AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

SCIENCE

ISSN 0036-8075
3 NOVEMBER 1989
VOLUME 246
NUMBER 4930

■ **SCIENCE is published weekly on Friday, except the last week in December, and with an extra issue in March by the American Association for the Advancement of Science, 1333 H Street, NW, Washington, DC 20005.** Second-class postage (publication No. 484460) paid at Washington, DC, and at an additional entry. Now combined with **The Scientific Monthly®** Domestic individual membership and subscription (51 issues): $75. Domestic institutional subscription (51 issues): $120. Foreign postage extra: Canada $46, other (surface mail) $46, air mail via Amsterdam $85. First class, airmail, school-year, and student rates on request. **Single copy sales:** Current issue, $3.50; back issues, $5.00; Biotechnology issue, $6.00 (for postage and handling, add per copy $0.50 U.S., $1.00 all foreign); Guide to Biotechnology Products and Instruments, $18 (for postage and handling add per copy $1.00 U.S., $1.50 Canada, $2.00 other foreign). Bulk rates on request. **Authorization to photocopy** material for internal or personal use under circumstances not falling within the fair use provisions of the Copyright Act is granted by AAAS to libraries and other users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that the base fee of $1 per copy plus $0.10 per page is paid directly to CCC, 27 Congress Street, Salem, Massachusetts 01970. The identification code for *Science* is 0036-8075/83 $1 + .10. **Change of address:** allow 6 weeks, giving old and new addresses and 11-digit account number. **Postmaster:** Send Form 3579 to *Science*, P.O. Box 1722, Riverton, NJ 08077. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

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COVER SYNGAMY II is one of a series of paintings by the Pennsylvania artist Peter Cohen on the first mitosis within the fertilized egg. The mitochondria, which have assumed the round shape seen in the painting, leave a clear space within the cytoplasm for the dance of the chromosomes on the luminous spindle. The paintings of Peter Cohen are currently on exhibit at AAAS in Washington as part of the AAAS Art of Science and Technology Program, which displays work reflecting the interaction of art and science. See the articles on the cell cyle that begin on page 603.

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The Cell Cycle

In each of our bodies there are molecular choreographers programming a minuet in which chromosomes appear from obscurity, line up with their partners, separate, rejoin, and then disperse. That minuet is called the cell cycle, and it must proceed according to certain rules and cadences if we are to lead normal lives. In embryonic cells, the cycle must frequently proceed very rapidly, in some adult cells more slowly, and in some neural tissue not at all. If the cycle fails in growing cells, death results. If it goes incorrectly in mature cells, cancer is caused.

The advent of the microscope made it possible to distinguish phases of this cycle such as anaphase, metaphase, and interphase on the basis of morphological changes. Inevitably in modern times the morphological studies have been followed by biochemistry and cell biology to find the molecules that direct and control this vital process. Further categorization followed, based on the time of DNA synthesis, which resulted in the addition of the following phases: G_1 (before DNA synthesis), S (DNA synthesis), G_2 (after DNA synthesis), and M (cell division). The combination of approaches has added greater understanding and complexity to this area of research. This issue of *Science*, assembled under the guidance of Barbara Jasny, describes the state of the art as seen by six leaders in the field.

As explained by Hartwell and Weinert, genetic and biochemical studies indicate two types of control. There is direct control, in which the completion of previous steps is essential to produce the substrate for the subsequent step. The other is indirect in that early steps release inhibitors of late steps and late steps feed back to control early steps. Pardee discusses G_1 in which nucleotide, histone, and enzyme synthesis occur to build up supplies for the S phase. Regulatory molecules can divert G_1 into a quiescent phase (G_0) or stimulate quiescent cells to active cycling. Quiescence can be deleterious if it lasts too long and uncontrolled proliferation can lead to cancer. A critical regulatory event occurs at a restriction or start point in the G_1 phase. If nutrients and control signals are appropriate, the cell passes through this start point and an inexorable chain of events is initiated.

Laskey *et al.* describe the S phase, which can take 10 hours in mature *Drosophila* or less than 4 minutes in the embryonic cells of the same species. Since a single replication fork moving at an observed rate of 3 kilobases per minute would require a month to replicate a human chromosome, synthesis must occur at many foci. This process, which is highly accurate, must therefore involve complex coordination. Not only the linear sequence but also the entire chromatin package must be reproduced with high fidelity.

Contrary to early guesses that major control points for embryonic cell cycles would occur in G_1, a great deal of regulation occurs in G_2 as discussed by O'Farrell *et al.* They have focused on the *string* gene, which appears to act as a mitotic trigger in early *Drosophila* embryogenesis. Murray and Kirschner describe the intricate relations of maturation promoting factor (MPF) and cyclin in the frog embryo. These two molecules seem to have a love-hate relationship in that changes in one can lead to activation or destruction of the other. Both increase and decrease at various stages, appearing as dei ex machina to control progress—but these powerful proteins use such common mechanisms as phosphorylation to accomplish their tasks. The finding that yeast proteins can replace frog proteins indicates high conservation of proteins and great similarity in mechanisms in different organisms.

McIntosh and Koonce describe the M phase in which mitosis occurs. This was the most mysterious part in the premolecular days because chromosomes were lined up and pulled apart by invisible and highly specific forces. This is now becoming explainable in terms of microtubules, spindles, and kinetochores. Both repulsive and attractive forces are needed to develop the reproducibility and specificity required.

The early microscope studies revealed an almost unbelievable event in which chromosomes were held in a meticulous alignment by unseen forces that appeared to arise spontaneously. Today we are a long way along the path of explaining those pictures in molecular terms. The molecules seem to be ordinary garden variety enzymes and receptors, but the cleverness of their feedback and feedforward relationships is as intellectually pleasing as the early microscopic pictures. Thus the molecular discoveries explain, but in no way diminish, the awe of the reader at the sophistication of the processes leading to the cell cycle.—DANIEL E. KOSHLAND, JR.