Study of Cell Division Sheds Light on Special Mechanism in Egg Cells

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In a study of egg cells using time-lapse microscopy, researchers at the University of California, San Diego School of Medicine and the Ludwig Institute for Cancer Research have discovered an unusual property of meiosis – cell division that produces reproductive cells in sexually reproducing organisms. The discovery of an "inside out" mechanism by which egg cell chromosomes separate from each other may shed light on mistakes made in chromosome distribution that can lead to Down syndrome, high miscarriage rates in humans, and the age-related decrease in fertility in human females. Their findings are reported in the September issue of *Nature Cell Biology*.

Sexual reproduction relies on the merger of chromosomes present in the sperm and egg at fertilization. Formation of sperm and egg cells requires the process of meiosis, which halves the chromosome number of each parent, so that the sperm-egg merger regenerates a cell with two copies of each chromosome. The reduction of chromosome number in meiosis is accomplished through two divisions without an intervening duplication of the genome.

Both meiotic and mitotic divisions require specialized protein polymers called microtubules. These polymers are organized into a football-shaped spindle with the polymer ends embedded in a special organelle – called the centrosome – at each end of the football. Egg cells, however, are unusual in that they lack centrosomes, and instead use a spindle that is self-organized from microtubules. Egg cells, especially in humans, are prone to mistakes in dividing the chromosomes during meiosis; mistakes which result in reproductive problems in humans such as Down syndrome, infertility and miscarriages.

Researchers led by Arshad Desai, PhD, professor of Cellular and Molecular Medicine and investigator with the Ludwig Institute at UC San Diego, used the roundworm *C. elegans*, as a model to study egg cell division. Julien Dumont, a postdoctoral fellow in the Desai lab, developed time lapse microscopy methods to observe egg cell meiosis with high precision.

Prior to this study, dividing cell chromosomes were thought to move apart by pulling on the microtubule polymers and moving into the ends of the spindle, like a person pulling himself up on

a rope. But the UCSD researchers discovered that, in *C. elegans* egg cells, chromosome move apart by being pushed in the middle – most likely caused by the growth of microtubule polymers between the chromosome halves.

Karen Oegema, PhD, professor at the Ludwig Institute and the UCSD Department of Cellular and Molecular Medicine was a co-contributor to the paper. This research was supported by grants from Human Frontiers Science Program, the National Institutes of Health and funding from the Ludwig Institute for Cancer Research.

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