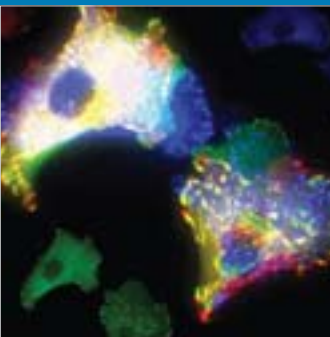
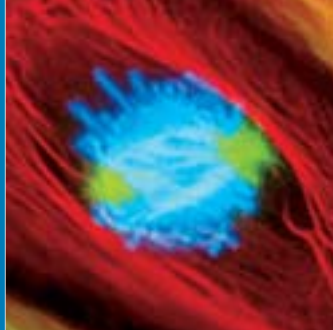




Curiosity Creates Cures

*The Value
and Impact of
Basic Research*



Whether they investigate how medicines work, study the life cycle of bacteria, or crunch numbers in a computer, scientists across the globe are united by a compelling desire: to better understand how life works. Rather than focusing on a specific disease, these basic biomedical scientists, many of whom are funded by the National Institute of General Medical Sciences (NIGMS) at the National Institutes of Health, seek to answer important biological questions like how cells talk to each other, how biological machines fold into their active shapes, and how genes are regulated.

Although these studies may not have an immediate impact on our health, such “untargeted” research often leads to new medicines, technologies, and research tools. Examples of advances that grew out of basic research include countless drugs to treat diseases ranging from cancer to AIDS; magnetic resonance imaging (MRI), which provides clear pictures of the body’s organs and tissues; and the polymerase chain reaction, a laboratory technique that is the basis of “DNA fingerprinting,” which revolutionized criminal forensics.

“Even if it brings no immediate benefits, scientific research that advances the frontiers of knowledge is necessary and should be supported.”

— 80 percent of respondents to a 2003 poll conducted by Research!America



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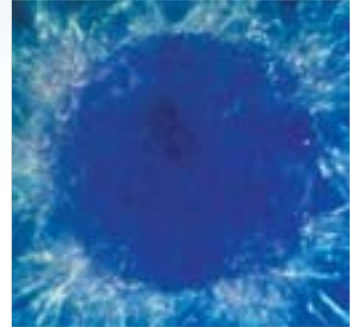
Basic Research Pays Off

“Basic research...pays off in terms of key discoveries almost twice as handsomely as other types of research and development combined.”

— a major conclusion of a landmark study that revealed that the most important advances in cardiovascular medicine grew out of the work of basic scientists.*

*Comroe JH, Dripps RD. Scientific basis for support of biomedical science. *Science* 1976; 192:105-11.

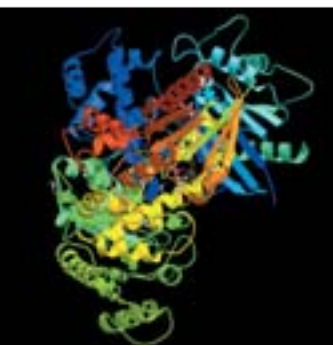
“If you think research is expensive, try disease.” This famous quote is attributed to Mary Lasker, a philanthropist and advocate for medical research. Her words acknowledge that by providing a solid understanding of the cellular and molecular changes that cause disease, basic research may help prevent disease or cure it in its early stages, yielding tremendous savings of both money and misery. The quote is clearly borne out by the numbers.

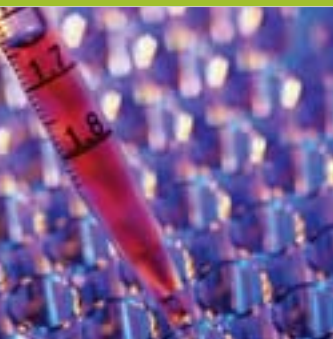


Regardless of what measure is used—reduced health care costs or increased productivity due to longer life and decreased illness—studies show returns on investment ranging from \$10 to more than \$80 for every dollar spent on basic research. Not surprisingly, the longer a medical advance is available, the greater the benefits.

Basic biomedical research also benefits the economy in more direct ways. Many nonbiomedical industries have been either created or enhanced by biomedical discoveries. Together, the following industrial applications contribute tens of billions of dollars to the U.S. economy every year:

- *Freeze-drying, which was developed to concentrate and preserve laboratory samples, is now widely used in the food industry.*
- *Basic studies of digestive enzymes led to improvements including meat tenderizers; bread dough conditioners; milk coagulants for cheese production; stain-removal additives in laundry detergent; and preservatives for beer, wine, and juice.*
- *Fundamental research on the role of immune factors in controlling herpes led to a vaccine for a deadly disease in chickens.*





UNTANGLING ALZHEIMER'S. The leading form of dementia in older people, Alzheimer's disease is caused in part when a protein, called tau, loses its normal shape. Tau forms knotty tangles that skew communication between nerve cells in the brain. Recently, a basic researcher studying cell division has identified an enzyme, dubbed Pin1, that restores tau's normal shape in laboratory experiments. The discovery helps researchers in the quest for new therapies to treat Alzheimer's disease and other neurodegenerative conditions.

CURIOSITY YIELDS CANCER DRUG. A scientist wondered why the body sometimes destroys its own proteins and why muscles waste away when they're not used. His research group discovered the culprit: cellular garbage-disposal-like structures called proteasomes. While creating compounds to clog proteasomes, the scientists noticed that one of their substances had anticancer properties. Under the name Velcade™, this drug is now used to treat multiple myeloma, the second most common blood cancer.

DESIGNER DRUGS FOR BLOOD CLOTS. While studying the structures of complex sugars, scientists developed prototypes of new drugs to help control blood clots, which can cause heart attacks and strokes, during surgery. Using "molecular scissors," the scientists tailored heparin, a commonly used blood thinner, into a much more potent form. They also developed a molecular tool that can selectively deactivate heparin after surgery, enabling doctors to control bleeding with minimal side effects.

GOT YOUR FLU SHOT? WILL IT WORK? To create effective flu vaccines, scientists must predict months in advance which strains of influenza are going to be most troublesome. A multidisciplinary research team used a computer-based approach to analyze a database containing DNA sequences of 560 flu viruses from 16 flu seasons. The team discovered patterns of genetic changes in the viruses that could help create more effective vaccines, saving many lives each year.

WHAT MAKES ANTHRAX SO DEADLY? Scientists recently revealed an answer by determining the structure of an anthrax protein. The protein, called edema factor, causes potentially fatal swelling and fluid buildup in the body. Its structure revealed that when it binds to another molecule in the body, edema factor changes shape to create a deep pocket in which deadly chemical reactions occur. This discovery—based on basic research into cell communication—may enable researchers to design drugs that clog the protein pocket and help disarm the lethal microbe.

HANG ON, BABY! Scientists studying carbohydrates on the surfaces of cells learned that these molecules are involved in the implantation of embryos in a woman's uterus. The research holds promise for understanding and treating infertility, because the failure of an embryo to implant properly is a common reason for problems in early pregnancy.



What Makes Good Research?

“It is hard to predict how science is going to turn out, and if it is really good science, it is impossible to predict.”

— Lewis Thomas
late biologist and writer

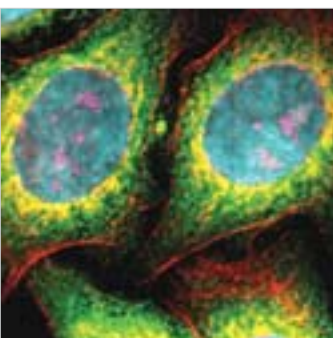
In a familiar science fiction scenario, a scientist knocks over a test tube and creates a medicine—or weapon—with incredible power. Although a number of important advances have occurred by chance, most scientific advances are not accidental. Neither are most findings made by lone scientists. They are products of years of intensive labor by teams of researchers that include many young scientists in training. Increasingly, groups of interdisciplinary scientists are working together to tackle problems that transcend their individual expertise. Each team contributes to the eventual “discovery.”

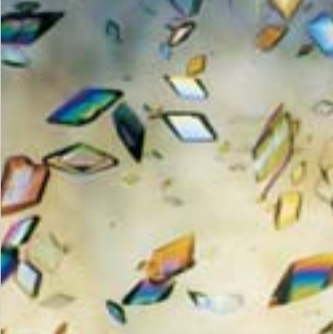


In many cases, basic research has unexpected applications. For example, studies in how viruses infect bacteria led to the discovery of restriction enzymes, which are a cornerstone of the biotechnology industry. Research on how electric fields affect bacteria led to an important cancer medication, cisplatin. And curiosity about substances that break down bacterial walls led to the identification of penicillin as an antibiotic drug.

Basic research often relies on studies in “model organisms” such as bacteria, fruit flies, or mice. Because human cells contain the same molecular building blocks and pathways as those of most other living things, researchers can learn much about the way our cells work by studying these simpler organisms. These creatures are easy to maintain in the laboratory and they allow scientists to tightly design and control their experiments. Scientists can select the type of model organism best suited to examine a specific problem or process. In the case of mice and some other animals, researchers can further tune the model to their work by choosing a strain that is prone to developing certain tumors, metabolic disorders, or other conditions.

Ingredients of good research include stimulating scientific collaboration, adequate funds, and the ability to shift directions to pursue promising leads. Sometimes, all it takes is having the right scientists in the right place at the right time. Whether it comes as blockbuster discoveries or incremental advances, history shows that over time, untargeted basic research yields inestimable rewards.





Great Benefits to Humankind

“The pursuit of curiosity about the basic facts of nature has proven, with few exceptions throughout the history of medical science, to be the route by which the successful drugs and devices of modern medicine were discovered.”

— Arthur Kornberg
1959 Nobel Laureate in physiology or medicine

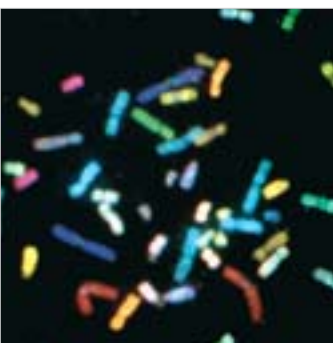
In his will, Alfred Nobel instructed that prizes be awarded to those who, in specific fields, “have conferred the greatest benefit on mankind.” The Nobel Prizes, the highest honors bestowed in science, are frequently awarded to basic researchers. Listed below are a few of the dozens of Nobel Prize-winning scientists supported by NIGMS.



NAME	NOBEL PRIZE	OFFICIAL CITATION
Paul C. Lauterbur	Physiology or Medicine 2003	For discoveries concerning magnetic resonance imaging.
Roderick MacKinnon	Chemistry 2003	For discoveries concerning channels in cell membranes, specifically his structural and mechanistic studies of ion channels.
H. Robert Horvitz	Physiology or Medicine 2002	For discoveries concerning genetic regulation of organ development and programmed cell death.
John B. Fenn	Chemistry 2002	For the development of methods for identification and structure analyses of biological macromolecules [specifically, for techniques in mass spectrometry].
Leland H. Hartwell	Physiology or Medicine 2001	For discoveries of key regulators of the cell cycle.
K. Barry Sharpless	Chemistry 2001	For work on chirally catalyzed oxidation reactions [a technique to selectively control the outcome of chemical reactions].

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