

Study finds protein that sets the stage for exchanges of DNA code in eggs and sperm

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A team led by a scientist at the University of Pittsburgh School of Medicine has discovered a regulatory protein that influences where genetic material gets swapped between maternal and paternal chromosomes during the process of creating eggs and sperm. The findings, which shed light on the roots of chromosomal errors and gene diversity, appear in tomorrow's issue of *Nature*.

Most cells contain 46 chromosomes, half coming from each parent. But eggs and sperm, known as germ cells, have half as many so that when they combine to form an embryo, the correct chromosome number is maintained, explained senior author Judith Yanowitz, Ph.D., assistant professor of obstetrics, gynecology and reproductive sciences, Pitt School of Medicine, a member of the Magee-Womens Research Institute, and former staff associate at the Carnegie Institution of Washington, Baltimore.

"When germ cells form, segments of DNA are exchanged, or recombined, between maternal and paternal chromosomes, leading to greater diversity in the <u>daughter cells</u>," she said. "Our research reveals a protein that plays a key role in choosing where those crossovers occur."

Crossing over is essential for the correct movement, or segregation, of chromosomes into the <u>germ cells</u>. Failure to exchange DNA properly can lead to offspring with the wrong number of chromosomes and, in humans, defects in this process are a leading cause of infertility, Dr. Yanowitz noted.



Despite the importance of this process for development, little is known about the factors that influence where crossovers occur and how they are regulated. In the genome of the tiny round worm C. elegans that the researchers studied, gene recombination typically occurs toward the ends of the chromosomes, which contains fewer genes.

But the "crossover landscape," as Dr. Yanowitz calls it, changed in two ways in worms that had a mutation in a protein called X non-disjunction factor (xnd-1): crossovers instead occurred in the gene-rich, central areas of the chromosomes; and crossovers on the X chromosome often did not occur.

"This is the first gene in any system that is specifically required for the segregation of single chromosomes," she said. "The fact that this is the X chromosome is interesting because the sex chromosomes play a unique role both in germ line and general development."

These observations led the researchers to suggest that xnd-1affects the way <u>chromosomes</u> are packaged into the nucleus of the cell as a DNA protein complex known as chromatin. They further showed xnd-1 alters a component of chromatin that has been maintained through species evolution and that this packaging is directly responsible for the effects on crossover formation.

Provided by University of Pittsburgh Schools of the Health Sciences

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