biology

Top scientists pinpoint the critical developments of the last 25 years and predict wonders yet to come

The ability to manipulate DNA is the central technology that has powered biomedical science over the past 25 years. We have gained the ability to cut and paste the long string of the DNA, to move snippets of DNA from one organism to another, to read DNA text and change it as well as to create new DNA segments at will. DNA technology has given us direct access to the central program of life and made it possible for us to harness the enormous reproductive and evolutionary power of living organisms for our advantage. It also enabled one of mankind's greatest technical achievements—the reading of the entire genetic code of a human being—and gave birth to a new industry, biotechnology, from which flow products that improve the lives and health of hundreds of millions of people worldwide. Progress in biomedicine over the next 25 years will be driven by our ability to manipulate human cells for healing. We have already learned to isolate and propagate human embryonic stem cells, those generators of life that hold the potential to become any cell, any tissue, and any organ of the human body. During the next quarter century we will learn to mold these plastic cells to restore, replace, and regenerate all parts of the body, whether they be injured by trauma, damaged by disease, or worn by time. With this new facility will also come the knowledge to similarly manipulate the myriad types of cells that compose our body, to usher in the new age of cellular therapy. What was once lost, will now be restored, be it muscle, brain, or bone.

WILLIAM HASELTINE, PRESIDENT OF THE WILLIAM A. HASELTINE FOUNDATION FOR MEDICAL SCIENCES AND THE ARTS; FOUNDER AND FORMER CHAIRMAN AND CEO OF HUMAN GENOME SCIENCES

I am impressed by observations, during the last 25 years that show the presence of many organic molecules, including amino acids and other biological constituents, in outer space and on extraterrestrial objects, not only in the solar system but probably also elsewhere in our galaxy and in others. Some of the processes involved are now being reproduced in the laboratory, under physical conditions (very low temperature, very high vacuum, high radiation) mimicking those that prevail in outer space. These findings have revealed that some of the main building blocks of life arise spontaneously in many parts of the universe as products of cosmic chemistry, available for the possible development of life wherever conditions allow. Predicting the future is not a scientific exercise. What I would find particularly exciting would be the discovery, around a nearby star, of an Earth-like planet exhibiting physical conditions under which the products of cosmic chemistry could give rise to living organisms, as they are suspected of having done on our planet 4 billion years ago. Many extrasolar planets have already been discovered. But technical improvements will be needed before an Earth-like planet can be detected.

CHRISTIAN DE DUVE, FOUNDER OF THE INTERNATIONAL INSTITUTE OF CELLULAR AND MOLECULAR PATHOLOGY, BRUSSELS; NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE, 1974

THE GREATEST DISCOVERIES

in biology over the last 25 years have undoubtedly been in the understanding and sequencing of the genome. However, the growing awareness of how whole sets of genes are expressed or suppressed by environmental influences early in life has drawn attention to the ways the developing organism is adapted to the world it is likely to inhabit. This awareness will have an enormous impact in the next 25 years and, to a large extent, reverse the past tendency of biological research to move from the level of the whole organism to that of the molecule. Increasingly, the focus will be on how intact biological systems work, how the environment shapes an organism's development, and on life-history tactics. Since developmental plasticity prepares the organism for the habitat that it is likely to occupy, rapid environmental change, such as that experienced by increasingly well-nourished modern humans, leads to inaccurate forecasts in early life, maladapted adults, and serious ill health resulting from diseases such as heart failure and diabetes. The discoveries to be made in biology will, I predict, have great significance for medical treatment of such disease and for the planning of public health.

SIR PATRICK BATESON, PROFESSOR OF ETHOLOGY, UNIVERSITY OF CAMBRIDGE; COAUTHOR WITH PAUL MARTIN OF *DESIGN FOR A LIFE,* (SIMON & SCHUSTER, 2000)

A series of discoveries between 1982 and 1986 revealed that RNA can be an enzyme. This provided the first tangible evidence that a different form of life may have existed on early Earth: one with RNA instead of DNA as its genetic material, and RNA instead of protein as its chief agent of catalytic function. These discoveries were recognized by the awarding of the Nobel Prize in Chemistry in 1989 to Thomas Cech and Sidney Altman. Over the past 20 years, it has become increasingly clear that RNA-based life preceded the DNA/protein-based life that has dominated our planet for the past 3.5 billion years. It is not known if RNA-based life was the first form of life on Earth, but our RNA ancestors have left a rich heritage in contemporary biology. Even today, RNA controls many of the most primitive processes of the cell, and almost every year new discoveries are made concerning the active roles that RNA can play.

GERALD F. JOYCE, PROFESSOR OF CHEMISTRY AND MOLECULAR BIOLOGY, SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

In the past 25 years, molecular biology has flourished. That includes the development of combinatorial chemistry, which could transform drug discovery. In this field, one generates large libraries of DNA, RNA, peptides, polypeptides, proteins, or small molecules and seeks a molecule with a defined function. The process works like this: Estrogen binds its receptor, lock and key; test a library for a second key molecule that fits the same estrogen-receptor lock; the new molecule is a candidate drug to mimic or antagonize estrogen. The idea generalizes to vaccines. This promise awaits its fulfillment. In the next 25 years, I hope the major new discovery will be in cancer research. There is growing evidence in many cancers that a subset of stem/progenitor cells may drive the proliferation of diseased cells. A new field of "differentiation therapy," which seeks to induce the benign behavior or death of these cells, may herald a new era in cancer therapy.

STUART KAUFFMAN, DIRECTOR, THE INSTITUTE FOR BIOCOMPLEXITY AND INFORMATICS, UNIVERSITY OF CALGARY; AUTHOR OF *AT HOME IN THE UNIVERSE* (OXFORD UNIVERSITY PRESS, 1995)

Advances in public health during the 20th century insulated us from the extreme hazards of our hostile world. This allowed most people in developed nations to live long enough to experience the full range of biological changes that occur as we age—both good and bad. One of the trade-offs for longer life was the modern rise of cardiovascular diseases and cancer. Twenty-five years ago these killer diseases began yielding to an arsenal of weapons developed in the biomedical sciences—including earlier detection, new surgical procedures, and pharmaceuticals—all leading to significant reductions in death rates at middle and older ages. In the next 25 years, the focus will shift to the underlying processes of aging itself. When scientists finally piece together enough of the puzzle of aging to slow it down in humans, we will for the first time in history believe we are the master of our own biological destiny. Discovering the unique alleles possessed by the world's longest-lived people could lead to genetic and pharmaceutical interventions that confer their protected and long-lived status to others. Likewise, understanding the genetics and cellular physiology that underlie variation in longevity between species may lead to the identification and manipulation of biologically conserved mechanisms that influence duration of life. There will be significant risks and moral dilemmas to be sure, but ultimately people alive today may be the first to sip from a genuine fountain of youth.

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