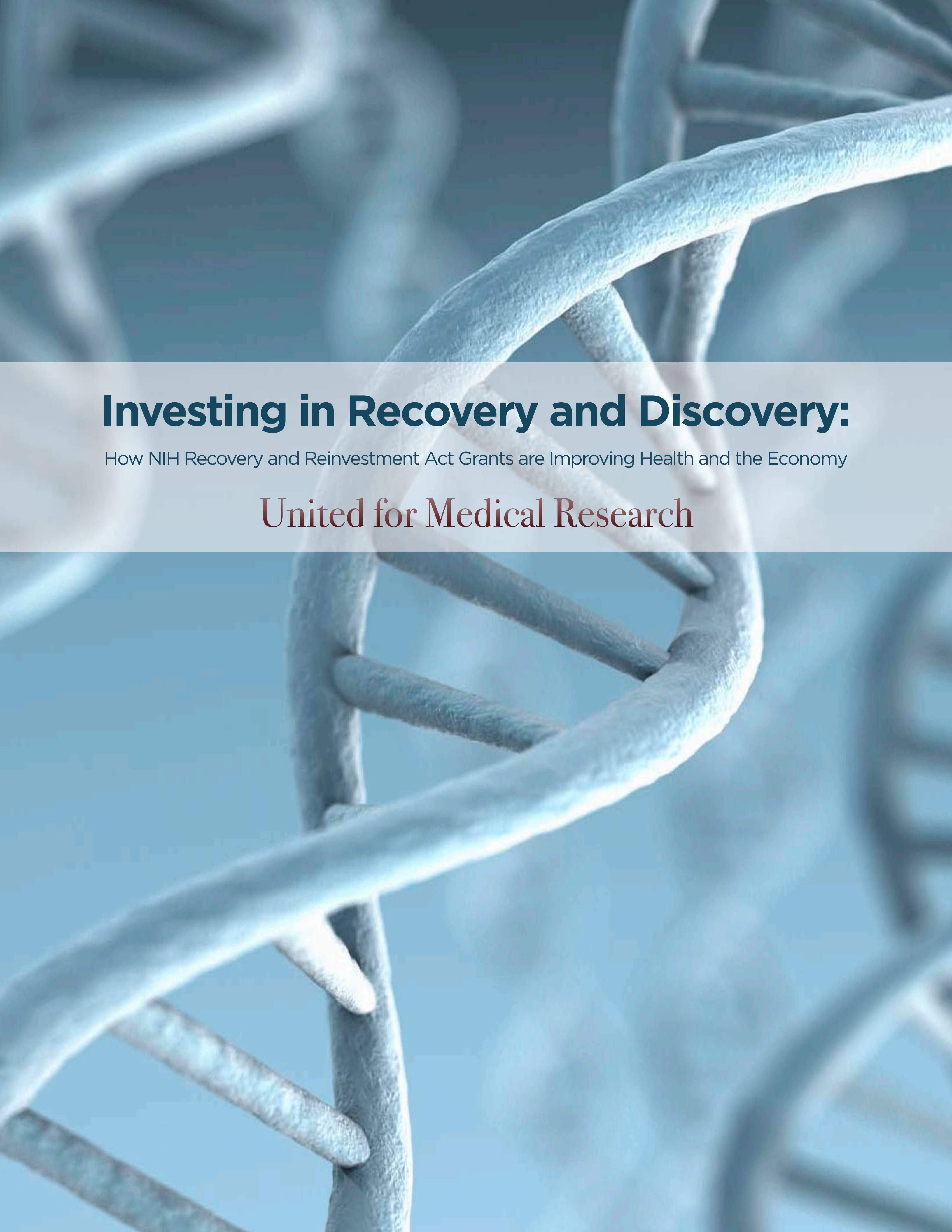

Investing in Recovery and Discovery:

How NIH Recovery and Reinvestment Act Grants are Improving Health and the Economy

United for Medical Research

Contents

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"Breakthroughs in medical research take far more than the occasional flash of brilliance, as important as that can be. Progress takes time; it takes hard work; it can be unpredictable; it can require a willingness to take risks and going down some blind alleys occasionally...all of this needs the support of government. It holds promise like no other area of human endeavor, but we've got to make a commitment to it."

— President Barack Obama
September 30, 2009[1]

I. NIH RECOVERY ACT FUNDING: A Unique Moment in Biomedical Research

The 2009 American Recovery and Reinvestment Act invested $10.4 billion over two years in biomedical research through the National Institutes of Health (NIH).[2] Much of those funds are now at work across the country in the service of better health and a healthier economy.

With an annual budget of over $30 billion, NIH is the single largest source of biomedical research funding in the world, and the catalyst for academic, clinical, and private work in the field.[3]

The Recovery Act investment in NIH comes at a propitious time in the history of biomedical science. Scientists now have the opportunity to combat disease using newly gained knowledge about biological structures and functions. They no longer merely describe the symptoms of disease, employ everything they have against it, and watch to see what works. Instead, in important areas, they can employ the knowledge gained through more than 40 years of arduous study to zero in strategically on a disease, its triggers and crucial moments of development. Using discoveries and new technologies made in just the last decade, they can now understand the molecular drivers of disease and affect them.

“In the pursuit of any scientific endeavor, there comes a time when the research progresses from simply describing and observing processes to actually understanding the underlying mechanisms that control these processes. When that transformation occurs, it becomes possible to actually manipulate the cellular events that govern function…That manipulative process is at the heart of every new diagnostic and therapeutic discovery. This transformational event is really where we are now in the life sciences. And we’re there, in large measure, because of the partnership that has been going on for several decades between the federal funding agencies, the NIH in particular, and the research intensive institutions of this country.”

— Dr. Steve Fluharty
Vice Provost for Research,
University of Pennsylvania

At this historic time, Recovery Act funding gives scientists the opportunity to pursue some of their most promising leads. Scientists are using Recovery Act funds to:

- Explore scientific strategies that were not possible even ten years ago, before advances in genomics, proteomics, and regenerative medicine opened up new avenues for research.
- Build upon the insights of previous discoveries to more quickly deliver new treatments for patients.
- Improve health care quality by finding the right treatment for each patient, forging a new age of personalized medicine.

This document highlights some of the most exciting projects funded and demonstrates the anticipated economic impact of these investments, such as job creation, industry growth, and health care cost reductions.

But the promise of Recovery Act NIH funding will not be fulfilled unless we build upon these investments in the NIH beyond 2010.

While many valuable projects will be completed in the Recovery Act’s timeframe, many more equally promising ideas do not fit into the two-year window of stimulus funding. And even with the Recovery Act infusion, past investments have created such an explosion of new opportunities that the US is still not pursuing even a quarter of what our smartest minds have to offer. Thousands of new ideas for translating scientific discovery into new treatments for patients could go unexplored in the years ahead, particularly if NIH funding declines back to pre-Recovery Act funding levels. Today, NIH is able to empower scientists to pursue roughly one in five of the nation’s most exciting biomedical ideas.[4] In 2011, if NIH funding returns to pre-Recovery Act levels, roughly only one in ten proposals would receive funding.[5] This would be a historically low funding rate and would stifle American innovation in this critical field.

Unfortunately, the nation has recently witnessed the results of similarly low funding rates. From 2003 to 2008, NIH funding increases failed to keep pace with medical research inflation, which meant that NIH lost more than 15% of its purchasing power.[6] Researchers struggled to secure funding for high-risk, high-reward ideas as scarce resources tended to fund surer scientific bets. And scientists often celebrated their 43rd birthdays before celebrating their first NIH grants.[7]

The unrealized potential for biomedical advancement was confirmed in early 2009, when NIH announced that it would fund several hundred new NIH Challenge grants, an award aimed at funding the nation’s most creative, high-risk, high-reward biomedical research projects. In the weeks and months that followed, NIH received more than 20,000 proposals for just a few hundred grants.[8]

As a nation, we cannot return to putting so much potentially life-changing science on hold, particularly now, when strong investments in medical research could pay extraordinary dividends to our health and economic well being. As baby boomers age, the next big economic threat will come from the costs associated with millions of people living longer with burdensome and as yet incurable diseases, including Alzheimer's, diabetes, cancer, heart disease, stroke and more.

But to date, there has been no indication that NIH funding momentum will be sustained in 2011 and beyond. The Recovery Act has demonstrated that in this historic moment of science, the big ideas are out there. How much the US Congress commits to the National Institutes of Health will determine how many — and how quickly — transformative ideas are brought to life for patients, their families and the American economy.

For more information or an interactive version of this report, visit www.investingindiscovery.com

"There is no blueprint on how Cancer deals with you, but thanks to research, there is a blueprint on how you deal with Cancer."

— Carol Roberts
Cancer Survivor
Merritt Island, FL

II. NIH RECOVERY ACT FUNDING:
For Better Health and A Stronger Economy

As of October 26, 2009, NIH had invested $4.35 billion of Recovery Act funding in 12,788 grants to researchers at major research institutions, medical schools, universities, and companies across the United States.[9] These grants are at once advancing American science, enabling better treatments and cures, and contributing to a better economy. The work underway will create jobs, stimulate entire industries, and reduce health care costs.

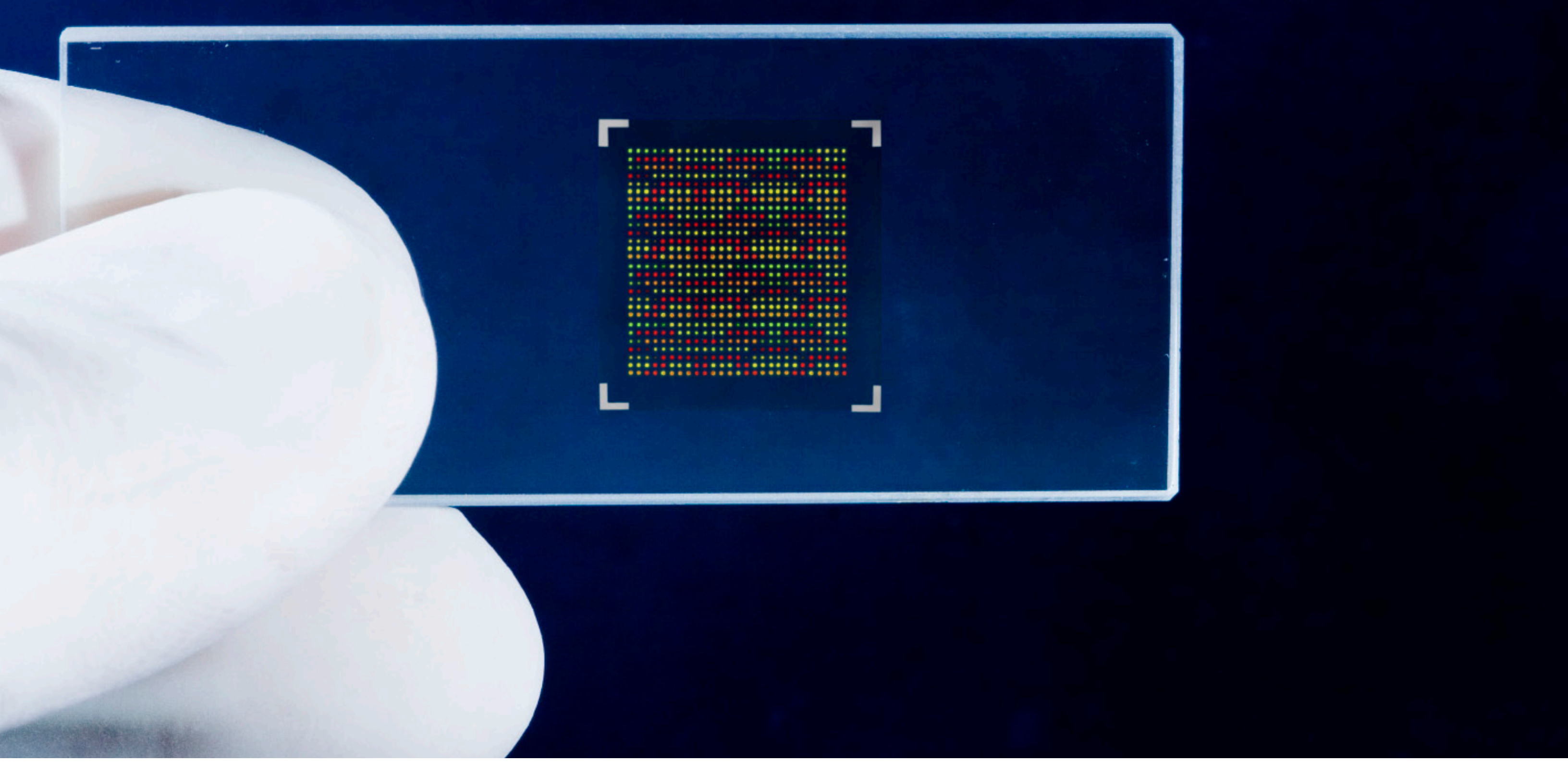
Creating Jobs Today

NIH funding supports hundreds of thousands of jobs directly in labs and research facilities across the country. The NIH has estimated that Recovery Act funds will create or retain 50,000 jobs.[10] And a Morgan Stanley Research report from December 2009 noted that on average, stimulus grantees intend to add two new lab members to their teams.[11]

These are well-paying jobs associated with public and private research institutions and universities. Laboratories often run like small businesses, employing a range of people — senior investigators, junior scientists, technicians — and they need space, research supplies and equipment. The investment in these labs and institutions also fosters indirect local job growth and business activity.

In addition, Congress also directed Recovery Act funds to scientific infrastructure projects such as new and renovated laboratories. These construction activities expand the employment benefits of research funding beyond scientific teams.

U.S. research universities and medical institutions are some of the largest and most stable employers in many cities and towns across America, forming the center of a community's strong, long-lasting economic growth. According to a 2008 study, some of the nation's leading medical schools and teaching hospitals employed 3.3 million people, and generated more than $22 billion in total state tax revenue. These institutions' combined total economic impact on the United States reached more than $512 billion in 2008, comprised of more than $222 billion in direct business volume impact and more than $289 billion in indirect economic impacts. Recovery Act funds will boost these figures at thousands of these organizations in every state.[12]



Technology is rapidly expanding the nature and scope of what's possible in research, and Recovery Act resources are funding the purchase of cutting-edge equipment. In the recent past, NIH has not been able to significantly support the acquisition of the new tools and infrastructure scientists need to pursue many great ideas.

Fortunately, The National Center for Research Resources, the NIH Center that provides these types of grants, received $1.6 billion in Recovery Act funding, the bulk of which will be distributed in the early part of 2010. This scale and type of funding can, over time, prove to be a key accelerator in moving the American scientific enterprise closer to better treatments and cures.

UCLA's Laboratory of Neuro Imaging (LONI), for example, is in the process of constructing a new $1.9 million computational cluster that analyzes the results of MRI, CT and other scans to better understand the brain and enable advances across Alzheimer's, schizophrenia, and brain development research. "The only way you can get a handle on the progression of these diseases is to be able to mathematically combine and better understand the characteristics and biomarkers of their various stages...These really are such complex problems for which you must have very sophisticated tools," says Arthur W. Toga, LONI's director.[13]

To this end, the new cluster will employ not only the latest in high density computational resources, but the lab will be using this project to drive a comprehensive project designed to help researchers more efficiently utilize these resources. By dynamically provisioning individual resources such as CPU cores, memory and storage bandwidth, the cluster can intelligently ensure that sophisticated workflows such as those used in neuroimaging analysis completely take advantage of today's computational technology.

The results of such investments are much-needed and long-lasting because the funding isn't just going to new business for the university, but also to the companies that supply such high-tech equipment and which employ tens of thousands of people across the country.

Investment analysts have concluded that the stimulus will have a significant positive impact on numerous US-based life science tools and technology providers. These companies supply the consumables and equipment used by biomedical researchers in public and private research institutions across the country. Morgan Stanley's analysis concludes that 20% of every NIH stimulus dollar will be spent purchasing reagents, liquid chromatographers, sequencing systems, real time PCR, analysis software, microarray instrumentation and the like, thereby driving growth in commercial firms as well as research labs.[14]

The NIH is...

27 institutes and centers

with an annual budget of over **$30 billion,**

funding **6,000** in-house scientists,

50,000 annual external grants, and

325,000 extramural researchers

at some **3,000** universities, medical schools

and other research institutions,

spurring countless more jobs in all

50 US States and territories, which all adds up to

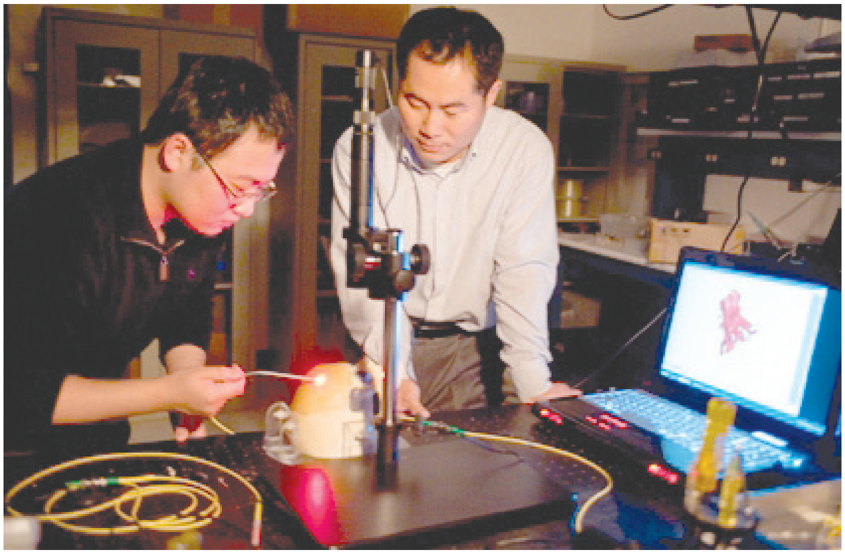
...an economic engine.[15]

A Foundation for Industry Growth

NIH-funded research goes far beyond immediate economic stimulus and direct job creation in the lab. It also provides the basis for further research and development in the private sector. It is estimated that every $1 of NIH funding results in more than $2 in additional business activity and economic output.[16] The Recovery Act's historic infusion of capital into biomedical research is solidifying this foundation for American innovation and competitiveness.

NIH Recovery Act funding is generating new technologies and the businesses that form around them. Indeed, a recent survey of the Biotechnology Industry Organization's members showed that 50 percent of those reporting said their companies were founded on licensed technologies and 76 percent said they have current licensing agreements in place with US universities.[17]

With a $450,000 NIH Recovery Act grant, Dr. Jin U. Kang of Johns Hopkins University is leading a team in the Department of Electrical and Computer Engineering in developing image guided smart surgical tools that will allow brain surgeons to safely locate and more closely examine cancerous tissue. In some cases, the device, which makes use of a scanning laser 3–dimensional imaging system called optical coherence tomography, will produce far sharper and more detailed imagery than that produced by traditional MRI or ultrasound equipment, and could eliminate the need to cut into the brain for a traditional biopsy — a procedure that poses significant risks to the patient. The images could then also guide doctors if surgery is indicated.



Dr. Kang works with a colleague at Johns Hopkins University.

Photo by Will Kirk/The John Hopkins University Gazette

Biosciences Industries' Economic Impact

The biotechnology and pharmaceutical industries that also build upon NIH funding are significant employers in the U.S. and important contributors to a thriving national economy.

- There were 1.3 million people employed in the biosciences in 2006 and the biosciences industry generated an additional 5.8 million related jobs throughout the remainder of the economy.
- Employment in the biosciences grew 5.7 percent between 2001–2006, compared with a 3.1 percent increase in employment in the overall private sector.
- The average annual wage of U.S. bioscience workers was $71,000 in 2006, more than $29,000 greater than the average private-sector annual wage.
- Jobs in bioscience were in all 50 states, Washington, DC, and Puerto Rico.[18]

Dr. Timothy Mitchison (right) and a colleague in his lab.
Photo by Graham Ramsay

The Full NIH Supply Chain: NIH to University to Industry to Patients

Dr. Timothy Mitchison at Harvard University will use an almost $1 million Recovery Act NIH grant to understand the responses of cancer cells with different genotypes to 15 small molecule candidate drug therapies. This will, in the end, help scientists more efficiently identify the most likely cancer therapy candidates earlier along the pipeline, save time and money in the drug development process with pharmaceutical companies, and help more effective drugs reach the market and patients, faster and more inexpensively than ever before.

"There's a reason why the United States leads the world in biosciences and it is largely because of the funding the American taxpayers have been willing to invest in NIH research. If we really want to realize the potential from what we've learned, from the human genome project, for example...we must continue to grow our commitment to the NIH."

— The Hon. Jim Greenwood,
President and CEO,
The Biotechnology Industry Organization (BIO)

From Research to Therapy: A CASE STUDY

Stories of better health and economic success born out of basic bioscience often speak louder than statistics. Take the example of the late Dr. Judah Folkman and angiogenesis. Beginning in the 1970s, Folkman worked for decades with NIH funding to discover a new way to fight cancer: stopping the growth of blood vessels that feed a tumor.

Folkman's work founded the field of angiogenesis research and paved the way for the development of a new class of drugs called angiogenesis inhibitors. These inhibitors block the formation of new blood vessels that provide oxygen and nourishment to cancer cells and help them spread to other parts of the body. If tumors can't create new blood vessels, they cannot invade nearby tissue.

A turning point for patients came in 2004 when the Food and Drug Administration approved an angiogenesis product by Genentech for treatment of colon and rectal cancers.[19] The approval essentially validated the concept of angiogenesis and spawned major interest from nearly every major pharmaceutical company. Since 2004, more than 10 angiogenesis inhibitors have been approved by the FDA. As of January 2008, more than 1.2 million patients worldwide had been treated with antiangiogenic therapy, not just for cancer, but also for other diseases involving abnormal growth of blood vessels, including the blinding eye diseases macular degeneration and diabetic retinopathy.[20]

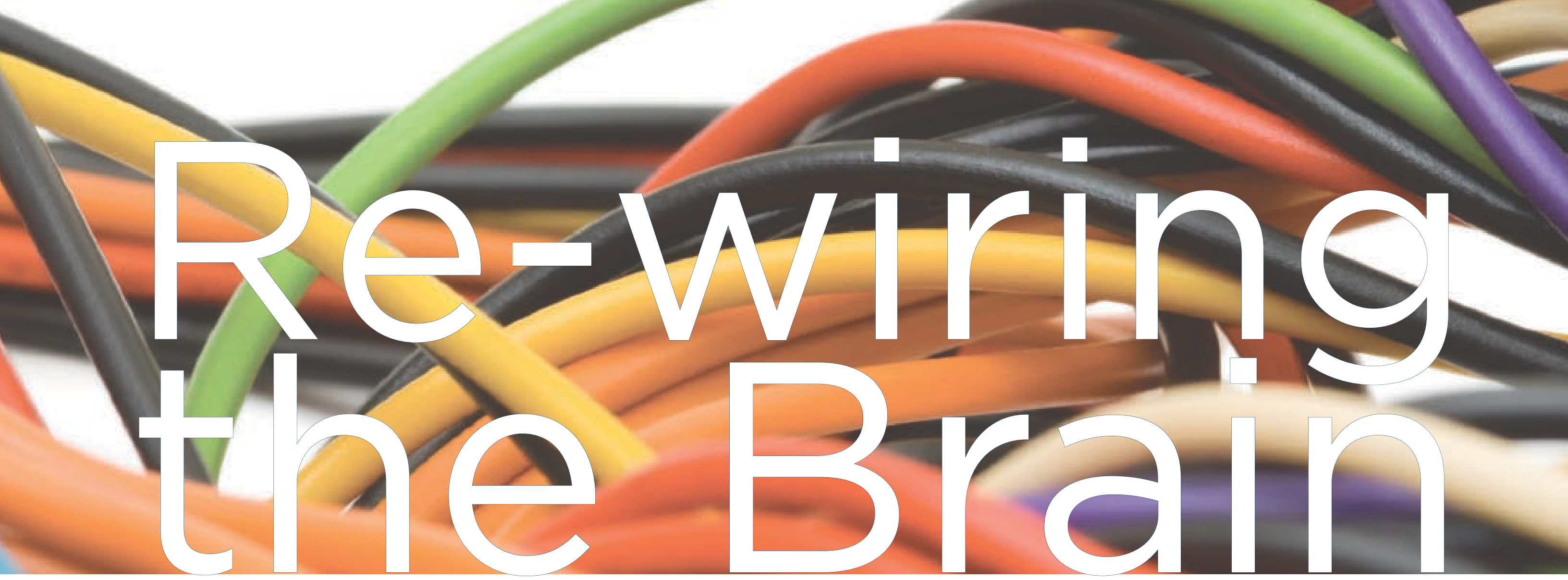
Other Game-Changing Pharmaceutical Treatments Born from Basic Research Include:[21]

- **Statins,** which lower cholesterol and help prevent heart attacks
- **Zanamivir,** first flu antiviral medicine
- **Captopril,** ACE-inhibitor that treats high blood pressure
- **Imatinib,** an enzyme inhibitor that targets a specific mutant kinase gene

Savings from Longer, Healthier Lives

In the long term, the only way the United States will overcome the unsustainable costs associated with chronic and acute disease within an aging population will be to find the treatments and cures that will keep people healthier, longer. Much of the latest science is uncovering the triggers of disease, long before symptom onset — which will lead us to treatments that prevent the disease from ever progressing.

It's possible, and it's already happening, thanks to NIH-funded breakthroughs. Daily, society is realizing savings that come with improved mortality rates and better quality of life. And while it's difficult to attribute a true dollar amount of savings associated with heart attacks that never happen, or cancers that never metastasize, a few top economists have done the analysis. It's been reported that a 10 percent decline in cancer mortality would have a positive economic impact of $4 trillion.[22] And delaying the average onset of Alzheimer's by five years would save $50 billion in health costs annually.[23] In the end, four big diseases alone, cancer, cardiovascular disease, diabetes, and arthritis account for hundreds of billions in yearly medical costs and lost productivity. There is enormous value in treatments and cures, in both emotional and fiscal terms.



Re-wiring the Brain AFTER STROKE

Cardiovascular disease is America's number one killer — and imposes an unbelievable economic toll on society: an estimated $503 billion in medical expenses and lost productivity in 2010.[24] Luckily, this is an area where discoveries to date have allowed scientists to make unparalleled strides toward treatments and cures. And thanks to NIH Recovery Act funding, researchers are entering a new age of both understanding and manipulating the factors underlying heart disease, strokes, and other cardiovascular disease.

At MIT, Dr. Emilio Bizzi is using more than $300,000 in his Recovery Act-funded NIH Challenge Grant to get us closer to a world where severe stroke victims can recover full rehabilitation of limbs, and where the brain can control prosthetic devices for amputees. His research is aimed at identifying the neural activity required to activate the muscles in the affected and unaffected arms of patients with strokes that have impaired movement in one side of the body. He will examine how the brain restructures motor function after a stroke by observing the changes in neural activity that occur during rehabilitation and the relationship between these changes and the person's clinical outcome. In other words, with NIH funding, Dr. Bizzi is studying whether there are ways we could help the brain rewire itself and the way it controls our bodies.

In addition, at the Salk Institute, a private non-profit research institution, Dr. David Schubert is studying promising compounds that could protect brain cells from the debilitating consequences of a stroke. When a stroke occurs, it is not simply the loss of oxygen to the neural cells that causes them to die. The lack of oxygen triggers an entire series of chemical events that can continue for hours or even days after a stroke has been identified and repaired. Scientists have already isolated several chemical compounds that could help break or stop this series of events, called the ischemic cascade, or that could protect the neural cells despite the course of the cascade. Dr. Schubert's work, with $1.6 million over two years, is selecting some of the most promising of these compounds, and testing and improving their neuroprotective properties, with the goal of getting a cascade-halting drug to market.

"Stroke research has changed my life.

- Without research carried out 45 years ago, I would not have benefited from electric shock therapy that made me understand the muscles that move my fingers.
- Without research conducted 30 years ago, I may not have been able to understand how to exercise my hand for dexterity.
- Without research performed ten years ago, the people around me would not understand the need to get me to the hospital quickly if I have another stroke.
- Without current support, researchers may never understand how to stop strokes before they happen or how to make current stroke survivors live healthier lives."

— **Susan Emery,** who suffered a stroke at age 9 and has been in and out of treatments all of her life.

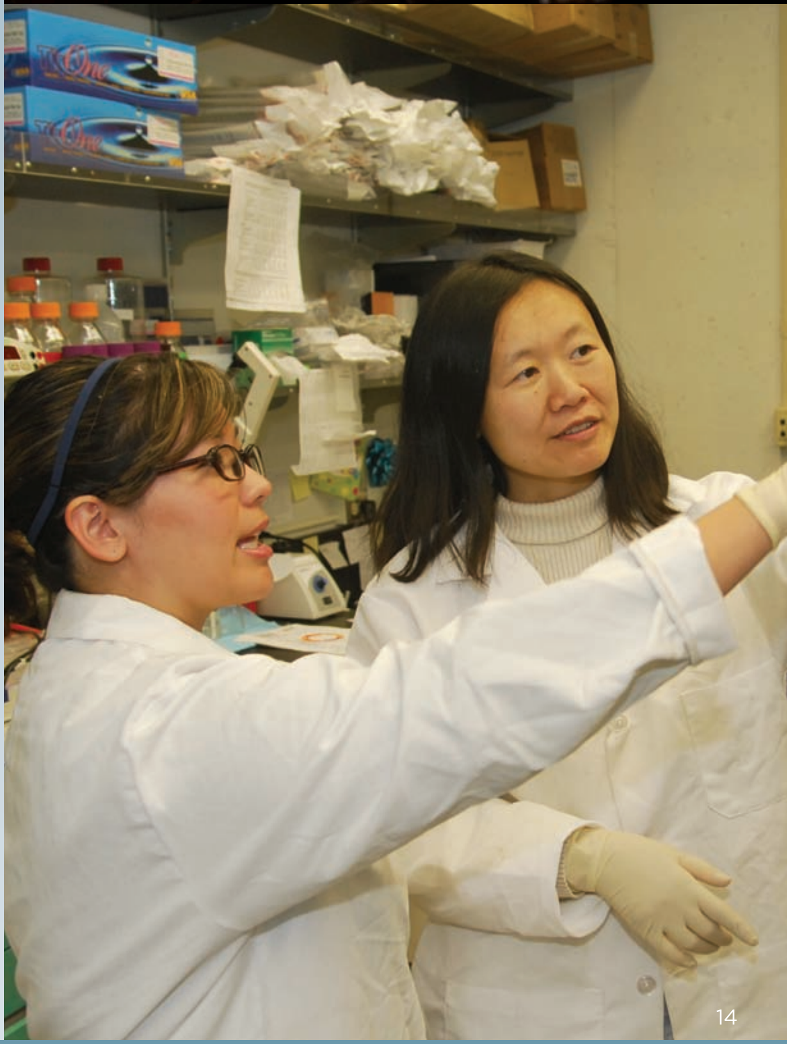
One–Two **Punch for DIABETES**

NIH Recovery Act funding recipients are also working hard to combat diabetes. At the University of Southern California (USC) Jennifer-Ann Bayan is a doctoral student pursuing a new field. She's examining how pancreatic stellate cells could help the body more naturally produce the right levels of insulin. Her work ultimately could be used in the treatment of type-2 diabetes.

"Diabetes runs on both sides of my family, and the disease has caused blindness and the need for amputations among the people that I love. Experiencing this makes me passionate about my work," Bayan says.[25]

At Washington University in St. Louis, Dr. Jim Cheverud has launched a novel study into the way genetic differences may change the way the body responds to a high-fat diet. "Some individuals respond to the high fat "Western" diet by becoming obese while others exposed to the same diet do not. This individual variation in response to dietary fat is, in part, due to genetic differences," says Dr. Cheverud.[26] Understanding these differences could lead to new diet and exercise regimens or other therapies that help alleviate the growing, costly epidemics of diabetes and obesity.

The only way to continue breaking new ground in all of these areas and more, to both improve health and beat back the long-term costs of care, will be with robust, consistent increases in NIH funding over the long-term.



RIGHT: Jennifer-Ann Bayan with faculty mentor, Dr. Bangyan Stiles, at the University of Southern California.

Photo by Don Milici

III. NIH RECOVERY ACT FUNDING:

Accelerating into a Healthier Century

NIH Recovery Act investments are working across the country, creating jobs and fostering new economic growth. However, the most important benefits of NIH Recovery Act funding cannot be measured in traditional economic terms. For example: neither scientist nor economist can estimate the human value of uncovering a new protein receptor in the kidney which researchers now manipulate so that it better regulates the amount of salt in the bloodstream, dramatically reducing life-threatening hypertension for millions. The primary goal of NIH investments will always be to advance biomedical science to enable new treatments and even cures for patients af icted with disease and other health care challenges. Simply put, the most important results of any NIH-funded research are priceless.

Previous investments in NIH have created an unusually rich period of scientific opportunity. Researchers are seizing those opportunities, using Recovery Act funds to:

- Explore new science that was not possible even ten years ago, before advances in genomics, proteomics, and regenerative medicine opened up new avenues for research.
- Build upon the insights of previous discoveries to more quickly deliver new treatments for patients.
- Improve health care quality by finding the right treatment for the right patient, forging a new age of personalized medicine.

> "The discovery process yields options. Options that make care more negotiable, more acceptable, more effective."
>
> **— Dr. Clyde Yancy,**
> President, the American Heart Association

New Science

NIH Recovery Act funding is allowing researchers to forge new scientific strategies that simply could not have been pursued just ten years ago. Thanks to the mapping of the human genome (completed in 2003 largely through the NIH) and the vast science that has followed on that work, scientists are able to understand the biology of disease more thoroughly and at earlier stages of its development. As, a recent White House report states, "through Recovery Act funded research, scientists will sequence over 2,300 complete genomes...This effort will allow researchers to make quantum leaps forward."[27] The following are just a few of the most exciting research projects making use of new science funded by the recovery act.

Shutting Off **A Gene,** Shutting Off **A Seizure**

Dr. Andrew Escayg of Emory University is pursuing a study that could lead to a new treatment for the many epileptic patients whose seizures cannot be controlled with any medicines currently available. Prior research has shown that lowering the expression level of a gene called SCN8A can reduce the excitability for the body's neurons, thus increasing resistance to seizures. Escayg's team plans to test a gene-therapy technique for shutting off the SCN8A gene in mice, a precursor to developing similar treatments for humans. The impact could be tremendous for the thousands of people who suffer from uncontrollable epileptic seizures — including young children, elderly adults, and soldiers returning from war with traumatic brain injuries (one of the causes of epilepsy).

UNRAVELING AUTISM

In recent years, autism has emerged as a particularly fearsome disorder for millions of families, and the federal government has recently reported a rise in the rate of autism to one in 110 children.[28] To help answer the call, there are many much-needed projects underway with $100 million in Recovery Act funds — the largest single infusion of funding for Autism research, ever.[29] Among these projects is the work of Dr. Margaret Pericak-Vance at the University of Miami who is using NIH Recovery Act funds to uncover the specific genes, their functions and interactions that may be leading contributors to the disorder. She is also studying the emergence and trajectory of children's autistic behaviors associated with those genes to elucidate the role that specific genes play in this complex genetic disorder. As Dr. Pericak-Vance notes, seeking the genetic roots of such a complex disease is critical: "If there is a genetic predisposition interacting with environmental factors, we need to know the responsible gene or genes before we can pinpoint which environmental risks are involved."[30]

In addition, Dr. Nirao Shah, MD, PhD, of the University of California, San Francisco, has received a roughly $700,000 NIH Pioneer Award to develop genetic tools to understand how the brain controls the ability to form long-standing social attachments. He seeks to understand the body's regulation of social ties and the profound inability to form interpersonal bonds that occur in disorders like autism.

The Cancer Genome, **and EPIGenome**

Over the last decade, researchers have learned that cancer is not one disease, but many, each caused by a different kind of malfunction in the genetic code of cells and/or in faulty interactions between genes and other chemicals in the cell's environment. With Recovery Act funding, NIH is accelerating the rate at which scientists can decode the individual genetic and epigenetic malfunctions that occur in major forms of cancer.

One of these projects is the Cancer Genome Atlas. The project is a coordinated effort across some of the nation's leading cancer research centers in universities and private research institutions. The effort will use $175 million in Recovery Act funding over the next two years. It will collect more than 20,000 cancer tissue samples, complete comprehensive maps of the genomic changes in 10 cancers and sequence and characterize at least 100 tumors of up to 15 additional cancers. By identifying the exact genetic malfunctions in each cancer, researchers will be able to specifically target treatments with far greater chances at success.

In addition, with $10 million, the University of Southern California is building one of the world's leading Epigenome Centers to explore the non-hereditary genetic changes affecting cancer. And at the Dana-Farber Cancer Institute, a private research institution based in Boston, scientists are using two grants totaling more than $3 million to develop bioinformatics and genetic data-crunching capabilities to systemically identify when viruses come into the genetic picture of cancers' development.

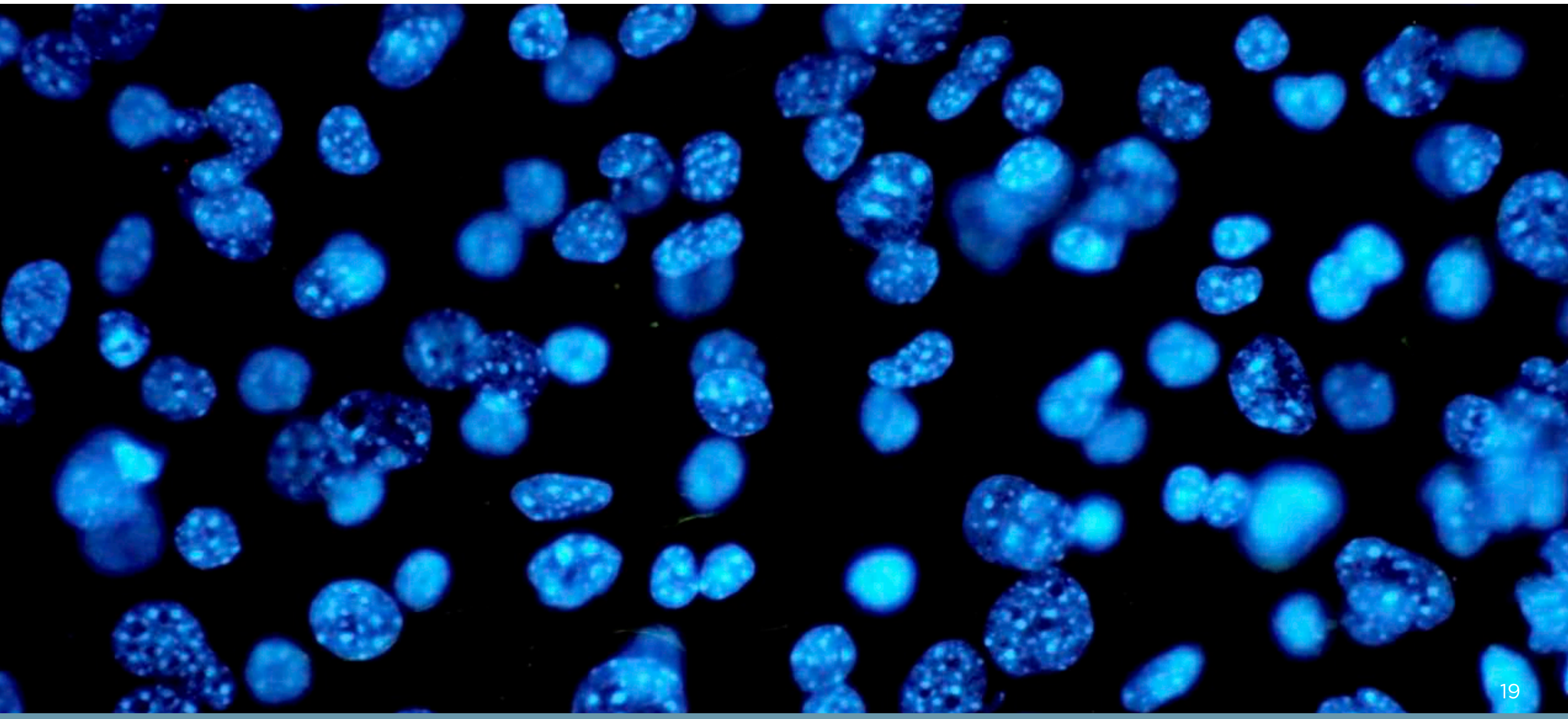
Recovery Act funding also is being deployed to create new models to study viruses in ways that may reveal how their actions contribute to cancer and other diseases. For example, recent studies have demonstrated that the hepatitis C virus, which infects more than 170 million people worldwide, is the leading cause of liver cancer in the United States. But a vaccine has proven elusive because scientists can only observe the virus accurately in living human liver tissue. To break through this barrier, Dr. Priscilla Yang and her team at Harvard University are using a roughly $200,000 NIH Recovery Act grant to create a mutation of the human hepatitis C virus that could live and be studied in the livers of lab mice. This model virus could provide the team directly with the insights it would need to move toward developing therapies and eventually, a vaccine. This tool could then be used to further research in related work across the US.

STEM CELLS in Action

For decades scientists had been able to observe that certain kinds of human cells had an impact on the generation of other cells. But it was only in the late 1990s that researchers were able to isolate stem cells and really study their properties, functions, and differentiating capabilities. Today, stem cell research is poised to launch into new areas of application that will be revolutionary for human health. For example, stem cells may help treat peripheral artery disease. The condition affects up to 12 million people in the U.S. today, and research shows that it is closely linked to cardiovascular disease, the number one killer. Peripheral artery disease is caused by a clogging of the arteries, leading to a loss of critical circulation in the legs.[31] With a roughly $1.6 million NIH grant funded through the Recovery Act, Dr. Arshed Quyyumi of Emory University's School of Medicine is studying whether the body's own growth factors can prod stem cells out of bone marrow and into the bloodstream where they may be able to repair blood vessels in the legs. This project is in a phase II clinical trial, a critical step in transforming such an innovative idea into a treatment.

"[People with PAD] are a group of individuals at a dead end; there is no good therapy but amputating their legs when the disease is advanced. If this is found to be a good modality of treatment, it will be hugely persuasive to get Phase III funding from NIH or industry. Even if it doesn't, it could also stimulate more research into [the field]. It moves the field forward," says Dr. Arshed Quyyumi.[32]

In another study, researchers at the University of Michigan in Ann Arbor received more than $350,000 in NIH Recovery Act funds to use stem cells to help combat Hirschsprung disease, a birth defect in which critical nerve cells in the colon never develop, causing severe bowel problems.[33] It occurs in one in 5,000 newborns and can be fatal. Right now, surgery is the only treatment for Hirschsprung disease. Dr. Sean Morrison and his team are working to uncover the mechanisms that underlie the development of Hirschsprung. Dr. Morrison notes, "These insights raise the possibility of treating this disease with stem cell therapies that would by-pass these defects."[34]



Between Genes and Symptoms

Huntington disease is a devastating neurodegenerative disorder with no cure. Because Huntington is a hereditary disease, researchers have been able to identify its genetic markers and inform patients of their condition long before symptoms set in. But until recently, that knowledge has never been analyzed in detail and compared across a large number of patients to help identify target moments within the disease process for treatment development. With $500,000, Dr. Jane Paulsen at the University of Iowa is continuing PREDICT-HD, a first-of-its kind, international, 31-site study that will help scientists understand the biological processes that take place in Huntington disease long before symptom onset. The project involves over 1,000 participants and includes annual measures of plasma, brain imaging, cognitive performance, psychiatric symptoms, and functional capacity.

This study will open up the likelihood for development of drugs that could delay or even prevent the manifestation of the disease. "We want to intervene and provide prevention tools as soon as the very first signs occur," says Dr. Paulsen "That's why it's so exciting. Because our work tries to push back the envelope, so to speak."[35]

Pursuing an Unexpected Killer

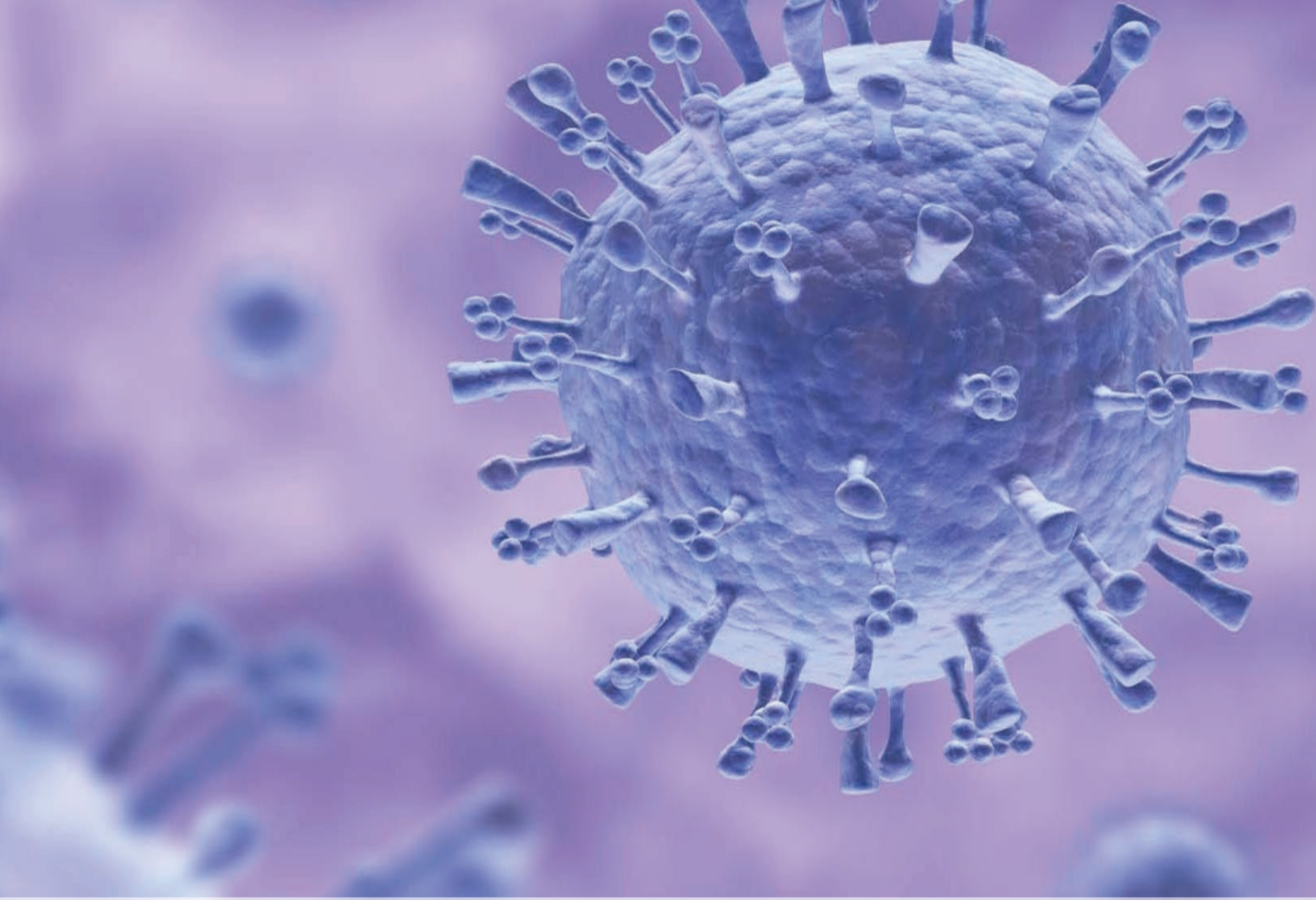
While healthy immune systems can fight off many fungal infections, patients with weakened immune systems often cannot. Few anti-fungal drugs have made it to market because of the complexity of these infections. Indeed, only one new class of anti-fungal medicine has been developed in the last decade. In recent years there has been a breakthrough: scientists identified an enzyme called hybrid histidine kinase, which regulates how a fungus changes, develops, and becomes more virulent. Dr. Bruce Steven Klein at the University of Wisconsin in Madison received an NIH Recovery Act-funded Challenge Grant to work with this enzyme and attempt to manipulate it as a more targeted and less damaging new drug candidate for a broad array of the most severe and life-threatening fungal infections.

Accelerating the Impact

Scientists are using NIH Recovery grants to build on previous investments and discoveries, translating research successes into new treatment possibilities for patients.

Disease Data-Crunching

With new techniques for diagnosing and tracking Alzheimer's disease, scientists across the country have amassed enormous databases of information. But it's all decentralized in various labs and consortiums across the country, so researchers have not been able to fully analyze and compare the information and use the data to find the causes of Alzheimer's disease. Today, Dr. Gerard Schellenberg at the University of Pennsylvania is using $5.5 million in Recovery Act funds over two years to collect much of this key data from across multiple organizations, programs, and consortiums with the goal of increasing understanding of this heartbreakingly elusive disease. In all, $92 million Recovery-Act NIH funds are going to new, high-tech projects like this one to collect and analyze sophisticated genetic and biological information sets in major disease areas in multi-organizational collaborative projects across the country.



STOPPING VIRUSES Before they Trigger Asthma

Scientists know that some of the greatest health risks associated with viral respiratory infections such as H1N1 are complications of the diseases including the onset of asthma and/or pneumonia. Medical researchers are beginning to define how viral infections in the lungs, previously considered to cause only transient and reversible illness, can trigger chronic diseases such as asthma and COPD. With almost $2.8 million in new funding, Dr. Michael Holtzman at Washington University in St. Louis is building upon his previous work showing that a part of the body's own natural immune system (called the "interferon signaling system") can be boosted to help fight off the more serious complications of viral infection. "In past research, we've shown that we can defeat flu viruses in mice and in human cells by genetically modifying the interferon signaling pathway so that it's more effective in controlling infections. We are now aiming to develop drugs that would mimic the effects that we saw in mice and cells," Holtzman explains.[36] In the first part of the new project, the team will study the biological processes that occur during influenza infection as well as the steps that occur when this type of infection turns into chronic lung disease. Understanding this process will provide new targets for therapy. In the second part of the project, the team will develop a drug discovery center based on a new screening system for antiviral drugs. This system will screen for drugs that boost efficacy of the interferon signaling system and thereby slow or stop the acute and chronic effects of viral infection. "We call it genome-guided drug screening — a new method of drug development that is being used in very few other places," he says. "We're putting together a specialized high-throughput system using robotic equipment that can rapidly screen many different compounds. The system will use high-fidelity cell models and gene expression data to help identify compounds that enhance our antiviral response and improve host defense."[37]

Connecting the Dots to Eliminate **Preemie Lung Disease**

Thanks to $3 million in Recovery Act funds, Dr. Hugh O'Brodovich and his team at Stanford's School of Medicine are able to connect key pieces of information about a devastating lung disease that attacks premature infants and causes respiratory harm throughout a patients' life. They are taking a pre-existing, large database of all the premature babies born in the state of California and matching it against each patient's genetic profile in order to be able to identify the genes and gene pathways which predispose premature infants to the disorder. Identifying the genes is key to developing better and more preventive treatments.

"This grant accelerates the scientific information we will have [in the 2-year time period]. It's truly remarkable. It would have taken us a decade or more to have gotten this together. This will enable treatments and new strategies to avoid this disease to be implemented much sooner than we ever dreamed."

— Dr. Hugh O'Brodovich, MD
Professor and Chair of Pediatrics,
Stanford School of Medicine[38]

Scientists now know that treatments that work for some people simply don't work for others because of differences in age, gender, genetic makeup, and other factors. Treatments' side effects among certain populations or individuals may outweigh the benefits. Researchers are studying these disparities to find the treatments that work for people who need them.

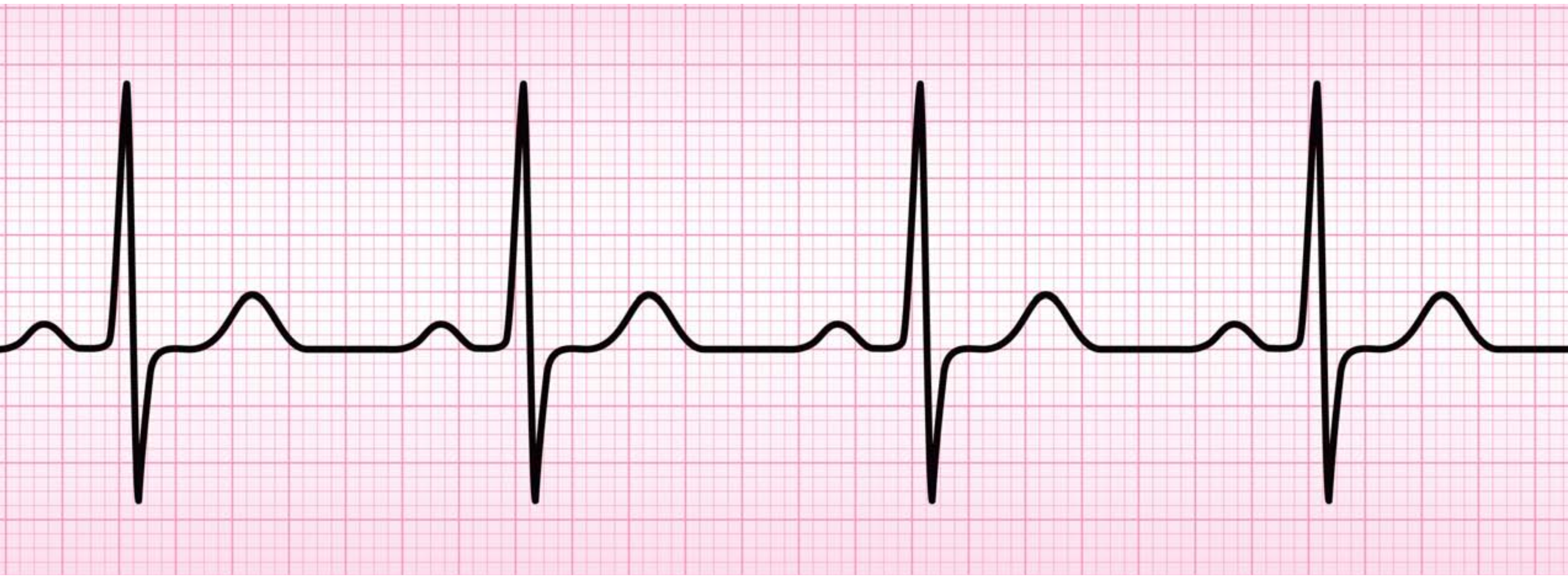
Cancer Treatments Adapted for Children

In recent years, great advances in molecularly-targeted cancer treatments have helped scientists develop better, less toxic treatments for certain cancers. One example of this new kind of medicine is Imatinib, which treats chronic myelogenous leukemia and gastrointestinal stromal tumors, sometimes with just one pill a day. But researchers and clinicians know that this targeted therapy revolution has had, thus far, only a limited impact in the childhood cancer setting. Within the walls of NIH's National Cancer Institute, researchers are using $25 million in Recovery Act funds and new technologies to understand this difference at the genetic and molecular levels and identify the therapeutic targets and treatment plans that will be more effective in children.

Rooting out **Disparities**

For years, health advocates have raised awareness of an otherwise quiet crisis occurring across the country. There is a gap between the quality of health in the general public and that within the nation's minority populations.[39] These disparities can be reduced with better access and distribution of health care services, but more diverse medical and clinical research conducted by NIH-funded scientists will also make a difference in understanding the physiological differences among various ethnic and gender populations. The unique demands of minority health in particular may have been overlooked in the past in part because there are also disparities in medical professionals and researchers. Minorities received only 6.5 percent of the Ph.D.s awarded in biological and biomedical sciences in 2007.[40] To help encourage minority entry into the research and medical fields, and provide essential training, Stanford University School of Medicine is using $400,000 to fund a program that directly creates 30 sub-internship opportunities for students from groups underrepresented in academic medicine. The program will help encourage diversification among translational scientists and academic faculty, and in the long term, improve the attention to and solutions for minority health.

Predicting and **Preventing Heart Failure**



Today, implantation of defibrillators is a common practice for patients with advanced heart disease at risk for sudden cardiac death. Defibrillators shock the heart to correct errant rhythms if they occur. However, it has been recognized that as few as one in ten patients with defibrillators may actually benefit from the device. Further defining which kinds of patients truly need one and those which do not is critical because implanting a defibrillator is an expensive and potentially hazardous surgery, which, if it could be avoided, would result in better health outcomes and lower costs for thousands of patients and the health care system as a whole. Supported by Recovery Act funds, Dr. Gordon Tomaselli, Director of the Johns Hopkins University School of Medicine's Cardiology Division, is identifying specific biomarkers that may indicate which patients are in fact more likely to need defibrillators. Dr. Tomaselli is extracting DNA and RNA from simple blood draws among 1,200 patients undergoing defibrillator surgery, and analyzing not only genetic markers, but also a wide range of other clinical and laboratory data already gathered on those patients. By sorting through all of these candidate factors, the work seeks to identify which patients are most likely to benefit from defibrillators, to reduce the number of sudden cardiac deaths, to cut repeated hospitalizations, and to help identify individuals with the greatest need for aggressive management programs to prevent heart failure.

IV. Looking Ahead

NIH Recovery Act funds are supporting new medical discovery at an historic moment for biomedical science. Standing on the shoulders of their predecessors and making use of previously unimagined tools and technology, today's investigators are leading the way to better health and a stronger economy.

The investment is creating and preserving jobs, supporting growth in multiple industries, and, over time, helping to reduce health care costs. It is also enabling exploration in new fields of science unreachable just ten years ago, accelerating the pace at which scientists can translate scientific discoveries into new treatments, and helping scientists tailor treatments to the unique needs of very different patient populations to ensure efficient and effective care.

Thanks to strong Recovery Act funding for NIH, scientists are poised to make new discoveries that will change and extend the lives of all Americans. Going forward, Congress and the President must provide the vital resources to keep up the momentum, or risk returning to a time of incremental progress when far too much breakthrough science waited in the wings.

This report was prepared by United for Medical Research, a partnership among university and private research institutions, industry, and patients. We believe that particularly in these tough economic times, Congress and the President must make robust funding for the National Institutes of Health a national priority. The nation can achieve better health and a stronger economy if it continues to invest in the National Institutes of Health.

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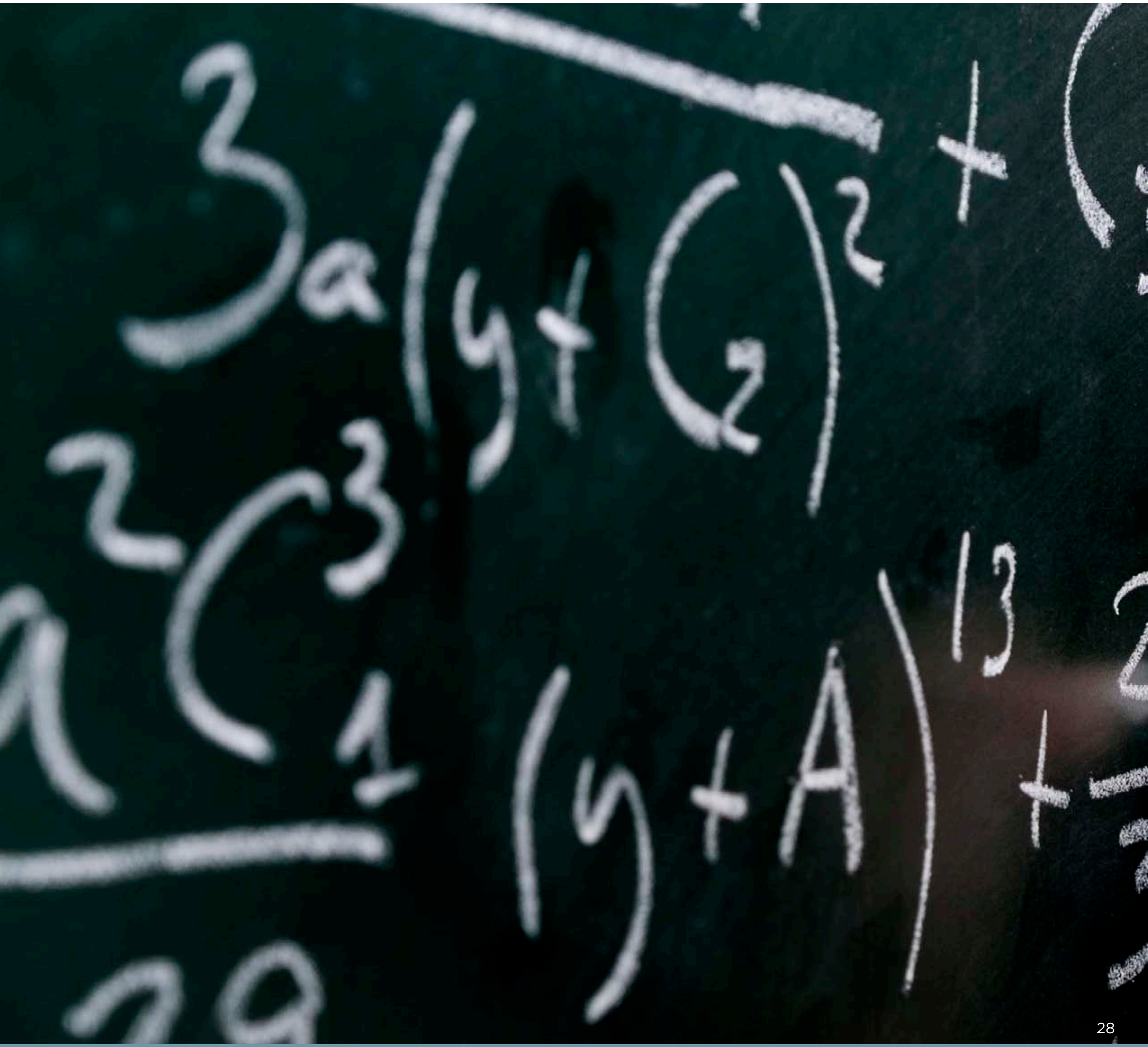

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1. Remarks Made by the President Remarks by the President on the American Recovery and Reinvestment Act at the National Institutes of Health, September 30, 2009, http://www.whitehouse.gov/the_press_office/Remarks-by-the-President-on-the-American-Recovery-and-Reinvestment-Act-at-the-National-Institutes-of-Health

2. Clive Cookson, "Stimulating Stimulus", Financial Times, December 7, 2009, http://www.ft.com/cms/s/0/71d245e2-dd53-11de-ad60-00144feabdc0.html

3. National Institute of Health (NIH), NIH Overview, http://www.nih.gov/about/NIHoverview.html

4. NIH Website, Research Project Success Rates by NIH Institute for 2008, http://report.nih.gov/award/success/Success_ByIC.cfm

5. Alvin Powell, Harvard Science, Stimulus funds provide welcome research boost, http://www.harvardscience.harvard.edu/culture-society/articles/stimulus-funds-provide-welcome-research-boost

6. Donna Young, THE DAILY BIOTECHNOLOGY NEWSPAPER, Collins: End of Stimulus Funds Could Send NIH Off Cliff in '11, August 18, 2009, http://www.unitedformedicalresearch.com/2009/08/18/2011-cliff-keeps-collins-awake-at-night/

7. A Broken Pipeline? Flat Funding of the NIH Puts a Generation of Science at Risk http://www.brokenpipeline.org/brokenpipeline.pdf

8. NIH, NIH Press Release, June 8 2009, http://www.nih.gov/news/health/jun2009/od-08.htm

9. NIH, PRELIMINARY NIH ARRA FY2009 FUNDING, October 26, 2009, http://report.nih.gov/PDF/Preliminary_NIH_ARRA_FY2009_Funding.pdf

10. NIH, PRELIMINARY NIH ARRA FY2009 FUNDING, October 26, 2009, http://report.nih.gov/PDF/Preliminary_NIH_ARRA_FY2009_Funding.pdf

11. Urist, Marshall, M.D., Ph.D., Medical Technology: The Anatomy of Stimulus, Morgan Stanley Research, North America, December 4, 2009

12. The Economic Impact of AAMC-Member Medical Schools and Teaching Hospitals, September 2008, https://services.aamc.org/publications/index.cfm?fuseaction=Product.displayForm&prd_id=268&prv_id=329

13. Anya Martin, The Wall Street Journal, Medical Research Spurt Offers Promise Of New Cures, NOVEMBER 5, 2009, http://online.wsj.com/article/BT-CO-20091105-711678.html?mg=com-wsj

14. Urist, Marshall, M.D., Ph.D., Medical Technology: The Anatomy of Stimulus, Morgan Stanley Research, North America, December 4, 2009

15. NIH, NIH Overview, http://www.nih.gov/about/NIHoverview.html

16. Families USA, How NIH Funding Helps Your State's Economy, June 2008, http://www.familiesusa.org/assets/pdfs/global-health/in-your-own-backyard.pdf

17. "BIO's 2009 Member Survey: Technology Transfer & the Biotech Industry,'' presented at BIO Technology Transfer Summit, San Francisco, Oct. 28, 2009, as featured in Universities, Inventors, and the Bayh-Dole Act BY SEN. BIRCH BAYH, JOSEPH P. ALLEN,AND HOWARD W. BREMER, Life Sciences Law & Industry Report, 3 LSLR 1266, 12/18/2009.

18. State Bioscience Initiatives 2008, June 2008, http://www.bio.org/local/battelle2008/State_Bioscience_Initiatives_2008.pdf

19. Food and Drug Administation, FDA NEWS RELEASE, May 8, 2009, FDA Approves Drug for Treatment of Aggressive Brain Cancer http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm152295.htm

20. Children's Hospital, Remembering Judah Folkman http://www.childrenshospital.org/cfapps/research/data_admin/Site2580/mainpageS2580P0.html

21. Federation of American Societies for Experimental Biology (FASEB), Timeline of Medical Advancement, http://opa.faseb.org/pdf/timelinemedical.pdf

22. SP Strickland, Harvard University Press, Politics, Science, and Dread disease., 1972. http://www.laskerfoundation.org/advocacy/pdf/rosenberg_economic.pdf

23. Research America! & the Lasker Foundation, Investment in Research Saves Lives and Money: Facts about Alzheimer's Disease, http://www.laskerfoundation.org/advocacy/pdf/factsheet4alzheimers.pdf

24. Heart Disease and Stroke Statistics—2010 Update, American Heart Association http://circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.109.192667

25. Gabrielle Olya, USC News, Stimulus Grants Enhance Therapeutic Work, October 8, 2009, http://uscnews.usc.edu/science_technology/stimulus_grants_enhance_therapeutic_work.html

26. The Jim Cheverud Lab, http://thalamus.wustl.edu/cheverudlab/Dietary%20Obesity%20and%20Diabetes.html

27. The White House, Office of the Press Secretary, FACT SHEET, Recovery to Discovery: $5 Billion Recovery Act Investment in Scientific Research and Jobs, September 30, 2009, http://www.whitehouse.gov/the_press_office/Fact-Sheet-Recovery-to-Discovery-5-Billion-Recovery-Act-Investment-in-Scientific-Research-and-Jobs/

28. Catherine Rice (Centers for Disease Control), Prevalence of Autism Spectrum Disorders --- Autism and Developmental Disabilities Monitoring Network, United States, 2006. http://www.cdc.gov/mmwr/preview/mmwrhtml/ss5810a1.htm

29. The White House, Office of the Press Secretary, FACT SHEET, Recovery to Discovery: $5 Billion Recovery Act Investment in Scientific Research and Jobs, September 30, 2009, http://www.whitehouse.gov/the_press_office/Fact-Sheet-Recovery-to-Discovery-5-Billion-Recovery-Act-Investment-in-Scientific-Research-and-Jobs/

30. Laurie Barclay, Medscape Today, Gene Linked to Autism: A Newsmaker Interview With Margaret Pericak-Vance, PhD, http://www.medscape.com/viewarticle/449158

31. The American Heart Association, Peripheral Vascular Disease http://www.americanheart.org/presenter.jhtml?identifier=4692

32. Anya Martin, The Wall Street Journal, Medical Research Spurt Offers Promise Of New Cures, NOVEMBER 5, 2009, http://online.wsj.com/article/BT-CO-20091105-711678.html?mg=com-wsj&mg=com-wsj

33. Lakshmi Pasumarthy & James W. Srour, PRACTICAL GASTROENTEROLOGY, A Case to Remember: Hirschsprung's Disease, JUNE 2008, http://www.practicalgastro.com/pdf/June08/PG_June08PasumarthyArticle.pdf

34. Sean Morrison, University of Michigan Health Systems, http://www.umich.edu/~mmgmed/faculty/bios/morrison.htm

35. Jane Paulsen, From Predictors to Prevention: The PREDICT-HD 2.0 Huntington Disease Study, http://www.youtube.com/user/PREDICTHD

36. Gwen Ericson, Recovery act funds new flu drug discovery center at Washington University, Washington University Press Release, Nov. 16, 2009, http://mednews.wustl.edu/news/page/normal/15099.html

37. Gwen Ericson, Recovery act funds new flu drug discovery center at Washington University, Washington University Press Release, Nov. 16, 2009, http://mednews.wustl.edu/news/page/normal/15099.html

38. Stanford University School of Medicine, Stimulus Funding's Effect on Science, Health Care and Economy, Nov 18, 2009, http://healthnewsdigest.com/news/National_30/Stimulus_Funding_s_Effect_on_Science_Health_Care_and_Economy_printer.shtml

39. Net Wellness, Statistics on Health Disparities Among African Americans, http://www.netwellness.org/healthtopics/aahealth/currentstats.cfm

40. Sandra Larson, Harvard talk addresses diversity in science faculty, http://www.baystatebanner.com/health22-2009-11-12


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