals, results in the formation of gametes or sex cells. While the biology of meiosis has been known for more than a century, major questions remain about how all the constituent cell parts must coordinate to make the process successful.

During the two stages of meiosis, chromosomes are first separated by type, ensuring that only one of each gene is represented and then separated in half again in preparation for fertilization. The authors showed that the first stage is orchestrated in part by the kinetochore that attaches chromosomes to the rest of the cell. When they suppressed a kinetochore protein called MIS12, the chromosomes no longer separated by type and jumped to the second stage before completing the first. These failures closely mimic those seen in eggs from older women.

The cell division processes that Dawe and Li studied have implications for other diseases—such as cancer—as well. And yet a genuine payoff may come in the form of genetically improved lines of corn.

Dawe's work opens the possibility of a more positive outcome: the ability to engineer so-called "artificial chromosomes" with useful genes into corn varieties. Though that may be years off, it could offer a way to create lines that could resist drought, disease and insect pests without harming the environment.

Researchers are racing to design artificial chromosomes that behave like natural ones. With such an engineered chromosome, the positives traits researchers could give to corn plants would be almost limitless.

"You could really put genes in there at will, stacking traits that would make the plants able to withstand problems that now limit production greatly all over the world," said Dawe. "But to get from theory to practice, we will need a much clearer understanding of meiosis."

Unfortunately, most early generation artificial chromosomes have failed at meiosis in a nearly identical manner as plants with reduced MIS12. By manipulating MIS12 or other similar proteins, Dawe hopes to correct these defects.

Source: University of Georgia (news : web)