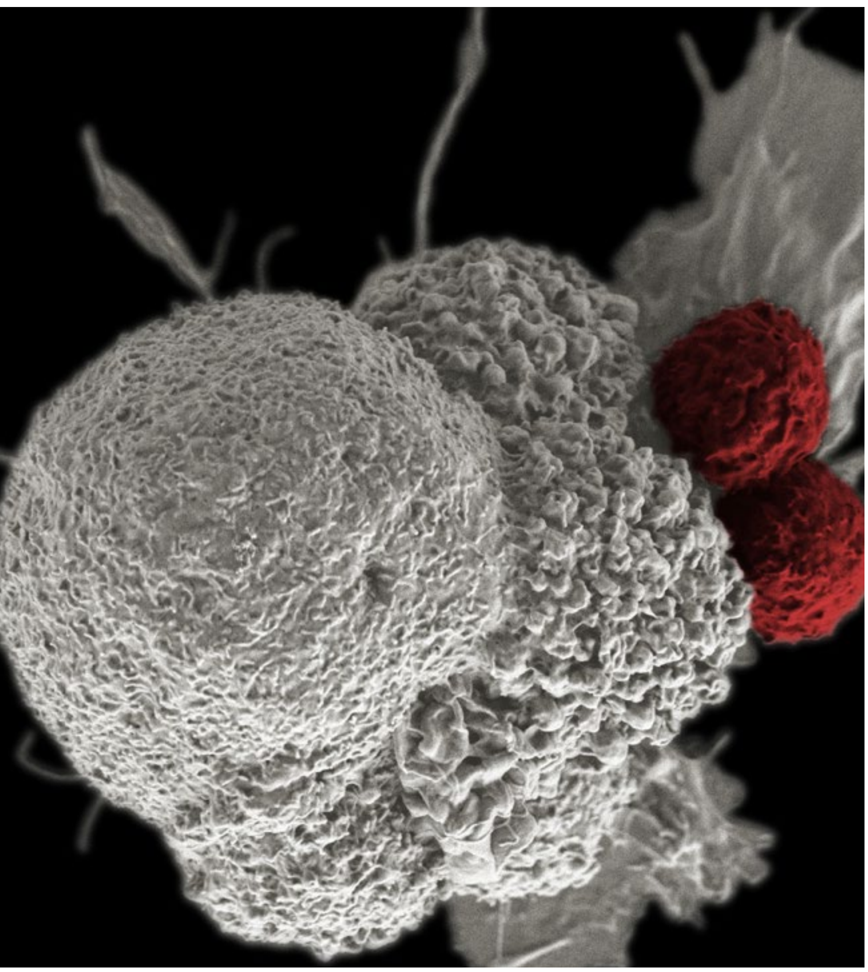
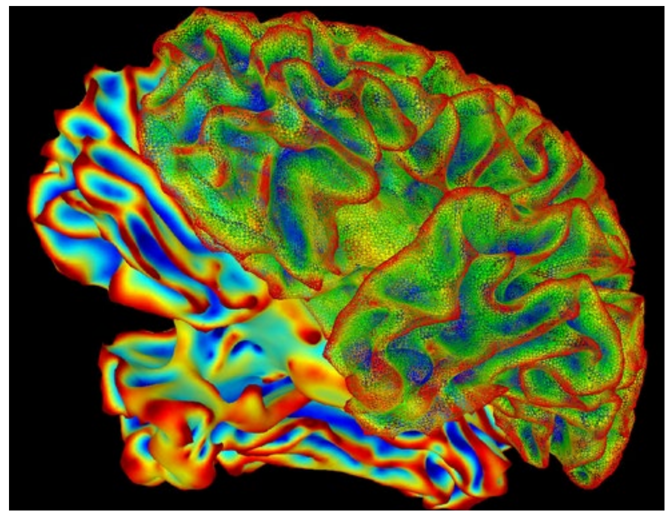
NIH TURNING **DISCOVERY** INTO **HEALTH**

U.S DEPARTMENT OF HEALTH & HUMAN SERVICES • NATIONAL INSTITUTES OF HEALTH





THE 21ST CENTURY NATIONAL INSTITUTES OF HEALTH

Created in 1887 as a one-room laboratory on Staten Island, NY, NIH was officially designated by Congress in 1930. Since then, the agency has grown to be the world's largest source of medical research funding and the driving force behind decades of advances that have expanded fundamental scientific knowledge and improved health.

NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and to apply that knowledge to enhance health, lengthen life, and reduce illness and disability.

TO CARRY OUT THIS MISSION, NIH SUPPORTS:

- **BASIC RESEARCH...** TO FUEL PROGRESS
- **TRANSLATIONAL RESEARCH...** TO MOVE BASIC DISCOVERIES FORWARD
- **CLINICAL RESEARCH...** TO TURN DISCOVERIES INTO PREVENTION, TREATMENTS, AND CURES
- **A CREATIVE AND DIVERSE WORKFORCE ...** SINCE PEOPLE ARE OUR MOST IMPORTANT RESOURCE
- **A BALANCED RESEARCH PORTFOLIO...** TO ENSURE HIGH RETURN ON INVESTMENT FOR U.S. TAXPAYERS

OUR BIGGEST HEALTH **CHALLENGES**

THANKS TO DECADES OF RESEARCH, AMERICANS ARE LIVING LONGER. YET CHRONIC DISEASES STILL AFFECT LARGE SWATHS OF THE POPULATION AND ARE UNEVENLY DISTRIBUTED, CREATING HEALTH DISPARITIES. THESE CHRONIC ILLNESSES ARE COMMON AND COSTLY, AND MANY ARE PREVENTABLE. NIH RESEARCHERS — BASIC, TRANSLATIONAL, CLINICAL, AND COMMUNITY-BASED — ARE TACKLING THESE CHALLENGES HEAD ON.

HEART DISEASE AND STROKE

In the years after World War II, heart attacks killed thousands of middle-aged Americans, many of them soldiers who had returned from conflict. Since then, NIH research has fueled major progress. Beginning with the landmark Framingham Heart Study in the 1940s, key risk factors were identified for cardiovascular disease, including smoking, cholesterol, high blood pressure, and diabetes. Research studies funded by NIH then tested interventions to reduce those risks, showing they could work. These included cholesterol- and blood pressure-lowering drugs and lifestyle modifications such as physical activity, a healthy diet, and quitting smoking. Since 1969, heart disease deaths have dropped nearly 70 percent.

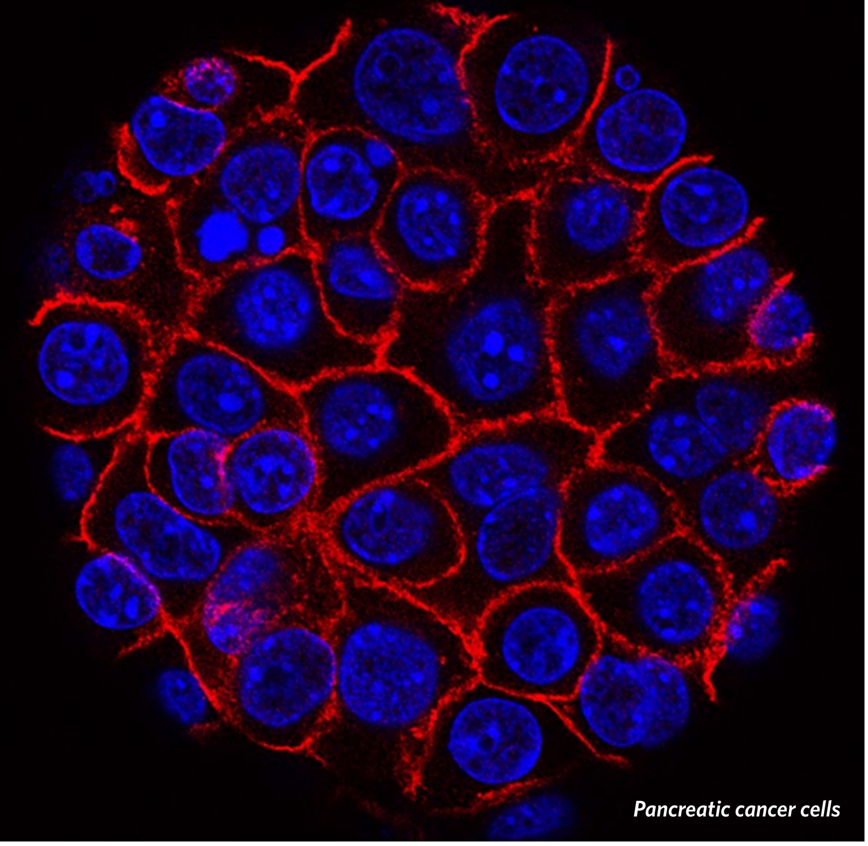
But stroke still strikes an American once every 40 seconds and can have catastrophic consequences for a person's ability to function. In the mid-90s, NIH research led to approval of the drug tissue-type plasminogen activator (tPA), which dissolves stroke-causing clots if given soon after symptoms appear. More recent studies showed that inserting balloon catheters to remove brain clots can prevent further damage in people suffering major strokes. NIH's *Know Stroke* awareness campaign has helped thousands learn to recognize stroke as a medical emergency and seek immediate help.

Yet, with heart disease and stroke still the leading causes of death for both U.S. men and women, more research is needed. NIH-funded scientists currently are looking to the power of precision medicine to better understand and manage these disorders. These efforts will combine molecular data with that from behavioral, imaging, environmental, and clinical studies to predict, prevent, diagnose, and treat illness based on a person's unique genes, lifestyle, and molecular signatures.

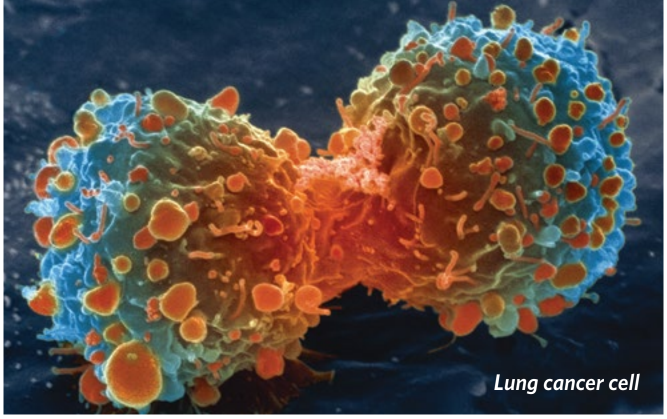
IMAGINE THE FUTURE ...

A HUMAN "TISSUE CHIP" CONTAINING MINIATURE VERSIONS OF HEART, LUNG, AND LIVER HELPS RESEARCHERS SCREEN NEW MEDICATIONS IN THE LAB BEFORE TESTING THEM IN HUMANS.

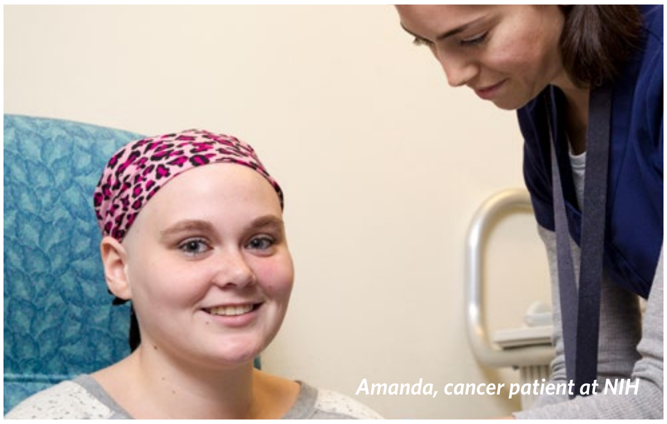
▶ More than 50% of U.S. economic growth since World War II has come from science and technology.



Pancreatic cancer cells



Lung cancer cell



Amanda, cancer patient at NIH

CANCER

Cancer is one of our nation's most feared diseases, with more than 1.6 million new cases diagnosed each year. But thanks to NIH research, this number is now falling. Between 1991 and 2014, cancer death rates went down 25 percent.

NIH research has transformed the way we think about cancer from affecting specific parts of the body to a much more precise understanding of the molecular cause. For example, the drug pembrolizumab is one of a new class of cancer drugs that works by engaging a patient's immune system to attack his or her tumors. Doctors already use this drug to treat some patients with several specific cancer types, including lung cancer and head and neck cancer. And, very recently, it became the first cancer therapy approved by the Food and Drug Administration (FDA) to treat any type of tumor, regardless of its location in the body, as long as the tumor has specific genetic features that make it much more likely to shrink after treatment with the drug.

This is just one example of how genomics has revolutionized our understanding of cancer (see Precision Oncology, p.18).

Despite gains, there is much work to do. Many clinical trials are testing new targeted treatments, as well as combinations of different cancer therapies. With other federal agencies, NIH is participating in the Cancer Moonshot℠, a bold initiative to accelerate cancer research that aims to make more therapies available to more patients while also improving our ability to prevent cancer and detect it at an early stage.

IMAGINE THE FUTURE ...

PEOPLE WITH PREVIOUSLY LETHAL CANCER MANAGE THEIR CONDITION WITH EFFECTIVE AND NON-TOXIC PRECISION MEDICATIONS AND ENJOY A NORMAL HEALTHY LIFE.

GOOD HEALTH FOR ALL

Many people in America are more likely to get certain diseases and to die from them, compared to the general population. One of NIH's greatest challenges is to understand and eliminate profound disparities in health outcomes for these individuals. We know the causes of health disparities are many. They include biological factors that affect disease risk; but most of the causes turn out to be non-biological factors such as socioeconomics, culture, and environment. Teasing apart health outcomes that differ among racial/ethnic groups is providing clues. For example, NIH research shows that among cigarette smokers, African Americans and Native Hawaiians are more susceptible to lung cancer than Whites, Japanese Americans, and Hispanics. Scientists are also intrigued by the "Hispanic paradox," in which U.S. Hispanics often experience similar or better health outcomes across a range of diseases compared with non-Hispanic Whites. Understanding this advantage may help us identify contributing factors and effective interventions.

OPIOID ADDICTION

Addiction used to be considered a lack of willpower that could be overcome with sufficient effort and restraint. We now know that misuse of substances disrupts brain circuits related to pleasure and reward, and that chronic substance use actually alters brain structures. These changes can persist long after a person stops using these substances, increasing risk for relapse.

Addiction to opioids – prescription pain relievers, heroin, and synthetic opioids such as fentanyl – is a national crisis. The epidemic's impact has been vast, disproportionately affecting military personnel and veterans, and estimates put the annual U.S. economic burden for prescription opioid misuse alone at more than $504 billion. NIH-supported research has led to effective strategies that can be implemented right now to save lives and to prevent and treat opioid addiction. For example, NARCAN® Nasal Spray can revive individuals from opioid overdose. NIH is working with other federal agencies and the pharmaceutical industry to develop new medications and technologies to prevent and treat opioid addiction.

A tandem issue to tackling opioid dependency is finding safe, effective, non-addictive strategies to manage chronic pain. NIH is actively involved in building a partnership with FDA and industry to accelerate these efforts. NIH researchers are also studying the neurobiology of pain and investigating complementary therapies such as yoga, acupuncture, and behavioral therapies to treat pain.

IMAGINE THE FUTURE ...

NEW OPIOID-BASED MEDICATIONS PROVIDE PAIN RELIEF WITHOUT DEPENDENCY.

INFECTIOUS DISEASES

Each year, about 23 million Americans visit a doctor's office or clinic seeking treatment for infections. Unlike many disorders, we know the exact source of most infectious diseases and in many cases, we have vaccines and treatments to fight them. One area of particular concern is antimicrobial resistance, a potentially deadly situation in which bacteria become resistant to most or all antibiotic drugs. We recognize this urgent threat, and our scientists are working to better understand how microbes develop resistance to antibiotics, finding new diagnostics that can more quickly detect resistance, and finding new antibiotic drugs and vaccines to prevent and treat bacterial infections.

But because no one knows when a new or re-emerging infectious disease will arrive and how dangerous it may become, NIH must remain vigilant and prepared with prevention strategies, such as the ability to launch rapid vaccine production. Readiness for such unwelcome health surprises also involves ongoing basic research on micro-organisms and the human immune system. The Ebola virus, which ravaged West Africa in 2013, killed more than 10,000 people and severely strained regional socioeconomic stability. When this crisis hit the world, NIH – home to the nation's largest medical research hospital – jumped into action as one of four designated U.S. research hospitals to care for infected health care workers. NIH scientists worked to rapidly test a promising preventive vaccine and experimental Ebola treatment.

AN AIDS-FREE GENERATION?

Since HIV/AIDS first appeared in the early 1980s, more than 70 million infections and 30 million deaths have occurred worldwide. Yet, after decades of intense work by NIH and other organizations, and with continued persistent effort, there is a real possibility of an AIDS-free generation in which virtually no child is born with HIV. NIH research has already enabled HIV-infected individuals to have a normal lifespan without medication-related side effects once considered unmanageable, as well as how to prevent the spread of HIV. If we can find and treat all HIV-infected people in the United States, we could prevent more than 90 percent of new infections every year. An effective HIV vaccine would get us to an AIDS-free generation sooner and, more importantly, would help sustain the result to create a world permanently without HIV/AIDS. An HIV vaccine that is even 50 to 70 percent effective, coupled with other proven HIV prevention tools, would be immensely effective at reducing the rate of new HIV infections.

Alternative pain therapies include yoga

DIABETES

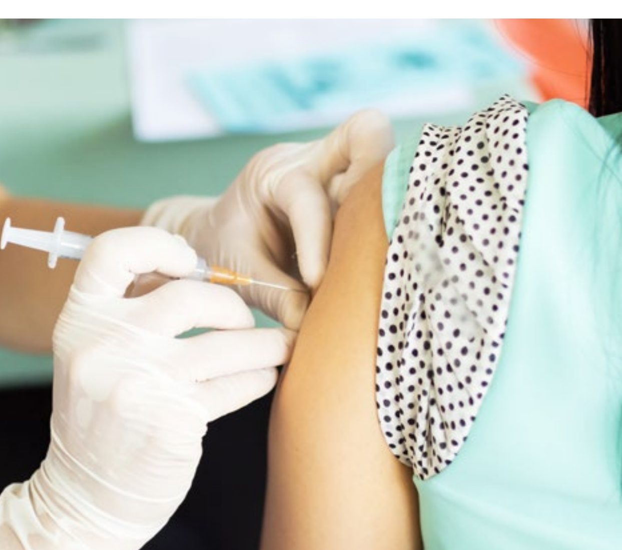
Diabetes affects 30 million American adults and children. People with the type 1 form of diabetes have an autoimmune disorder and are unable to produce sufficient amounts of the hormone insulin, which is made by the pancreas. NIH research contributed to development of a “bionic pancreas,” which connects a smartphone app to a small implanted sensor-pump system that measures blood sugar every 5 minutes and delivers insulin when needed.

The vast majority of Americans with diabetes have the type-2 form of the disorder, in which the body does not manage its insulin levels correctly. Genetics research has identified more than 80 heritable risk factors, but NIH research has shown that lifestyle changes, such as diet and physical activity, can significantly lower the risk of developing type 2 diabetes in high-risk adults.

NIH-funded technological advances offer much promise. For example, using electronic health records and genomic data, scientists have identified what appear to be three distinct subtypes of type 2 diabetes. Since each may cause different health complications such as blindness, cancer, or high blood pressure, this information should eventually help doctors provide individualized treatment.

IMAGINE THE FUTURE ...

MEDICATIONS TREAT TYPE 2 DIABETES BY RESETTING METABOLISM IN PEOPLE AT RISK.



UNIVERSAL FLU VACCINE

Influenza, or “the flu,” is for many a seasonal nuisance, but for others it is a serious health threat. Each year, the flu causes thousands of hospitalizations and deaths in the United States and costs the U.S. economy about $87 billion. NIH scientists are currently testing various potential methods to create a universal flu vaccine — designed to produce broad protection against virtually all strains of the flu for extended periods of time. A promising approach has been to identify and target molecular portions of the flu virus that don’t change from year to year. A universal flu vaccine may avert the need for annual flu shots, as well as reduce the risk of a global pandemic.

A HEALTHY **MIND**

ONLY A FEW CENTURIES AGO, IT SEEMED FANCIFUL THAT A PHYSICAL ORGAN, THE BRAIN, COULD CONTROL ACTIVITIES SUCH AS THINKING AND FEELING. WE NOW KNOW THAT THIS AMAZING BIOLOGICAL MACHINE MADE UP OF ROUGHLY 86 BILLION NEURONS AND TRILLIONS OF NERVE CIRCUITS IS THE COMMAND CENTER FOR MANY OF THE BODY'S VITAL PROCESSES. IT IS ALSO CENTRAL TO CHRONIC CONDITIONS INCLUDING MENTAL ILLNESS, ADDICTION, AND MOVEMENT DISORDERS.

ALZHEIMER'S DISEASE

Alzheimer's disease is the most common cause of dementia in older adults, affecting more than 5 million Americans – and, sadly, this toll is likely to rise as the U.S. population ages. Still others have related conditions, including fronto-temporal, vascular, and Lewy body dementia. In addition to severely impairing memory and the ability to recognize family and friends, in its late stages, Alzheimer's disease restricts a person's ability to manage basic body functions.

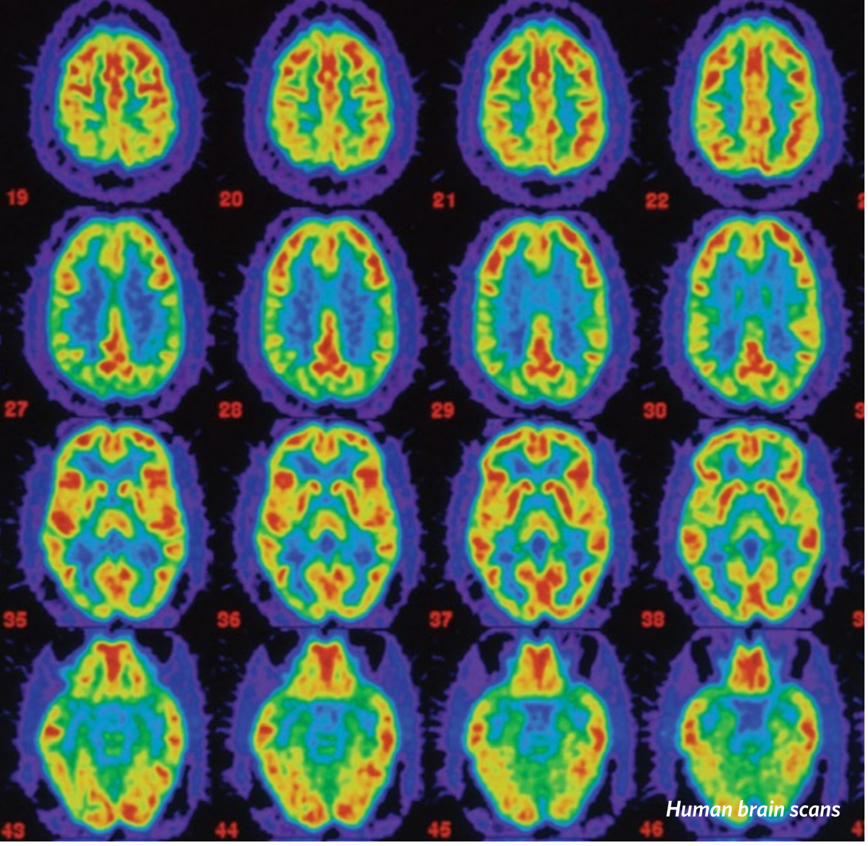
As recently as 30 years ago, we knew very little about Alzheimer's disease. NIH research has generated a much better understanding of brain function, risk factors, treatment, and prevention. For example, scientists have used specialized images of the brain to uncover dramatic insights into how the disease starts. Because of that work, new treatments can now be tested at the earliest stages of disease, ideally years before symptoms appear.

While there is currently no cure for Alzheimer's disease, basic research has led to the development of several drugs that help people maintain mental function and some that seem to delay disease progression. A groundbreaking partnership between NIH and industry has identified a long list of new potential therapeutic targets (see "Speeding Drugs to Market," p.13). More than 90 drugs are in clinical trials, and many more are in the pipeline.

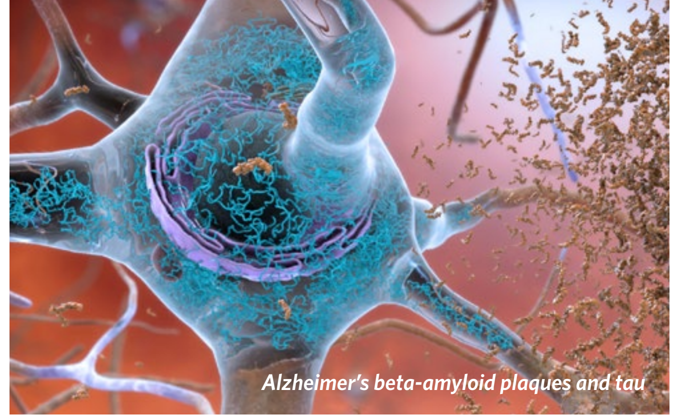
IMAGINE THE FUTURE ...

NEW TECHNOLOGIES DETECT ALZHEIMER'S DISEASE RISK LONG BEFORE MEMORY LOSS OCCURS, WHEN IT MAY BE POSSIBLE TO TREAT OR PREVENT THIS DISEASE.

▶ NIH research produces an extraordinary return on investment for local businesses across the nation; on average, every NIH grant creates 7 high-quality jobs.



Human brain scans



Alzheimer's beta-amyloid plaques and tau

TRAUMATIC BRAIN INJURY

Traumatic brain injury (TBI) due to accidents or sports is a leading cause of death and disability in children and young adults in the United States. TBI is also a major concern for people 75 and older, who are prone to falls. All told, an estimated 5 million Americans live with the challenges of a long-term TBI-related disability. NIH-funded researchers are currently working to better understand TBI, toward creating guidelines to improve recovery and reduce disability.

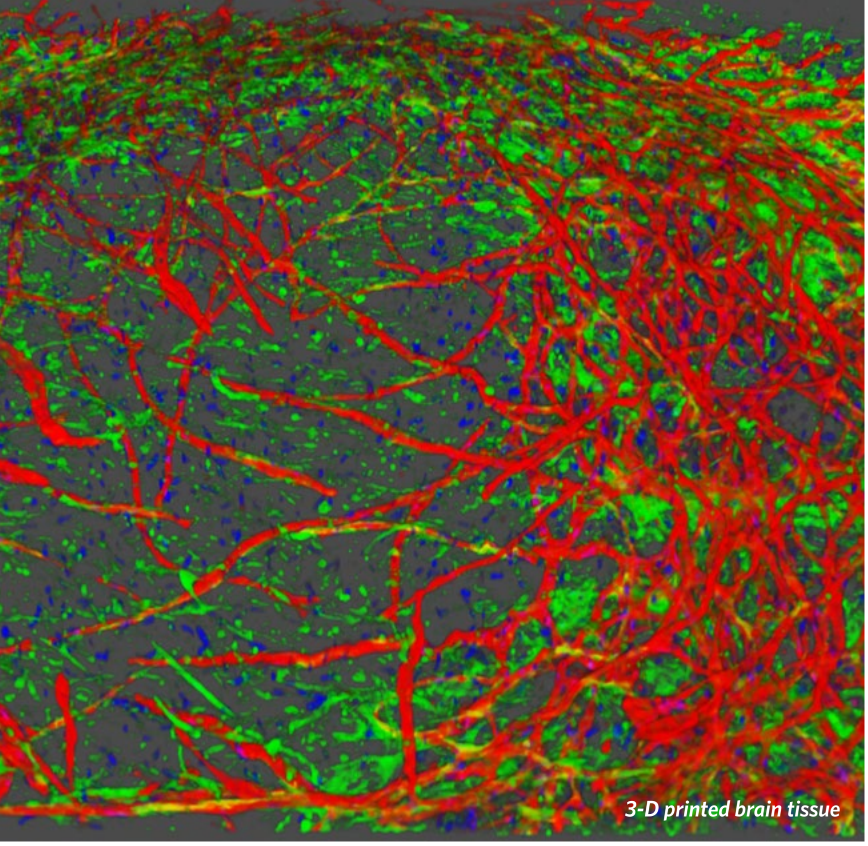
Concussions are among the mildest forms of TBI, but NIH research is showing that cumulative damage over time from concussions may be especially harmful. Scientists have observed that people who experience repetitive head trauma, such as in contact sports like football or hockey, are much more likely than those who do not incur such injuries to develop the degenerative brain disorder chronic traumatic encephalopathy.

People suffering a TBI may also be at risk for developing post-traumatic stress disorder (PTSD). NIH research is looking for PTSD biomarkers – molecular signatures – in people who have suffered serious head injuries amid harrowing environmental influences, such as military combat. This knowledge could revolutionize care for individuals at high risk for PTSD and suicide.

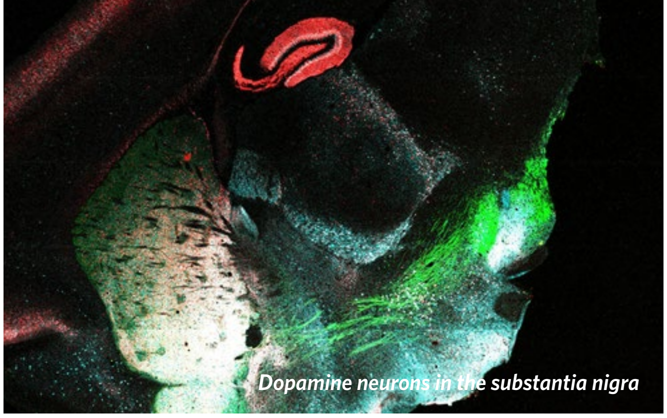
IMAGINE THE FUTURE ...

COMPUTER-BASED SCREENING TOOLS INDIVIDUALIZE CARE OF PEOPLE WITH HEAD TRAUMA.

NIH is the largest single public funder of biomedical research in the world.



3-D printed brain tissue



Dopamine neurons in the substantia nigra

PARKINSON'S DISEASE

A half-century ago, the seemingly miraculous recovery of people suffering from severe rigidity and tremors due to Parkinson's disease renewed hope for thousands. The drug levodopa – a mimic of the brain chemical dopamine that is depleted in Parkinson's disease – helped these individuals regain control of movement, but the effects were incomplete. Levodopa did not slow underlying neurodegeneration and became less effective as the condition progressed.

NIH research has led to discoveries about how the brain controls movement and to a procedure known as deep brain stimulation (DBS). DBS improves symptoms of Parkinson's disease by electrically stimulating brain cells in areas of the brain that control movement, using implanted electrodes. DBS is currently being tested in other conditions, such as treatment-resistant depression and dementia.

In recent years, NIH research has provided much more detail about what causes Parkinson's disease. We now know that several genes can cause a rare inherited form of it. Scientists now know how to reprogram ordinary skin cells from people with Parkinson's disease into stem cells that can be coaxed to grow into the nerve cells that die in this disease. This advance offers a powerful tool for developing and testing new therapies.

IMAGINE THE FUTURE ...

STEM CELLS WILL REPLACE BRAIN CELLS LOST TO PARKINSON'S DISEASE OR ACT AS DELIVERY VEHICLES FOR NERVE-CELL SURVIVAL-PROMOTING FACTORS.

THE BRAIN® INITIATIVE

The Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative is a bold, ambitious endeavor that will require the energy of thousands of our nation's most creative minds working together over a decade. It aims to revolutionize our fundamental understanding of the human brain, the most complicated biological structure in the known universe. Through development of innovative technologies, researchers will be able to produce a new dynamic picture of the brain that, for the first time, shows how individual cells and complex neural circuits interact. Long desired by scientists seeking new ways to treat, cure, and even prevent brain disorders, this picture will fill major gaps in our current knowledge and provide unprecedented opportunities for exploring how the brain enables the body to record, process, utilize, store, and retrieve vast quantities of information, all at the speed of thought.

MENTAL HEALTH

Like other chronic diseases, mental illnesses arise from the interplay of genes, environment, and many other factors. Using research to gain a better understanding of these complex interactions will guide the development of personalized strategies for diagnosing, treating, and preventing these debilitating disorders.

DEPRESSION

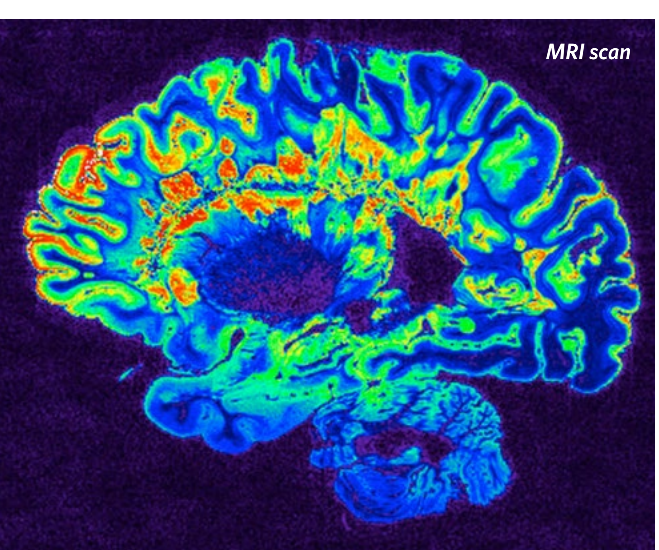
Major depression is one of the most common mental disorders in the United States, affecting nearly 7 percent of U.S. adults and about 5 percent of children. It is two to four times more common in girls and women. Many people with depression also have other mental illnesses, including addiction, and they are at a higher risk for suicide. While effective treatments — both medications and psychosocial therapies — are available for depression, NIH research is searching for a wider range of options. Commonly used medications for depression, for example, may take weeks to take effect and they do not work for everyone. To that end, NIH scientists are testing a substance called ketamine that can relieve symptoms of depression within hours. NIH research is also studying brain-stimulation therapies that hold promise for treating individuals with severe depression who do not respond to medication or psychotherapies.

SCHIZOPHRENIA

Each year, about 100,000 American teens and young adults unexpectedly experience their first episode of psychosis, a terrifying symptom of schizophrenia and other psychiatric disorders characterized by delusions, hallucinations, and altered behavior. These symptoms can make it very difficult to function at home, school, or work. NIH scientists have identified more than 100 gene variants associated with risk for schizophrenia, providing new avenues for understanding the causes of this disorder and developing new treatments. NIH research has also shown the effectiveness of individualized treatment plans combining different types of therapy and support, coordinated by a specialty-care team that includes a young individual with first-episode psychosis, his or her family, and mental health specialists. This work has shown that the earlier young people with schizophrenia are diagnosed and treated, the better they respond to therapy.

AUTISM SPECTRUM DISORDER

About one in every 68 U.S. children is affected by an autism spectrum disorder (ASD). The causes for this increased incidence are not completely understood, though a possible connection to childhood vaccines has been resoundingly rejected by rigorous scientific studies. The central features of ASD include difficulty with social communication and restricted, repetitive behaviors. While ASD symptoms are often recognized in the toddler years, NIH research has shown that the condition begins in very early development — most likely in the womb — and that early intervention can alleviate behavioral and learning difficulties. Toward identifying ASD sooner, NIH researchers have found that obtaining brain scans of high-risk infants as they slept naturally could predict which children would later be diagnosed with ASD. Those infants' brains showed unusually rapid growth from infancy to age 2. Other NIH research is providing knowledge about genetic variants that contribute to ASD risk. These gene patterns are giving scientists clues to the changes in the brain that underlie ASD and may provide targets for therapy.


MRI scan

▶ The United States is the top producer of published science & engineering articles.

THE FUTURE OF
BIOMEDICINE

TO ACHIEVE ITS GOAL OF TURNING DISCOVERY INTO HEALTH AND TO MAINTAIN ITS ROLE AS THE WORLD'S PREMIER BIOMEDICAL RESEARCH AGENCY, NIH MUST SUPPORT THE BEST SCIENTIFIC IDEAS AND BRIGHTEST SCIENTIFIC MINDS. THAT MEANS LOOKING TO THE FUTURE – BEING SURE THAT WE HAVE A STRONG AND DIVERSE WORKFORCE TO CATALYZE DISCOVERY IN ALL FIELDS OF BIOMEDICINE INCLUDING EMERGENT AREAS LIKE DATA SCIENCE.

TOMORROW'S SCIENTISTS

Although we learn science from teachers, scientific facts come from researchers working in labs and in the field. Acquiring the skills and knowledge to conduct research takes time, and given the unpredictable nature of scientific inquiry, requires freedom and tools to explore over many years.

Part of the NIH mission is supporting the next generation of scientists, funding thousands of graduate students and postdoctoral fellows across the United States. This support helps to launch the future careers of highly talented women and men who are thrilled by discovery and driven to help people. NIH puts a major focus on these early-career scientists just starting their labs. NIH's Next Generation Researchers Initiative, launched in 2017, ensures that sufficient resources will be available to provide support over time for these individuals as their careers progress.

NIH also follows closely specific areas of biomedical research in which workforce training must adapt to meet growing needs, including revitalizing physician-scientist training, fostering recruitment to expand the data-science workforce, and promoting cross-training of basic scientists, clinical scientists, and physician-scientists to maximize opportunities for discovery that lead to health advances.

▶ The NIH-led Human Genome Project has resulted in nearly $1 trillion of economic growth — a 178-fold return on investment — at a cost of only $2 per year for each U.S. resident.

Virtual reality treadmill

INNOVATION THROUGH DIVERSITY

Given the complexity of current health challenges and the enormous opportunity of 21st century biomedicine, diversity in all its forms – among research projects and the researchers themselves – invites innovation. Research is an intensely human endeavor that benefits from different points of view that are formed in part by racial/ethnic heritage, socioeconomic background, sexual/gender identity, physical ability, geographic location, and many other self-identifying features.

We know that diversity increases creativity, innovation, and productivity in the workforce. But we also know that the U.S. scientific workforce is not as diverse as it could be – especially at the level of faculty at the nation's colleges and universities, where the vast amount of federally-funded biomedical research takes place. Enhancing diversity in the NIH-funded workforce is urgent, given shifting U.S. demographics and the need to draw insights from all corners of America.

In 2014, NIH launched a landmark initiative to enhance U.S. scientific workforce diversity through a research-based lens. This effort, the Diversity Program Consortium, is using scientifically-driven approaches to understand which recruitment and retention approaches work, and in what context – to help colleges and universities attract and develop future scientists from diverse backgrounds. Another key component of the Diversity Program Consortium is the National Research Mentoring Network aimed at helping highly trained scientists from diverse backgrounds achieve career success. This highly integrated network helps connect junior and senior scientists across the nation through online tools.

DATA SCIENCE

Due to major technology advancements in recent decades, including the Human Genome Project and its resulting data deluge, biomedical research is increasingly reliant on computers both for finding new knowledge and for understanding what it means. NIH is catalyzing this historic research opportunity to use "Big Data" by bringing different types of researchers together and encouraging rapid, open sharing of data and common standards among scientists working with it. One expectation is that data-science advances occurring at the intersection of computer science and biology will enable basic scientists to conduct more experiments using computer models alone. An important NIH focus in data science is developing and testing tools located "in the cloud," instead of on individual computers, that are accessible to researchers regardless of location and resource availability. Already, NIH researchers have used data-science analyses to make discoveries about extremely complex conditions like diabetes and heart disease, as well as how to improve the development of new drugs for a range of disorders.

TRANSFORMATIVE **TECHNOLOGIES**

IN A CYCLIC FASHION, TECHNOLOGY DRIVES SCIENCE, AND SCIENCE CREATES TECHNOLOGIES TO TACKLE SCIENTIFIC PROBLEMS AS THEY ARISE. TECHNOLOGY DEVELOPMENT OFTEN REQUIRES INPUT FROM MANY TYPES OF MINDS, INCLUDING NOT ONLY BIOLOGISTS AND CHEMISTS BUT ALSO MATHEMATICIANS, ENGINEERS, AND COMPUTER SCIENTISTS. 21ST CENTURY BIOMEDICINE IS A HOTBED OF DISCOVERY OF NEW DEVICES AND TOOLS THAT PROMISE TO REVOLUTIONIZE HEALTH.

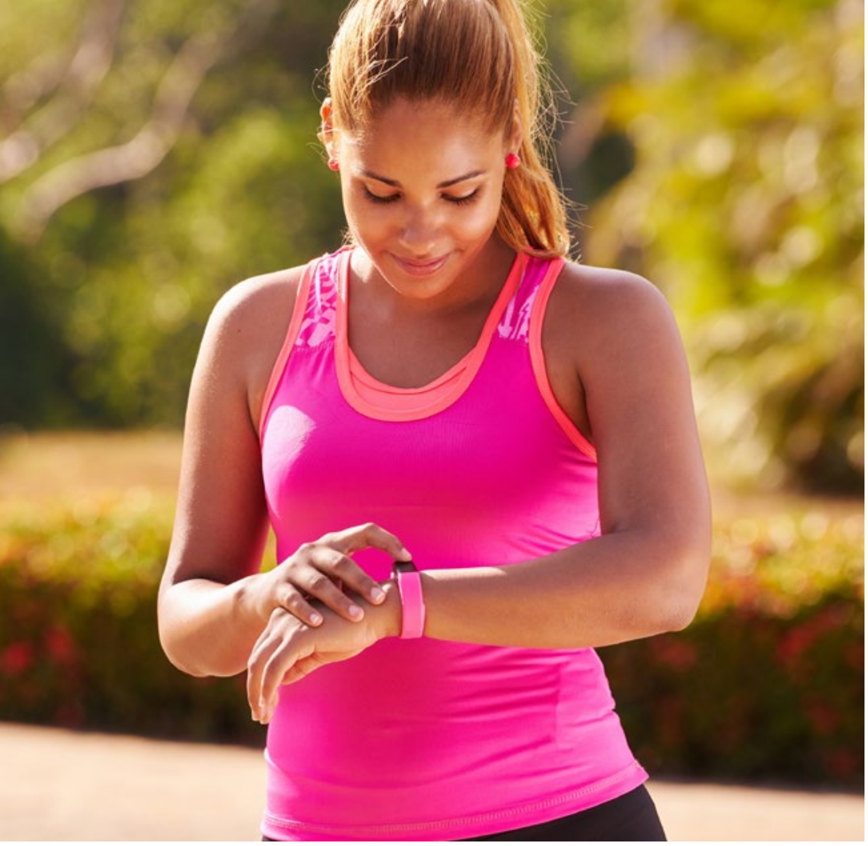
REGENERATIVE MEDICINE

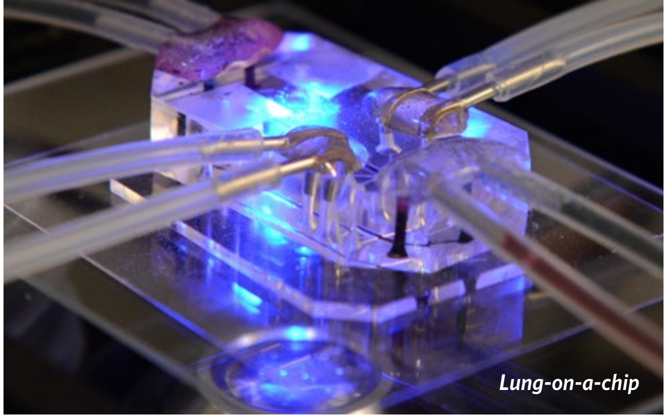
Instead of trying to compensate for failing organs, what if we could readily replace diseased or injured body parts with brand-new versions made in the lab? Researchers working in the field of regenerative medicine have already made amazing progress, creating artificial organs and miniature labs-on-a-chip. The return on investment for this area of research is expected to be dramatic: better understanding of how diseases develop and spread, accurate screens for testing new drugs, and cell-based therapies for diabetes, arthritis, Parkinson's disease, and many other conditions that affect millions of Americans. NIH researchers have already created miniature "hearts" that beat rhythmically in a culture dish and contain all the different cell types that make up a human heart. Scientists have also developed a lung-on-a-chip. When intermittent suction is applied, the cells in this thumb-sized device flex and stretch rhythmically just as they do in our lungs when we breathe. For individuals with kidney failure, the potential of using their own skin cells to build a new kidney might now be within reach – given years of hard work and the necessary research investment.

THE CRISPR REVOLUTION

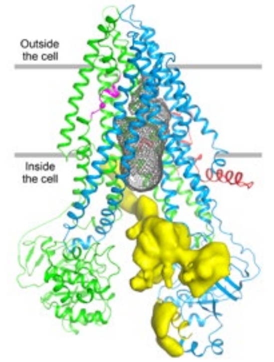
The human genome is a 3-billion letter instruction book, using a 4-letter DNA alphabet. Just a single typo can lead to a devastating disease. Imagine the ability to, like a copy editor, quickly fix DNA spelling errors so that the genetic words and sentences read flawlessly. NIH scientists are getting close: they have developed a revolutionary new way to edit genomes precisely inside living cells, without even removing the DNA as was once necessary. Researchers are testing the value of this method, named CRISPR, for hundreds of applications. Some include creating malaria-resistant mosquitoes, and correcting gene errors in diseases known to be caused by one or just a few mutations. Recently, NIH researchers successfully edited the disease-causing mutation in blood-forming cells taken directly from people with sickle-cell disease. These gene-edited cells survived when transplanted into mice, suggesting that such a treatment might be long-lasting or possibly even curative if tested in humans. If CRISPR could be targeted effectively to cells in a living person, then the thousands of genetic diseases that currently lack treatment might be cured.

▶ Each year, NIH research funding can be expected to generate more than 100 new inventions.





Lung-on-a-chip



Cystic fibrosis transmembrane conductance regulator (cryo-EM)

WEARABLE SENSORS

Millions of Americans leave for school or work each day wearing devices that count their steps, check their heart rates, and help them stay fit. The next generation of "wearables," used by individuals in partnership with their health-care providers, might be able to monitor vital signs, blood oxygen levels, and a wide variety of other measures of personal health. Toward making this a reality, NIH scientists recently conducted a study involving 40 adults who wore a commercially available smartwatch over many months. The devices were programmed to provide a continuous daily stream of accurate personal health data that researchers could access and monitor. When combined with standard laboratory blood tests, the information, which totaled more than 250,000 bodily measurements a day per person, could detect early signs of infections simply through changes in heart rate.

MOLECULAR FREEZE-FRAME

One of the oldest tools in a biomedical scientist's toolbox is the microscope, which scientists have been using since the 17th century to study cells, tissues, and organs. Yet a new development in microscopy is eclipsing even the instruments available just a few years ago. This new technique, cryo-electron microscopy (cryo-EM) – so named for the requirement to flash-freeze a biological sample before viewing it – is transforming our understanding of cells and their many working parts. This approach can provide detailed images of proteins and other macromolecular structures that were previously only available using X-ray crystallography – a tedious and expensive approach that often fails when applied to biomolecules. NIH-supported scientists are using cryo-EM to capture stunningly accurate details of disease-causing viruses like Ebola, Zika, or HIV, as well as proteins involved in conditions like cystic fibrosis, cancer, and Alzheimer's disease. Such knowledge helps researchers who are crafting vaccines and drugs for many conditions.

SPEEDING DRUGS TO MARKET

The vast majority of drugs entering the development pipeline never emerge as patient-ready therapies. Most distressing is when a drug fails late in the process, after years of work has been done and millions of dollars have been spent. This happens because scientists often don't know how to choose the right molecules to target at the outset. Through the Accelerating Medicines Partnership (AMP), a public-private partnership between NIH, FDA, numerous biotechnology companies, and nonprofit organizations, we are transforming the current model for developing new diagnostics and treatments. Together, AMP is jointly identifying and validating promising biological targets for new drugs, focusing on four major health challenges: Alzheimer's disease, type 2 diabetes, autoimmune diseases, and Parkinson's disease. Other partnerships on cancer immunotherapy and the opioid crisis are under development.

RESEARCH FOR **HEALTHY LIVING**

SCIENTIFIC AND TECHNOLOGICAL BREAKTHROUGHS GENERATED BY NIH RESEARCH HAVE HELPED PEOPLE IN THE UNITED STATES AND ALL OVER THE WORLD LIVE LONGER, HEALTHIER LIVES. THESE ADVANCEMENTS WERE ACHIEVED BY MAKING DISEASES LESS DEADLY THROUGH EFFECTIVE INTERVENTIONS TO PREVENT AND TREAT ILLNESS AND DISABILITY.

OBESITY AND NUTRITION

More than one-third of U.S. adults — and about 17 percent of U.S. children — are obese. Obesity puts people at risk for many health issues including heart disease, stroke, type 2 diabetes, arthritis, and certain types of cancer. Because these conditions are some of the top preventable causes of chronic illness and death, NIH has a considerable interest in addressing obesity.

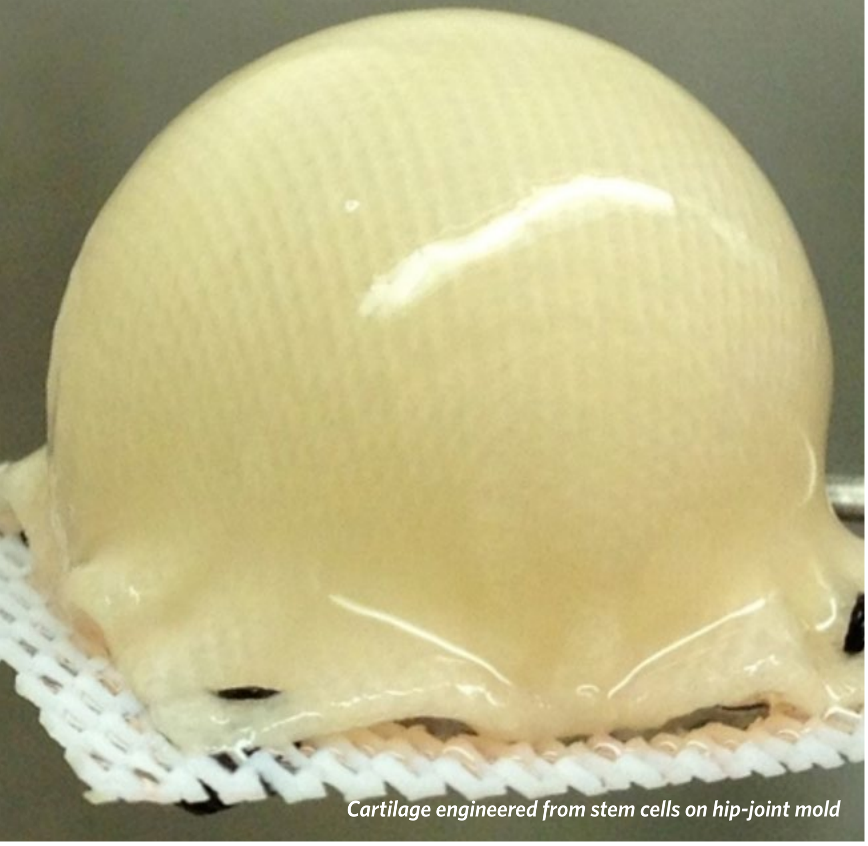
The problem of obesity seems straightforward: When we eat more calories than we burn, our bodies store this extra energy as fat. Yet, we all know how hard it can be just to lose a few pounds. And solving this problem on a population-sized scale has proven to be tremendously difficult. That is because so many factors play a role: where we live and work, how much time we spend sitting – and the availability of safe spaces for exercise – and the fact that many people cannot choose alternatives. Access to nutritious food can be a major barrier for many with low incomes or mobility limitations.

Heredity also has an impact. For example, NIH research shows that certain gene variations that occur in one of six people of European descent translate into an extra 7 pounds, on average. Those discoveries are pointing to pathways involved in obesity that suggest potential ways to prevent undesirable weight gain. Research on the social factors contributing to obesity also offers ideas for intervention. When people are provided funds to buy food once a week, instead of monthly, they are more likely to buy fresh fruits and vegetables instead of pre-packaged (and often less-nutritious) goods. We also know that affordable housing programs lead to better nutrition, because people no longer must compromise on food in order to pay rent.

IMAGINE THE FUTURE ...

THOUSANDS OF DEATHS ARE AVERTED AND BILLIONS OF HEALTH CARE DOLLARS ARE SAVED BY PREVENTING OBESITY-RELATED COMPLICATIONS.

NIH research funding across the nation generated $65 billion in new economic activity in 2016.



Cartilage engineered from stem cells on hip-joint mold

ARTHRITIS

Many people, as they age, notice discomfort in their knees, hips, hands, or other joints. They also feel stiff when they get up. Over time, people with osteoarthritis, which causes these symptoms, can develop physical deformities that affect mobility, productivity, and quality of life.

Over the past decades, scientists have made important strides toward helping people manage osteoarthritis. This research has shown that successful treatment programs involve a combination of patient-guided therapies – including exercise, weight control, and rest and relief from stress on joints. In addition, novel approaches to combining pain medicines, surgery, and complementary and alternative therapies have provided millions with relief. New approaches utilizing regenerative medicine may ultimately provide benefit, but are still very much in the experimental phase (see “Regenerative Medicine,” p.12).

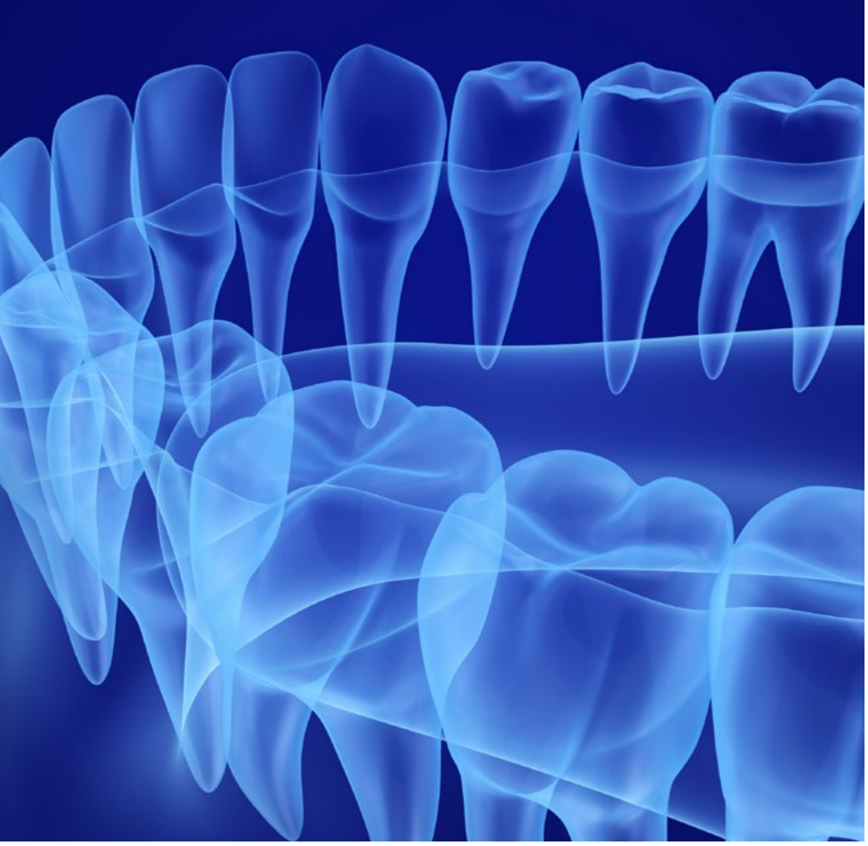
Osteoarthritis is the most common form of arthritis, but there are about 100 rheumatic diseases in all. Thanks to NIH research, the outlook has improved dramatically for rheumatoid arthritis, which generally appears much earlier in life than osteoarthritis. As recently as 30 years ago, treatment was limited to aspirin, gold salts, and heat rubs such as methyl salicylate (the active ingredient in BENGAY®), none of which worked well and could produce serious side effects. NIH research led to three FDA-approved medicines that have had a remarkable effect on the lives of people who live with rheumatoid arthritis, reducing pain and swelling, increasing energy, and even helping to repair joint damage.

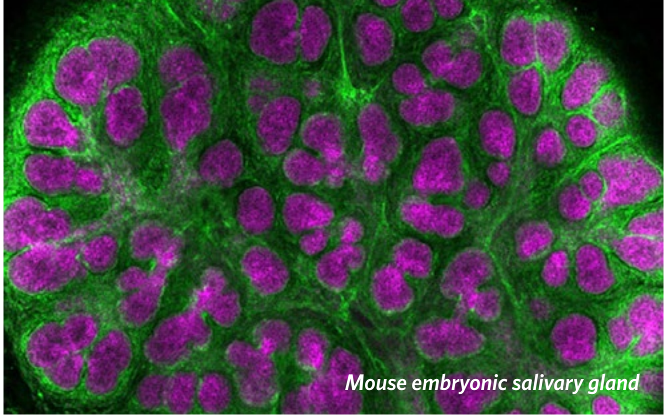
IMAGINE THE FUTURE ...

OSTEOARTHRITIS TREATMENTS STOP DISEASE PROGRESSION RATHER THAN SIMPLY TREATING SYMPTOMS.

RESEARCH WITHOUT BORDERS

Online communication and wide availability of international travel have led to globalization of knowledge, business, education, as well as many other things, including disease. Science and medicine know no borders, and knowledge gained through NIH research has had a dramatic impact internationally on both infectious and non-infectious diseases. Major technology advances have allowed scientists to read the genetic language of disease-causing bacteria, viruses, and parasites. That information has led to effective ways to manage well-known threats like malaria, tuberculosis, and HIV/AIDS, but also to new approaches for managing conditions that are uncommon in the United States, but rampant in the developing world. These include diarrheal diseases caused by viruses and many infections triggered by parasites. The globalization of chronic, non-communicable diseases like cancer, heart disease, obesity, and depression contribute to more than half of all deaths in the developing world and substantial disability, and NIH collaborations are tackling this ongoing crisis that has ripple effects on regional economic health and stability.





Mouse embryonic salivary gland

ORAL HEALTH

In the early part of the 20th century, it was common for women and men to lose many teeth as they aged, leaving them to rely on dentures. That story began to change dramatically in the 1940s and 1950s, when NIH scientists showed that the rate of tooth decay fell more than 60 percent in children who drank fluoridated water. This discovery laid the foundation for a major component of modern dental health.

Today, research on oral health extends far beyond teeth. NIH researchers consider the mouth an expansive living laboratory to understand infections, cancer, and even healthy development processes. For example, we know that oral tissues and fluids, which are home to about 600 unique microbial species, can have remarkable protective roles against infection and possibly other conditions.

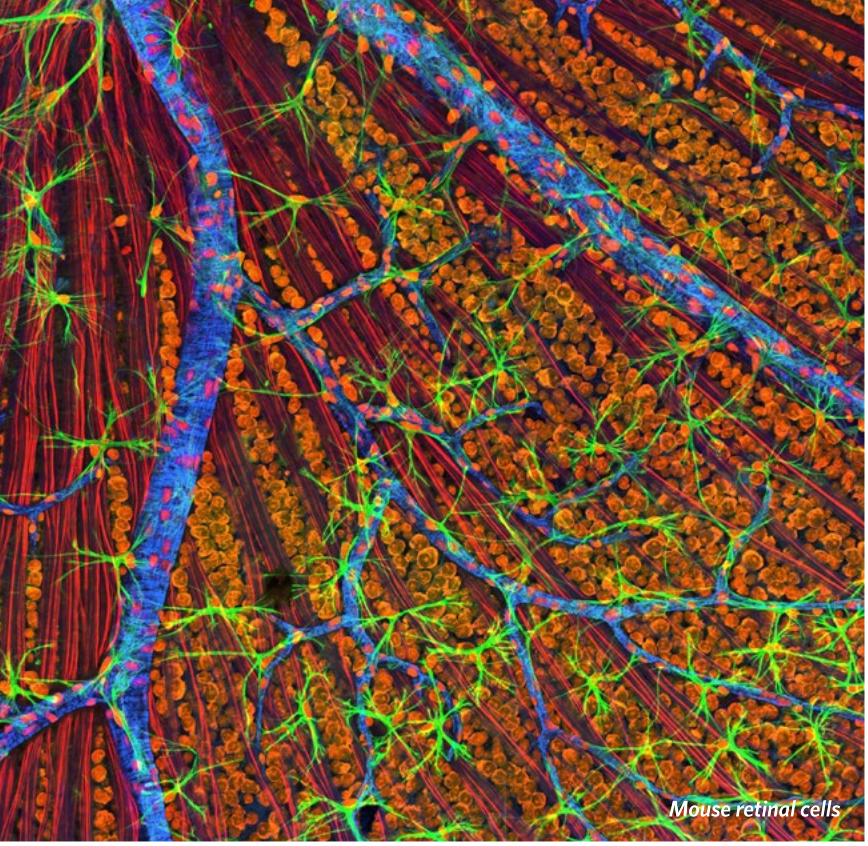
NIH research on oral health is working to understand and manipulate the body's innate ability to repair and regenerate damaged or diseased tissues. These approaches will guide prevention and treatment of health problems not only in teeth and in the mouth, but also in other organs and tissues.

IMAGINE THE FUTURE ...

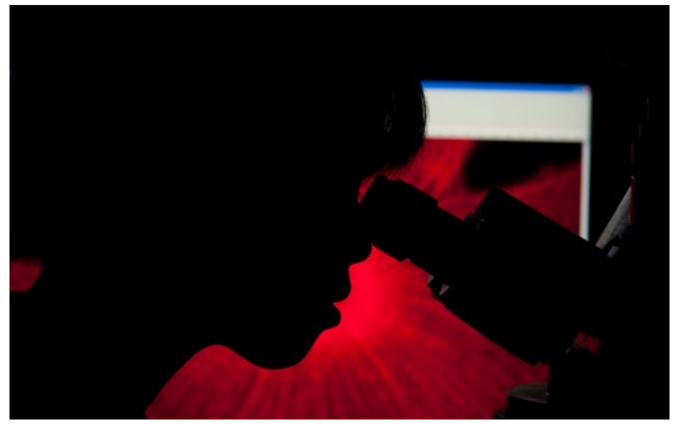
A DROP OF SALIVA WILL ENABLE EARLY DETECTION OF VARIOUS MEDICAL CONDITIONS, RANGING FROM ORAL DISEASES TO CANCER TO DIABETES.

OPTIMAL HEALTH FOR WOMEN AND MEN

Certain health conditions are more common in women than in men, such as osteoporosis, depression, and autoimmune diseases. Others are more common in males, such as autism and color blindness. And there are those conditions that affect women and men differently, such as heart disease. While chest pain is common to both women and men suffering a heart attack, women may experience other symptoms such as nausea, back or neck pain, and fatigue, which they may not link to problems of the heart. NIH researchers are studying these differences, toward providing personalized care for individuals. The sexes can also have very different responses to even very common drugs like aspirin. So, NIH research ensures that females, including pregnant women when it is safe to do so, are included in sufficient numbers in clinical trials that test new medicines. Currently, slightly more than half of clinical trial participants are women.



Mouse retinal cells



VISION

Not long ago, age-related macular degeneration (AMD) was an untreatable disease — the leading cause of new cases of blindness in people over age 65. The disorder made it difficult, if not impossible, to read, recognize faces, drive a car, or perform many other simple tasks.

Thanks to NIH research, we know a lot about the underlying causes of vision loss. For example, we know that AMD is caused by the formation of abnormal, leaky blood vessels in the eye. Eye injections of anti-vascular endothelial growth-factor drugs, such as ranibizumab and bevacizumab, inhibit the growth and leakage of fluid from these abnormal blood vessels and, in some cases, even reverse vision loss.

In addition to AMD, cataracts, glaucoma, and inherited eye disorders cause either blindness or low-vision in millions of Americans. NIH research is providing hope. For example, a recent study in mice showed that cells within an injured eye can be coaxed into regenerating neurons that appeared to integrate themselves into the eye's nerve circuitry. NIH scientists are also developing several technologies to help people with low vision or blindness navigate their surroundings more safely and confidently. These include a GPS-guided cane, a robotic glove, and a smartphone app for safely navigating crosswalks.

IMAGINE THE FUTURE ...

IMPLANTABLE SUSTAINED-RELEASE NANOPARTICLES DELIVER DRUGS OR GENETICALLY ENGINEERED CELL THERAPY TO DAMAGED EYES.

On average, every $10 million increase in NIH funding generates 3 additional private-sector patents.

THE PROMISE OF PRECISION MEDICINE

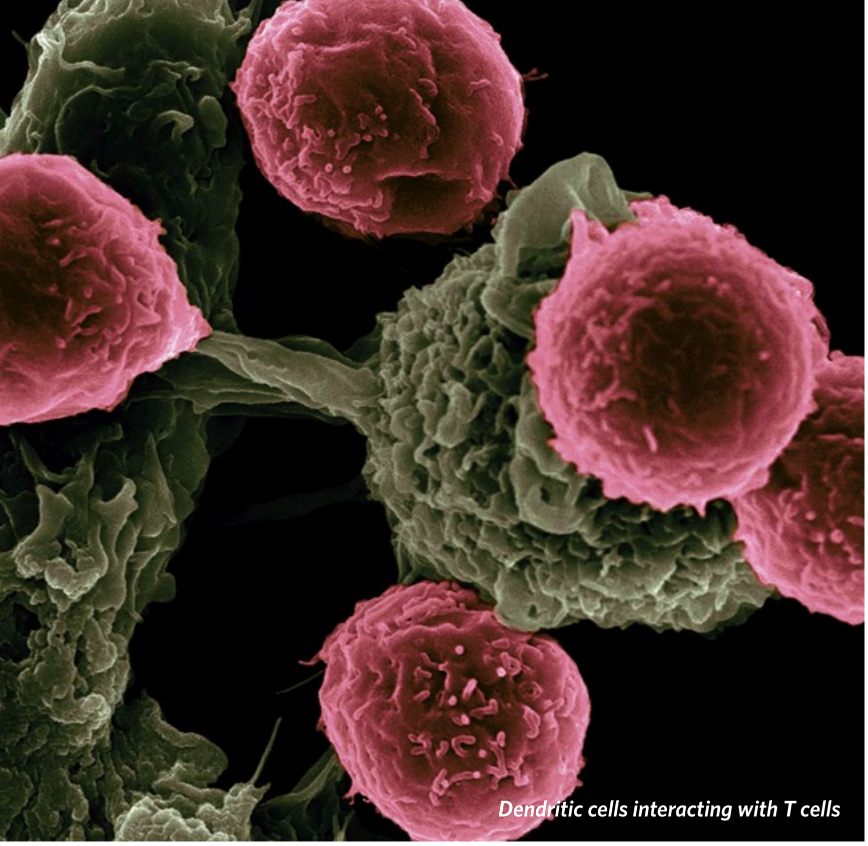
HISTORICALLY, DOCTORS HAVE HAD TO MAKE MOST RECOMMENDATIONS ABOUT DISEASE PREVENTION AND TREATMENT BASED ON THE EXPECTED RESPONSE OF AN AVERAGE PATIENT. THIS ONE-SIZE-FITS-ALL APPROACH WORKS WELL FOR SOME PATIENTS AND SOME CONDITIONS, BUT NOT SO WELL FOR OTHERS. PRECISION MEDICINE IS AN INNOVATIVE APPROACH THAT TAKES INTO ACCOUNT INDIVIDUAL DIFFERENCES IN PATIENTS' GENES, ENVIRONMENTS, AND LIFESTYLES. MILLIONS OF PEOPLE HAVE ALREADY BEEN TOUCHED BY THE ERA OF PRECISION MEDICINE THAT HAS GROWN DIRECTLY FROM BIOMEDICAL RESEARCH.

PRECISION ONCOLOGY

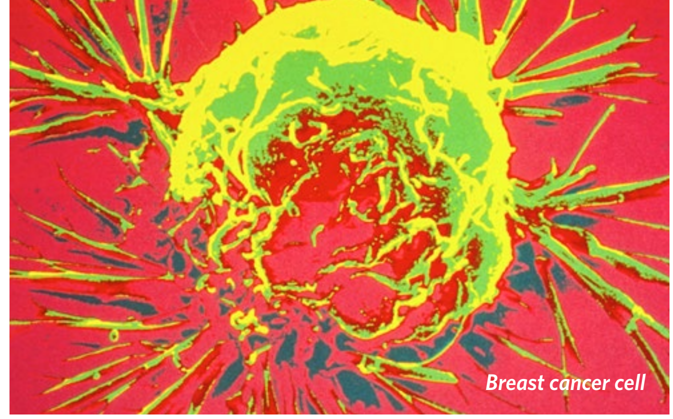
It's still the case in most medical care systems that cancers are classified mainly by the type of tissue or part of the body in which they arose: lung, brain, breast, colon, pancreas, and so on. But a radical change is underway. Researchers are now identifying the molecular fingerprints of various cancers and using them to divide cancer's once-broad categories into far more precise types and subtypes. They are also discovering that cancers that develop in totally different parts of the body can sometimes, on a molecular level, have a lot in common. From this new perspective emerges an exciting era in cancer research called precision oncology, in which doctors are choosing treatments based on the DNA signature of an individual patient's tumor. In one example, using advanced technology to analyze both tumor and blood samples from a large number of children who'd been newly diagnosed with cancer, NIH researchers uncovered genetic signatures that could refine diagnosis, identify inherited cancer susceptibility, or guide treatment for nearly 40 percent of the children.

ALL OF US

The *All of Us* Research Program is an ambitious effort to gather data over time from 1 million or more people living in the United States, with the ultimate goal of accelerating research and improving health. Unlike research studies that are focused on a specific disease or population, *All of Us* will serve as a national research resource to inform thousands of studies, covering a wide variety of health conditions. Researchers will use data from the program to learn more about how individual differences in lifestyle, environment, and biological makeup can influence health and disease. By taking part, people will be able to learn more about their own health and contribute to an effort that will advance the health of generations to come. Participants in *All of Us* will be invited to use wearable sensors that will provide real-time measurements of their health and environmental exposures, significantly expanding this type of research (see "Wearables," p. 13).



Dendritic cells interacting with T cells



Breast cancer cell

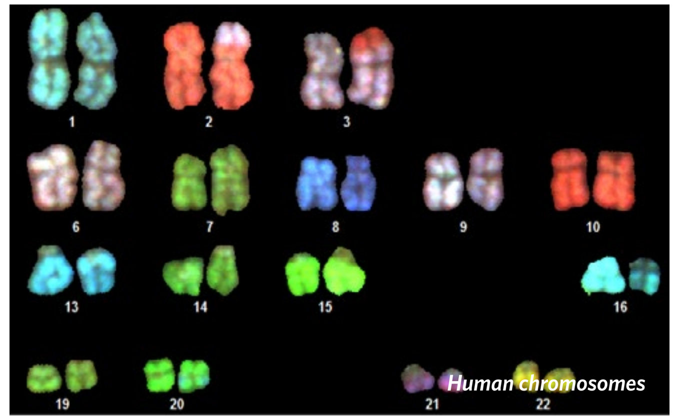
Cancer survivor Emily Whitehead. Emily Whitehead Foundation

CANCER IMMUNOTHERAPY

Another powerful ally in precision oncology has been there all along – the body's immune system. Our immune system's natural ability to detect and destroy abnormal cells prevents many cancers from ever developing, just like it protects us from infections. However, cancer cells can sometimes evade this system of immune surveillance. In the relatively new field of cancer immunotherapy, scientists are beating cancer cells at their own game – enlisting a person's own immune system to control and, in some cases, even cure their cancer. Decades of NIH research has led to several types of cancer immunotherapy drugs. These include mimics of natural immune-system molecules, such as anti-cancer antibodies, supercharged immune cells, or treatment vaccines that "teach" an individual's immune system to attack tumors. Because the treatments enlist the immune system, they do not kill every dividing cell like traditional chemotherapy drugs. Unfortunately, they don't yet work in everyone. NIH researchers, however, are busy investigating the factors that affect whether a tumor will respond to immunotherapy, providing clues for matching tumors to drugs.

Each $1 increase in public basic research stimulates an additional $8.38 of industry R&D investment after 8 years.


DNA-sequencing robot

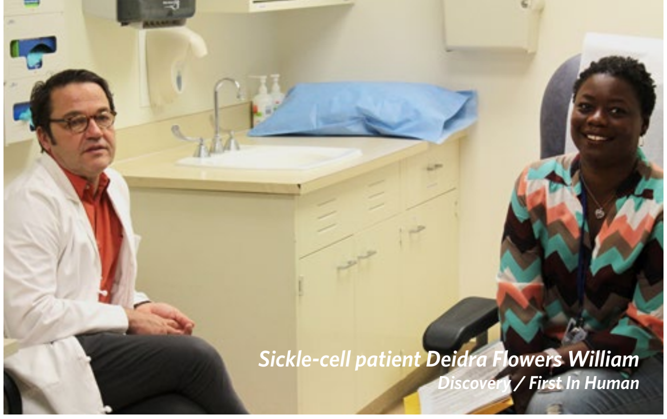


Human chromosomes

PHARMACOGENOMICS

In the 1970s, NIH research gave us genetic engineering and launched what is today the $100 billion biotechnology industry, a major source of high-paying U.S. jobs. Virtually every biomedical research lab and pharmaceutical company uses the power of the genomic revolution every day to demystify diseases and search for new cures. Companies today can read the entire DNA sequence of an individual for less than $1,000, and the cost is dropping quickly. This ability to study massive amounts of DNA has helped the field of pharmacogenomics mature rapidly. In this area of science, researchers match DNA patterns in individuals with how they respond to medications. The goal is to move away from one-size-fits-all dosing – because we now know that many factors aside from sex, age, and body size influence how our bodies react, or don't, to many drugs. Research results in this important area of biomedicine have prompted FDA to include pharmacogenomic information in drug labeling, toward more precise and safer drug responses for patients. A significant goal of precision medicine is to implement this strategy broadly in medical care – focusing on the right drug at the right dose at the right time for the right patient.

Leg muscle fiber from mouse model of Pompe disease



Sickle-cell patient Deidra Flowers William
Discovery / First In Human

Friedreich's ataxia pediatric patients Claire & Jake Yuip at NIH

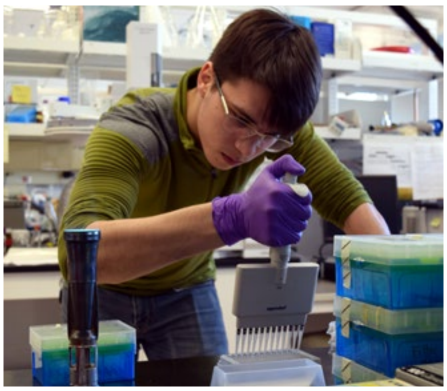
RARE DISEASES

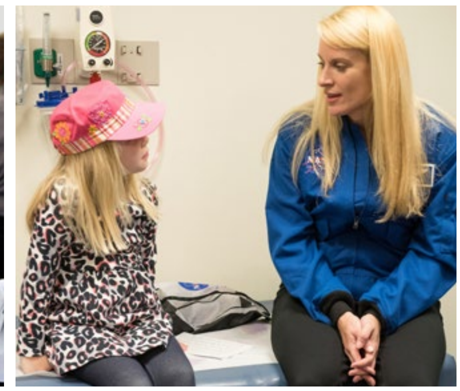
Rare diseases were once considered medical curiosities with little public-health impact. But though such diseases are individually rare, collectively an estimated 25 to 30 million Americans are affected. NIH's Undiagnosed Disease Program focuses on the most puzzling medical cases referred to the NIH Clinical Center in Bethesda, Maryland. UDP has received nearly 10,000 inquiries, reviewed more than 3,000 applications, and admitted about 900 patients to the NIH Clinical Center for comprehensive weeklong evaluations. Some of these patients with rare diseases have taught us more about common conditions such as osteoporosis, kidney stones, and viral infections. Building on the early successes of the NIH UDP, NIH has extended the program into a network of sites across the country. Advances in diagnosis of rare diseases are gratifying, but are not enough: Of the 7,000 identified rare and neglected diseases for which we know the molecular cause, only about 500 have approved treatments. Through the Therapeutics for Rare and Neglected Diseases program of the National Center for Advancing Translational Sciences (NCATS) and other research efforts, NIH is collaborating with multiple partners to speed up the development of effective treatments.

TRACKING CHILDREN'S HEALTH

NIH research has taught us that many diseases take root in the body long before symptoms show up, perhaps early in life or even before birth. Many experiences and exposures during sensitive developmental windows throughout childhood can have long-lasting effects on health. NIH recently launched the Environmental influences on Child Health Outcomes (ECHO) Program, a 7-year research initiative, that aims to determine what factors give children the highest probability of achieving the best health outcomes over their lifetimes. In particular, ECHO is focused on lung health and development, obesity, and brain and nervous system development. To discover factors that contribute to these health issues, and to identify ways for as many children as possible to have optimal health outcomes, ECHO is following about 50,000 children from diverse backgrounds.

LOOKING **FORWARD**





Throughout this brochure, example after example shows – through countless stories and statistics– how NIH is turning discovery into health. NIH research saves lives and strengthens our economy through job creation and improved quality of life for millions of Americans. There is little doubt that this research investment is one of the wisest moves we can make as a nation.

NIH is also a leading source of scientific knowledge for the world, which bolsters the nation's strength in lasting ways. NIH fundamental research has led to 153 Nobel Prizes and 198 Lasker Prizes. Often dubbed "America's Nobel," the Lasker Prize honors groundbreaking contributions to our understanding of human disease.

And for thousands of patients around the world, NIH is known as the "National Institutes of Hope." Since the NIH Clinical Center opened in 1953, more than half a million patients from all over the world who qualify for studies have come here to be treated, often when no other options remain.

Their participation in clinical research has brought forth numerous advances, some shown on the facing page, and is vital in our ongoing quest to improve health for all Americans.

BECAUSE OF NIH RESEARCH ...

- BLOOD-THINNING DRUGS SUCH AS TPA PREVENT STROKES AND SAVE LIVES
- ONCE THE LEADING CAUSE OF BACTERIAL MENINGITIS IN CHILDREN, HAEMOPHILUS INFLUENZAE TYPE B HAS BEEN NEARLY ELIMINATED
- THE CURE RATE FOR THE MOST COMMON CHILDHOOD LEUKEMIA IS 90%
- FLUORIDE IN WATER PROTECTS OUR TEETH FOR LIFE
- THE U.S. BLOOD SUPPLY IS CLEAN AND SAFE FROM VIRUSES LIKE HIV AND HEPATITIS
- CHOLESTEROL-LOWERING STATINS PREVENT HEART DISEASE, AND HEART ATTACK DEATHS ARE DOWN BY 70%
- MODEST WEIGHT LOSS AND REGULAR EXERCISE PREVENT TYPE 2 DIABETES IN PEOPLE AT RISK
- EFFECTIVE MEDICINES TREAT MILLIONS WITH DEPRESSION
- QUITTING SMOKING PREVENTS MANY DISEASES LIKE CANCER AND HEART DISEASE
- HIV/AIDS IS NO LONGER A DEATH SENTENCE, AND CAN BE EFFECTIVELY TREATED FOR DECADES
- MEDICINES BLOCK MOTHER-TO-CHILD HIV TRANSMISSION
- ARTIFICIAL SKIN ALLOWS SEVERE BURNS TO HEAL
- THE SEQUENCING OF THE HUMAN GENOME HAS OPENED A WORLD OF UNPRECEDENTED OPPORTUNITIES FOR SCIENCE, MEDICINE, AND HEALTH

IMAGINE THE FUTURE ...

NIH INSTITUTES

NCI	National Cancer Institute — *Est. 1937*
NEI	National Eye Institute — *Est. 1968*
NHLBI	National Heart, Lung, and Blood Institute — *Est. 1948*
NHGRI	National Human Genome Research Institute — *Est. 1989*
NIA	National Institute on Aging — *Est. 1974*
NIAAA	National Institute on Alcohol Abuse and Alcoholism — *Est. 1970*
NIAID	National Institute of Allergy and Infectious Diseases — *Est. 1948*
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases — *Est. 1986*
NIBIB	National Institute of Biomedical Imaging and Bioengineering — *Est. 2000*
NICHD	*Eunice Kennedy Shriver* National Institute of Child Health and Human Development — *Est. 1962*
NIDCD	National Institute on Deafness and Other Communication Disorders — *Est. 1988*
NIDCR	National Institute of Dental and Craniofacial Research — *Est. 1948*
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases — *Est. 1950*
NIDA	National Institute on Drug Abuse — *Est. 1974*
NIEHS	National Institute of Environmental Health Sciences — *Est. 1969*
NIGMS	National Institute of General Medical Sciences — *Est. 1962*
NIMH	National Institute of Mental Health — *Est. 1949*
NIMHD	National Institute on Minority Health and Health Disparities — *Est. 1993*
NINDS	National Institute of Neurological Disorders and Stroke — *Est. 1950*
NINR	National Institute of Nursing Research — *Est. 1986*
NLM	National Library of Medicine — *Est. 1956*

NIH CENTERS

CC	NIH Clinical Center — *Est. 1953*
CIT	Center for Information Technology — *Est. 1964*
CSR	Center for Scientific Review — *Est. 1946*
FIC	Fogarty International Center — *Est. 1968*
NCATS	National Center for Advancing Translational Sciences — *Est. 2011*
NCCIH	National Center for Complementary and Integrative Health — *Est. 1999*

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National Institutes of Health
Turning Discovery Into Health

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