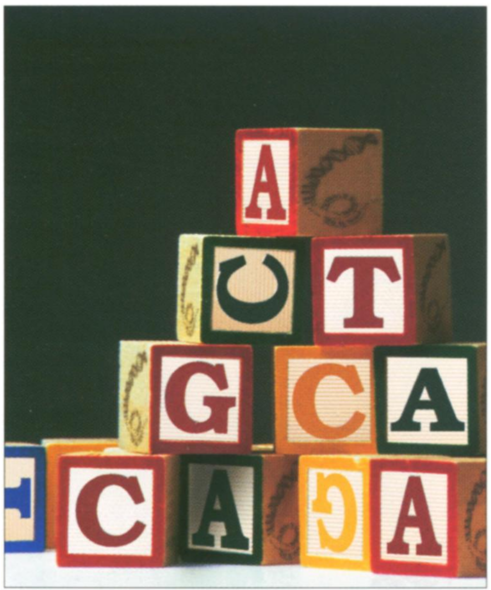
Biology's Periodic Table

By JOHN TRAVIS

A few years ago, as the pace of gene discovery quickened, scientists and journalists alike began to joke about gene-of-the-week stories. That notion seems almost quaint, now that whole genomes, the complete collection of an organism's genes, are being unveiled left and right.

Minimalist viral genomes debuted first, followed recently by several bacterial genomes. Last year, yeast joined the party, offering scientists a tantalizing glimpse of the genetic menu used by cells similar to our own. A member of the so-called third branch of life, the oddball microorganisms called archaea, has also bared its genes, to the delight of biologists.



For many scientists, those achievements are but precursors of the main event: the Human Genome Project. Conceived in the mid-1980s and officially launched on Oct. 1, 1990, this $3 billion international effort has outlasted the skepticism that greeted its audacious goal. By 2005, biologists will have catalogued and sequenced the 80,000 to 100,000 genes used by humans, as well as the rest of our genetic material, which we almost certainly mistakenly dismiss as "junk DNA."

Ranging from tests that spot diseases decades before symptoms appear to cures that replace disease-causing DNA, the clinical dreams of the Human Genome Project have been well documented, as have the ethical quandaries it will bring. Yet the project should no less certainly recast our understanding of pure biology and the discussion of how the seemingly endless array of life-forms on this planet came to be.

The Human Genome Project has been likened to many past endeavors—particularly the Manhattan Project, which led to the atomic bomb, and the Apollo missions, which reached the moon. Noting that the genome project is largely laying the foundation for future research rather than addressing life's mysteries directly, Eric C. Lander of the Whitehead Institute for Biomedical Research in Cambridge, Mass., offers perhaps the most apt analogy.

"The Human Genome Project," he wrote recently, "is best understood as the 20th century's version of the discovery and consolidation of the periodic table. In the period from 1869 to 1889, chemists realized it was possible to systematically enumerate all atoms and position them in an array that captured their similarities and differences. The building blocks of chemistry were rendered finite, and the predictability of matter gave rise to the chemical industry on one hand and the theory of quantum mechanics on the other. The Human Genome Project aims to produce biology's periodic table—not 100 elements, but 100,000 genes, not a rectangle reflecting electronic valences, but a tree structure depicting ancestral and functional affinities among human genes."

The new periodic table will force a sea change in the experiments that biologists perform. Rather than probe the roles of individual genes and the proteins they encode, investigators will monitor the activity of every human gene in a single cell. "People won't pick one gene and make a career of it. They will focus more on the interactions of families of genes," observes Victor McKusick of Johns Hopkins University in Baltimore.

While the Human Genome Project's name may suggest there's a single standard sequence, individual genomes vary tremendously, a fact that will rise to prominence in the years to come. Much as a chemical element exists as distinct isotopes, genes can come in several alleles. The distribution of these alleles explains much of human diversity and enables scientists to track the migrations and evolution of our ancestors.

J. Craig Venter of the Institute for Genomic Research in Rockville, Md., stresses that the Human Genome Project is but a single effort in the genome revolution now under way. "By the time the human genome is sequenced, there could be a thousand other genomes done," he says. "Over the next 5 to 10 years, there's going to be 400,000 to 500,000 new genes discovered."

This deluge of data should change molecular evolution from a fledgling enterprise into a sophisticated discipline. Most of the speculative trees of life drawn by today's molecular evolutionists stem from species differences in a single gene that encodes a subunit of a cellular organelle. The controversy over whether this gene's evolution is relevant to that of an entire species will become moot once dozens of complete genomes are available for comparison. "We're trying to develop genome-based evolutionary studies because the genomes are what evolved," says Venter.

Genomes probably hold answers to some of life's fundamental mysteries. They should settle, for instance, the question of how complex genes arose from simpler DNA sequences, an issue that lies at the heart of the origin of life.

Finally, the genome revolution promises to alter biology's status among the sciences. The Manhattan Project's devastating success over Hiroshima and Neil Armstrong's first steps on the moon reflect the preeminence of physics and engineering in the 20th century. Yet as the Superconducting Supercollider's failure to get funding and the international space station's struggles attest, those fields' heady days are over.

"We're going from the century of physics to the century of biology," Venter says. □

1938 Description of how Earth's orbit caused ice ages

1939 Astronomers explain how stars burn

1939 DDT discovered

1940 Stone Age paintings found in France's Lascaux cave

1942 Sustained nuclear chain reaction

1944 Discovery that genes are made of DNA

1946 Carbon-14 dating method developed

1948 Transistor invented

1949 Theory that strengthening neuron connections causes learning

1949 Birth of X-ray astronomy