Absent protein causes chromosomal breakup

Perhaps even more than fans of Godzilla films, fruit fly biologists love mutants. For decades, these investigators have studied strange and unusual examples of the fast-breeding insect, both natural mutants and those induced by chemicals or X rays.

In 1968, researchers captured an intriguing mutant near a winery outside Rome. As they studied this mutant strain, scientists found that the insects had problems making the cells that would become sperm or eggs. Sometimes too much genetic material would end up in sperm cells, for example; other times sperm were a bit light on DNA.

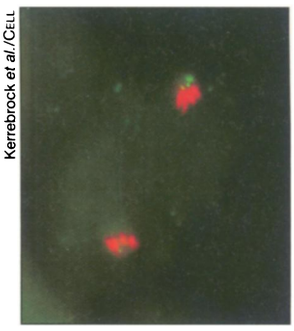
Now, a group led by Terry L. Orr-Weaver of the Whitehead Institute for Biomedical Research in Cambridge, Mass., has finally discovered the broken gene responsible for these reproductive troubles. It appears to describe a protein that briefly glues chromosomes together while sperm and egg cells are made.

Investigators hope the advance will help them understand why human sperm and egg cells often have inappropriate numbers of chromosomes. Conception with these sperm or eggs may result in early miscarriages or children with diseases such as Down's syndrome.

"This is really important work. [Orr-Weaver] is tying up this incredibly long, beautiful story," says R. Scott Hawley of the University of California, Davis, who coauthored a commentary that appears in the Oct. 20 CELL with the report of the Whitehead investigators.

In genetics shorthand, the mutant insects Orr-Weaver studies are known as *mei-S332* flies because their difficulties arise during meiosis, the two-stage process in which a precursor cell divides twice to form four sperm or eggs.

Mei-S332 flies appear to have no problems with the first division. To begin with, the cell contains 4 pairs of chromosomes, one of each pair derived from the insect's father and the other from its mother.



Kerrebrock *et al.*/CELL

In this image of a cell undergoing meiosis, the protein made by the mei-S332 *gene shows up as bright green spots on separating chromosomes (red). The hazy green glow is background fluorescence.*

Each chromosome then makes a copy of itself. Now called sister chromatids, the two identical chromosomes remain linked at their midpoint, an area called the centromere. Next, maternal sister chromatids pair up with their paternal counterparts, usually exchanging stretches of DNA before the first cell division in meiosis separates the maternal and paternal chromosomes into two cells.

In the second stage of meiosis, the sister chromatids, still tightly linked at their centromeres, gather at the centers of the two cells. As cell division begins again, an apparatus called the spindle forms within each cell and gently pulls the sister chromatids apart, just as the maternal and paternal pairs are separated for the first division. Once the sister chromatids part, the two cells divide, forming four cells, each with half the original number of chromosomes.

But in *mei-S332* flies, "you can see the sisters prematurely disjoining," says Orr-Weaver. As a result, she explains, "some cells get too many chromosomes, others get too few."

When Orr-Weaver and her Whitehead colleagues Anne W. Kerrebrock, Daniel P. Moore, and Jim S. Wu found the *mei-S332* gene, they discovered it contained instructions for a kind of protein never seen before. To explore the protein's function, they fused it to a fluorescent marker by joining the marker's gene to a working *mei-S332* gene. They inserted the genetic blend into *mei-S332* flies.

Adding these joined genes not only corrected the mutation in the insects, it enabled the Whitehead team to watch the gene's protein as they examined the formation of fruit fly sperm. During the first stage of meiosis, the protein shows up initially where the sister chromatids join and then disappears from the centromeres during the second stage, right before the sisters break apart.

The *mei-S332* protein is the first protein shown to play a direct role in holding sister chromatids together, says Hawley. Orr-Weaver and her colleagues plan to look for similar proteins in mammals and examine what happens to the gluelike protein right before the sisters free themselves. It may simply disperse off the DNA, or another protein may degrade it, Orr-Weaver notes.

— J. Travis

Ozone depletion research wins Nobel

For their work elucidating how Earth's protective ozone layer forms and decomposes, three scientists received this year's Nobel Prize in Chemistry.

The Nobel committee honored Paul Crutzen, a Dutch scientist at the Max Planck Institute for Chemistry in Mainz, Germany; Mario J. Molina of the Massachusetts Institute of Technology; and F. Sherwood Rowland of the University of California, Irvine, for showing "how sensitive the ozone layer is to the influence of anthropogenic emissions of certain compounds."

In explaining the mechanisms affecting the ozone layer's thickness, said the committee, the three scientists have contributed to "our salvation from a global environmental problem that could have catastrophic consequences."

The stratospheric ozone layer consists of three-atom oxygen molecules (O_3) sparsely distributed more than 15 kilometers above sea level. Though relatively few in number, ozone molecules capture much of the sun's ultraviolet rays, protecting life on Earth from their damaging effects.

In 1970, Crutzen first showed that nitrogen oxides (NO_x)—produced by decaying nitrous oxide from soil-borne microbes—react catalytically with ozone, hastening its depletion. His findings, the committee said, sparked research on "global biogeochemical cycles" as well as the effects on the stratosphere of nitrogen oxide–spewing supersonic transport planes.

In 1974, Molina and Rowland postulated that human-made chlorofluorocarbons—widely used in spray cans, refrigerators, and air conditioners—could, in the stratosphere, transform into ozone-depleting agents. Within a decade, scientists worldwide acknowledged the impact of certain industrial gases on the upper atmosphere, prompting nations to ban production of the most environmentally noxious agents.

"This is really a prize for the scientific community," says Molina, "which has done an excellent job of dealing with this global environmental issue."

Calling the award "highly appropriate," Daniel L. Albritton, an atmospheric chemist at the National Oceanic and Atmospheric Administration in Boulder, Colo., says the recognition highlights "basic science also done for the benefit of humankind."

"Traditional chemistry has mainly involved laboratory work and theoretical calculations," says Rowland. "This award validates the field of environmental chemistry." Noting that this now applied research began as basic science, Rowland adds that this Nobel strengthens the case for "curiosity-driven" investigations.

"We were trying to figure out how the world works, without thinking specifically about how to use the results," he says. "There are distinct advantages to letting people try to understand things, and in doing so pursue questions that might later lead to applications."

Perhaps a better term for such research, Rowland says, would be "understanding-driven." *— R. Lipkin*