Contemporary Readings for General Biology

FIFTH EDITION

FOR STARR AND TAGGART'S

BIOLOGY

The Unity and Diversity of Life

AND STARR'S

BIOLOGY

Concepts and Applications

John W. Crane

Contemporary Readings for General Biology

Fifth Edition, 1998 Edition

To Accompany Starr and Taggart's
BIOLOGY
The Unity and Diversity of Life

and

Starr's
BIOLOGY
Concepts and Applications

John W. Crane
Washington State University

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PREFACE

For the memories of Nancy Antonia Crane, who always listened to the owl

The quality of all life depends on a human understanding of the intricacies of the biotic/abiotic connection, for we not only control this connection, but also depend upon it for our own existence. Biologists now recognize the importance of diversity, both biotic and abiotic, in the maintenance of properly functioning and viable ecosystems. But the owl and salmon speak—and we still refuse to listen! Their diminishing populations are trying to inform us that if we continue to reduce the viability of their ecosystems through habitat destruction and pollution, we reduce our own fitness as well. Based on an objective assessment of our environmental quality, the outlook appears dim. Earth, air, and water qualities continue to suffer and are in worse shape than they have ever been—and we still don't pay attention. Listen to the owl—the future quality of all life depends upon the message!

New information regarding other biological concerns also makes headlines. News emanating from the biological sciences affects our lives on a scale never before imagined. Almost daily we hear of diseases such as AIDS, lupis, and hemorrhagic fever, for which no cures exist. AIDS, which results from destruction of the human immune system by the HIV virus, results in almost certain death. Research into the causes of cancer, lupis, heart disease, and a host of other diseases continues. Although surgical, drug, and other forms of therapy aid in treatment, prevention and finite cures still elude us. Lung cancer and heart diseases in women are increasing at alarming rates and will cause more deaths in the United States in 1996 than at any time in our history. And yet there is hope. Investigations in cellular biology, biochemistry, genetic engineering, and physiology are producing new medical breakthroughs. Genetic engineering, encompassing the fields of gene manufacture and gene substitution, holds much promise for preventing, and perhaps curing, various diseases. In fact, genetic treatment of human patients has already begun.

As we explore new biological constructs, we also continue to examine older concepts such as evolution in the attempt to refine these doctrines in light of modern scientific inquiry. Efforts to explain the absence of observable continuity between species have resulted in the concept of "punctuated equilibrium"—evolution by bursts rather than by gradual change. The reexamination of Darwin's hypotheses reveals that, with some modifications, his doctrines hold true.

In producing the Fifth Edition of *Contemporary Readings for General Biology,* we retain our original goal: to demonstrate the importance, dynamic nature, and impact of the biological sciences for all of us—including the owl.

John W. Crane

CROSS-REFERENCE GUIDE

to Starr and Taggart's Biology: The Unity and Diversity of Life, *Eighth Edition*

This cross-reference guide correlates selected readings in this book with units and chapters in Starr and Taggart's *Biology: The Unity and Diversity of Life,* Eighth Edition.

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The Cellular Basis of Life

Human life, as does most, begins with but a single cell. In our case we each begin as a cell containing 46 chromosomes—23 from each parent. From this beginning we eventually mature to an individual containing an almost uncountable number of cells, many of which are far different from the original. The eventual fate of each cell is, of course, death; perhaps produced, as some biologists believe, by an innate genetic program. Apoptosis, or programmed cell death, is currently receiving scientific attention regarding the molecular mechanisms causing the event. For not only does it apparently cause cellular death, apoptosis is believed to be responsible for preventing webbed fingers in humans and may underlie metamorphosis of amphibians and insects. Apoptosis may also have a "dark side" as recent findings implicate it as a potential cause of cancer and a possible factor in AIDS and other autoimmune diseases. Why and how these cells evolve from a single ancestor to widely divergent cellular components and then perish is receiving much scientific investigation as biologists begin to probe the genetics of programmed cell death.

Relative to apoptosis are many unanswered questions regarding human fetal development. The question of how, in nine months, a zygote measuring about 0.025 of an inch develops into an infant containing a myriad of cells is receiving much attention. Biologists are currently focusing on "master control" genes that may program other cellular systems to change directions in their eventual fates. In fact, certain "master control" genes are implicated in producing morphological variations when inserted into developing embryos. As developmental research continues we will begin to understand how all living systems integrate the various genetic messages that eventually culminate in the production of an adult form.

Also, as population growth continues, we are observing a concomitant increase in the number of older members within our communities. As the population ages, medical attendants are seeing a rise in the number of patients with Alzheimer's and other age-related diseases. Very recent medical/genetic research suggests that at least one form of Alzheimer's disease can be traced to a genetic cause. Other studies suggest that Alzheimer's disease may result when proteins produced by cells and known as "complements" are unleashed against the fragile cells of the brain itself.

But all is not gloom. Potential treatments are on the horizon for many cellular diseases, running the gamut from AIDS and lupus to sickle-cell anemia. Of course much remains to be done, but the scientific community continues to gain momentum in its attempt to understand the basic unit of life—the cell.

1

A Time to Live, a Time to Die

Biologists probe the genetics of programmed cell death

By Carol Ezzell

"First, you murder," Michael O. Hengartner forthrightly told a horde of expectant faces. "Next, you get rid of the body. Then, you hide the evidence," he explained, pacing back and forth in the dimly lit room.

Hengartner wasn't instructing a group of apprentice hit men. Instead, the Massachusetts Institute of Technology (MIT) biologist was addressing a gathering of cancer researchers, detailing the functions of a recently identified set of genes that controls life's only inevitable process: death.

Together, Hengartner and his MIT colleagues constitute one of scores of research teams around the world who are reviving scientific interest in the molecular mechanisms of a phenomenon called apoptosis, or programmed cell death. Among other things, this phenomenon (pronounced apa-tosis, with the second "p" silent) prevents humans from having webbed fingers and eliminates cells of the immune system that can't tell "self" from "nonself." It also underlies metamorphosis—the magic wand that turns caterpillars into butterflies and tadpoles into frogs. In adults, it phases out old body cells so they can be replaced by new ones.

Over the past year, biologists from a range of disciplines have uncovered evidence that this seemingly salutary process has a dark side. Several new studies suggest that apoptosis can play roles in AIDS and autoimmune diseases; others indicate that disruptions in the usual orderly progression of apoptosis lead to the uncontrolled cell growth of cancer.

Apoptosis—which means "dropping off" in Greek—was first described in 1951 as a step in animal development. The process takes its name from its appearance as it unfolds under the microscope: Within minutes, cells undergoing apoptosis shrink and shed tiny, membranous blebs that neighboring cells quickly gobble up, mirroring Hengartner's colorful description. In contrast, during necrosis—cell death arising from injury—cells swell for hours and then burst, spraying their contents about as a chemical signal that attracts immune-system cells to fight the injurious microbe or substance.

In the late 1960s and early 1970s, researchers began gathering evidence that apoptosis occurs as part of the normal turnover and replacement of worn-out tissues in adult organisms. They discovered that apoptosis resembles suicide in some ways: Old cells actively participate in their own demise by turning on genes and making new proteins that will shortly cause their death.

They discovered that apoptosis resembles suicide in some ways: Old cells actively participate in their own demise by turning on genes and making new proteins that will shortly cause their death.

Since the mid-1980s, cell biologists and geneticists have started sorting out the causes and implications of apoptosis in a wide range of animals, including humans. Last spring they began reporting evidence of the role played in apoptosis by the cancer-causing c-myc gene—named for its initial discovery in myelocytomas, tumors consisting of tightly packed bone marrow cells.

The c-myc oncogene becomes overactive in a wide range of mammalian tumors, including human cancers of the breast, bladder, colon, lung, and cervix (SN: 6/1/91, p.347). In many cases, c-myc's hyperactivity begins when a cell inexplicably creates extra copies of the gene, reproducing it over and over within the cell nucleus.

Because cells with such c-myc amplifications grow and divide nonstop—and further, because the c-myc gene encodes protein-containing regions that can bind to DNA—scientists hypothesize that c-myc regulates other genes involved in cell division. Ironically, Gerard I. Evan of the Imperial Cancer Research Fund Laboratories in London and his colleagues reported in the April 3 CELL that c-myc can also cause apoptosis under certain conditions .

Evan's group found that while laboratory-cultured cells with hyperactive c-myc genes can grow faster than cells with less active c-myc genes, they also die faster than those cells when deprived of growth medium. Moreover, the researchers noted, the cells with overactive c-myc genes died with all the visible hallmarks of apoptosis.

Evan and his co-workers conclude that c-myc functions as a two-edged sword: While it usually acts to keep a healthy cell dividing, it can also trigger cell death if outside conditions

aren't right for continued cell proliferation or if the cell has become genetically damaged. In this way, c-myc can function as a built-in cellular self-destruct mechanism.

So how does c-myc cause cancer? According to a model developed by Evan and his co-workers, damage to the c-myc gene—caused either by slips in the DNA-repair machinery or by environmental injury—usually results in cell death. But some cells sustain such genetic damage and go on to develop a mutation that activates, or turns on, a second gene. This second gene somehow overrides c-myc's death command, allowing the cells to grow into tumors.

Two papers in the Oct. 8 NATURE provide evidence that this second gene is bcl-2, an oncogene named for its initial discovery in human immune-system cancers called B-cell lymphomas. In the first paper, a team led by Douglas R. Green of the La Jolla (Calif.) Institute for Allergy and Immunology reports that death-prone cells containing extra c-myc genes survive much longer following insertion of an activated bcl-2 gene, which produces a protein with unknown function.

"In the absence of bcl-2, c-myc induces death," summarizes Green, "but in the presence of bcl-2, there's no death." Cancer results, he asserts, "not just because the [mutated] cells grow faster, but also because they die more slowly."

In the second paper, a team led by the Imperial Cancer Research Fund's Evan reports similar results and provides evidence suggesting that the bcl-2 mutation can help cancer cells resist the deadly effects of chemotherapeutic drugs. Many such drugs kill cancer cells by causing them to undergo apoptosis.

Evan's group administered the anticancer drug etoposide, also known as VP16, to death-prone rat cells genetically engineered to contain the activated bcl-2 gene. The researchers found that the bcl-2 gene prevented many of the cells from undergoing apoptosis and delayed its onset in others.

Further evidence that bcl-2 increases the resistance of cancer cells to chemotherapy is published in the Oct. 1 CANCER RESEARCH. Toshiyuki Miyashita and John C. Reed of the University of Pennsylvania School of Medicine in Philadelphia inserted copies of the activated human bcl-2 gene into mouse lymphoid tumor cells. They found that the genetically engineered cells survived a dose of the steroid drug dexamethasone roughly 100 times larger than that required to kill cells lacking the bcl-2 gene. Moreover, the cells resisted death induced by several other chemotherapeutic drugs, including the widely used cancer therapies vincristine and methotrexate.

The findings "may open the door to a whole new approach for the treatment of cancer," says Reed, who is now at the La Jolla (Calif.) Cancer Research Foundation. "If you could use drugs to reduce the expression of bcl-2 [in cancer cells], you might make the cells more sensitive to existing chemotherapeutic drugs," he suggests.

Reed and his colleagues are working with Genta, Inc., a San Diego-based biotechnology company, to develop so-called antisense drugs to block the activity of bcl-2. Antisense drugs—which consist of the same chemical building blocks that make up the genetic material DNA—turn off specific genes by binding to and inactivating messenger RNA, the intermediate compound that genes use to tell a cell to make a given protein (SN: 2/16/91, p.108).

Reed says initial tests in laboratory-cultured cells show that antisense drugs that target bcl-2 make cancer cells more vulnerable to apoptosis induced by chemotherapeutic drugs. "We're hoping to get our [bcl-2] antisense drug into clinical trials soon," says Reed. "We'd love to see if we could get it to work [in cancer patients]."

"There's a possibility that in all [the processes that turn cells cancerous] there may be mechanisms that favor cell death," adds Green. "If other genetic changes override that, you get full-scale transformation [into a cancer cell]."

In the meantime, MIT's Hengartner has found that the tiny roundworm *Caenorhabditis elegans* has a gene that resembles human bcl-2. He reported last month that the structure of bcl-2 is similar to that of a roundworm gene called ced-9, for *C. elegans* death (SN: 10/10/92, p.229). Moreover, like bcl-2, ced-9 protects cells from programmed cell death, Hengartner and his colleagues reported in the April 9 NATURE.

Hengartner says that ced-9 regulates the activity of two other genes, ced-3 and ced-4, that actually cause cells to undergo apoptosis. When ced-9 is "on," it shuts off ced-3 and ced-4, allowing a cell to live. But when ced-9 is inactivated by a mutation, ced-3 and ced-4 start up, prompting a cell to commit suicide.

This feedback mechanism ensures that so-called stem cells in a developing roundworm die when they are no longer needed, says Hengartner. Scientists know that the minuscule roundworm generates 1,090 cells during its embryonic development. However, 131 of these cells die, so an adult roundworm consists of exactly 959 cells.

Hengartner's team has shown that roundworms with an abnormally activated ced-9 gene develop superfluous body parts, presumably because the extra 131 cells never die. In contrast, the researchers report, the offspring of roundworms lacking functional ced-9 genes die as embryos, evidently because the ced-3 and ced-4 genes functioned unchecked, killing all of the young organism's cells prematurely.

"Ced-9 is the switch between life and death" in the developing roundworm, concludes Hengartner.

Two studies published earlier this year demonstrate that the mammalian immune system may employ a similar set of cell-death genes. In the first study, a group led

by Shigekazu Nagata of the Osaka Bioscience Institute in Osaka, Japan, has found that mice genetically predisposed to an affliction resembling the human autoimmune disease systemic lupus erythematosus (SLE) have defects in a protein required for apoptosis in white blood cells.

Accordingly, Nagata and his colleagues report in the Mar. 26 NATURE, the mice fail to purge themselves during embryonic development of white blood cells that attack their own tissues. As a result, the animals develop the swollen lymph glands, lethargy, and tissue damage characteristic of lupus.

The results reported by Nagata's team "are the first hint of a cell-death link with a real disease model," comments Green. "It looks like a gene that is involved in the programmed cell death process is defective in this strain of mouse with horrendous autoimmune problems."

In the second paper, which appeared in the July 10 SCIENCE, a group led by Frank Miedema of the University of Amsterdam in the Netherlands reports evidence that AIDS resembles the other side of the same coin. Miedema and his colleagues took white blood cells called T-cells from male AIDS patients. When they stimulated the cells' CD3 receptors using antibodies, up to one-fourth of the cells committed suicide by apoptosis. In contrast, the antibody treatment failed to induce significant levels of apoptosis in T-cells isolated from men not infected with the AIDS-causing HIV virus.

Miedema and his colleagues suggest that HIV infection "hyperactivates" T-cells, giving them a hair-trigger tendency toward suicide. They say this mechanism may explain why AIDS patients show a decrease in all types of T-cells, not just those bearing the CD4 receptor that HIV uses to enter and infect some T-cells.

Developments such as these signal renewed interest in the study of cell death among researchers from a variety of fields, say many biologists. "This will be a very fruitful area of research for some time to come," predicts Reed.

THOUGHT EVOKERS

- Explain the concept of apoptosis.
- Why has it been suggested that apoptosis might have a "dark side" regarding the human autoimmune system?
- Describe how the c-myc oncogene is believed to be involved in causing cancer.

2

Body building from scratch

Breakthroughs in developmental biology teach us how we grow

By Traci Watson

It is one of life's most splendid mysteries: In nine months, a 0.025-inch fertilized egg somehow turns into a kicking, crying human baby. No topic could be more intriguing—or less understood. Humans start life small and inglorious, as "little, slug-like things," says one developmental biologist. But the "slug" somehow conjures up eyes, a brain, and other organs. How it does so is finally being worked out by scientists.

Thanks to new laboratory methods, scientists are gaining awesome insights into what makes the embryo tick. Study of the embryo "is enormously fun because we're learning so much so fast," says Cliff Tabin, a developmental biologist at Harvard University. In the past six months alone, researchers have done important work on genes for head and eye formation. Last week, scientists reported the first discovery of genes directing the left-right orientation of the body. And in the ultimate sign of trendiness, biotech companies have recently taken an interest in developmental biology, once considered a backwater of useless knowledge.

The resulting mouse pups had normal bodies below the neck. Above the neck, they had . . . nothing.

Much of the attention is being lavished on "master control" genes that tell parts of the body how to form. In one startling finding, a Swiss research team reported in March that it had created fruit flies with eyes in the oddest places—on their wings, their legs, their antennae. To make these all-seeing flies, the scientists simply gave a fly gene called eyeless—probably a master-control gene—to fly embryos. All by itself, eyeless tells a growing fly to make an extra eye. Mice and humans also have a version of eyeless.

Growing heads. Dramatic as eyeless is, it seems mundane next to the gene named Lim-1. In a paper published in March, researchers at the M. D. Anderson Cancer Center in Texas reported that they had created very young mouse embryos lacking Lim-1. The resulting mouse pups had normal bodies below the neck. Above the neck, they had . . . nothing.

Examining these freakish results, the M. D. Anderson scientists realized that they had found an important clue to the powerful, mysterious region called the head organizer. Located in the very young embryo, the organizer somehow tells a group of cells, "Become a head," which they do. The new study shows that one of the organizer's key agents is Lim-1, a finding that will help reveal all the steps required to grow a head.

Just because an embryo has a head, however, doesn't mean it knows how to proceed. A developing animal must also figure out which way is up and which down, which way is back and which front. And the genes that control those commands are now being tracked down. Chief among them are the 39 "Hox" genes. So fundamental is this genetic family that it is found in nearly the exact same form in all animals with backbones. The list of body parts the Hox genes help form reads like the index of an anatomy textbook: nervous system, sexual organs, skeleton.

A barrage of recent experiments have shown that at least some of the Hox genes help the embryo tell head from tail. Certain Hox genes, it seems, switch on only at the embryo's front; others switch on at the rear. By looking at which Hox genes are on, cells know what to become. A series of recent studies show that if a single Hox gene is removed from one part of the embryo, that part develops like the section closer to the head.

But knowing front from back isn't enough. An embryo also needs to know its left from its right, because the two halves of an animal aren't mirror images. The heart is slightly tilted to one side, for example. This isn't trivial: People born with reversed organs often suffer cardiac ailments and infertility.

Right and left. Last week, the journal *Cell* carried a report that has other scientists cheering: A research team led by Harvard's Tabin has discovered three proteins that control left-right patterning. The researchers found that one of the proteins appears on the right side of the embryo's chest. The other two proteins appear only on the left side. This lopsided pattern prompts the budding heart to tilt leftward and probably affects the slant of other organs, too.

Even more is known about how limbs form. For example: Take a look at your arm. When it was forming, the young cells had to know whether they were closer to the thumb or the pinkie. The signal for that information was a protein now called sonic hedgehog (after a computer game character). A second protein told the arm cells whether they were closer to the shoulder or the fingertips; a third protein, whether they were closer to the back or the palm of the hand. If just one protein had been missing, your arm could

have had two palms or no thumb or a hand joined to the shoulder.

This kind of detailed information has not gone unnoticed by other scientists. To evolutionary biologists, the genes and proteins at play in the embryo are a gold mine: They provide a window on how new types of animals arose, even in the distant past.

If just one protein had been missing, your arm could have had two palms or no thumb or a hand joined to the shoulder.

When Sean Carroll of the Howard Hughes Medical Institute at the University of Wisconsin at Madison began studying how insect wings develop, he was surprised to find that the butterfly's gorgeous sails and the fruit fly's plain little flappers are sculpted by many of the same genes. Butterfly and fly embryos simply turn on their wing genes in different patterns. So one key to forming new bodies—and thus new species—lies in how embryos play the genes they've already got. It's only fitting that the miracle of life's diversity is being revealed by the miracle of how each creature—human, butterfly, bird—comes to life.

THOUGHT EVOKERS

- What is a "master control" gene?
- Why are the 39 "Hox" genes considered fundamental for animal development?
- Describe what is meant by the phrase "left-right patterning."