

Chapter 2

NIAID International Research Programs: Global Impact

NIAID conducts and supports a global program of research aimed at improving diagnosis, treatment, and prevention of immunologic, allergic, and emerging infectious diseases. This research has led to new therapies, vaccines, diagnostic tests, and other technologies that have improved the health of millions of people in the United States and around the world (<http://www3.niaid.nih.gov/topics/GlobalResearch/default.htm>).

Note: Whenever relevant, further detailed information on NIAID international research programs is described in the separate book chapters that follow.

Several unique NIAID international programs designed to promote scientific advances and cooperation on important infectious diseases and pathogens include:

- *International Research In Infectious Diseases (IRID)*. The International Research In Infectious Diseases (IRID) initiative is intended to encourage the submission of *ROI applications of investigators from institutions in eligible foreign countries* (who do not currently have NIAID-funded research grant awards) to conduct studies and establish and/or extend collaborative infectious diseases research among investigators and institutions at international sites where NIAID has significant investment in research and/or infrastructure, including such international research programs as: (i) The International Centers of Excellence in Research (ICERs); (ii) International Collaborations for Infectious Diseases Research (ICIDRs); (iii) The Tropical Medicine Research Centers (TMRCs); and (iv) The Tuberculosis Research Program. Clinical trials will not be supported through IRID.
- *International Collaborations for Infectious Diseases Research (ICIDR)*. The International Collaborations for Infectious Diseases (ICIDR) program is designed to promote collaborative research between U.S. investigators and scientists in about 15 countries where *tropical infections are endemic*. In 1999, the ICIDR program was re-competed to include a companion program from the Fogarty International Center, entitled “*Actions for Building Capacity (ABC)*,” which supports training of foreign investigators in the context of the ICIDR program. There are 14 NIAID-supported sites and 4 additional sites with support from NICHD and NIDA. There are nine ABC awards in the ICIDR program.
- *Tropical Disease Research Units (TDRU)*. The Tropical Disease Research Units (TDRU) program is a *domestic grants award program* intended to provide support for multiproject, interdisciplinary studies that seek to develop new strategies to control diseases by *protozoa and helminths*.
- *Tropical Medicine Research Centers (TMRC)*. The Tropical Medicine Research Centers (TMRC) is a program that is intended to support 4 foreign institutions—currently located in Mali, China, Colombia, and Brazil—in conducting research of direct relevance to the health of the people in tropical environments and to promote collaborations and exchange of information between foreign and U.S. scientists (<http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-06-006.html>). This program was initiated in 1991 to support International Centers located in disease endemic areas in conducting research in major tropical diseases. The 2006 initiative solicited applications in the areas of leishmaniasis, Chagas’ disease, and human African trypanosomiasis to facilitate translational research using the recently published genomes of the trypanosomatids.
- *International Centers for Tropical Diseases Research (ICTDR)*. Institutions supported by grants from TDRU, ICIDR, and the TMRC programs and other large international research sites, along with the NIAID’s Division of Intramural Research (DIR), comprise the NIAID Network of International Centers for Tropical Diseases Research (ICTDR). The ICTDR program incorporates NIAID-supported intramural and extramural tropical disease research centers into an interactive network focused on tropical infectious disease problems.
- *Tuberculosis Research Unit (TBRU)*. The Tuberculosis Research Unit (TBRU) is a contract to Case Western Reserve University intended to develop surrogate markers of disease and human protective immunity and to

conduct clinical trials of potential new TB therapeutic, preventive, and diagnostic strategies. In addition, well-characterized clinical samples will be available for distribution to TBRU investigators and their collaborators through a newly established repository. The activities of the TBRU are coordinated with other major organizations involved in tuberculosis research, including CDC, U.S. Department of Agriculture (USDA), U.S. Food and Drug Administration (FDA), WHO, Global Alliance for TB Drug Development, and the International Union Against Tuberculosis and Lung Disease (IUATLD), and with interested industrial partners.

- *Vaccine Action Program (VAP)*. The Indo-U.S. Vaccine Action Program (VAP) was initiated in 1987 as a bilateral program that focuses on the development of safe and effective vaccines for major communicable diseases of interest to India and the United States through joint research and development. Currently, the focus of VAC is on HIV/AIDS, malaria, and tuberculosis.
- *U.S.-Japan Cooperative Medical Science Program*. This is a 36-year-old bilateral, cooperative research program involving U.S. and Japanese scientists who convene on a regular basis to address *public health priorities in Asia*; for example, the U.S.-Japan Workshops in Medical Mycology (<http://www.niaid.nih.gov/dmid/fungal#2e>). The goals of these workshops have been to initiate interactions; build collaborations; identify research needs; turn needs into opportunities; stimulate molecular research in medical mycology; and summarize recommendations emerging from workshop proceedings (1).
- *International Training and Research in Emerging Infectious Diseases (ITREID)*. The International Training and Research in Emerging Infectious Diseases (ITREID) has been established as collaboration between NIAID and the Fogarty International Center (FIC) to support international training and research. The intent of this program is to enable NIH grant recipients to enhance laboratory, epidemiologic, clinical, and social sciences research and to train scientists and public health workers from developing countries and their U.S. counterparts in research, control, and prevention strategies.
- *International Malaria Research Training Program (IMRTP)*. The IMRTP initiative is a joint collaborative program of the Fogarty International Center and NIAID aimed at training and/or expanding the capabilities of scientists and health professionals from developing countries in which malaria is endemic and to engage in research relevant to severe malarial anemia (<http://grants.nih.gov/grants/guide/rfa-files/RFA-TW-01-006.html>).
- *International Cooperative Biodiversity Groups Program (ICBG)*. The International Cooperative Biodiversity Groups is a program with a threefold mission: conservation of biodiversity, economic growth for develop-

ing countries (e.g., Central and South America, Nigeria, Cameroon, Madagascar, Jordan, Central Asia, Papua New Guinea, Laos, and Vietnam), and discovery of pharmaceuticals from natural products. NIAID, together with the National Cancer Institute (NCI), National Institute of Mental Health (NIMH), National Heart, Lung, and Blood Institute (NHLBI), National Institute on Drug Abuse (NIDA), FIC, the National Science Foundation, and the USDA, are the co-sponsors of ICBG. The current awards are given to multidisciplinary research groups that also include in-country, research-capacity collections, and *partnerships with a pharmaceutical company*. The ICBG program has been widely recognized as a model for research partnerships that acknowledge intellectual property ownership of indigenous communities.

- *International Clinical Studies Support Centers (ICSSC)*. The primary goal of the International Clinical Studies Support Centers (ICSSC) is to enhance the capacity of *international clinical sites* to perform clinical research in accordance with international standards, such as the International Conference on Harmonization's (ICH) Good Clinical Practices (GCP), and to facilitate the planning and conduct of clinical epidemiologic studies and clinical trials that range from small, early-phase trials to large, multicenter efficacy trials. These studies are conducted throughout the world, primarily in Africa, South and Central America, and Asia.
- *Ethical Aspects of Research in Developing Countries*. NIAID sponsors workshops on the Ethical Aspects of Research in Developing Countries with the participation of the NIH Department of Bioethics. To date, there have been workshops held in Malawi and Ghana.
- *U.S.-South Africa Science and Technology Agreement*. A Framework Agreement between the U.S. government and the government of the Republic of South Africa concerning cooperation in scientific, technologic, and environmental fields, including areas of public health, was signed on December 5, 1995. This agreement is still in effect.

2.1 Global Research: Africa

As operationally defined by WHO, the African Region (WHO/AFRO) comprises 46 countries. Other countries in the African continent belong to another operationally defined region of WHO (<http://www3.niaid.nih.gov/topics/GlobalResearch/Africa/default.htm>).

As Africa confronts the 21st century, it faces several challenges. Some of the major challenges are in the interrelated areas of economic development and health. According to WHO, an estimated 45% of the population of Africa lives below the poverty line, on less than US\$1.00 per day. As WHO reports, life expectancy is only 47 years, and people

suffer from a wide range of diseases, several of which are NIAID's highest priorities for research:

- The majority of cases of malaria each year occur in Africa, primarily in children under 5 years of age
- HIV/AIDS has had a more devastating effect on Africa than on any other region of the world
- Tuberculosis (TB) is a major cause of death among people living with HIV/AIDS, and Africa bears the brunt of the HIV-fueled TB epidemic

2.1.1 Countries with NIAID-Funded Research Activities

African countries with current NIAID-funded activities (Fig. 2.1) include:

| | |
|--|-----------------------|
| Benin | Malawi |
| Botswana | Mali |
| Burkina Faso | Mauritius |
| Cameroon | Mozambique |
| Central African Republic | Nigeria |
| Côte d'Ivoire | Republic of the Congo |
| Democratic Republic of the Congo (DRC) | Rwanda |
| Gabon | Senegal |
| Gambia, The | South Africa |
| Ghana | Tanzania |
| Kenya | Uganda |
| Liberia | Zambia |
| Madagascar | Zimbabwe |

Additional countries where NIAID is conducting and supporting research will continue to be added. However, this information is not meant to be a complete list of NIAID research and NIAID-sponsored activities. It is intended to serve as an overview.

Research Focus. NIAID has funded research activities in 26 African countries, mostly in southern and eastern Africa. However, NIAID has also developed a major research presence in Mali in West Africa (<http://www3.niaid.nih.gov/topics/GlobalResearch/Africa/default.htm>).

HIV/AIDS, TB, and malaria are three of the most serious infectious diseases in Africa, causing millions of deaths each year. These three diseases are a major cause of poverty through their debilitating impact on the workforce and significantly affect the economic development and stability of the region. NIAID supports HIV/AIDS research in all of these 26 countries, with most projects conducted in areas with the highest incidence of infection and disease, namely Botswana, Kenya, Malawi, Rwanda, South Africa, Zambia, and Zimbabwe.

The recent emergence of multidrug-resistant TB (MDR TB) and extensively drug-resistant TB (XDR TB), especially

in the context of HIV/AIDS infection, is being addressed by NIAID-funded projects conducted in South Africa, Tanzania, and Uganda.

Malaria remains a major threat, and NIAID conducts clinical, epidemiologic, drug, and vaccine research in east African countries such as Kenya, Malawi, Tanzania, and Uganda, and in Mali, Cameroon, Ghana, and The Gambia in central and West Africa.

Neglected diseases such as filariasis and schistosomiasis are receiving renewed attention, with NIAID projects in Kenya, Malawi, and South Africa. Diarrheal and respiratory diseases and vector-borne diseases, such as African trypanosomiasis (sleeping sickness), are also of concern.

2.1.1.1 The Gambia

The largest NIAID investment in The Gambia is in malaria, particularly severe malaria in children, and methods of controlling mosquito larvae. NIAID also has a program on *Helicobacter pylori* and two programs on HIV/AIDS. A major program on a Phase III pneumococcal conjugate vaccine study in Basse, The Gambia, involved collaboration among NIAID, the British Medical Research Council (MRC), Wyeth Pharmaceuticals, WHO, the Program for Appropriate Technology in Health (PATH), and the United States Agency for International Development (USAID). This study was successfully completed in 2005 and has provided data to show that serious infections and deaths can be prevented by the incorporation of a pneumococcal conjugate vaccine into the local expanded program on immunization (EPI) (<http://www3.niaid.nih.gov/research/topics/bacterial/clinical/GambiaPneumococcalVaccineTrial.htm>).

The MRC facility has offered the U.S. researchers the opportunity to undertake human clinical vaccine trials that comply fully with FDA regulations. Among these trials were a Phase II pneumococcal vaccine trial and a malaria vaccine involving the U.S. Department of Defense. Vector-borne diseases, including dengue, Crimean-Congo hemorrhagic fever, and yellow fever, remain endemic. Water-borne diseases include bacterial and protozoal diarrhea, hepatitis A, and typhoid fever.

Selected Current and Recent NIAID-Funded Research (Non-HIV/AIDS). The following information is not necessarily a complete list of NIAID research and NIAID-sponsored activities. It is intended to serve as an overview.

- *Malaria*
 - (i) Severe malaria in African children—Michigan State University
 - (ii) Antilarval measures in malaria control—University of Durham, United Kingdom



Fig. 2.1 Map of African countries with NIAID-funded activities—world regions as defined by WHO

- *Helicobacter pylori*

- Genotypes of *Helicobacter pylori* in The Gambia—MRC, Banjul, The Gambia

2.1.1.2 Kenya

Kenya is a major site of NIAID funding, with 29 recently funded activities. The heaviest investments are in HIV/AIDS, malaria, schistosomiasis, and vector studies. There are opportunities for further research in TB (especially in the context of HIV/AIDS) and vector-borne diseases, especially Rift Valley fever (RVF), a serious zoonosis (a disease that primarily affects animals, but occasionally causes disease in humans) (<http://www3.niaid.nih.gov/topics/GlobalResearch/Africa/Kenya.htm>).

According to WHO data, child mortality remains high in the country. Kenya has a high risk of food- and water-borne diseases, particularly bacterial and protozoal diarrhea, hepatitis A, schistosomiasis, and typhoid fever. Malaria is

endemic in many areas, especially around Lake Victoria, and vector-borne diseases in general remain a threat, particularly RVF. HIV/AIDS prevalence is 7.4% and, according to WHO, the incidence of TB is high. The appearance of MDR TB and emergence of XDR TB are potential threats. Kenya reported two cases of polio in 2006, although it is not regarded as a highly endemic country.

Selected Current and Recent NIAID-Funded Research (Non-HIV/AIDS). The following information is not necessarily a complete list of NIAID research and NIAID-sponsored activities. It is intended to serve as an overview.

- *Malaria*

- Associating genetic variation with resistance in severe malaria in East Africa—Harvard University Medical School
- Human immunity to merozoite surface protein-1 in western Kenya—Case Western Reserve University
- Fetal immunity to falciparum malaria—Case Western Reserve University

- (iv) Redefining cerebral malaria—Michigan State University
- (v) Malaria transmission and immunity in highland Kenya—University of Minnesota
- *Schistosomiasis*
 - (i) Toward a molecularly defined vaccine for schistosomiasis—Southwest Foundation for Biomedical Research
 - (ii) Evo-epidemiology of *Schistosoma mansoni* in western Kenya—University of New Mexico
 - (iii) Determinants of resistance in human schistosomiasis—University of Georgia
- *Vectors*
 - (i) Population genomics of mosquito *Anopheles gambiae* in Africa—University of California at Davis
 - (ii) Nutritional ecology of adult *Anopheles gambiae*—Ohio State University
 - (iii) Microbial control of immature *Anopheles* mosquitoes—University of Illinois at Champagne-Urbana
 - (iv) Insecticide mosaics and sustainability of treated nets—Michigan State University
- *Other*
 - (i) Immunologic studies of Burkitt's lymphoma—Case Western Reserve University
 - (ii) Clinical epidemiology of *Mycoplasma genitalium*—University of Washington, Seattle

2.1.1.3 Mali

NIAID maintains on-site staff in Bamako, Mali, working in close association with the Faculty of Medicine, Pharmacy, and Odonto-Stomatology (FMPOS) at the University of Bamako. The intramural research program has been active in Mali since the late 1980s; in 2002, the FMPOS/University of Bamako was selected as an NIAID International Center of Excellence in Research. Milestones in the intramural collaborations with the FMPOS include the establishment of the Malaria Research and Training Center at the University of Bamako; the development of clinical field sites to test candidate malaria vaccines and to conduct studies on malaria and lymphatic filariasis; the development of a collaborative program to study HIV/AIDS and tuberculosis co-infection; the renovation of a BSL-3 laboratory for use in the co-infection studies; and the establishment of the Mali Service Center.

Mali's climate is highly stratified: hot and arid in the north and wetter and more humid in the south. This affects vector-borne diseases such as malaria. Food- and water-borne diseases, particularly associated with the Niger River, include

bacterial and protozoal diarrhea, hepatitis A, typhoid fever, and schistosomiasis.

Selected Current and Recent NIAID-Funded Research (Non-HIV/AIDS). The following information is not necessarily a complete list of NIAID research and NIAID-sponsored activities. It is intended to serve as an overview.

- *Malaria Clinical Research*
 - (i) Malaria Vaccine Trials in Mali—University of Maryland, Baltimore
 - (ii) Vaccines: Phase II trials in children (Bandiagara, Donéguebouyou, Bancoumana), and Phase I trial in adults (Donéguebouyou)—NIAID intramural program
 - (iii) Preterm and infant mortality observational study—Gabriel Toure Hospital, Bamako
 - (iv) Multidisciplinary studies of malaria protection by hemoglobinopathies and glucose-6-phosphate dehydrogenase (G6PD) deficiency—NIAID intramural program
- *Malaria*
 - (i) Genetic basis for natural resistance to malaria in *Anopheles gambiae*—NIAID intramural program
 - (ii) Identification of genetically susceptible *Anopheles gambiae* to *Plasmodium falciparum* by location—NIAID intramural program
 - (iii) Genomics of mosquito resistance to *Plasmodium*—University of Minnesota at Twin Cities
 - (iv) Niono Irrigation Project and Malaria: A Computer Model—University of California at Los Angeles
- *Filariasis Clinical Research*
 - (i) Albendazole dosage/frequency-ivermectin/albendazole trial—NIAID intramural program
 - (ii) Doxycycline to reduce microfilaremia in co-infections, safety and efficacy—NIAID intramural program
- *HIV/TB Clinical Research*
 - (i) CD4⁺ T-cell immune responses to *Mycobacterium tuberculosis*—NIAID intramural program
 - (ii) Establishment of normal parameters for blood and sputum with samples obtained from volunteers in Bamako—NIAID intramural program

2.1.1.4 Mozambique

NIAID supports three projects in Mozambique, all linked to the country's high prevalence of HIV/AIDS. However, Mozambique's health priorities are more complex.

Mozambique suffers from high infant mortality, an expanding HIV/AIDS epidemic, malaria (*Plasmodium falciparum*) as the primary cause of mortality among children under 5 years of age, and recent severe outbreaks of cholera. Extensive malnutrition among children and an increasing burden of TB, according to WHO, are also of concern (<http://www3.niaid.nih.gov/topics/GlobalResearch/Africa/Mozambique.htm>).

2.1.1.5 Rwanda

All of NIAID's current funding in Rwanda involves HIV/AIDS—the adult prevalence rate in Rwanda is approximately 5%.

However, malaria is a major problem and probably contributes to the country's high infant mortality rate (WHO). There was a regional outbreak of meningococcus that caused as many as 636 cases in 2002, leading to a mass immunization program. As in many other countries in this region, water-borne diseases, such as bacterial diarrhea, hepatitis A, and typhoid fever, are prevalent. In addition, TB is a problem (WHO) that has remained steady over several years, with emerging MDR TB. Immunization rates are generally low.

2.1.1.6 South Africa

Currently, NIAID is funding more than 50 projects in South Africa, most of them involving HIV/AIDS research. However, the institute is also supporting research on TB, malaria, and other diseases or vectors. These projects focus primarily on treatment and pathogenesis. NIAID also supports some prevention and epidemiology studies in these areas and provides direct funding to seven institutions in South Africa involving 17 projects (<http://www3.niaid.nih.gov/topics/GlobalResearch/Africa/SouthAfrica.htm>).

The incidence of TB in South Africa is high, according to WHO. The recent emergence of MDR TB, and now XDR TB, is a major and urgent new challenge. Better surveillance for drug resistance is urgently needed to determine the level and extent of MDR and XDR TB, especially in relation to HIV status. HIV-associated infections such as *Cryptococcus neoformans* are increasingly found. Drug-resistant *Staphylococcus aureus* is a major health problem. There has been a rapid resurgence of chloroquine-resistant malaria strains, and schistosomiasis is endemic in rivers in eastern South Africa. Crimean-Congo hemorrhagic fever is also endemic. Despite a low life expectancy at birth (WHO), diseases such as diabetes mellitus and obesity are expected to increase significantly.

Selected Current and Recent NIAID-Funded Research (Non-HIV/AIDS). The following information is not nec-

essarily a complete list of NIAID research and NIAID-sponsored activities. It is intended to serve as an overview.

- *Tuberculosis*

- (i) A smart microscope for the detection of tuberculosis in ZN-stained sputum smears—University of Cape Town, South Africa
- (ii) Diagnostic yield of induced sputum for rapid diagnosis of pulmonary tuberculosis—University of Cape Town, South Africa
- (iii) Inherited resistance in Beijing with isolates of *M. tuberculosis*—University of Stellenbosch, South Africa
- (iv) Protective immunity induced by newborn Bacillus Calmette-Guérin (BCG) vaccination—University of Cape Town, South Africa
- (v) Regulation of dormancy in *M. tuberculosis*—University of Pennsylvania
- (vi) Ecology, genetics, and physiology of insect vectors—Iowa State University
- (vii) Host and pathogen determinants of *M. tuberculosis* latency—Public Health Research Institute, Newark
- (viii) Molecular approaches for understanding TB dynamics—Harvard University Medical School
- (ix) A second-generation patch test for tuberculosis—Sequella, Inc., Rockville, Maryland
- (x) Development of novel resistance management strategies—Liverpool School of Tropical Medicine, United Kingdom
- (xi) The role of the granuloma in *M. tuberculosis* infections—Cornell University, New York

- *HIV/TB Research*

- (i) BCG as an HIV vaccine vector—University of Cape Town, South Africa
- (ii) Novel TB prevention regimens for HIV-infected adults—Johns Hopkins University

- *Malaria Research*

- (i) Development of novel resistance management strategies—Liverpool School of Tropical Medicine, United Kingdom

2.1.1.7 Tanzania

NIAID funds research programs in Tanzania related to HIV/AIDS, TB, and malaria, among other diseases (<http://www3.niaid.nih.gov/topics/GlobalResearch/Africa/Tanzania.htm>). In comparison with its neighboring countries, the child mortality rate in Tanzania is lower, but the HIV/AIDS prevalence rate is higher. Major infectious

diseases including food- or water-borne diseases, such as bacterial diarrhea, hepatitis A, and typhoid fever, and vector-borne diseases, such as malaria, remain serious. There has also been plague and a March 2007 outbreak of Rift Valley fever with clusters of human cases. Schistosomiasis is an important water contact disease. TB prevalence is high according to WHO, with a small percentage of TB cases identified as MDR TB. Noncommunicable diseases such as diabetes mellitus are rising significantly.

Selected Current and Recent NIAID-Funded Research (Non-HIV/AIDS). The following information is not necessarily a complete list of NIAID research and NIAID-sponsored activities. It is intended to serve as an overview.

- *Tuberculosis*

- (i) Nutrition, immunology, and epidemiology of TB—Harvard University School of Public Health
- (ii) TB clinical research: training the next generation—Centralized HIV-1 genes as vaccines—Duke University
- (iii) Training African giant rats as a cheap diagnostic tool for early TB detection—APOPO vzw, Antwerp, Belgium, and Tanzania

- *HIV/TB*

- (i) Disseminated tuberculosis in HIV infection—Dartmouth College
- (ii) Adjunct vitamin A therapy for tuberculosis and HIV/AIDS—Johns Hopkins University

- *Malaria*

- (i) Severe falciparum malaria: mechanisms of hypoargininemia—University of Utah
- (ii) Hyperphenylalaninemia in cerebral malaria—University of Utah
- (iii) Pathogenesis of falciparum malaria in infancy—Seattle Biomedical Research Institute
- (iv) Preventing pregnancy malaria: maternal-infant outcomes—Seattle Biomedical Research Institute
- (v) Nitric oxide and severe malaria—Duke University

- *Other*

- (i) Effect of zinc supplementation on pneumonia in children—Muhimbili University College of Health Sciences, Dar-es-Salaam, Tanzania

2.1.1.8 Uganda

Currently, NIAID is funding approximately 28 projects in Uganda related to HIV/AIDS, malaria, and TB (<http://www3.niaid.nih.gov/topics/GlobalResearch/Africa/Uganda.htm>). Among them are the program at Tufts University on

cryptococcus; four core activities to support HIV/AIDS research; work on the interactions of HIV/AIDS and TB and of HIV/AIDS and malaria; and malaria drug studies.

Despite expending 7.6% of the gross domestic product (GDP) on health in 2004, Uganda has a high infant mortality rate and low life expectancy (WHO). HIV prevalence declined from 15% in 1991 to 5% by 2001, but this decline has stopped. The government has announced a countrywide plan to implement male circumcision as an HIV/AIDS preventive method. As in neighboring countries, tuberculosis incidence is high (WHO), and cases of MDR TB have been found. Outbreaks of meningococcal meningitis have occurred in 2006 and 2007, cholera in 2003, and Ebola in 2000. In addition, bacterial diarrhea, hepatitis A, typhoid fever, vector-borne diseases—malaria and African trypanosomiasis (sleeping sickness)—and water-contact schistosomiasis are high risks in some locations.

Selected Current and Recent NIAID-Funded Research (Non-HIV/AIDS). The following information is not necessarily a complete list of NIAID research and NIAID-sponsored activities. It is intended to serve as an overview.

- *HIV Interactions with Other Diseases*

- (i) Associating genetic variation with resistance in severe malaria in East Africa—Harvard University Medical School
- (ii) Human immunity to merozoite surface protein-1 in western Kenya—Case Western Reserve University
- (iii) Clinical studies of interactions between HIV and malaria—University of California at San Francisco

- *Tuberculosis*

- (i) Tuberculosis immunity in young children—Oregon Health & Science University
- (ii) Sample processing cartridges for rapid polymerase chain reaction (PCR) TB detection—Cepheid, Sunnyvale, California

- *Malaria*

- (i) Clinical and molecular studies of drug resistant malaria—University of California at San Francisco
- (ii) Utility of rapid diagnostic tests for malaria—University of California at San Francisco

- *Cryptosporidium*

- (i) Studies on *Cryptosporidium parvum* type 1—Tufts University

- *Chlamydia*

- (i) Immunopathogenesis of *Chlamydia trachomatis* infection—NIAID intramural research

2.2 Global Research: Asia

International Collaboration in Influenza Research. Within the NIH, the NIAID is tasked with performing and supporting research to prevent, detect, and treat infectious diseases such as influenza. During the past 5 years, NIAID influenza research funding grew from US\$16.8 million to US\$196.3 million in fiscal year 2006.

The NIAID influenza research effort covers the spectrum from basic research to clinical trials, leading to the discovery and implementation of influenza vaccines, therapeutics, and diagnostics. Like research on other diseases, influenza research progress hinges upon collaboration and shared resources (http://www.usminstitute.org/spotlight_23.html).

Seasonal influenza is a fairly predictable annual occurrence. WHO estimates that influenza epidemics result in 250,000 to 500,000 deaths globally per year. In contrast, the impact of pandemic influenza, an unpredictable but historically proven threat, can range from fairly mild (1968) to catastrophic (1918).

An influenza virus that causes illness in humans, to which the majority of the human population has little or no immunity, and that is easily transmissible among humans, constitutes a pandemic virus. Of the existing potential pandemic viruses, the highly pathogenic avian influenza (HPAI) H5N1 virus that has become endemic in poultry in Southeast Asia, Eastern Europe, and several countries in Africa presents a source of concern to scientists and health officials around the world.

Not surprisingly, seasonal influenza preparedness and prevention are inherently linked to pandemic influenza preparedness and prevention. Both seasonal influenza research and pandemic influenza research depend on collaboration, especially at the international level. NIAID participates in several international influenza research efforts regarding pandemic preparedness. Several international partners identified the need for a clinical research network focused on therapeutics. Thus, in 2005 the NIAID Division of Clinical Research, with multilateral partners, established the *Southeast Asia (SEA) Influenza Clinical Research Network* to advance the scientific knowledge and management of human influenza through integrated, collaborative clinical research. Partners include hospitals and institutions in Vietnam, Indonesia, Thailand, the United Kingdom, and the United States. The network is committed to building independent research capacity within the SEA countries involved. NIAID and the Wellcome Trust provide financial support. Initial clinical studies will evaluate appropriate dosage levels of the influenza antiviral drug oseltamivir in patients with severe seasonal or avian influenza. Pharmacokinetics studies of oseltamivir in Asian subjects began in autumn 2006 at the Network Pharmacokinetics Unit at Mahidol University in Thailand.

NIAID Research on SARS. NIAID maintains a long-standing commitment to conducting and supporting research on emerging infectious diseases, such as SARS, with the goal of improving global health. In carrying out its global health research mission, the institute is supporting SARS research, including intramural and extramural research and collaborations with international agencies and organizations, to rapidly initiate the development of diagnostics, therapeutics, and vaccines against SARS.

Through a grant supplement to the Chinese Center of Disease Control (China CDC) and their collaborators, NIAID has funded three different SARS projects. Approaches undertaken include:

- Developing immune correlates of protection through study of pediatric and adult serum, stool, and cellular clinical samples obtained longitudinally from SARS patients
- Developing a panel of human SARS-associated coronavirus (SARS-CoV) antisera that can be used to standardize diagnostic assays. This project will be a collaboration with FDA and CDC
- Attempting to identify animal reservoirs of SARS-CoV through surveillance of live animal markets.

NIAID has assembled a multidisciplinary working group to develop a broad-based program that addresses the research needed to combat SARS. Key NIAID intramural laboratories have begun to pursue a range of research strategies to develop a SARS vaccine as well as therapeutics, including immune-based therapies, and the institute extramural programs are poised to help as well. NIAID has also initiated and expanded collaborations with other federal agencies, academia, and private industry. In addition, NIAID has released “Sources Sought” announcements, a special mechanism to rapidly identify contractors who can develop treatment strategies, vaccines, and antibody preparations to address SARS (<http://energycommerce.house.gov/reparchives/108/Hearings/05072003hearing917/Fauci1435print.htm>).

NIAID has purchased several hundred SARS microarrays—essentially a reference strain of the SARS coronavirus embedded in a quartz chip—and distributed the arrays at no cost to qualified researchers worldwide (http://findarticles.com/p/articles/mi_pnih/is_200306/ai_1336428103).

Seroprevalence Studies. As part of the international avian influenza effort, NIAID has funded several seroprevalence studies in Southeast Asia. A study of close contacts of infected individuals is being conducted by the China CDC. A case-control study of infected individuals is also planned to examine risks associated with infection. Basic research on the cross-reactivity of immune responses to the influenza H5N1 strain is also being carried out at the Chinese Academy of Medical Science. Bird isolates will be evaluated at the Chinese Academy of Science.

In addition, a population-based seroprevalence study will be conducted in three provinces of Vietnam. This study will be coordinated by the National Institute of Hygiene and Epidemiology in collaboration with the AFRIMS laboratory in Thailand.

Enteric Diseases. NIAID has established an Interagency Agreement with the U.S. Department of Defense to support the AFRIMS (Armed Forces Research Institute of Medical Sciences) site in Thailand to develop a non-human primate model of shigellosis and to conduct clinical trials of vaccines against shigellosis and other enteric pathogens.

2.3 Partnerships

- *Product Development Public-Private Partnerships (PDPPPs).* In 2006, a new initiative was announced by NIAID that calls attention to the vital role played by PDPPPs in developing new products directed against the neglected tropical diseases. NIAID is seeking to provide support to PDPPPs that have diagnostic or therapeutic products requiring additional targeted funding in order to complete the preclinical phase of development and enable an Investigational New Drug (IND) or Investigational Device Exemption (IDE) to be submitted for transition to clinical development.
- *The Global Alliance for TB Drug Development (GATB).* GATB is a nonprofit organization involving many public and private partners, which is contributing to the development of new drugs to shorten or simplify the treatment of TB and facilitate TB control in high-burden countries. More than 30 organizations are stakeholders in this public-private partnership, including the Bill & Melinda Gates Foundation, CDC, NIAID/NIH, the Rockefeller Foundation, USAID, the World Bank, and WHO (<http://www.tballiance.org/>).
- *Bill & Melinda Gates Foundation.* The Bill & Melinda Gates Foundation has collaborated with NIAID by funding a symposium at the larger NIAID-organized U.S. – Japan Cooperative Medical Sciences Program, Panel Meeting and Scientific Conference on Cholera and Related Bacterial Enteric Infections (the symposium title: “Challenges in Translational Research: Symposium on Vaccine Development—Pathways to Licensure,” Boston, Massachusetts, December 1, 2005).
- To enhance dialogue between NIAID-funded scientists working on malaria and the implementing organizations of the President’s Malaria Initiative (PMI), NIAID convened a 3-day meeting in Kampala, Uganda, entitled “Malaria Research into Practice: Research to Advise Policy, Policy to Advise Research.” Twenty-eight scientists from Africa and the United States participated in the meeting, which began on April 25, 2006, the African Malaria Day.
- *Multilateral Initiative on Malaria (MIM).* NIAID continues to support the MIM through grants to African researchers at African institutions under the MIM/TDR Program (<http://www.who.int/tdr/diseases/malaria/mimprojectsall.htm>).
- *Federal Malaria Vaccine Coordinating Committee (FMVCC).* NIAID continues to participate in FMVCC and provides support to the *MIM/TDR Task Force* to advance malaria research and strengthen research capacity at African institutions. NIAID also participates in the *Malaria Vaccine Advisory Committee* established at the *WHO Initiative for Vaccine Research (WHO/IVR)* and in the External Scientific Advisory Committee of the *Medicines for Malaria Venture*, a public-private partnership that fosters the accelerated development of new antimalarial compounds.
- *The International Cooperative Biodiversity Groups.* This NIAID-sponsored initiative addresses the interdependent issues of biodiversity conservation, economic capacity, and human health through discovery and development of therapeutic agents for diseases of importance in developing countries, as well as those of importance in developed countries. Five comprehensive awards and seven planning grants were announced (<http://www.nih.gov/news/pr/dec2003/fic-16.htm>). Areas of research include discovery of natural products for treatment of HIV, TB, malaria, and other tropical diseases, with screening of extracts from Uzbekistan, Kyrgyzstan, Papua New Guinea, Laos, Vietnam, Panama, Jordan, and Costa Rica. Two additional comprehensive awards co-funded by NIAID were awarded in 2006 (<http://www.nih.gov/news/pr/jan2006/fic-03.htm>) from the planning grants.
- *2006 NIAID Research Conference.* As part of its mission to reduce the burden of human disease, NIH—and NIAID in particular—has committed to encouraging the accelerated translation of biomedical discoveries into new treatments outside the United States. One direction for NIAID has been to broaden research opportunities and collaborations with scientists and research and educational institutions in Europe and in particular of countries from Central and Eastern Europe, the Baltics, Russia, Ukraine, and other newly independent states of the former Soviet Union. To this end, the Office of Global Research at NIAID took the initiative to organize the 2006 NIAID Research Conference in Opatija, Croatia (June 26–30, 2006) (<http://www3.niaid.nih.gov/program/croatia>).

The Scientific Program of the Conference covered a wide range of sessions by invited speakers on topics reflecting the broad scope of scientific activities

of NIAID. The 2006 NIAID Research Conference also featured plenary lectures delivered by distinguished scientists, roundtable discussions on a wide variety of topics, and poster sessions open to all participants (2).

Prior to the conference (June 24–25, 2006), a Satellite Symposium was held on “Grants Opportunities and Preparation” (grantsmanship, technology transfer, regulatory affairs, and FDA regulations with concurrent workshops) and on training opportunities at NIH by the Fogarty International Center. The training courses were conducted by staff members from the Division of Extramural Activities at NIAID and the NIH Offices of Technology Transfer and Regulatory Affairs (2).

About 300 participants from 39 countries in Europe, Asia, and North America have attended the 2006 NIAID Research Conference. As a direct result of the conference, 13 new collaborations in biomedical research were established by U.S. and foreign scientists.

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