Research News

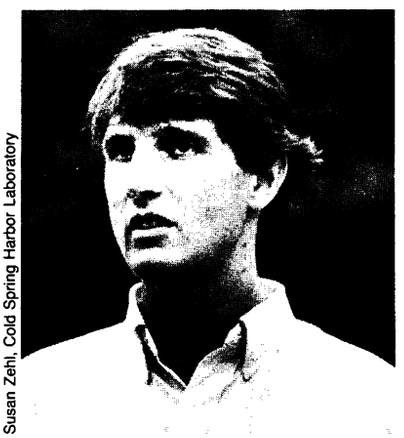
The Cell Cycle Coming Under Control

Two disparate lines of research merge, revealing that the biochemical machinery for controlling cell division is the same in species ranging from yeast to man

WITHIN THE PAST YEAR, researchers have made rapid strides toward understanding one of the critical events in the life cycle of the cell—namely, cell division. And as they have identified the biochemical machinery that controls this event, they have made a welcome discovery: the basic mechanisms are apparently the same in species ranging from yeast to man. "That's the wonderful thing," says David Beach of Cold Spring Harbor Laboratory. "Cell cycle control is now much simpler than it was 2 years ago. It's the grand unification theory of the moment."

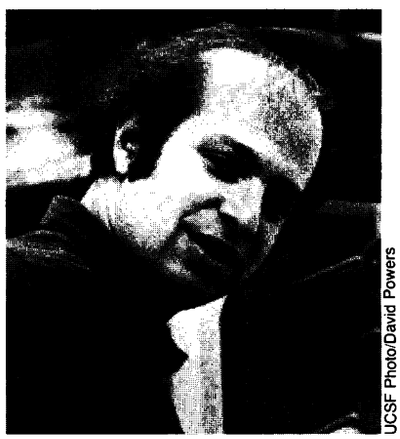
This increasingly detailed picture of cell cycle control has emerged from the confluence of two previously disparate lines of research. In one set of laboratories around the world, geneticists used the classical methods of their discipline to identify the genes controlling cell division in the simple yeasts. Meanwhile, the cell biologists and biochemists were applying their traditional methods to isolate the proteins regulating cell division in clam, sea urchin, and frog eggs. In the end, everyone found that they were studying the same proteins.

As Joan Ruderman of Duke University puts it, sea urchins and clams "are little things that people laugh at. But the pathway that we have got onto here seems to be universal."



Susan Zehl, Cold Spring Harbor Laboratory

David Beach. *One of the yeast geneticists whose work helped to uncover the molecular machinery that tells cells that it is time to divide.*



UCSF Photo/David Powers

Marc Kirschner. *A cell biologist whose studies of maturation promoting factor in* Xenopus *eggs recently intersected with the yeast results.*

As biological mechanisms go, the pathway discovered by the yeast geneticists and cell biologists is relatively simple, involving just two major proteins. One of these is a particular type of enzyme, a kinase which adds phosphate groups to other proteins. Such phosphate additions and removals are commonly used by cells to modify protein activities. Although researchers do not fully understand how the kinase they have identified works, they do know that its activation is the signal that sets in motion the cellular changes necessary for division.

And this is where cyclin, the other major protein of the cell cycle, comes in. Cyclin concentrations fluctuate, going up just before cells divide and turning on the kinase, although the cyclin may do this indirectly. The cyclin concentrations then drop precipitously and the kinase activity also subsides, allowing the cells to complete the division cycle. Resynthesis of cyclin can then trigger another round of division.

Although simple, this picture was nearly 20 years in the making. The going was slow for much of this time. But then suddenly in the past year or two, the rate of advance surged—at least partly because of the readiness of the various groups to communicate and collaborate with one another. "We're a pretty friendly lot," comments Tim Hunt of the University of Cambridge, England. "It's competitive, but on the whole information has been flowing freely."

The first glimmerings of the cell cycle story emerged back in 1971 when Yoshio Masui and Clement Markert of Yale University and, independently, L. D. Smith and Richard Ecker of Argonne National Laboratory discovered that immature eggs from the frog (*Xenopus laevis*) produce a factor that causes them to undergo meiosis and mature, preparing them for fertilization. This factor is known as "maturation promoting factor" or MPF.

Meiosis is a special type of cell division, occurring only in the germ cells that give rise to eggs and sperm. But researchers soon found that the maturation factor could also induce mitosis—the division of ordinary somatic cells.

Not only that, key experiments done in the early 1980s by John Gerhart and Michael Wu of the University of California, Berkeley, and Marc Kirschner of the University of California, San Francisco, showed that MPF activity in frog eggs fluctuates during the cell cycle; it rises as cells enter meiosis or mitosis and then drops sharply after they divide. Activation of the factor appeared to serve as sort of an internal clock that tells cells when to divide. "All the aspects of the cell cycle one is familiar with can be caused by the addition and withdrawal of MPF," Kirschner says.

Correction

An article in our 30 June issue ("'Dangerous' liaisons in cell biology," p. 1539), which discussed the commentary in the 2 June issue of the journal *Cell* by Max L. Birnstiel and Meinrad Busslinger regarding the transgenic mice experiments of Corrado Spadafora and coworkers, stated that Vienna's Institute of Molecular Pathology (IMP), for which Birnstiel and Busslinger work, was seeking patents on extensions of the Spadafora experiments. On further investigation, we have learned that this is not correct. At present no applications have been applied for or granted to IMP or its parent companies Genentech and Boehringer Ingelheim. We wish to correct the record, apologize to Dr. Birnstiel and Dr. Busslinger for this misstatement, and alert our readers to their letter, which is printed in our Letters section on page 243.