NIAID Global Research:
Improving Health in a Changing World

NIAID

National Institute of Allergy and Infectious Diseases

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

CONTENTS

2 Foreword

4 About NIAID

6 NIAID's International Involvement: Taking the Lead to Improve Global Health Research

8 Confronting the AIDS Pandemic

10 Responding to Emerging and Re-Emerging Threats

- **11** Tuberculosis
- **12** Malaria
- **14** Influenza

16 Calling Attention to Neglected Tropical Diseases

17 Improving Understanding of the Immune System

18 Funding Opportunities for Foreign Scientists and Institutions

20 Training Opportunities for Foreign Scientists

21 NIAID Contact

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Foreword

Medicine and science have become international enterprises, far less constrained by national borders than at any other time in history. Diseases rampant in one region can affect the health, stability, and security of nations far removed, and global collaboration has become essential to the biomedical research needed to improve health everywhere.

In recent years, improving global health has become a key priority of developed nations not only for humanitarian reasons, but also because of a growing realization that, in our interconnected society, disease outbreaks have worldwide implications, both directly through the transmission of disease and indirectly through the economic and political instability that these health concerns can provoke.

The HIV/AIDS pandemic in many ways marked the beginning of the new interest in global health. First recognized in developed nations, efforts to control the threat of HIV/AIDS were concentrated within borders. It slowly became clear, however, that HIV/AIDS was a health crisis devastating the developing world, and that the humanitarian, economic, and political dimensions of HIV/AIDS would negatively affect all nations.

Attempts to address this burgeoning pandemic in developing countries have brought the world's attention to other devastating diseases that pose potential threats to global health. For example, tuberculosis claims the lives of an estimated 1.7 million people each year, and emerging drug-resistant strains of *Mycobacterium tuberculosis* threaten to reverse gains made in the control of the disease. Malaria, which in 2006 caused an estimated 880,000 deaths worldwide, is growing resistant to treatment and returning to areas where it was previously eradicated. And we have seen increasing numbers of humans infected by highly virulent strains of avian influenza in Asia and elsewhere.

The National Institute of Allergy and Infectious Diseases (NIAID) is at the forefront of efforts to address these and other international health challenges. We support projects in approximately 90 countries and have dramatically increased

Anthony S. Fauci, M.D.
Addressing the United Nations
General Assembly
Special Session on HIV/AIDS
June 10, 2008

spending on international activities in the past decade. Our strategy is not only to devote more resources within the United States to the study of diseases with global health importance, but also to develop the capacity for advanced research within resource-poor nations. Doing so involves increasing support for domestic grantees to expand their collaborations with scientists abroad and increasing NIAID participation in the extensive network of international partnerships among scientists, governments, companies, and non-governmental organizations.

NIAID's global research efforts have produced many notable successes. For example, NIAID-supported trials in Africa showed that two inexpensive doses of nevirapine, one administered to HIV-infected mothers at childbirth and a second to their infants soon after birth, dramatically reduce mother-to-child transmission of HIV. More recently, clinical trials demonstrated that medically supervised circumcision of adult African men reduces their risk of acquiring HIV via heterosexual intercourse. Additionally, the newly sequenced genomes of the malaria parasite *Plasmodium falciparum* and its mosquito vector *Anopheles gambiae* promise to produce new methods for fighting malaria.

These and other research efforts illustrate how actively engaging with international researchers can achieve global health goals. Although we have made important strides, there is much work left to accomplish. The opportunities for improving global health have never been greater, and we must use our momentum to move forward, recognizing that solving the enormous health challenges facing humanity will require global collaboration and a long-term commitment.

Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases

The National Institute of Allergy and Infectious Diseases (NIAID) is one of the 27 institutes and centers that comprise the National Institutes of Health (NIH), an agency of the U.S. Department of Health and Human Services (HHS). NIAID is one of the largest institutes at NIH, with a budget of approximately $4.6 billion in 2008. More than 8 percent of the NIAID budget supports international research and training, and NIAID is one of the few NIH institutes to have an Associate Director for International Research Affairs to facilitate international activities.

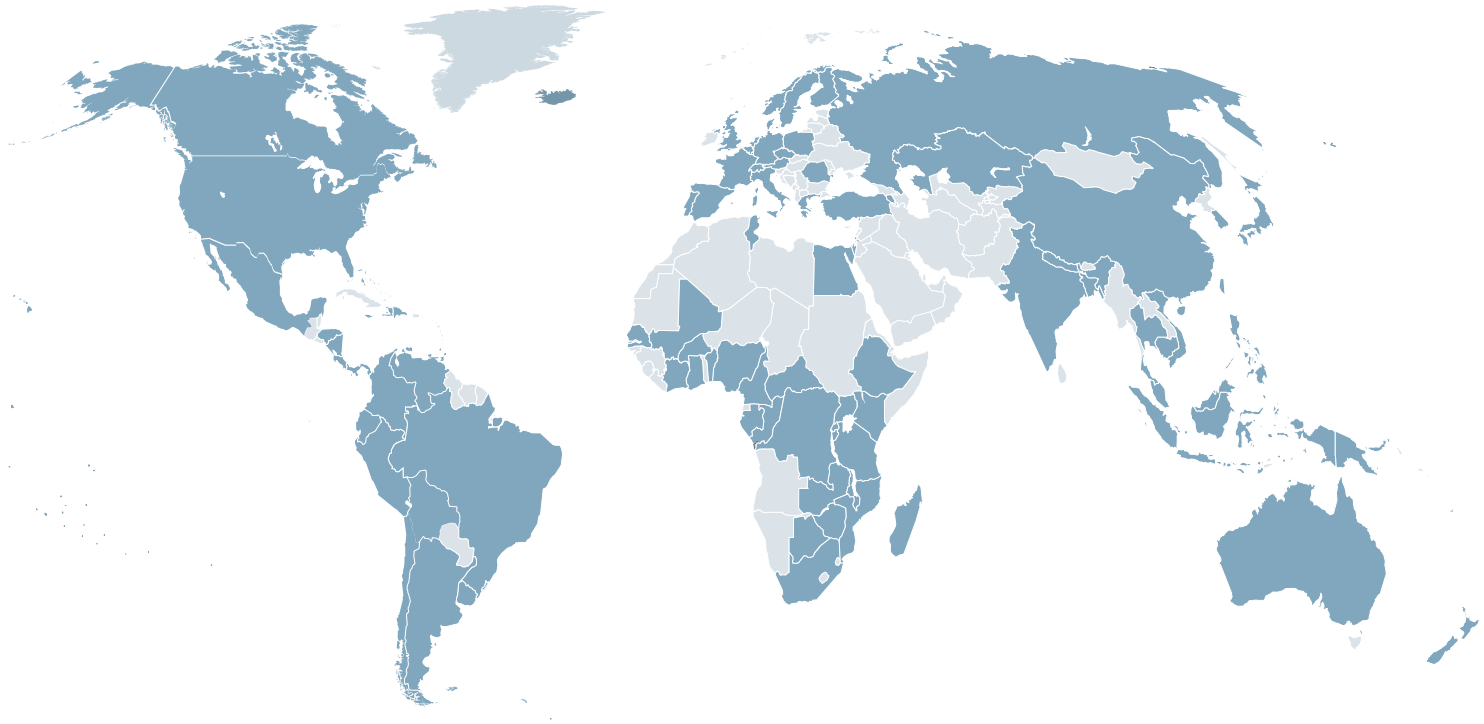
As with other large NIH institutes, most of the NIAID budget is used to support biomedical research at academic and research institutions outside NIAID through grants, contracts, and cooperative agreements (called extramural research). The remaining budget is used to fund research within NIAID's own laboratories (called intramural research) and to support administrative functions.

NIAID Extramural Research

Extramural research is managed by the following NIAID divisions:

- **Division of Acquired Immunodeficiency Syndrome**—supports research aimed at improving basic understanding, prevention, and treatment of HIV/AIDS and its complications and co-infections
- **Division of Allergy, Immunology, and Transplantation**—supports research on basic immunology and the etiology, treatment, and prevention of immune-mediated diseases, including rejection of transplanted organs, tissues, and cells; autoimmune diseases; and asthma and allergic diseases
- **Division of Microbiology and Infectious Diseases**—supports research to control and prevent diseases caused by virtually all human infectious agents except HIV; major priorities include emerging and re-emerging infectious diseases and biodefense
- **Division of Extramural Activities**—serves NIAID and its extramural research community by overseeing policy and management for grants and contracts, managing NIAID's research training and international programs, and conducting initial peer review of grant applications

NIAID supported biomedical research in approximately 90 countries during fiscal year 2008.



NIAID Intramural Research

Most NIAID intramural laboratories are located on the NIH campus in Bethesda, Maryland, and in nearby Rockville, Maryland. NIAID also has a large research campus in Hamilton, Montana, known as the Rocky Mountain Laboratories, and research collaborations at sites in Mali, Uganda, and India through its International Centers of Excellence in Research program.

The NIAID intramural program includes the following divisions:

- **Division of Intramural Research**—conducts basic and clinical research in a wide range of disciplines related to immunology, allergy, and infectious diseases. Its global activities include HIV, malaria, and dengue vaccine development; research to develop better therapies for tuberculosis; and lab and field research on neglected tropical diseases, such as filariasis and leishmaniasis

- **Dale and Betty Bumpers Vaccine Research Center**—conducts research that facilitates the development of effective vaccines for human disease. Its global activities include studies on HIV, Ebola and Marburg viruses, and avian influenza

- **Division of Clinical Research**—facilitates the efficient performance of NIAID clinical research programs in the United States and abroad. Its global activities include research projects in Mali, South Africa, and Southeast Asia

NIAID Office of Global Research

The Office of Global Research (OGR), within the NIAID Office of the Director, facilitates and coordinates international activities and collaborative research programs. OGR works closely with other NIH institutes and centers such as the Fogarty International Center and with other offices and agencies of HHS, including the Office of Global Health Affairs within the Office of the Secretary, the Centers for Disease Control and Prevention, and the Food and Drug Administration. OGR also collaborates with other U.S. government agencies, such as the Department of State and the U.S. Agency for International Development, and with numerous foreign government agencies.

Online Resources

NIAID Organization
www.niaid.nih.gov/about/organization

NIAID Director's Page
www.niaid.nih.gov/about/directors

NIAID Global Research
www.niaid.nih.gov/topics/globalresearch

Office of Global Research
www.niaid.nih.gov/about/findingpeople/ogr.htm

Division of Acquired Immunodeficiency Syndrome
www.niaid.nih.gov/about/organization/daids

Division of Allergy, Immunology, and Transplantation
www.niaid.nih.gov/about/organization/dait

Division of Clinical Research
www.niaid.nih.gov/about/organization/dcr

Division of Extramural Activities
www.niaid.nih.gov/about/organization/dea

Division of Intramural Research
www.niaid.nih.gov/about/organization/dir

Division of Microbiology and Infectious Diseases
www.niaid.nih.gov/about/organization/dmid

Vaccine Research Center
www.niaid.nih.gov/about/organization/vrc

NIAID's International Involvement:

Taking the Lead to Improve Global Health Research

Issues related to global health have captured the attention of world leaders, philanthropists, policy makers, academia, and the general public. Developed nations have realized that disease outbreaks in distant countries can have worldwide social, economic, and political ramifications. This heightened awareness has presented a welcome opportunity for those in biomedical research and public health to emphasize international collaboration and promote new and existing global health programs.

NIAID has embraced its leadership role in global health with innovative scientific research programs that seek to not only advance knowledge of ever-changing pathogens, but also help translate new scientific discoveries into medical tools that improve diagnosis, prevention, and treatment of infectious diseases.

NIAID accomplishes its mission by fostering collaborations between domestic and international scientists and by supporting development of research capacity in regions with high burdens of disease. Through partnerships with academia, private industry, philanthropic organizations, and other research-supporting agencies, NIAID helps guide and enhance medical research that improves the quality of human life around the world.

ICER Program Fosters Research Collaborations in Developing Countries

The NIAID International Centers for Excellence in Research (ICER) program was launched in 2002 to develop and sustain research programs in resource-poor countries through partnerships with local scientists. NIAID has developed core programs at the ICER sites—currently located in Mali, Uganda, and India—and, over time, has facilitated the expansion of research capacity by improving laboratory and clinical infrastructure and enhancing information technology capabilities.

The ICER program builds on experience gained from NIAID's long-standing malaria research collaboration with scientists in Mali. Today, the Mali ICER includes the Malaria Training and Research Center; the Entomology Unit of the Faculty of Medicine, Pharmacy, and Dentistry of the University of Bamako; and the Centre de Recherche et Formation.

Malian researchers collaborate with NIAID scientists on several ongoing programs, including studies on mosquito vectors, malaria drug resistance, and candidate malaria vaccines; research on leishmaniasis and its vectors; and immunologic and microbiologic studies of patients with HIV and tuberculosis.

The ICER site in Uganda, which includes a field laboratory in the Rakai district and facilities at Makerere University in Kampala and the Uganda Virus Research Institute in Entebbe, conducts clinical research on HIV and sexually transmitted infections, including studies on prevention. The ICER site in India, located at the Tuberculosis Research Centre in Chennai, conducts collaborative studies on filariasis and, more recently, on tuberculosis-filarial and HIV-filarial co-infection.

THROUGH PARTNERSHIPS WITH ACADEMIA, PRIVATE INDUSTRY, PHILANTHROPIC ORGANIZATIONS, AND OTHER RESEARCH-SUPPORTING AGENCIES, NIAID HELPS GUIDE AND ENHANCE MEDICAL RESEARCH THAT IMPROVES THE QUALITY OF HUMAN LIFE AROUND THE WORLD.

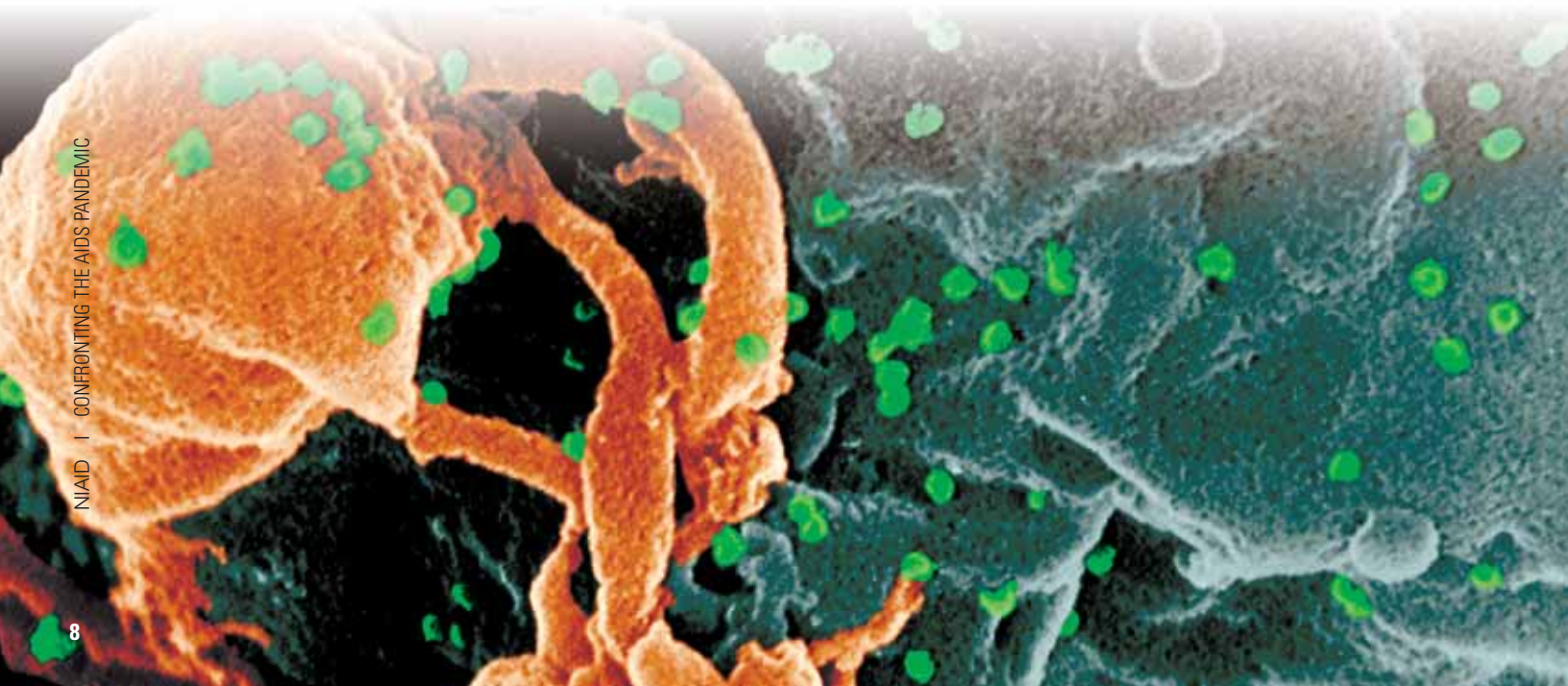
Confronting the AIDS Pandemic

Since its recognition in 1981, AIDS has claimed more than 25 million lives, the majority of them in the developing world. While extraordinary scientific, medical, and public health accomplishments have been made in the battle against HIV/AIDS, major challenges remain, especially in the delivery of therapies and prevention tools to the resource-poor countries that need them the most.

NIAID's investment in HIV/AIDS research has generated promising findings in preventing and treating HIV/AIDS and in advancing scientific understanding of the disease. For example, NIAID-funded researchers have recently demonstrated that medically supervised adult male circumcision reduced by more than 50 percent the risk of heterosexual African men becoming infected with HIV. Researchers hope that this finding and other advances in HIV prevention research will form the basis of a comprehensive toolkit that will markedly decrease new HIV infections over the next two decades. Furthermore, a recent NIAID-supported study suggests that earlier intervention with antiretroviral therapy, as opposed to delaying treatment until clinical signs of disease appear, could help HIV-infected patients live longer. This advance and others like it could lead to a change in the global standard of care for managing HIV disease.

Conducting AIDS research in international settings allows NIAID-supported scientists to study the disease under a variety of environmental and social conditions. For example, the NIAID-funded HIV Prevention Trials Network (HPTN) comprises more than 20 clinical sites in the United States, Africa, Asia, and South America. HPTN evaluates the effectiveness of multiple HIV prevention strategies—from the use of antiretroviral therapy to prevent HIV and other sexually transmitted infections to community education and counseling—in different populations to better understand and ultimately control the spread of HIV on a global scale.

NIAID also supports international researchers studying the underlying mechanisms of HIV infection. For example, the Center for HIV/AIDS Vaccine Immunology (CHAVI) brings together investigators in the United States, Africa, Australia, and Europe to conduct fundamental research on the major scientific obstacles hindering HIV vaccine design and development. Recent CHAVI studies have identified human genes associated with control of HIV infection, knowledge that could inform the design of therapeutic HIV vaccines—those given to an infected person to boost the immune system's ability to identify and clear HIV from the body.



Clinical Trials Network Evaluates Microbicides to Reduce Spread of HIV

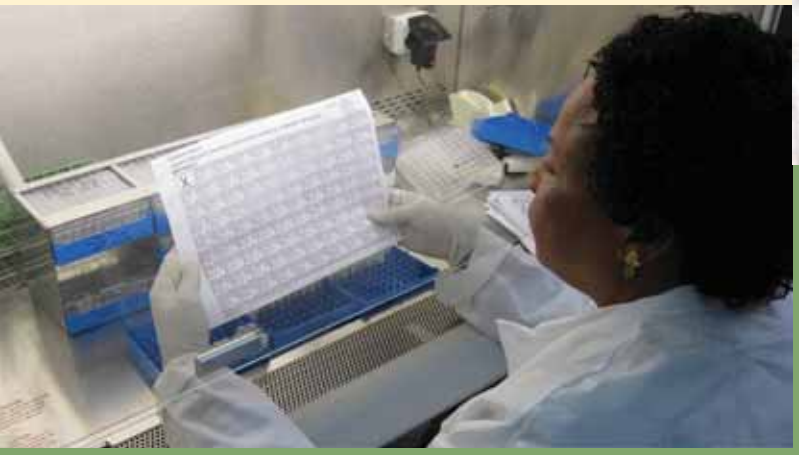
Women and girls account for nearly half of all people living with HIV, according to UNAIDS estimates. Globally, the vast majority of women with HIV/AIDS became infected through heterosexual intercourse, frequently in settings where refusing sex or insisting on condom use is not an option because of cultural factors, lack of financial independence, and even the threat of violence.

In response to these and other issues, NIAID established the Microbicide Trials Network (MTN) in 2006 to develop and evaluate products that could be used by women daily or prior to sexual intercourse to prevent infection with HIV and other sexually transmitted agents. Safe and effective microbicides would give women the ability to protect themselves when negotiating with sexual partners is difficult or impossible.

The MTN conducts its multicenter studies at sites in Malawi, South Africa, Uganda, Zambia, Zimbabwe, India, and the United States. The network has several ongoing microbicide studies, including some inherited from the NIAID-supported HIV Prevention Trials Network (HPTN). For example, the HPTN 035 trial seeks to determine whether candidate microbicides BufferGel and PRO 2000 can prevent the sexual transmission of HIV in 3,100 sexually active HIV-negative women in Africa and the United States. Another study, HPTN 059, aims to assess the safety and acceptability of an antiretroviral-based candidate microbicide called tenofovir gel. It is the first study that evaluates daily use of a gel, which is an approach to HIV prevention that researchers believe may be more acceptable to women than having to apply gel shortly before intercourse.

The MTN is structured to allow for active representation and participation by community stakeholders in every stage of clinical study development and implementation. In addition to including a community representative on its Executive Committee, the MTN has established a Community Working Group (CWG), comprising one Community Advisory Board member and one community educator from each site. The CWG aims to ensure the successful conduct of studies through community and researcher partnerships and to build capacity within local communities for providing input into the planning and conduct of MTN trials.

As part of its effort to be more responsive to the needs and perspectives of local communities, the MTN also has adopted the Regional Physician Model, a successful component of the Bill & Melinda Gates Foundation-funded Partners in Prevention. Regional Physicians are MTN's local ambassadors in Africa, providing support to clinical sites and educating local providers and community groups about microbicide research, MTN-specific trials, and safety measures designed to protect all trial participants.

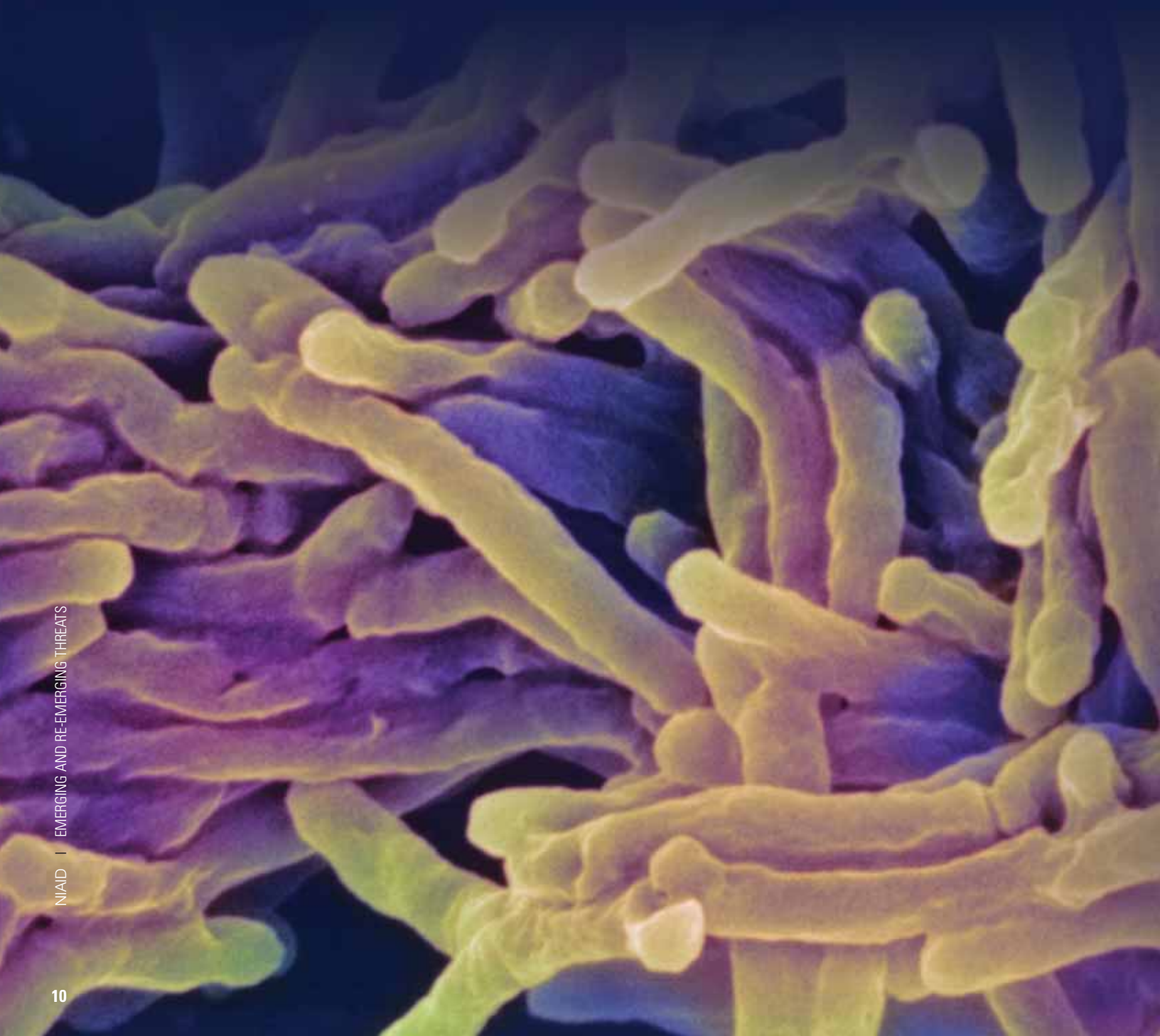


WOMEN AND GIRLS ACCOUNT FOR NEARLY HALF OF ALL PEOPLE LIVING WITH HIV, ACCORDING TO UNAIDS ESTIMATES.

Responding to Emerging and Re-Emerging Threats

Scientists have made extraordinary progress toward containing or nearly eliminating many infectious diseases, such as diphtheria, tetanus, polio, and measles. Despite these advances, the world still faces numerous threats from new microbes that emerge naturally, and from familiar pathogens that re-emerge with enhanced properties or in unusual settings. Drug-resistant tuberculosis and influenza viruses with pandemic potential are of particular concern.

NIAID research programs combating these threats emphasize collaborations with domestic and international partners to improve knowledge; stimulate the pipeline of new drugs, diagnostics, and preventive measures; and enhance existing research infrastructure to effectively confront outbreaks where they occur.



Tuberculosis

Tuberculosis (TB) is an example of a re-emerging threat. In 2006, an estimated 9.2 million new cases of TB were reported worldwide, and an estimated 1.7 million people died of the disease. Antiquated techniques for accurately diagnosing TB, complex and lengthy drug regimens, and an increase in the prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB continue to present major challenges to effective control of the disease.

NIAID TB research programs harmonize domestic and international efforts to prevent and control the spread of TB and to slow the development and spread of MDR and XDR strains of *Mycobacterium tuberculosis* (Mtb), the bacterium that causes the disease. NIAID is leading and sponsoring research activities to create a foundation of knowledge for the discovery of new diagnostics, drugs, and vaccines. Many of these programs are providing critical information. For example, researchers from the United States and South Africa recently determined that small but significant differences exist between the genomes of MDR and XDR strains of Mtb. These and similar studies advance the understanding of factors contributing to drug resistance and provide new leads for diagnosing and treating drug-resistant forms of TB.

SQ109, an anti-TB drug candidate developed through a partnership between NIAID and Sequella, was recently granted orphan drug status by the U.S. Food and Drug Administration and the European Medicines Agency for potential use against drug-susceptible and drug-resistant TB. NIAID also assisted in the preclinical development of another candidate drug, PA-824, currently in clinical trials in South Africa sponsored by the nonprofit Global Alliance for TB Drug Development. In addition, NIAID recently formed a partnership with the Eli Lilly Foundation, the Infectious Disease Research Institute of Seattle, and others to further stimulate TB drug discovery.

U.S.-South Korean Collaboration Seeks to Advance TB Care

In 2003, NIAID scientists and clinical researchers at South Korea's National Masan Tuberculosis Hospital joined forces to develop potential new drug regimens for effective treatment of the disease. The hospital is the national referral center for tuberculosis treatment failures in South Korea and has one of the largest populations of in-patient MDR TB cases in the world.

One of the first tasks of the NIAID-South Korean team was to oversee construction of a new biosafety-level 3 (BSL-3) facility where research on MDR TB could be performed safely. The BSL-3 lab—opened at a newly founded institute, called the International Tuberculosis Research Center, adjacent to the hospital—supports clinical studies to test new drugs for both latent and MDR TB. All funding for the BSL-3 lab's construction and operation is provided by the South Korean Ministry of Health, Welfare, and Family Affairs.

The U.S. and South Korean researchers have conducted numerous clinical research studies and have more than 600 patients participating in trials. Two trials of existing drugs (metronidazole and linezolid) in patients with highly drug-resistant TB are ongoing using imaging technologies (PET/CT) that have never before been applied to TB patients. In addition, researchers are collecting information about rates and causes of MDR and XDR TB in two groups of patients: those who are having an initial episode of active TB and those who have recurrent TB. Investigators also are studying bacterial and human genomes to further understand the relationship between the expression of specific bacterial and human genes and the acquisition and development of XDR TB infection.

Recently, NIAID scientists led by Clifton E. Barry, III, Ph.D., have been working with colleagues at the hospital and with the manufacturers of the drugs meropenem and clavulanate to evaluate a combination of these drugs in individuals who have MDR or XDR TB. Laboratory tests have shown the drug combination to be effective in killing drug-susceptible strains of TB bacteria as well as XDR TB.

IN 2006, AN ESTIMATED 9.2 MILLION NEW CASES OF TB WERE REPORTED WORLDWIDE, AND AN ESTIMATED 1.7 MILLION PEOPLE DIED OF THE DISEASE.

Malaria

Malaria continues to pose an enormous global health burden, particularly in countries in tropical and subtropical regions. The World Health Organization (WHO) estimates that in 2006 there were 247 million cases of malaria worldwide. That same year, approximately 880,000 people, mostly African children under the age of 5, died from the disease, and nearly half of the world's population was at risk of infection.

NIAID has a long-standing interest in malaria research and supports global efforts to reduce death and suffering from the disease. To accomplish these goals, NIAID works closely with organizations such as the U.S. Agency for International Development, the WHO, the European Malaria Vaccine Initiative, the Program for Appropriate Technology in Health Malaria Vaccine Initiative, the Wellcome Trust, and the Bill & Melinda Gates Foundation. Additionally, NIAID has joined with the NIH Fogarty International Center, the National Library of Medicine, and other institutions to form the Multilateral Initiative on Malaria, whose mission is to enhance worldwide research on malaria by facilitating multinational cooperation and by supporting the career development and research efforts of African scientists working in malaria-endemic areas.

Such collaborations have yielded notable successes. For example, NIAID-supported scientists have sequenced the genome of the most deadly malaria parasite, *Plasmodium falciparum*. Researchers have also decoded the genome of the parasite *Plasmodium vivax,* which is the leading cause of relapsing malaria. These and similar studies promise to reveal potential new targets for drug and vaccine development.

In Malawi, NIAID-funded research has suggested that chloroquine, the once-standard medication for preventing and treating malaria, may again be effective in that country, thanks to the reduced prevalence of the genetic mutation responsible for parasitic resistance to the drug. This finding, along with subsequent studies, may eventually lead to low-cost chloroquine being reintroduced in parts of Africa for use in combination with other drugs. Finally, NIAID remains committed to the development of safe and effective vaccines for malaria. Several vaccine candidates that target different lifecycle stages of the malaria parasite are in development, including those designed to either destroy parasites in the bloodstream or inhibit parasites from infecting red blood cells. NIAID supports clinical trials of these and other vaccine candidates in malaria-endemic countries.

IN 2006, APPROXIMATELY 880,000 PEOPLE, MOSTLY AFRICAN CHILDREN UNDER THE AGE OF 5, DIED FROM MALARIA.

Scientists Target Mosquito Larvae in Battle Against Malaria

Malaria is rampant in sub-Saharan Africa, and effective control of the disease is being threatened by growing drug resistance in the malaria parasite and insecticide resistance in malaria-transmitting mosquitoes.

In The Gambia, NIAID-supported researchers from the United Kingdom are testing an alternate strategy for malaria control: the use of larvicides that kill larvae of *Anopheles gambiae*, the main mosquito species responsible for spreading the disease. The goal of this study is to determine if widespread use of microbial larvicides (i.e., those based on bacteria that produce larvae-killing toxins) will suppress the development of adult mosquitoes to such an extent that the prevalence and transmission of malaria in local communities will also decline.

To test their hypothesis, the researchers are assessing the effectiveness and impact on transmission of two microbial larvicides: *Bacillus thuringiensis var.israelensis* (Bti) and *B. sphaericus* (Bs). Both larvicides are desirable because they specifically target mosquito larvae and do not appear to elicit resistance.

Researchers established four study sites along the River Gambia covering roughly 100 square kilometers each. During the rainy season (July to November), the river rises and floods wide areas, resulting in higher transmission of malaria and an increase in clinical cases of the disease.

So far, the researchers have been able to identify the sources of larval mosquitoes in each of the four study areas and have established the most effective strategy for killing them using Bti and Bs, including the best combination of the two larvicides and the most efficient length of time before re-treatments. They have also developed a method for large-scale application in the study areas.

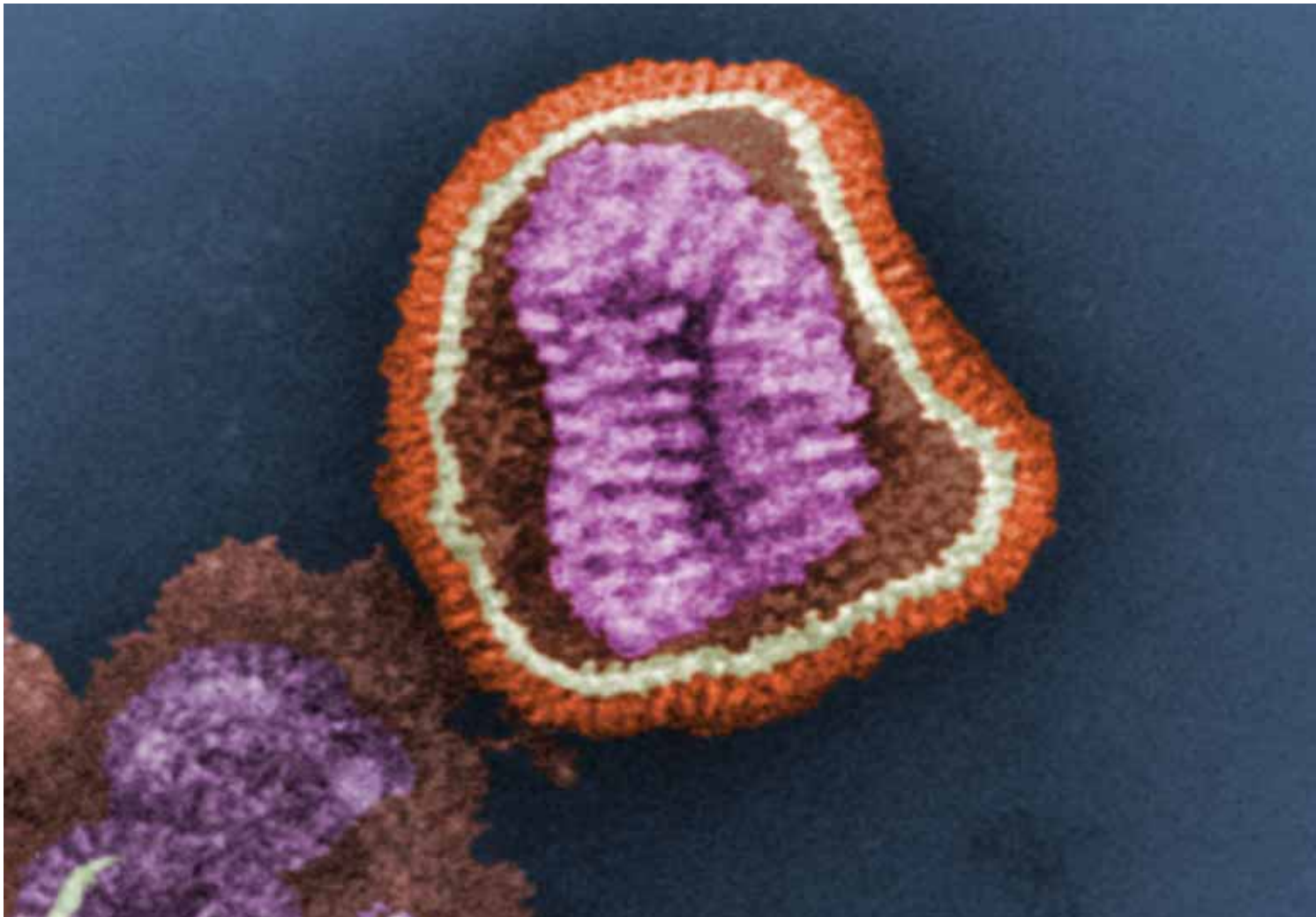
Influenza

Seasonal influenza, caused by viruses that vary slightly from year to year, is a classic example of a re-emerging infectious disease. Influenza viruses can also undergo more dramatic genetic changes that periodically enable them to evade pre-existing immunity and cause a pandemic, such as the 1918 influenza pandemic that is estimated to have killed more than 50 million people worldwide.

NIAID supports a broad portfolio of influenza research, including basic and applied research on the development of vaccines, diagnostics, and therapeutics against both seasonal and pandemic influenza. This work has underpinned the significant progress made in the development of new medical tools against influenza. For example, in 2007, based on clinical data from NIAID-funded research, the U.S. Food and Drug Administration approved the first vaccine for humans against the H5N1 avian influenza virus.

More recently, a study co-supported by NIAID found that influenza viruses, rather than persisting in low levels year-round in the northern and southern hemispheres, emerge anew each year from tropical zones such as Southeast Asia before spreading into temperate regions around the world. This finding promises to help public health officials determine more quickly and accurately which virus strains to use in the annual influenza vaccine.

Today, the Southeast Asia Influenza Clinical Research Network (SEA ICRN), co-supported by NIAID and the Wellcome Trust, brings together hospitals and institutions in Indonesia, Singapore, Thailand, the United Kingdom, the United States, and Vietnam to advance scientific knowledge and clinical management of human influenza caused by avian or human viruses. SEA ICRN studies aim to improve patient care and help inform public health policy on influenza treatment. The network also works with national ministries of health and



other authorities to facilitate the sharing of samples of influenza viruses for research purposes.

In the United States, NIAID-funded repositories are providing researchers around the world with vital data to help improve the understanding of how influenza viruses evolve, spread, and cause disease. For example, the NIAID Influenza Genome Sequencing Project helps scientists identify sequences in the influenza genome that could be potential targets for vaccines or therapies. To date, more than 3,000 complete influenza virus genomes have been sequenced and made available in the public domain.

CASES OF HUMAN DISEASE FROM AVIAN INFLUENZA VIRUSES HAVE BECOME MORE FREQUENT, SOMETIMES RESULTING IN SEVERE ILLNESS AND DEATH.

Centers Expand Global Reach of Influenza Research and Surveillance

In 2007, NIAID established the Centers of Excellence for Influenza Research and Surveillance (CEIRS) to expand its worldwide influenza surveillance program and bolster influenza research in key areas, including understanding how the virus causes disease and how the immune system responds to infection with the virus. The goal of the CEIRS program is to provide essential information for the development of public health strategies crucial to lessening the impact of seasonal influenza and to responding to a pandemic.

The CEIRS program is built upon a foundation of NIAID-supported international influenza research. For example, following the 1997 Hong Kong outbreak of avian influenza in humans, NIAID-supported researchers conducted surveillance of influenza viruses in aquatic birds and live bird markets in Hong Kong, which helped shed light on the natural history of flu viruses. Furthermore, scientists conducted training courses in animal influenza surveillance, developed diagnostic tools to detect animal flu viruses, and generated viruses suitable for use in developing human influenza vaccines.

Current activities by the centers lay the groundwork for the development of control measures against emerging and re-emerging influenza viruses, including determining the prevalence of avian influenza in animals that routinely come into close contact with people; understanding how flu viruses evolve, adapt, and transmit infection; and identifying immunological factors that can determine whether a flu virus causes death or only mild illness. Additionally, some centers monitor for international and domestic cases of animal and human influenza to rapidly detect and characterize viruses that may have pandemic potential and to create vaccine candidates targeted to those viruses.

Calling Attention to Neglected Tropical Diseases

Though little known to most in the United States, tropical diseases such as dengue, lymphatic filariasis, trachoma, leishmaniasis, and schistosomiasis take a tremendous toll on global health. For example, in 2008, Brazil experienced an explosive outbreak of the mosquito-borne illness dengue. By October of that year, the disease had sickened more than 700,000 people and resulted in over 200 deaths. Elsewhere in South America, as well as in parts of Africa and Asia, parasitic worm diseases such as schistosomiasis continue to inflict widespread suffering, particularly in areas where sanitation is poor and living conditions are crowded.

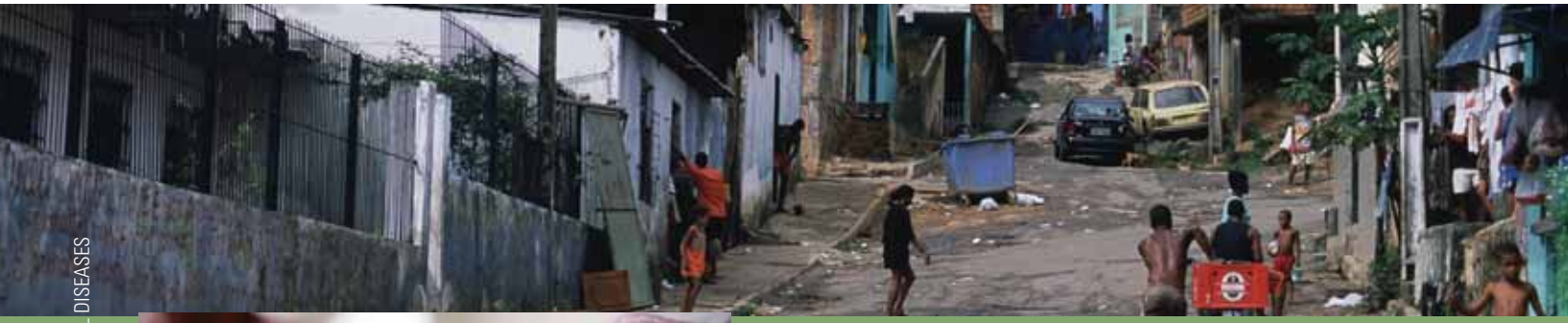
NIAID has a robust program of research devoted to better understanding and combating neglected tropical diseases. In 2005, NIAID-supported investigators sequenced the genomes of *Trypanosoma brucei, Trypanosoma cruzi,* and *Leishmania major*, the three parasites that cause the tropical diseases African sleeping sickness, Chagas disease, and leishmaniasis, respectively. Researchers also have sequenced the genome of *Aedes aegypti*, the mosquito species commonly associated with the transmission of dengue, yellow fever, and chikungunya fever.

This new genetic information promises to help researchers design better ways to diagnose, treat, and prevent diseases caused by these organisms.

The newly sequenced genome of *Aedes aegypti* is particularly important because the mosquito, which has become increasingly resistant to existing insecticides, is expanding into temperate regions. Researchers hope that studies of the sequence will lead to new methods of controlling the mosquito, such as genetically altering the species so that it is resistant to agents that cause disease.

Through its Partnerships with Public-Private Partnerships program and Tropical Diseases Research Units, NIAID is actively supporting the discovery and development of treatments for parasitic tropical diseases. For example, researchers in the program are developing a low-cost treatment for visceral leishmaniasis and identifying new drugs for African sleeping sickness and Chagas disease.

Recently, scientists supported in part by NIAID identified chemical compounds that hold promise as potential new therapies for schistosomiasis, which afflicts more than 200 million people worldwide. The compounds, known as oxadiazoles, can inhibit an enzyme vital to the survival of the worms that spread the disease. The search for new drugs for schistosomiasis is vital, as public health experts fear that the worms will become resistant to praziquantel, which has been used to treat the disease since the 1980s.



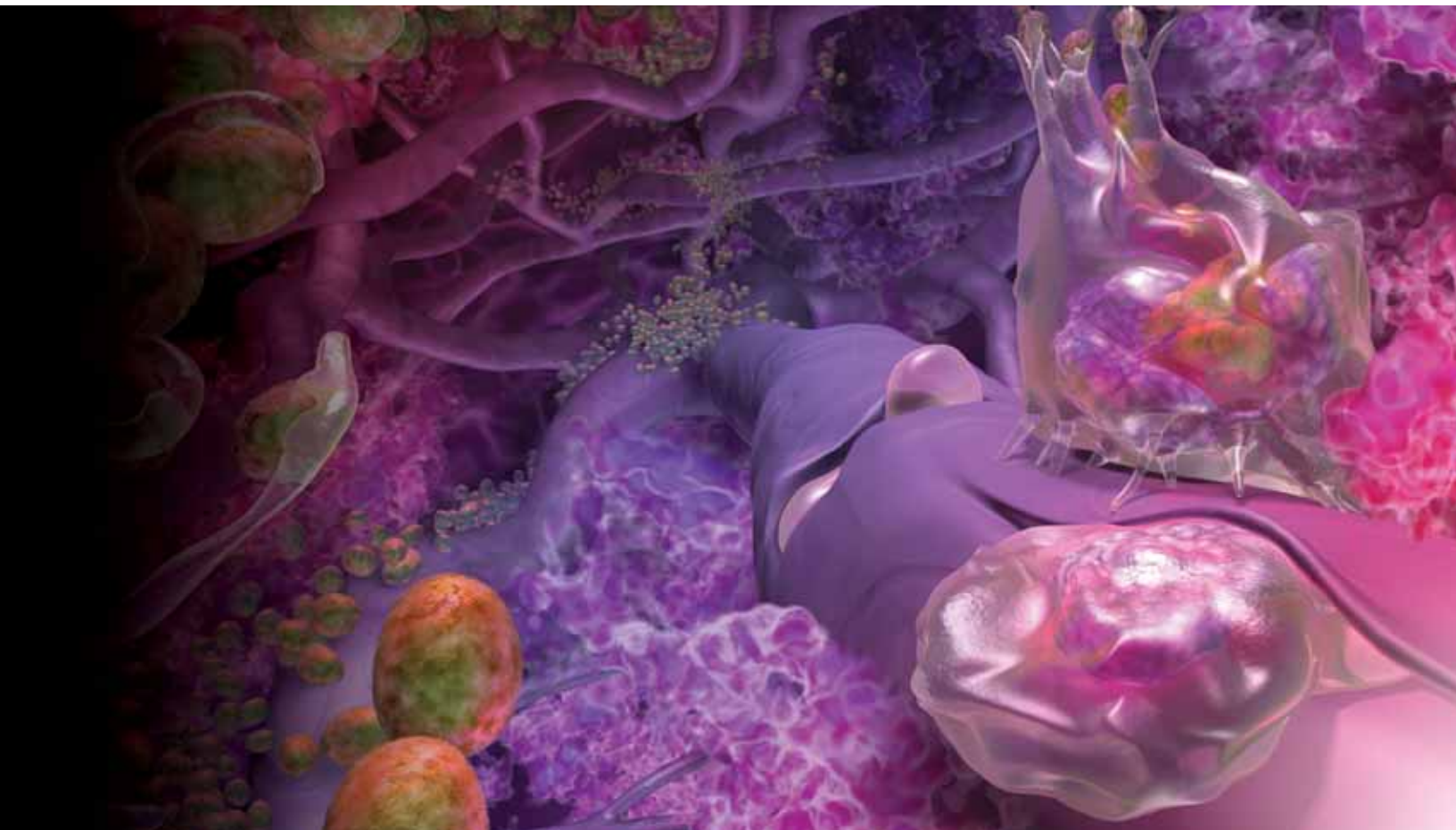
TROPICAL DISEASES SUCH AS DENGUE AND LEISHMANIASIS TAKE A TREMENDOUS TOLL ON GLOBAL HEALTH.

Improving Understanding of the Immune System

Basic immunology is the foundation for much of the research being conducted on HIV/AIDS, malaria, tuberculosis, and other global infectious diseases. Immunology is also vital in the fight against autoimmune diseases, allergic diseases, asthma, transplant rejection, and other disorders of the immune system that cause chronic disease and disability on a global scale.

NIAID supports and conducts basic and clinical immunology research to advance understanding of the mechanisms that underlie immune system disorders and to develop new strategies to detect, prevent, and treat them. For example, the Immune Tolerance Network, an international collaboration of more than 80 researchers co-funded by NIAID, is making steady progress toward reducing the need for costly and potentially risky immunosuppressive drugs that are the current standard treatment to prevent rejection of transplanted organs and tissues. To date, more than 10 kidney and liver transplant recipients are surviving without immunosuppressive drugs, some for as long as four years.

NIAID also supports clinical trials in food allergy, including studies aimed at preventing the development of allergies to particular foods and reversing established allergies to milk, eggs, peanuts, and others. For instance, a United Kingdom study supported in part by NIAID is exploring if early-life exposure to peanuts contributes to lower rates of peanut allergy. The researchers are comparing peanut avoidance to daily peanut consumption in children from 4 to 10 months of age using a peanut snack eaten by more than 90 percent of Israeli children during the first year of life. Though peanuts are commonly consumed by infants in Israel, the rate of peanut allergy in the country is quite low and does not appear to be increasing. In the United Kingdom and North America, however, peanut avoidance is recommended during infancy, yet the prevalence of peanut allergy continues to rise.



Funding Opportunities for Foreign Scientists and Institutions

NIAID funds biomedical research through various mechanisms such as grants, cooperative agreements, and contracts.

Grants are used to foster creative scientific research with minimal NIAID involvement. Cooperative agreements are types of grants NIAID uses to fund projects in which substantial NIAID scientific or programmatic involvement is needed to guide and coordinate the research. NIAID uses contracts to fund clearly defined projects of scientific need or interest. NIAID closely supervises projects funded by contracts.

NIAID IRIDA Program

The NIAID International Research in Infectious Diseases including AIDS (IRIDA) Program solicits R01 applications from organizations/institutions in eligible foreign countries that propose research related to infectious diseases. NIAID funds up to 10 IRIDA grants each year to encourage the development of scientific expertise and research infrastructure and to increase collaborative research partnerships at NIAID-funded international sites.

Grants

Investigators need not be U.S. citizens to apply for select NIH research grants, including the following:

- R01s—provide support for health-related research and development based on the NIH mission
- R03s—support small research projects that can be carried out in a short period of time with limited resources
- R21s—encourage exploratory research projects by providing support for the early and conceptual stages of development

Another opportunity for funding is the NIH Pathway to Independence Award (K99/R00), which is available to investigators with a clinical or research doctorate and no more than five years of postdoctoral research training at the time of application.

The K99/R00 does not require citizenship or permanent U.S. residency, but the applicant should have a visa that allows him or her to be in the country for the duration of the grant.

Studies may be proposed for the IRIDA program on any aspect of infectious diseases (except clinical trials). The following are some examples:

- Epidemiology, pathogenesis, and immunopathogenesis of infectious diseases
- Identification of resistance patterns
- Characterization of susceptible cohorts for a particular pathogen
- Pilot and feasibility studies in preparation for larger studies

How to Apply for Grant Funding

Research funds are paid to institutions only, not to individual scientists. Foreign institutions must be registered with Grants.gov and with the NIH Electronic Research Administration Commons Web site prior to applying for NIAID or other NIH grants. It may take four to six weeks to complete the registration process, so interested institutions should start well in advance of the application due date.

Before applying, institutions should read current NIAID funding opportunity announcements and consider whether their projects fit within the NIAID mission. Successful grant applications often depend on collaborations. Scientists from foreign countries may find it helpful to partner with U.S. institutions when applying.

Contracts

NIAID uses contracts to purchase items it needs or to perform research and development. NIAID uses a variety of contract mechanisms to accomplish its research goals, such as contracts for developing animal models, developing and testing vaccines, conducting clinical trials, and developing and maintaining reagent and specimen repositories for investigators.

CRADAs

NIAID often uses Cooperative Research and Development Agreements (CRADAs) to facilitate the development of specific technologies or projects that originate in NIAID laboratories. Under a CRADA, NIAID may provide personnel, services, facilities, equipment, or other resources. See the CRADA Web site listed on the right of this page for more information.

Online Resources

International Grants and Contracts
www.niaid.nih.gov/ncn/grants/int

IRIDA Program Announcement
grants.nih.gov/grants/guide/pa-files/PAR-08-130.html

K99/R00 Program Announcement
grants.nih.gov/grants/guide/pa-files/PA-07-297.html

Grants.gov
www.grants.gov

Electronic Research Administration Commons
commons.era.nih.gov/commons

Cooperative Agreements
www.niaid.nih.gov/ncn/sop/coopagree.htm

CRADAs
ott.od.nih.gov/CRADAs

THROUGH PARTNERSHIPS WITH ACADEMIA, PRIVATE INDUSTRY, PHILANTHROPIC ORGANIZATIONS, AND OTHER RESEARCH-SUPPORTING AGENCIES, NIAID HELPS GUIDE AND ENHANCE MEDICAL RESEARCH.

Training Opportunities for Foreign Scientists

Training at NIH

The NIH Visiting Program provides opportunities for foreign postdoctoral scientists to train and conduct collaborative research. Annually, more than 2,000 scientists from other nations conduct research in the basic and clinical science laboratories on the NIH campus in Bethesda, Maryland, and in several field units across the United States. NIH has long considered close interaction with foreign scientists in the conduct of collaborative research to be an essential ingredient in achieving its objectives.

There are two categories of Visiting Program participants: Visiting Fellows, who receive awards for research training, and Visiting Scientists, who receive appointments to conduct research. Each participant works closely with a senior NIH investigator who serves as a sponsor or supervisor during the period of award or appointment.

Visiting Scientists and Visiting Fellows hosted by NIAID receive a salary or stipend according to their particular appointment.

How to Apply for Training Opportunities

Foreign postdoctoral scientists who wish to participate in the Visiting Program must first secure an invitation from a senior scientist at NIH. The award (Visiting Fellow) or appointment (Visiting Scientist) is offered based on a candidate's qualifications and the research needs of the host laboratory.

Individuals interested in an NIAID fellowship or appointment should write to an NIAID senior scientist who works in the same research field, enclosing a resume and brief description of their particular research area and interests.

Guest and Volunteer Researchers

Foreign predoctoral and postdoctoral scientists may work at NIAID without salary or stipend as Volunteer Researchers. It is also possible for foreign scientists to receive a salary or stipend from their home institution and work at NIAID as Guest Researchers. Interested individuals should contact a senior scientist at NIAID who works in the same research field, enclosing a resume and brief description of their particular research area and interests.

ICSSC Assists Clinical Investigators in Developing Countries

The International Clinical Sciences Support Center (ICSSC) provides support to clinical investigators funded by the NIAID Division of Microbiology and Infectious Diseases and whose work focuses on treatment, prevention, and control of infectious diseases in developing countries.

This support includes the following:

- Assistance with research planning, protocol development, and study implementation
- Training and workshops on topics such as study design, data management, and ethical conduct of trials
- Opportunities to communicate and share experiences with other investigators

The ICSSC Web site includes a service-request form and links to resources such as protocol templates, informed consent checklists, and online tutorials.

Online Resources

International Clinical Sciences Support Center
www.icssc.org

Training in NIAID Labs
www.niaid.nih.gov/labs/training

Opportunities at NIH for Non-U.S. Citizens
www.jobs.nih.gov/jobsearch/noncitizen.htm

NIAID Contact

Office of Global Research
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
U.S. Department of Health and
Human Services

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Inside front cover: Worker at Kilimanjaro Christian Medical Centre, Moshi, Tanzania; NIH/J. Haliski

Page 3: Anthony S. Fauci, M.D., addressing the United Nations General Assembly Special Session on HIV/AIDS, June 10, 2008; UN Photo/ Evan Schneider

Page 6: Leishmaniasis study in Mali; NIAID

Page 7 (top): District of Baraoueli in Mali; NIAID

Page 7 (bottom): Family in Delhi, India; WHO/P. Virot

Page 8: Scanning electron micrograph (SEM) of HIV-1 budding from cultured lymphocyte; CDC

Page 9 (left): Worker at Kilimanjaro Christian Medical Centre in Moshi, Tanzania; NIH/J. Haliski

Page 9 (right): Ethiopian girl; WHO/P. Virot

Pages 10 and 11: SEM of *Mycobacterium tuberculosis*; Photo Researchers

Page 11: Investigator at South Korea's National Masan Tuberculosis Hospital; NIAID

Page 12: SEM of a human red blood cell infected with a malaria parasite; Photo Researchers

Page 13 (background): *Anopheles* mosquito; CDC

Page 13 (left): Distribution of insecticidal bed nets in Bohicon, Benin; WHO/Benoist Carpentier

Page 13 (right): Mosquito larvae (*Anopheles stephensi*) at water surface; Photo Researchers/ G. I. Bernard

Page 14: Negative-stained transmission electron micrograph of an influenza virus particle; CDC

Page 15: Food market in Alem Kitmama, Ethiopia; WHO/P. Virot

Page 16 (top): Shanty town in Rio De Janeiro, Brazil; iStockphoto/Joseph Luoman

Page 16 (bottom): Boy with dengue fever in Bangkok, Thailand; Christopher Brown/IHT/Redux

Page 17: Neutrophils responding to infection; Photo Researchers

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