The Role of Life Sciences in Transforming America's Future: Summary of a Workshop

ISBN
978-0-309-13156-8

31 pages
8.5 X 11
2009

Committee on a New Biology for the 21st Century: Ensuring the United States Leads the Coming Biology Revolution, National Research Council

Prepublication Copy

2008 National Academies Biology Summit

The Role of the Life Sciences in Transforming America's Future Summary of a Workshop

December 3, 2008

Committee on a New Biology for the 21st Century:
Ensuring the United States Leads the Coming Biology Revolution

Board on Life Sciences
Division on Earth and Life Studies

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

THE NATIONAL ACADEMIES PRESS
Washington, D.C.
www.nap.edu

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This study was supported by Contract/Grant No. DHHS-5294, TO#209 between the National Academy of Sciences and the National Institute of Health and Contract/Grant No. NSF-8893 between the National Academy of Sciences and the National Science Foundation. Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the author(s) and do not necessarily reflect the views of the organizations or agencies that provided support for the project.

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Printed in the United States of America

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COMMITTEE ON A NEW BIOLOGY FOR THE 21ST CENTURY: ENSURING THE UNITED STATES LEADS THE COMING BIOLOGY REVOLUTION

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Acknowledgements

This workshop summary has been reviewed in draft form by persons chosen for their diverse perspectives and technical expertise in accordance with procedures approved by the National Research Council's Report Review Committee. The purposes of this review are to provide candid and critical comments that will assist the institution in making the published summary as sound as possible and to ensure that the summary meets institutional standards of objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following for their participation in the review of this summary:

Deborah Blum, University of Wisconsin, Madison
Thomas Connelly, E. I. du Pont de Nemours and Company
Margaret McFall-Ngai, University of Wisconsi, Madison
Robert Nerem, Georgia Institute of Technology
Muriel Poston, Skidmore College
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Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse, nor did they see the final draft of the workshop summary before its release. The review of this summary was overseen by Marvalee H. Wake, University of California, Berkeley. Appointed by the National Research Council, she was responsible for making certain that an independent examination of this summary was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this summary rests entirely with the author and the National Research Council.

Preface

Many of the great global challenges of the 21st century – providing an expanding population with adequate food and water, reducing and adapting to climate change, conquering disease, ensuring adequate supplies of energy – could be met through the application of ideas emerging from the life sciences. In university, corporate, and government laboratories across the United States and throughout the world, scientists and engineers are creating the new knowledge and technologies that could create a better life for the billions of people living on earth today and the billions more who will be born during this century. Human ingenuity can solve the problems we face, just as it has many times in the past. But we need to move quickly to create the conditions that will allow human ingenuity to flourish.

The tremendous potential of the life sciences was the central theme of a December 3, 2008, "Biology Summit" held by the National Academies' Board on Life Sciences at the headquarters of the American Association for the Advancement of Science in Washington, D.C. Some of the nation's leading scientists were asked to put aside their day-to-day administrative concerns and talk instead about where they see the life sciences headed and how to get there. The result was a fascinating mixture of visionary optimism and hard-headed policy advice. Nobel Prize winners, university and corporate presidents, and top government officials spoke enthusiastically about the research occurring in their laboratories and institutions and where that research could lead. They expressed frustration at opportunities that are not yet being grasped because of organizational, intellectual, or financial obstacles, and they offered ideas about how to make the future arrive sooner. Speakers at the meeting also discussed two of the most important developments taking place in science today: the ongoing unification of the life sciences, and the merging of important parts of the life sciences with the physical sciences and engineering into a single "transdisciplinary" endeavor directed at solving the major problems facing human society. This reorganization of science -- the most profound shift in the scientific enterprise since the professionalization of science in the second half of the 19th century -- could mark a turning point in the application of human knowledge to meet human needs.

This publication summarizes the main points made at the Summit and highlights, in sidebars accompanying the main text, some of the new ideas and technologies described by the speakers. The meeting was organized by the Committee on a New Biology for the 21st Century: Ensuring the United States Leads the Coming Biological Revolution, which the two of us co-chair. The committee was formed by the National Academies to recommend actions that federal policymakers can take to ensure that the United States maintains and builds on its lead in the life sciences. The meeting served as input to a consensus report being prepared by the committee that lays out steps that can be taken to help achieve the great potential offered by the life sciences today. While it was not possible to cover all of the thriving areas of the life sciences in a one-day meeting -- for example, important work now being done on the functioning of whole organisms did not receive much discussion -- the Summit provided a broad overview of the field and a sense of the excitement that surrounds it.

In his introductory remarks at the Summit, National Academy of Sciences president Ralph Cicerone made a remarkable observation. If each person living today were allotted an equal space of all the world's landmasses, that person would have to survive on a square of land measuring 150 meters on a side – about the area of four American football fields. With that much land per person, we must grow all our food, extract all our energy, sequester all our wastes, derive all our water, build all our roads and structures, and set aside space for the preservation of nature. Furthermore, by the year 2050, the global population is expected to grow from today's 6.7 billion to more than 9 billion – reducing the area per person to three football fields.

Humans could not have become as numerous and as successful as we are without science and technology. As our numbers grow, we will not continue to prosper without continued major advances in science and technology. The life sciences could lead the way to an even more successful future. All of us have a responsibility to help realize that vision.

Thomas Connelly, DuPont Company
Phillip Sharp, Massachusetts Institute of Technology

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A Critical Time for the Life Sciences

Speaker after speaker at the Summit agreed: the life sciences are poised to usher in a period of unprecedented health and prosperity. Basic scientific research into how living things function is producing new understanding of how living systems work and new ways of using biological processes to meet human needs. If current opportunities are grasped, the life sciences can help produce enough food for a growing population, cure chronic and acute diseases, meet future needs for energy, and manage the preservation of earth's biological heritage for future generations. From the perspective of the life sciences, we live in the most exciting and promising period in human history. Yet even though the potential is enormous, speakers emphasized that the benefits will be achieved more quickly if financial and institutional barriers to newly emerging capabilities are reduced.

The potential of the life sciences today has two roots. First, powerful tools are allowing biologists to collect and analyze vastly more information about complex systems, from single cells to global biogeochemical cycles, than has been possible before. This information is helping to uncover not just the molecular mechanisms that underlie biological processes but the ways that biological subsystems interact in whole organisms and in terrestrial and marine ecosystems. In this way, ongoing research is helping to unify biology by revealing the commonalities among organisms and by linking biological processes at different levels of organization.

Second, a profound reorganization within science is occurring. Important segments of the life sciences are merging with the physical sciences and engineering to create "transdisciplinary" scientific endeavors focused on pressing global problems. This blending of disciplines is leading to new insights into life processes and creating new opportunities to translate those insights into practical applications, just as the synthesis of the physical and mathematical sciences with engineering in the 20th century created the electronics and information revolutions that have transformed our lives.

> If current opportunities are grasped, the life sciences can help produce enough food for a growing population, cure chronic and acute diseases, meet future needs for energy, and manage the preservation of earth's biological heritage for future generations.

Scientists, policymakers, and research administrators cannot predict which new technologies and industries will emerge from the unification of biology and the convergence of the life sciences, the physical sciences, and engineering. Yet steps can be taken now, multiple speakers pointed out, to ensure that the great potential of the life sciences bears fruit as quickly as possible, thereby giving rise to a steady stream of new ideas and new applications of science. Public and private funders can support the high-risk, transformational research that is commonly underfunded, especially during times of stagnant budgets. They can support younger researchers, who face daunting challenges in competing for scarce funds yet often have important insights that can spur progress.

They can help break down the barriers among disciplines that continue to inhibit transdisciplinary research. And they can foster educational programs that will produce the transdisciplinary scientists and engineers of the future.

The Promise of the Biological Sciences

Investments in the life sciences pay off in three broad areas, observed Massachusetts Institute of Technology (MIT) President Susan Hockfield. They improve human health. They foster industries that boost the economy while addressing a wide range of environmental, energy, health, and agricultural challenges. And they further human understanding of some of the most fascinating systems in the universe.

Improving Human Health

The biological sciences have enabled most of the world's population to enjoy higher living standards and longer life spans than ever before, said National Academies President Ralph Cicerone. New understanding of the links between disease and sanitation, the role trace nutrients play in health, and the potential of vaccines and antibiotics, among many other research results, have improved the lives of people everywhere.

The progress made in combating heart disease is a prime example of the payoffs from investment in the life sciences, said Hockfield. Over the past 30 years, the National Institutes of Health (NIH) has invested about $4 per American per year in cardiovascular research. That investment has helped reduce the rate of death from heart disease and stroke by more than half. Knowledge of cholesterol metabolism led to the development of the drugs known as statins, which have reduced heart attacks and strokes. The development of drug-eluting stents has enabled physicians to open occluded blood vessels. Study of receptors on the surface of nerve cells has led to new beta blockers that are being used to treat hypertension and heart disease.

Similar advances have produced benefits throughout medicine, observed Thomas Cech, President of the Howard Hughes Medical Institute, and Harold Varmus, President of the Memorial Sloan-Kettering Cancer Center. Greater understanding of the role of tumor necrosis factor in inflammatory disease has led to antibody treatments that have changed the lives of many people with rheumatoid arthritis. Materials science is producing spare parts for bones, arteries, and other tissues and organs.

The Artificial Retina

The artificial retina is an implantable microelectronic device designed to restore useful vision in people blinded by retinal diseases like macular degeneration. It is being developed by six Department of Energy (DOE) national laboratories, four universities, and private industry. A camera mounted in eyeglasses sends a signal to a microprocessor worn on a belt that converts the camera's image to an electronic signal. This signal is fed to an array of electrodes positioned on the retina of the eye. The electrodes are coated with diamonds so they do not decay in the salty environment inside the eye, and they are springloaded so they do not destroy the cells inside the eye that convey images to the brain.

The first model consisted of 16 electrodes and was implanted in six patients between 2002 and 2004. A second, much smaller model consisting of 60 electrodes is currently being tested in humans, and a third model containing more than 200 electrodes is now being designed. "When you see a patient who has been blind for 30 to 40 years recognize objects and be able to read large-scale newsprint, you begin to appreciate the consequences of the convergence of the physical and life sciences," said DOE's Raymond Orbach.

Basic research into retroviruses motivated by their role in some cancers built the base of understanding that proved critical in first identifying the cause of the AIDS epidemic and then developing drugs to control the disease. "If we as a country hadn't made the investment in the basic science, in the understanding of retroviruses, we would probably still today have a rapidly expanding global AIDS epidemic," Cech said.

Continued basic research into fundamental biological processes could yield a wealth of new medical advances.

A Genetic Fountain of Youth?

Many biologists have assumed that living things inevitably age and die. But recent research has shown that the rate of aging in many animals is at least partially under genetic control, suggesting that many organisms may be able to live longer than they do normally.

In the 1990s, Cynthia Kenyon and her colleagues at the University of California, San Francisco, began looking for genes that might control aging in the tiny worm *C. elegans*. They found a worm with a mutation in a gene called *DAF-2,* which encodes a hormone receptor, that had a healthy life span twice that of normal worms. Mutants found since then have lifespans up to ten times that of normal worms.

Kenyon and her colleagues also found that another gene called *DAF-16* is needed for *DAF-2* mutations to extend the lifespan. *DAF-16* encodes a protein that turns other genes on and off. When another technique called RNA interference was used to regulate these genes one by one, many turned out to have an effect on aging in *C. elegans*. Furthermore, many of these genes may be involved in disease processes, since long-lived mutants have a remarkable resistance to disease.

Similar genetic pathways have been identified in flies, mice, and humans. Study of families and populations with unusual longevity also are beginning to turn up genetic variants associated with long life. "It is looking as though these variants can affect human lifespans, which means that we could potentially increase longevity and youthfulness in humans by modulating components of this pathway," said Kenyon.

Investigations of bacterial genetics could provide new treatments for infectious diseases, including diseases caused by microbes that have evolved mechanisms to evade existing treatments. Bioengineered stem cells could provide regulated insulin secretion in people with diabetes, for example, or repair severed spinal cord nerves. Study of chronic diseases such as cancer, heart disease, and mental illness, which now account for the bulk of health care costs, could lead to personalized treatments that reflect a disease's unique characteristics in each individual.

However, the translation of basic research findings to applications is not always straightforward or quick, Cech observed. Even where understanding of biological processes is extensive, vast amounts of work must be done, often by people in different disciplines and sectors working collaboratively, to apply new knowledge in medicine.

From Discovery to Treatment

A combination of deep biological understanding and innovative biotechnology has dramatically changed outcomes for many women with breast cancer.

In the 1980s, researchers discovered a gene in rats that is involved in the origin and spread of cancer. The products of this gene could be blocked using a monoclonal antibody – a special kind of protein made using the tools of biotechnology. Researchers also discovered that this gene is related to a human gene called *HER2* that encodes a growth factor receptor on the surface of human cells.

Further research showed that women with breast cancer who had extra copies of the HER2 receptor on tumor cells survived with the disease only about half as long, on average, as did women with the normal number of receptors. In 1991 the Food and Drug Administration (FDA) received an application requesting that a monoclonal antibody directed against the receptor called trastuzumab (or Herceptin) be studied in clinical trials. In 2006, FDA approved the drug for use in patients undergoing breast cancer treatment who test positive for elevated expression of the receptor.

That is not fast enough, said Susan Desmond-Hellmann, President of Product Development for Genentech, Inc. The drug should have been available sooner, and far more drugs similar to Herceptin need to be in the drug development pipeline than is the case today.

Many questions remain unanswered about Herceptin. Why do some patients relapse despite being treated with the antibody? Why does Herceptin cause cardiac problems in some of the women who receive it? As Desmond-Hellmann said, "We need more, more, more basic science." Also, scientists from academia, industry, and government need to be able to interact extensively to answer such questions. For example, noninvasive ways approved by regulators to monitor and diagnose cancers would catalyze the development of new drugs.

Fostering Industries to Counter Global Problems

The life sciences have applications in areas that range far beyond human health. Life-science based approaches could contribute to advances in many industries, from energy production and pollution remediation, to clean manufacturing and the production of new biologically inspired materials. In fact, biological systems could provide the basis for new products, services and industries that we cannot yet imagine. Microbes are already producing biofuels and could, through further research, provide a major component of future energy supplies. Marine and terrestrial organisms extract carbon dioxide from the atmosphere, which suggests that biological systems could be used to help manage climate change. Study of the complex systems encountered in biology is producing insights into similarly interconnected networks encountered in many other areas of science – and vice versa.

Take agriculture as an example. The agricultural biotechnology industry is just a little more than a decade old, said Robert Fraley, Executive Vice President and Chief Technology Officer at Monsanto – the first bioengineered crop, a soybean seed with a gene providing tolerance for a common herbicide, was launched in 1996. Yet biotechnology crops are today being planted on 20 percent of the world's farmland, and the percentage is projected to double as new crops are introduced and countries like India and China move toward full adoption of the technology. "This is the most rapidly adopted new technology in the history of agriculture," Fraley said.

The ability to introduce multiple genes into an ever-expanding array of crops has not only increased yields but has produced significant environmental benefits. By altering the characteristics of crops, agricultural biotechnology has made it possible for farmers to use fewer pesticides and other chemicals. Fewer trips through the fields on tractors mean less greenhouse gas emissions and reduced compaction of soils. Furthermore, the revolution in agricultural biotechnology has just begun, Fraley said. Within a few years, agricultural companies will be selling seeds with ten or more introduced genes. Crops can be modified to improve human health; for example, soybeans have been genetically modified to produce healthy rather than unhealthy fatty acids. Future crops will need far less water, a crucial consideration as climate change alters rainfall patterns and groundwater aquifers are depleted. As Fraley said, "As much as we have seen happen in the last decade, it is really just the beginning."

Advances in the underlying science of plant and animal breeding have been just as dramatic as the advances in genetic engineering. Results from basic research have allowed plant and animal breeders to produce organisms with desired combinations of genetic traits. Say, for example, that a breeder wants to assemble 20 desirable genetic traits in the same plant. Using traditional breeding methods, the odds of achieving exactly that combination of traits in a single plant would have been one in a trillion – essentially zero. Using the new techniques made possible through genetic research, the odds are one in five. Over the last half century, plant breeders have been able to achieve a nearly one percent annual increase in corn yields using traditional breeding techniques. With the new techniques, yields are now going up by two to three percent annually. "We can now pick traits and combinations of genes that it never would have been possible to produce in the history of agriculture," said Fraley. "That says a lot when you consider that humans have been trying to do this for 8,000 years."

Many other technologies derived from basic scientific research are boosting agricultural yields. Automated gene sequencers test genetic markers in thousands of individual seeds per day. Magnetic resonance imaging can look inside plants and animals to characterize traits. Using tractors equipped with global positioning system devices, farmers can put down a band of fertilizer, come back six months later, and plant seeds exactly on that row, reducing the need for fertilizer, pesticides, and other agricultural inputs.

Fraley said that the global agricultural system needs to adopt the goal of doubling the current yield of crops while reducing key inputs like pesticides, fertilizers, and water by one third. “It is more important than putting a man on the moon,” he said. Doubling agricultural yields would “change the world.” Another billion people will join the middle class over the next decade just in India and China as economies continue to grow. And all people need and deserve secure access to food supplies.

Continued progress will require both basic and applied research, as scientists learn more about the fundamental biology of plants and collaborate with others in putting that knowledge to work. “Just as the basic biomedical research in the future is not going to be done by the pharmaceutical companies, [oil companies and agribusinesses] aren't going to do the fundamental research in photosynthesis and plant development and plant hormones that is going to lay the groundwork for a future understanding of how plants work,” said Cech. For the life sciences to have a dramatic effect on nutrition, the world’s food supply, and the renewable energy problem, “we need to keep reinvesting in understanding the biology.”

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Answering Fundamental Questions

The life sciences can answer some of the most fundamental, interesting, and difficult questions that human beings can ask. How did the great diversity of living things come to be? How do cells function on a molecular level? What is the role of life in changing the surface of the earth?

The evolution of life “put earth under new management,” Collins said. Understanding the future state of the planet will require understanding the biological systems that have shaped the planet.

Consider this last question, said James Collins, who is currently on leave from Arizona State University to serve as Assistant Director for Biological Sciences at the National Science Foundation. According to a recent estimate, of the approximately 4,300 types of minerals on the earth, about 3,000 are the products of biological processes. The evolution of life "put earth under new management," Collins said. Understanding the future state of the planet will require understanding the biological systems that have shaped the planet.

Many of these biological systems are found in the oceans, which cover 70 percent of the earth's surface and have a crucial impact on weather, climate, and the composition of the atmosphere. In the past decade, new tools have become available to explore the microbial processes that drive the chemistry of the oceans, observed David Kingsbury, Chief Program Officer for Science at the Gordon and Betty Moore Foundation. These technologies have revealed that a large proportion of the planet's genetic diversity resides in the oceans. In addition, many organisms in the oceans readily exchange genes, creating evolutionary forces that can have global effects.

The oceans are currently under great stress, Kingsbury pointed out. Nutrient runoff from agriculture is helping to create huge and expanding "dead zones" where oxygen levels are too low to sustain life. Toxic algal blooms are occurring with higher frequency in areas where they have not been seen in the past. Exploitation of ocean resources is disrupting ecological balances that have formed over many millions of years. Human-induced changes in the chemistry of the atmosphere are changing the chemistry of the oceans, with potentially catastrophic consequences. "If we are not careful, we are not going to have a sustainable planet to live on," said Kingsbury. Only by understanding the basic biological processes at work in the oceans can humans live sustainably on earth.

The prospect of answering basic questions about the nature and history of life attracts many students to the life sciences, especially when they see that putting that knowledge to work can contribute to building a cleaner and healthier world, said several speakers at the meeting. How did the first living organisms arise from the inanimate compounds present on the earth? What biological mechanisms give rise to consciousness? Have living things evolved on other planets in our solar system or elsewhere in the universe? These are the kinds of questions that can spark the imaginations and convictions of students and researchers alike.

The Rise of Transdisciplinary Science

The way that biological research is being done "is changing right in front of our eyes," according to Collins. Researchers from different fields of biology are working together on projects that transcend divisions within the discipline. Similarly, life scientists are increasingly working in partnerships with physical scientists and engineers on problems that no one discipline could solve on its own.

The Unification of the Life Sciences

Since the emergence of biology as a profession in the 19th century, the discipline has included two major intellectual strands, said Collins. One strand focused on understanding life, as exemplified by Charles Darwin's identification of natural selection as the explanation for the diversity and distribution of living things. The other strand focused on controlling life, as exemplified by the work of Jacques Loeb, a German biologist who worked at the University of Berlin and the University of Chicago in the late

19th and early 20th centuries, to understand and modify the physiological mechanisms responsible for biological processes.

Over the course of the 20th century, these two streams of scholarship blended. The effort to understand organisms led to the study of biological processes on progressively smaller scales. As former NIH Director Elias Zerhouni put it, “Just as physicists went from gross phenomena to atomic structure to subatomic particles, we have gone from understanding organs and their general functions to trying to understand molecular events.” This research led to the discovery that all organisms rely on essentially the same basic molecular mechanisms, so investigations of one organism can yield insights that apply throughout biology. It turn, new understandings of the molecular constituents of organisms have made it possible to adapt biological mechanisms for specific purposes.

Today, the ongoing unification of the life sciences is also evident in a contrasting endeavor: the effort to build upward in scale from an understanding of molecular mechanisms to an understanding of entire organisms and ecosystems. Living things, from bacteria to humans, consist of biological subsystems that are connected in complex, interacting networks. Biologists now have a fairly good understanding of many of these subsystems, said Zerhouni. But they need to develop ways of integrating their knowledge of subsystems to understand the behavior of organisms and assemblies of organisms. Computing, robotics, and other technologies allow life scientists to generate immense amounts of data. But “the generation of data is not equal to the generation of knowledge,” said Zerhouni. Understanding the complexity inherent in organisms is another grand challenge that could inspire the best efforts of students and scientists.

“The generation of data is not equal to the generation of knowledge,” said Zerhouni. Understanding the complexity inherent in organisms is another grand challenge that could inspire the best efforts of students and scientists.

“We have to encourage young people to take up this next challenge,” Hockfield said. “[We need] to grab the attention of kids from K to 12 to say, ‘wow, this is cool stuff, I want to be doing science and engineering and math.”

The Rise of Transdisciplinary Research

To continue to make progress on basic scientific questions and on the application of new knowledge to human needs, life scientists are discovering that they must join in partnerships with physical scientists and engineers. This convergence of disciplines is “the defining intellectual movement of our time,” according to Hockfield.

In crucial respects, the life sciences are undergoing a transition analogous to a transition that the physical sciences underwent at the beginning of the 20th century. Basic research in the physical sciences at the end of the 19th century and the beginning of the 20th produced a deep understanding of the physical world. This fundamental scientific research revealed the structure and nature of matter. It demonstrated the nature of the cosmos and our place within the cosmos. It was a triumph of knowledge for knowledge's sake.

This new understanding of the physical world also yielded what Hockfield called a "parts list" for the physical world – a basic understanding of the constituents and interactions of physical objects. Having this parts list enabled scientists and engineers to incorporate the insights of physics into a wide array of practical applications. The resulting convergence of the physical sciences and engineering spawned the electronics industry, the computer industry, and the information industry. "If you contrast daily life today with what it was like a century ago, you would be hard-pressed to name a set of technologies and industries that have had a more transformative impact on our lives and on how we do our work," Hockfield said.

The biological sciences are poised on the brink of a comparable transformation. The discovery of the structure of DNA in the middle of the 20th century drove a worldwide effort to construct the parts list of biological organisms. The construction of this list, which has been a tremendously exciting intellectual adventure in its own right, is also having revolutionary practical outcomes, such as the biotechnology revolution in medicine and agriculture and the application of knowledge from the life sciences to energy and environmental issues.

From Genetics to Genomics to Metagenomics

The first large-scale transdisciplinary project centered on the life sciences was the Human Genome Project (HGP). It drew on concepts and technologies from many disciplines, including physics, engineering, computer science, and mathematics. Many of the technologies needed for ultrafast genetic sequencing were not available when the HGP started in 1990, and some biologists wondered if the data generated by the project would ever have broad applications. In fact, the HGP greatly accelerated the development of many new technologies, and the data and techniques generated by the project have had revolutionary effects throughout biology. For example, said Sloan-Kettering's Harold Varmus, the availability of the human genome has "completely changed our approach to cancer," including diagnostics, classification, prevention, and treatment.

The HGP marked the transition from genetics – the study of the DNA sequences that constitute genes – to genomics – the study of the complete DNA sequences of organisms. Now the continued development of sequencing technologies is giving rise to metagenomics – in which the collective 'genome' of entire communities of microorganisms is studied. Metagenomics reveals the characteristics of organisms that cannot be cultured in the laboratory, and it helps show how organisms relate to each other in natural environments. It also has revealed a range and diversity of DNA sequences -- and even organisms -- previously unknown to science.

In the past, biologists simply borrowed tools from the physical sciences and engineering to solve problems within their own discipline. Today, biological and physical scientists and engineers are working as equal partners on problems. In the process, they are forging a "strong and fruitful new synthesis," said Hockfield.

This work represents a step beyond interdisciplinary research, in which researchers from different disciplines contribute elements to a common problem, or multidisciplinary research, where disciplines overlap. The convergence of the life sciences, the physical sciences, and engineering has the potential to produce a transdisciplinary science in which separate disciplines merge into something new. In laboratories such as that of Stanford's Lucy Shapiro (see sidebar), this convergence is generating not just new results but new approaches to research. As Keith Yamomoto, Professor and Executive Vice Dean of the School of Medicine at the University of California, San Francisco, put it, "disciplines that were thought to be distinct begin to melt together and be able to contribute different kinds of expertise and thought processes to solving problems."

A Wiring Diagram for Cells

Cellular systems can be represented in "wiring diagrams" analogous to those of electronic circuits. But the components in the diagram are proteins, nucleic acids, and other biologically active molecules while the wires are interactions among those components.

Lucy Shapiro's laboratory at the Stanford University School of Medicine chose a simple organism -- a bacterium called *Caulobacter crescentus* -- and set out to understand all the integrated processes that this organism needs to function as a living cell. Among these processes are the biochemical circuits that control cell division and differentiation. Four proteins serve as master regulators of these processes, Shapiro and her colleagues have found. Rising and falling quantities of these proteins in in particular parts of the cell produce "an exquisite coordination of events in a three-dimensional grid."

Building these circuit diagrams has allowed researchers to identify nodes that control cellular functions and are attractive targets for drugs designed to alter the functioning of cells. Research in Shapiro's lab, for example, has led to drug development projects for two new antibiotics and an antifungal agent.

Shapiro's lab members are about half biologists and half physicists and engineers. Each has had to learn the language of the others so that they can work together. "You put all these people together and amazing things happen," Shapiro said. "Now we understand in a completely different way how this bacterial cell works."

Maximizing the Return on our Life Sciences Research Investment

In many places, life sciences research is already being done in new ways, but several speakers emphasized that changes in how life sciences research is funded, how students are educated, and how academic institutions are organized could speed the emergence of new ideas and applications from the life sciences research community. The tremendous potential of the life sciences demands new approaches not just by researchers but by the policymakers and administrators who fund and oversee scientific research. While many steps can be taken to strengthen the scientific enterprise, speakers at the meeting emphasized two in particular: supporting high-risk, high-payoff science, and educational initiatives at all levels to prepare the scientists and engineers of the future.

Taking Risks

Stagnant funding for the life sciences over the past five years has had major consequences for research. When funding is tight, science almost always becomes more conservative. Funders focus on projects that have a high likelihood of succeeding, not on projects that could have great payoffs but may be less likely to succeed. "Potentially transformative or high-risk, high-reward research is discouraged," said Cech.

At the same time, younger scientists tend to have a harder time getting research grants—especially when funding is constrained. They have less of a track record, so their proposals tend not to score as highly in reviews of their proposals. Also, because of the shift in science toward work that combines disciplines, many projects tend not to fall neatly within disciplinary boundaries, even though the panels set up to review proposals tend to be organized by discipline. Today, the average age at which biologists get their first R01 grants as independent investigators from NIH is 43. "I find this astonishing," said Hockfield. "I got my first NIH R01 when I was 30, and I was not considered to be a young receiver of an award."

According to Zerhouni, "The greatest risk in periods of tight economic times and tight budgets is to stop taking risks." Funding mechanisms need to cut across different institutes within NIH and across federal agencies. While the principles of peer review need to be maintained to ensure the quality of the research that is funded, several speakers suggested that a new kind of proposal review mechanism may be needed that has a multidisciplinary foundation. "Our funding agencies and not just our scientists need to be collaborators," said Hockfield.

Zerhouni suggested several ways that more adventurous science could be encouraged. For example, a small percentage of support could be set aside at each research-funding agency as a "venture budget." These funds could be used to take advantage of fast-emerging opportunities and to support small-scale projects to gauge the likelihood of success for a larger project. Also, program officers could be given some authority to override study sections to support innovative projects with the potential for important advances, allowing researchers to spend their time doing science instead of writing grant applications. Finally, it is important for federal agencies to have "flexible funding mechanisms to support unconventional self-assemblies of scientists with ideas beyond the typical framework of grants."

Zerhouni – along with several other speakers - further asserted that federal agencies need to find ways of supporting younger scientists. The panels that review grant proposals could be organized in such a way that expectations are appropriate for the career stages of applicants. Programs may also be needed that move promising young researchers from initial, small-scale grants into mainstream funding mechanisms.

Steps in these directions have occurred in both the public and private sectors. NIH, NSF, and the Department of Defense have new grant programs to support younger researchers. Private philanthropies like the Howard Hughes Medical Institute and the Gordon and Betty Moore Foundation have instituted programs that essentially fund people rather than projects. "We identify the best people that we see coming up and invest in them," said Kingsbury. "It has been incredibly powerful and transformative in our view." The Bill & Melinda Gates Foundation has been supporting small-scale explorations of promising but high-risk ideas. The federal government's support of the life sciences would benefit by incorporating more of this spirit of innovation, said Zerhouni.

At the same time, research administrators need the tools to do their jobs more effectively. Today it can be difficult to determine what kinds of science are being funded even within a single agency such as NIH. The diversity of funding sources is a strength rather than a weakness of the U.S. research system, said Kingsbury, but program officers need some way of knowing whether important research is being overlooked.

New policies also are needed to promote efforts designed to move discoveries from the laboratory to the marketplace. For example, some work progresses best in an academic environment and some progresses best in an industrial setting, said Hockfield. Researchers from both settings need to be able to work together with clearly spelled out policies on conflict of interest that facilitate research without compromising its integrity.

Producing the Scientists and Engineers of the Future

Fifty years ago, the challenge posed by the Soviet Union's launch of Sputnik helped generate a response in the Unites States that caused a generation of students to become excited about science and engineering. The potential of the life sciences to address major global problems could create a similar level of enthusiasm for science, technology, engineering, and mathematics (STEM) subjects today, said Hockfield. "We have to encourage young people to take up this next challenge," she said. "[We need] to grab the attention of kids from K to 12 to say, 'wow, this is cool stuff, I want to be doing science and engineering and math.'"

Education in STEM subjects needs to reflect the changing nature of science. The disciplinary structure of university departments organizes knowledge in a coherent way for teaching and research. But it also erects barriers to the kind of across-discipline research and education needed to address many of today's major challenges. Universities need to find ways to reduce the institutional, physical, and attitudinal barriers between departments, said several speakers at the meeting. Students throughout the sciences and engineering need a "broad education," said Hockfield, "so that the material they study has a common element that equips them to cross talk."

Education in the life sciences also needs to be more quantitative, more analytic, and more computationally oriented, said Kingsbury. This emphasis needs to be in place both at the molecular level and at the organismal and ecological levels so that data and insights travel freely and quickly within the life sciences and between the life sciences and other disciplines.

In addition, STEM education needs to reflect the changing nature of students. Young people are growing up in a world saturated with information technologies. They interact electronically with social networks, contribute to wikis and other distributed collaborations, and receive information in ways different from those of previous generations. Students themselves are more multidisciplinary than in the past and recognize the importance of working on problems that transcend disciplinary boundaries. Before graduate school, and even before college, the groundwork needs to be laid for the integration of the life sciences, the physical sciences, and engineering. "We need to find more and more ways, . . . starting at least at the high school level, to teach topics from a multidisciplinary point of view," said Cech. According to Varmus, changes at the precollege level require “high school teachers who are better paid and who approach science not from textbooks but from experiential approaches.” College instructors also need more funding and support to develop the kinds of innovative classes that combine elements from different disciplines.

The life sciences have an intrinsic advantage in education because of the innate interest students have in learning about things that are alive, said Cicerone. “That sense of wonder and curiosity . . . is what drives so many students.”

Conclusion

One hundred years ago, the airplane and the tungsten filament light bulb were five-year-old inventions. “No one could have predicted where those inventions would have taken us,” said Yamamoto.

Today the life sciences are in a comparable position. It is impossible to predict what new technologies and new industries will arise from today’s basic research. What can be predicted is that the world will undergo dramatic changes in the next one hundred years, and that the life sciences can help ensure that those changes produce a better life for people everywhere.

While the potential for significant advances is enormous, many challenges need to be to overcome. Achieving the promise of the life sciences articulated by the Summit speakers will require investment, creative approaches to how life sciences research is organized and funded, and attention to improving science education at all levels.

The Summit demonstrated that many of the ingredients for success are already in place. Many policy-makers, university officials, and scientists have begun to implement the changes that will allow the life sciences to transform America’s—and the world’s—future. Expanding these initiatives to a broader set of funding agencies, universities, and industrial entities will help ensure that the 21st century will be, as many have predicted, the century of biology.

Appendix A - Statement of Task

Committee on A New Biology for the 21st Century:
Ensuring the United States Leads the Coming Biology Revolution

An ad hoc committee will examine the current state of biological research in the United States and recommend how best to capitalize on recent technological and scientific advances that have allowed biologists to integrate biological research findings, collect and interpret vastly increased amounts of data, and predict the behavior of complex biological systems. Among the questions the committee may address are:

- What fundamental biological questions are ready for major advances in understanding? What would be the practical result of answering those questions? How could answers to those questions lead to high impact applications in the near future?

- How can a fundamental understanding of living systems reduce uncertainty about the future of life on earth, improve human health and welfare, and lead to the wise stewardship of our planet? Can the consequences of environmental, stochastic or genetic changes be understood in terms of the related properties of robustness and fragility inherent in all biological systems?

- How can federal agencies more effectively leverage their investments in biological research and education to address complex problems across scales of analysis from basic to applied? In what areas would near term investment be most likely to lead to substantial long-term benefit and a strong, competitive advantage for the United States? Are there high-risk, high pay-off areas that deserve serious consideration for seed funding?

- Are new funding mechanisms needed to encourage and support cross-cutting, interdisciplinary or applied biology research?

- What are the major impediments to achieving a newly integrated biology?

- What are the implications of a newly integrated biology for infrastructural needs? How should infrastructural priorities be identified and planned for?

- What are the implications for the life sciences research culture of a newly integrated approach to biology? How can physicists, chemists, mathematicians and engineers be encouraged to help build a wider biological enterprise with the scope and expertise to address a broad range of scientific and societal problems?

- Are changes needed in biology education-- to ensure that biology majors are equipped to work across traditional subdisciplinary boundaries, to provide biology curricula that equip physical scientists and engineers to take advantage of advances in biological science, and to provide nonscientists with a level of biological understanding that gives them an informed voice regarding relevant policy proposals? Are alternative degree programs needed or can biology departments be organized to attract and train students able to work comfortably across disciplinary boundaries?

The subgroup of the committee will organize a Biology Summit to garner input from a broad spectrum of stakeholders—government and private agencies that fund biological research, the biotech and pharmaceutical industries, universities and medical schools—to consider barriers to progress and to highlight exciting new areas of research that cross traditional disciplinary boundaries. The Summit's proceedings will be published as a separate, type-3 workshop report. In a subsequent consensus report, the committee will recommend actions that federal policy makers can take to ensure that the United States takes the lead in the emergence of a biological science that will support a higher level of confidence in our understanding of living systems, thus reducing uncertainty about the future, contributing to innovative solutions for practical problems, and allowing the development of robust and sustainable new technologies. The committee will not make specific budgetary or government organizational recommendations.

Appendix B - Agenda

The Role of the Life Sciences in Transforming America's Future
The 2008 National Academies Biology Summit

December 3rd, 2008
1200 New York Avenue NW
Washington, D.C. 20005

8:30 a.m.	Welcome from the President Ralph Cicerone, President of the National Academy of Sciences
8:45 a.m.	James P. Collins Assistant Director for Biological Sciences, National Science Foundation
9:15 a.m.	Raymond L. Orbach Undersecretary for Science in the United States Department of Energy
9:45 a.m.	Thomas R. Cech President of the Howard Hughes Medical Institute
10:15 a.m.	David T. Kingsbury Chief Program Officer for Science, Gordon and Betty Moore Foundation
10:45 a.m.	Break
11:00 a.m.	Susan Hockfield President of the Massachusetts Institute of Technology
11:30 a.m.	Susan Desmond-Hellmann President of Product Development, Genentech
12:00 p.m.	Harold Varmus President of the Memorial Sloan-Kettering Cancer Center
12:30 p.m.	Panel Discussion
1:00 p.m.	Lunch Break
2:15 p.m.	Cynthia Kenyon American Cancer Society Professor, UCSF
2:45 p.m.	Lucy Shapiro Ludwig Professor of Cancer Research, Stanford University
3:15 p.m.	Break
3:30 p.m.	Robert Fraley Executive Vice President and Chief Technology Officer, Monsanto
4:00 p.m.	Elias A. Zerhouni former Director of the National Institutes of Health
4:30 p.m.	Panel Discussion
5:00 p.m.	Closing Remarks Keith Yamamoto Chairman, Board on Life Sciences, National Research Council

Appendix C - Speaker Biographies

Dr. Ralph J. Cicerone is president of the National Academy of Sciences and chair of the National Research Council. He is an atmospheric chemist whose research on climate change has shaped science and environmental policy at the highest levels nationally and around the world. His research was recognized on the citation for the 1995 Nobel Prize in chemistry, and he has been consistently honored for his fundamental contributions to the understanding of greenhouse gases, ozone depletion, and human impact on the environment. The Franklin Institute named him the 1999 laureate of the Bower Award and Prize for Achievement in Science, one of the most prestigious American awards in science. While on the faculty at the University of California, Irvine, he served as founding chair of the Department of Earth System Science, then dean of the School of Physical Sciences, and subsequently chancellor before his election as president of the NAS.

Dr. James Paul Collins received his B.S. from Manhattan College in 1969 and his Ph.D. from The University of Michigan in 1975. He is Virginia M. Ullman Professor of Natural History and the Environment in the School of Life Sciences at Arizona State University where he was chairman of the Zoology, then Biology Department from 1989 to 2002. He is currently on leave at NSF serving as Assistant Director for Biological Sciences. In addition to his obligations as Assistant Director, Collins is responsible for coordinating collaborations between NSF and other federal agencies as Chair of the Subcommittee on Biotechnology and co-Chair of the Interagency Working Group on Plant Genomics though the National Science and Technology Council. Dr. Collins's research focus is host-pathogen biology and its relationship to population dynamics and species extinctions. The role of pathogens in the global decline of amphibians is the model system for this research. The intellectual and institutional factors that have shaped Ecology's development as a science are also a focus of his research, as is the emerging research area of ecological ethics. Dr. Collins is a Fellow of the American Association for the Advancement of Science and a Fellow of the Association for Women in Science.

Dr. Raymond Lee Orbach is the Under Secretary for Science at the U.S. Department of Energy. Dr. Orbach is responsible for planning, coordinating and overseeing the Energy Department's research and development programs and its 17 national laboratories, as well as the department's scientific and engineering education activities. From 1992 to 2002, he served as Chancellor of the University of California (UC), Riverside. Dr. Orbach's research in theoretical and experimental physics has resulted in the publication of more than 240 scientific articles. He has received numerous honors including two Alfred P. Sloan Foundation Fellowships, a National Science Foundation Senior Postdoctoral Fellowship at Oxford University, a John Simon Guggenheim Memorial Foundation Fellowship at Tel Aviv University, the Joliot Curie Professorship at the Ecole Superieure de Physique et Chimie Industrielle de la Ville de Paris, and the Lorentz Professorship at the University of Leiden in the Netherlands. He is a fellow of the American Physical Society and the American Association for the Advancement of Science. Dr. Orbach received his Bachelor of Science degree in Physics from the

California Institute of Technology in 1956. He received his Ph.D. degree in Physics from the University of California, Berkeley, in 1960.

Dr. Thomas R. Cech obtained his B.A. in chemistry from Grinnell College and his Ph.D. in chemistry from the University of California, Berkeley, and then engaged in postdoctoral research in the department of biology at the Massachusetts Institute of Technology. In 1978 he joined the faculty of the University of Colorado, Boulder, where he became a Howard Hughes Medical Institute investigator in 1988 and Distinguished Professor of Chemistry and Biochemistry in 1990. The discovery by Dr. Cech and his research group of self-splicing RNA provided the first exception to the long-held belief that biological reactions are always catalyzed by proteins. In January 2000, Dr. Cech became president of the Howard Hughes Medical Institute, the nation's largest private biomedical research organization. Dr. Cech received the Heineken Prize of the Royal Netherlands Academy of Sciences and the Albert Lasker Basic Medical Research Award in 1988, the Nobel Prize in Chemistry in 1989, and the National Medal of Science in 1995. In 1987 Dr. Cech was elected to the U.S. National Academy of Sciences and also awarded a lifetime professorship by the American Cancer Society. In April 2009, Dr. Cech will return full-time to the University of Colorado as the director of the Colorado Institute for Molecular Biotechnology.

Dr. David Kingsbury is the Chief Program Officer, Science at the Gordon and Betty Moore Foundation. Prior to joining the Moore Foundation he worked in the biotechnology industry at Chiron Corporation. From 1992 to 1997 he was on the faculty at The Johns Hopkins University School of Medicine where he was an Associate Dean of the School of Medicine and held several other academic positions. Between 1984 and 1988 he served as the Assistant Director for Biological, Behavioral and Social Sciences at the National Science Foundation, where he was Acting Director for several months in 1984. At the time of his appointment to the NSF he was Professor of Virology at the University of California, Berkeley. While at NSF he served as the Chair of two White House committees on biotechnology policy and regulation.

Dr. Susan Hockfield has served as the sixteenth President of the Massachusetts Institute of Technology since December 2004. A noted neuroscientist whose research has focused on the development of the brain, Dr. Hockfield is the first life scientist to lead MIT. She holds a faculty appointment as Professor of Neuroscience in MIT's Department of Brain and Cognitive Sciences and is a member of the American Academy of Arts and Sciences. Dr. Hockfield earned her Ph.D. from the Georgetown University School of Medicine, while carrying out her dissertation research in neuroscience at the National Institutes of Health (NIH). She was an NIH postdoctoral fellow at the University of California at San Francisco, and then joined the scientific staff at the Cold Spring Harbor Laboratory. Before assuming the presidency of MIT, she was Provost at Yale University, where she had taught since 1985 and had also served as Dean of the Graduate School of Arts and Sciences. She serves as a director of the General Electric Company; a trustee of the Carnegie Corporation of New York and the Woods Hole Oceanographic Institution; an overseer of the Boston Symphony Orchestra; and a member of the Foundation Board of the World Economic Forum.

Dr. Susan Hellmann is President of Product Development at Genentech, where she is responsible for Genentech's Development, Process Research & Development, Business Development, Product Portfolio Management, Alliance Management and Pipeline Planning Support functions. She is a member of Genentech's executive committee. Hellmann is also an adjunct associate professor at the University of California, San Francisco (UCSF). She is board-certified in Internal Medicine and Medical Oncology and completed her clinical training at UCSF. Prior to joining Genentech, Hellmann was associate director of clinical cancer research at Bristol-Myers Squibb's Pharmaceutical Research Institute, where she was the project team leader for Taxol. In July 2008, Hellmann was appointed to the California Academy of Sciences Board of Trustees. She was named to the Biotech Hall of Fame in 2007 and as Healthcare Businesswomen's Association's "Woman of the Year" for 2006. Hellmann was also named to FORTUNE magazine's "Top 50 Most Powerful Women in Business" list in 2001 and each year from 2003 to 2008.

Dr. Harold Varmus, former Director of the National Institutes of Health and co-recipient of the 1989 Nobel Prize in Physiology or Medicine, has served as the President and Chief Executive Officer of Memorial Sloan-Kettering Cancer Center in New York City since January 2000. Dr. Varmus received the Nobel Prize (jointly with Michael Bishop, his former colleague at the University of California, San Francisco) for the discovery of cellular genes that are progenitors of retroviral oncogenes. He is a member of the U.S. National Academy of Sciences and the Institute of Medicine and has received the National Medal of Science, and the Vannevar Bush Award. Dr Varmus has been an advisor to the Federal government, pharmaceutical and biotechnology firms, and many academic institutions. He served on the World Health Organization's Commission on Macroeconomics and Health from 2000 to 2002; is a co-founder and Chairman of the Board of Directors of the Public Library of Science; chairs the Scientific Board of the Gates Foundation Grand Challenges in Global Health and leads the Advisory Committee for the Global Health Division; and is involved in initiatives to promote science in developing countries. His current research at the Sloan-Kettering Institute mainly addresses molecular mechanisms of oncogenesis, using mouse models of human cancer.

Dr. Cynthia Kenyon is the Herbert Boyer Distinguished Professor of Biochemistry and Biophysics and American Cancer Society Professor at the University of California, San Francisco. In 1993, Kenyon and colleagues' discovery that a single-gene mutation could double the lifespan of C. elegans sparked an intensive study of the molecular biology of aging. These findings have now led to the discovery that an evolutionarily conserved hormone signaling system controls aging in other organisms as well, including mammals. Dr. Kenyon is a member of the US National Academy of Sciences, the American Academy of Arts and Sciences, and the Institute of Medicine and she is a past president of the Genetics Society of America. She is now the director of the Hillblom Center for the Biology of Aging at UCSF. Cynthia Kenyon graduated valedictorian in chemistry and biochemistry from the University of Georgia in 1976 and received her PhD from MIT in 1981.

Dr. Lucy Shapiro is a professor and the founding chair of the Department of Developmental Biology and Ludwig Professor of Cancer Research at the Stanford University School of Medicine. She is also director of Stanford's Beckman Center for Molecular and Genetic Medicine and is a member of the Spogli Institute for International Studies. Her research uses a systems engineering approach to define the genetic circuitry that links bacterial cell differentiation and cell cycle progression. She has shown that the bacterial cell is highly organized with internal structure and regulatory mechanisms that oscillate in time and space. Dr. Shapiro received an A.B. in fine arts in 1962 from Brooklyn College and a Ph.D. in molecular biology in 1966 from the Albert Einstein College of Medicine. Her many honors include FASEB's Excellence in Science Award, the 2005 Waksman Award in Microbiology from the National Academy, and election to the National Academy of Sciences, the Institute of Medicine, and the American Academy of Arts and Sciences.

Dr. Robert T. Fraley oversees Monsanto's integrated crop and seed agribusiness technology and research with facilities in most world areas. Dr. Fraley has held several positions at Monsanto, including Co-President of Monsanto's Agricultural Sector and President of Monsanto's Ceregen business unit with responsibilities for the discovery, development and commercialization of new crop chemical and biotechnology products. Author of more than 100 publications and patent applications relating to technical advances in agricultural biotechnology, Dr. Fraley received the National Medal of Technology from President Clinton in 1999. He received the 2008 National Academy of Sciences (NAS) Award for the Industrial Application of Science for his work on the improvement of crops through biotechnology. Dr. Fraley holds a PhD in microbiology/biochemistry from the University of Illinois and a Bachelor of Science from the University of Illinois.

Dr. Elias A. Zerhouni served as director of the National Institutes of Health from May 2002 to October 2008. During his tenure he oversaw the completion of the doubling of the NIH budget and initiated the NIH Roadmap for Medical Research. Prior to joining the NIH, Dr. Zerhouni served as executive vice-dean of Johns Hopkins University School of Medicine, chair of the Russell H. Morgan department of radiology and radiological science, Martin Donner professor of radiology, and professor of biomedical engineering. Dr. Zerhouni was born in Nedroma, Algeria and earned his medical degree at the University of Algiers School of Medicine in 1975. In 2000, he was elected to the National Academies' Institute of Medicine. Dr. Zerhouni has won several awards for his research including a Gold Medal from the American Roentgen Ray Society for CT research and two Paul Lauterbur Awards for MRI research. His research in imaging led to advances in Computerized Axial Tomography (CAT scanning) and Magnetic Resonance Imaging (MRI) that resulted in 157 peer reviewed publications and 8 patents.