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Outgrowing meiosis

Study finds that a fertilized egg doesn't immediately start dividing mitotically.

Fertilization triggers an upheaval in the egg, including a switch from meiosis to mitosis as the method of cell division. Courtois et al. show that this transition is gradual and isn't complete until after the embryo's 8th division (1).

Meiosis and mitosis differ in several ways. Unlike the bipolar mitotic spindle that is anchored by a centrosome at either end, the meiotic spindle starts out with multiple poles anchored by structures called microtubule-organizing centers (MTOCs). The meiotic spindle is barrel shaped, with flattenened ends, and is longer than the mitotic spindle, which has tapered ends. Researchers have assumed that once the egg is fertilized it begins dividing mitotically immediately. But observations of centrioles—key components of centrosomes—suggest otherwise. The egg destroys its centrioles, and in most species sperm provide the structures (2). In rodents, however, the sperm centrioles also disappear before fertilization (3). Researchers have noted that centrioles are not present until the 64-cell stage embryos of mice, implying that the early divisions don't rely on centrioles (4).

Courtois et al. tracked the changes in spindle formation and architecture through the pre-implantation stage of mouse embryos. To their surprise, the first three divisions after fertilization were similar to meiosis. Centrosomes were absent, and several MTOCs within each cell established a multipolar spindle that eventually became barrel shaped. Two motor proteins necessary for shaping the meiotic spindle, dynein and kinesin-5, were active at this time. Moreover, previous work has shown that efficient division without centrosomes requires RanGTP (5). The researchers found that blocking Ran in zygotes delayed or thwarted anaphase, suggesting that division was occurring through a meiosis-like mechanism.

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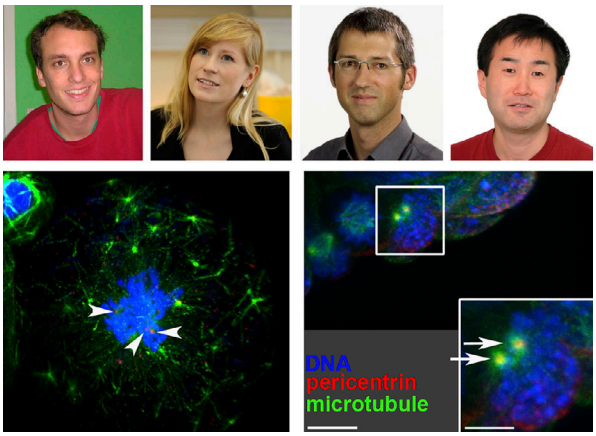
Cells did display some mitotic characteristics in these early divisions, however. During meiosis, for instance, chromosomes stick to a glob of microtubules in the middle of the cell, but the researchers saw no evidence of this so-called microtubule ball. Another way in which these divisions resemble mitosis is the source of the MTOCs that spawn the spindle. In the egg, MTOCs from all around the cytoplasm become part of the spindle. But the team observed that, in mouse zygotes, only MTOCs near the future cell nuclei joined up, a sign that the spindle is shifting toward a mitotic-type organization.

Courtois et al. found that the major changes happened between the 8-cell and the 64-cell stages. During this period, the size and number of MTOCs in each cell declined. The length of the spindle decreased as the cells in the embryo became smaller with each division. Around this time, cells began manufacturing two centrosomes, and only two MTOCs remained in each cell.

"The transition from meiosis to mitosis was not immediate and took several divisions," says senior author Takashi Hiiragi. Whether cells can manufacture new centrioles or have to rely on hand-me-downs has been controversial. The work suggests that, like the shift to mitosis, the synthesis of centrioles occurs in stages. The team found that one centriole ingredient, pericentrin, is present in the egg. But other key centriole components, such as centrin, odf2, and CP110, were not available for centrosome construction until later stages.

Focal Point



PHOTOS (LEFT TO RIGHT) COURTESY OF: AURÉLIEN COURTOIS, NEIL GRANT, HUGO NEVES, AND HUGO NEVES

(Left to right) Aurélien Courtois, Melina Schuh, Jan Ellenberg, and Takashi Hiiragi observed that early mouse embryos undergo a gradual transformation in spindle structure during the first few divisions after fertilization. One change is from a multipolar spindle organized around microtubule-organizing centers to a bipolar one anchored by centrosomes. In this dividing two-celled embryo (bottom left), each cell sports three microtubule-organizing centers (arrowheads) in prometaphase. But by the time the embryo contains more than 128 cells, only two microtubule-organizing centers remain during prophase (arrows, bottom right).

What spurs the embryo to start building centrioles? The concentration of MTOC components could be the trigger, Hiiragi says. The embryo might have to make do with the limited amount of MTOC ingredients contained in the egg. With each division, a cell receives a smaller share of this finite supply, until eventually a shortage of MTOCs might make it necessary to start constructing centrioles.

The researchers don't know if this gradual transition from meiosis to mitosis holds true for other organisms, including humans, in which the sperm delivers centrioles to the egg. Whether these centrioles have a role in the early divisions after fertilization isn't clear, Hiiragi says.

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2. Schatten, H., et al. 1986. *Proc. Natl. Acad. Sci. USA*. 83:105–109.
3. Manandhar, G., et al. 1998. *Dev. Biol.* 203:424–434.
4. Gueth-Hallonet, C., et al. 1993. *J. Cell Sci.* 105:157–166.
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