

## OFFICE OF THE DIRECTOR

The Office of the Director (OD), NIAID, provides policy guidance, program development and evaluation, and overall operational and administrative coordination for the Institute. OD is the focal point of relationships with the Director of the NIH as well as with other components of the Department of Health and Human Services (DHHS), other Federal agencies, Congress, professional societies, voluntary health organizations, and other public groups. The activities of OD also include advising and guiding NIAID's key leaders on the principles, practices, laws, regulations, and policies of the Federal equal employment, affirmative action, civil rights, and minority programs. Offices within OD provide critical management and administrative support to the Institute. By carrying out their individual tasks, OD offices play a key role in helping the Institute achieve its mission. Brief descriptions of OD offices follow.

**The Office of Administrative Services (OAS)** assists NIAID staff in carrying out their responsibilities by providing administrative and acquisition management support services. These services include procurement, space management, and travel. OAS also develops internal controls in areas such as property accountability and financial monitoring, and coordinates and analyzes organizational changes.

**The Office of Clinical Research** manages and coordinates those NIAID research programs conducted at the Warren Grant Magnuson Clinical Center located on the NIH Bethesda campus. The Office promotes interactions and collaborations between intramural and

extramural investigators and oversees NIAID's Institutional Review Board to provide initial and continuing review of intramural clinical research protocols to protect the welfare of human subjects recruited to participate in biomedical or behavioral research. The Office also provides relevant information from NIAID's intramural clinical research programs to the NIH community and other Government agencies, as well as to public and private organizations.

**The Office of Communications and Public Liaison (OCPL)** enables NIAID to meet an important part of its mission by conveying the goals and results of its research programs to health professionals, the news media, and the public. In addition to responding to more than 10,000 requests for information annually, the Office plans educational and media campaigns; develops and disseminates brochures, fact sheets, news releases, and audiovisual products; and produces educational exhibits for national and regional meetings. OCPL also coordinates NIAID's Web site activities.

**The Office of Equal Employment Opportunity** is responsible for planning, implementing, evaluating, and monitoring programs and initiatives to increase the number of minorities, women, and persons with disabilities in all scientific and administrative areas of the Institute. The Office also develops initiatives that further enhance biomedical research programs at historically black colleges and universities and at Hispanic-serving institutions, and coordinates all activities to implement NIH minority-assistance programs and objectives relevant to the mission of NIAID.

**The Office of Ethics** provides advice regarding conflict of interest of individuals involved in the conduct of biomedical research, including Government employees, advisory committee members, and non-government employees such as peer reviewers and Data Safety Monitoring Board members. The Office also administers a comprehensive NIAID ethics program that reflects statutory responsibilities and integrity in service to the public.

**The Office of Financial Management** provides overall financial planning, management, and budget analysis to the Institute Director and all NIAID components and provides budget-related materials for the NIAID Director's briefings with DHHS, the NIH Director, the Office of Management and Budget, and Congress.

**The Office of Global Affairs (OGA)** provides overall coordination of NIAID international activities through a matrix of international liaisons; it accomplishes its work with other NIH components and DHHS agencies through the Fogarty International Center. OGA also meets and greets international visitors and delegations, coordinates NIAID participation in bilateral and multilateral programs, negotiates and provides administrative support for the long-term assignment of NIAID staff and representatives overseas, and supervises the OGA/NIAID Epidemiology Group in support of intramural and extramural international projects.

**The Human Resources Operations Branch C (NIAID)**, Division of Human Resources Operations, Office of Human Resources, NIH, provides human resource services for the Institute management, employees, and

applicants. These services encompass recruitment and staffing, position management and classification, pay and compensation, employee relations, employee benefits, employee development, and advisory services.

**The Office of Management for New Initiatives (OMNI)** is responsible for managing the establishment of key resources for new NIAID scientific and administrative initiatives. OMNI also is charged with acquiring and developing physical, human, and contractual infrastructure to fulfill new and expanded NIAID mission requirements.

**The Office of Policy Analysis** provides support and serves as liaison to program managers to coordinate, integrate, and articulate long-range program goals and strategies; develop and coordinate the Institute's annual planning and reporting process; advise on material for all stages related to congressional budget presentations; direct and coordinate the legislative liaison, tracking, and analysis for the Institute; manage the Executive Secretariat function; direct and coordinate Freedom of Information Act (FOIA) activities; provide the secretariat function for selected advisory groups, such as the NIAID Executive Committee; prepare the NIAID Director for meetings with various constituency groups; and brief the NIAID Director in preparation for trans-NIH policy meetings.

**The Office of Technology Development (OTD)** supports NIAID's intramural and extramural research programs by facilitating collaborations between NIAID researchers and external research and development organizations. OTD's staff uses scientific, legal, and business expertise to negotiate

agreements with universities, small biotechnology companies, large national and multinational pharmaceutical concerns, and other government institutions. OTD manages NIAID's portfolio of patents and inventions and serves as NIAID's resource for all issues concerning intellectual property. OTD also manages the receipt of Cooperative Research and Development Agreement (CRADA) funds, supports the NIH's licensing program, and tracks license royalty receipts. In addition, OTD provides NIAID investigators with training on NIH technology transfer policies and regulations and guidance on conflict-of-interest issues.

**The Office of Technology Information Systems (OTIS)** manages technologies supporting NIAID biomedical research programs. The Office provides a spectrum of management, technologies development, applications/software engineering, bioinformatics support, and professional development. OTIS works closely with NIAID intramural, extramural, and administrative staff to provide technical support, liaison, coordination, and consultation on a wide variety of ventures. These projects and initiatives are aimed at ensuring ever-increasing interchange and dissemination of scientific information within the Federal Government and among the worldwide scientific network of biomedical researchers.

## OUTREACH ACTIVITIES

The NIAID Office of Communications and Public Liaison (OCPL) is the focal point within the Institute for disseminating research results to the media, health professionals, and the public. An important part of NIAID's mission, this activity includes producing and disseminating print, audiovisual, and Web-based materials; distributing materials at professional and community meetings; and sponsoring workshops and conferences for community healthcare providers and the public.

OCPL produces materials on topics ranging from allergic and immunologic diseases, to AIDS and other sexually transmitted diseases, to potential illnesses caused by agents of bioterrorism. These materials include press releases, information sheets, and booklets, which are distributed to more than 10,000 people who contact the Institute from around the world each year. In addition, hundreds of thousands more download or request materials from the NIAID Web site ([www.niaid.nih.gov](http://www.niaid.nih.gov)), which is now visited 1.5 million times each month.

The NIAID Web site is a searchable site containing a wealth of information about NIAID's organization and research programs, as well as descriptions of NIAID's laboratories. The Extramural Information Center includes program announcements, contact information for key personnel, and many other items of interest to current and potential grantees and contractors.

OCPL has reprinted its very popular low-literacy booklets on tuberculosis (TB)—*Tuberculosis* and *Tuberculosis Infection*. Both are available in Spanish. OCPL staff also have

updated and printed the booklet titled *Malaria*. Malaria, like TB and HIV/AIDS, is a serious disease that kills millions of people worldwide. OCPL has distributed thousands of copies of the previous edition of *Malaria* to researchers and healthcare providers around the world. All publications also are available on the NIAID Web site.

A new OCPL communications initiative expands NIAID's efforts to keep more than 400 voluntary and scientific organizations updated about Institute activities. Periodic e-mails provide timely news on NIAID research advances that relate to the specific research interests of the organizations. In addition, OCPL disseminates news from the NIH Offices of Public Liaison, which include NIAID.

Exhibiting at scientific and health-related meetings is a key element of OCPL's outreach efforts. Institute staff distribute materials and answer questions about NIAID research and job opportunities at conferences, including the American Academy of Allergy, Asthma and Immunology; the American Society for Microbiology; the National Conference on Blacks in Higher Education; the Hispanic Association of Colleges and Universities; the American Public Health Association; and the Congressional Black Caucus. OCPL has been involved extensively in the outreach efforts of NIAID's Dale and Betty Bumpers Vaccine Research Center (VRC). VRC is the first facility at the NIH dedicated solely to vaccine research and production. To help the Center recruit for HIV vaccine trials, OCPL is helping to construct community partnerships by targeting local news media, visiting local churches and other community organizations,

and attending HIV/AIDS-related conferences and meetings.

The NIAID Division of AIDS (DAIDS) is conducting a national HIV vaccine communications campaign to foster a better public awareness of HIV vaccine research. The campaign is designed to create a public dialogue to help the public better understand the research, support it, and support those who may volunteer for clinical trials. The Institute implemented a qualitative comprehensive research effort, including both primary research (for example, 28 focus groups representing communities most affected by HIV/AIDS) and secondary, or existing, research. Staff used the findings to plan and target the campaign strategy and message development.

A key component for the first year of the campaign was to engage “early adopters,” those individuals and organizations that represent target audiences and are currently involved in HIV/AIDS prevention and treatment efforts. Roundtable discussions were held with leaders in the African-American and Hispanic communities to refine strategies and to engage participants in ongoing activities, such as materials development and outreach.

In coordination with NIAID’s HIV Vaccine Trials Network, DAIDS implemented an advertising campaign targeting opinion leaders, especially in communities most affected by HIV/AIDS, along with a substantial print and broadcast outreach that publicly reveals key messages about HIV vaccine research. Workshops on HIV vaccine research were featured at scientific conferences, including the Conference on Retroviruses and Opportunistic Infections.

## RESEARCH PLANNING

NIAID has a long-standing tradition of rigorous and prospective research planning, involving the development and prioritization of specific research initiatives on an annual basis and long-range, strategic planning. NIAID's planning process was cited as a model by the Institute of Medicine in its 1998 report titled *Scientific Opportunities and Public Health Needs: Improving Priority Setting at the National Institutes of Health*. The two pillars of this research planning process are the annual Winter Program Review (WPR) and the Summer Policy Retreat (SPR).

### Program Reviews

NIAID's annual program reviews provide an opportunity to focus on future research opportunities and to review proposed research initiatives for new and ongoing research programs.

The specific objectives of the annual program reviews follow:

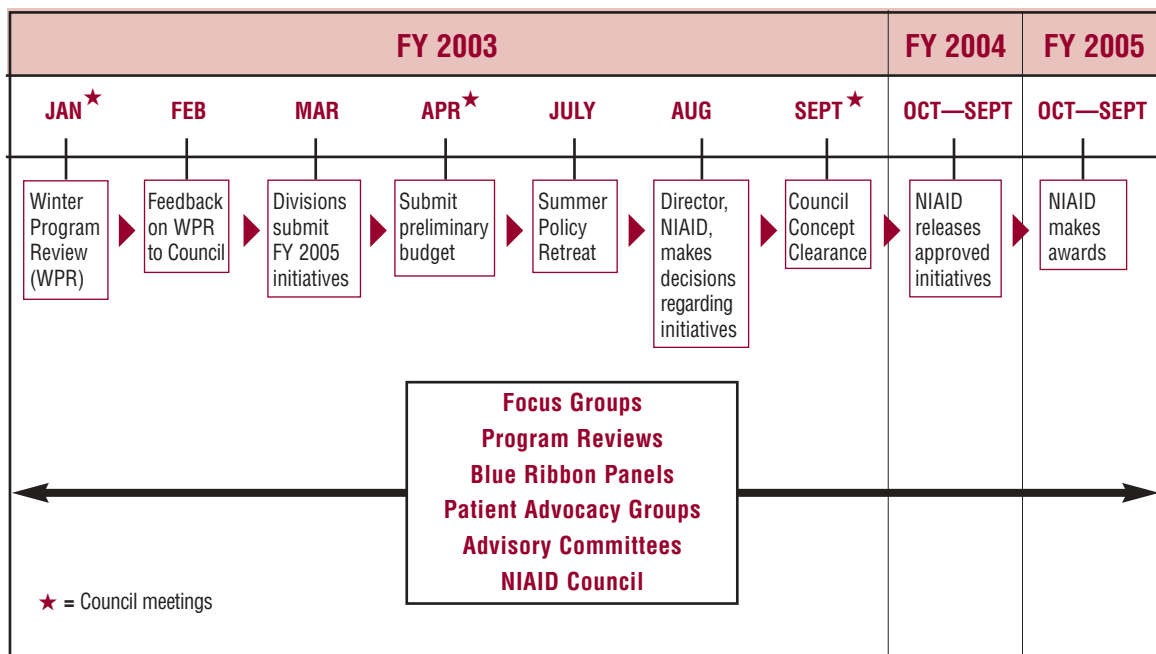
- Identify major public health, scientific, legislative, and budget directions that will influence NIAID programs;
- Discuss the scientific framework for and priority of new and ongoing research programs in the context of the above factors; and
- Use this information to make decisions about research activities and initiatives to be implemented in the future budget year.

### Policy Retreats

The planning process is further enriched through annual policy retreats that provide opportunities for the following:

- Focus on broad scientific issues, opportunities, gaps, and directions;
- Identify the basis for scientific opportunities and gaps;

## NIAID PRIORITY-SETTING PROCESS



- Ensure that scientific planning addresses the interests and priorities of the Congress, the Administration, the Department of Health and Human Services (DHHS), and the NIH Director;
- Propose approaches for responding to newly identified opportunities and needs;
- Identify the implications of changes in scientific or programmatic direction; and
- Prioritize newly identified opportunities and needs within the future budget year.

Throughout the year, NIAID convenes scientific workshops, blue ribbon panels, and program reviews to evaluate progress and to determine future needs and opportunities for the many diseases and areas of research within the Institute's purview. The NIAID Director and each research division consult extensively with NIAID stakeholders, including scientific experts, professional societies, and patient advocacy groups, to develop long-range, strategic plans as well as specific research initiatives. Areas of emphasis articulated in strategic plans, as well as those identified by DHHS, the NIH, Congress, the White House, and others, also help shape the Institute's decisionmaking and priority-setting process for new and continuing research programs.

Planning for future research initiatives is a multistep process that begins 2 years in advance of the projected implementation date. At each step in the process, the concepts for research initiatives are reviewed and refined. Concepts are first subjected to internal discussion during the annual program review, followed by a second level of review and clearance by the National Advisory Allergy and Infectious Diseases Council. Approved

concepts are then developed by NIAID staff into various forms of grant and contract solicitations and announced to the scientific community. Proposed research projects are then peer reviewed and awarded on the basis of scientific merit, program relevance, and need.

## Strategic Planning

NIAID's comprehensive strategic plan, *NIAID: Planning for the 21st Century*, is the product of an intensive effort that included a task force of national experts. The plan describes broad-based priorities to guide NIAID programs, policies, and initiatives through the next 3 to 5 years. The cornerstones of the plan are (1) immune-mediated diseases; (2) human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS); (3) emerging infectious diseases and global health; and (4) vaccines. The full text of the plan can be accessed at [www.niaid.nih.gov/strategicplan](http://www.niaid.nih.gov/strategicplan).

The Institute's guiding principles for global health research are articulated in the *NIAID Global Health Research Plan for HIV/AIDS, Malaria, and Tuberculosis*. This plan identifies short-term, intermediate, and long-term research goals to address these devastating international killers. The plan can be accessed at [www.niaid.nih.gov/publications/globalplan.htm](http://www.niaid.nih.gov/publications/globalplan.htm).

Since the anthrax mail attacks of 2001, biodefense research has become a major component of NIAID's mission. The vigorous growth of the NIAID biodefense program is guided by expert recommendations and an intricate strategic planning process. In 2002, NIAID convened the first Blue Ribbon Panel

on Bioterrorism and Its Implications for Biomedical Research to assist in developing the *NIAID Strategic Plan for Biodefense Research*, the *NIAID Biodefense Research Agenda for Category A Agents*, and the *NIAID Biodefense Research Agenda for Category B and C Priority Pathogens*. The strategic plan emphasizes basic research on microbes, host defense mechanisms, and the development of drugs, vaccines, and diagnostics. The biodefense research agendas articulate immediate and longer term goals for research on Category A pathogens, which include smallpox, anthrax, Ebola virus, plague, botulinum toxin, tularemia, Marburg virus, Rift Valley fever, and Lassa virus, and goals for research on Category B and C priority pathogens. The agendas also address the research resources, facilities, and scientific manpower needed to conduct basic and applied research on these potential agents of bioterrorism. Both the strategic plan and the research agendas can be accessed at [www.niaid.nih.gov/publications/bioterrorism.htm](http://www.niaid.nih.gov/publications/bioterrorism.htm). Tremendous progress has been made since these reports were first released. NIAID has

increased the breadth and depth of biodefense research and has made progress in meeting the specific goals of the Blue Ribbon Panel. The *NIAID Biodefense Research Agenda for CDC Category A Agents Progress Report* describes the progress made toward addressing the immediate goals outlined in the research agenda and can be accessed at [www.niaid.nih.gov/biodefense/research/category\\_A\\_Progress\\_Report.pdf](http://www.niaid.nih.gov/biodefense/research/category_A_Progress_Report.pdf).

Another important strategic planning effort focuses on how to further stimulate research activities to address health disparities. The *NIAID Strategic Plan for Addressing Health Disparities* articulates specific action plans for reducing disparities through (1) research on HIV/AIDS, transplantation, autoimmune diseases, tuberculosis, hepatitis C virus, and sexually transmitted diseases; (2) support for research infrastructure and research training; and (3) support for community outreach projects. The full text of the health disparities strategic plan can be accessed at [www.niaid.nih.gov/healthdisparities/niaid\\_hd\\_plan\\_final.pdf](http://www.niaid.nih.gov/healthdisparities/niaid_hd_plan_final.pdf).

## DIVISION OF ACQUIRED IMMUNODEFICIENCY SYNDROME

### Mission

The Division of Acquired Immunodeficiency Syndrome (DAIDS) ([www.niaid.nih.gov/daids](http://www.niaid.nih.gov/daids)) was formed in 1986 to develop and implement the national research agenda to address the HIV/AIDS epidemic. Specifically, the mission of DAIDS is to help ensure an end to the HIV/AIDS epidemic by increasing basic knowledge of the pathogenesis and transmission of the human immunodeficiency virus (HIV), supporting the development of therapies for HIV infection and its complications and co-infections, and supporting the development of vaccines and other prevention strategies. DAIDS accomplishes its mission through planning, implementing, managing, and evaluating programs in (1) fundamental basic research, (2) discovery and development of therapies and treatment strategies for HIV infection, its complications, and co-infections, and (3) discovery and development of vaccines, topical microbicides, and other prevention strategies.

To achieve its mission, DAIDS actively supports and promotes public and private-sector alliances to maximize available research opportunities and resources. By surveying developments in key research areas, DAIDS assesses ongoing needs in biomedical research as well as requirements for outreach activities and training scientific investigators. As part of this process, DAIDS works with advisory groups and community and health professional organizations, evaluating and redirecting program emphasis to respond to changing global research needs. DAIDS' commitment to advancing research worldwide has led to a

steady increase in international activities, particularly in the developing world. This situation reflects the global impact of HIV/AIDS and the critical need for cost-effective prevention and treatment strategies in those limited-resource regions where more than 95 percent of HIV infections occur.

### Scientific Areas of Focus

#### Basic Research

Basic research continues to increase our understanding of the biology of HIV and how the immune system responds to the virus. Knowledge gained from these studies enhances the ability of researchers to create new therapeutic agents and vaccines to combat HIV infection. DAIDS is studying the natural history of HIV progression in men and women through its cohort studies. The Women's Interagency HIV Study (WIHS) is a collaborative, multi-site longitudinal study designed to investigate the impact of HIV infection on women in the United States (<http://statepiaps.jhsph.edu/wihs>). The Multicenter AIDS Cohort Study (MACS) is an ongoing study of the natural history of HIV infection in homosexual men (<http://statepi.jhsph.edu/mac/mac.html>). MACS began in 1983 and was able to capture information on a large number of men who seroconverted while enrolled in the study. The Women and Infants Transmission Study (WITS) ([www.niaid.nih.gov/daids/wits.htm](http://www.niaid.nih.gov/daids/wits.htm)) examines the natural history of HIV disease in the context of pregnancy, focusing on clinical, laboratory, and psychosocial aspects of maternal/infant transmission. WITS currently is investigating the long-term consequences of exposure to HIV and antiretrovirals in the children born during the study. Programs that study men and women separately give

researchers the ability to make gender-based comparisons, thereby adding value to the analyses.

DAIDS also supports a large portfolio of investigator-initiated grants in HIV pathogenesis in a variety of areas, including mechanisms of viral entry and infection; the structure, function, and mechanism of action of viral genes and proteins; the roles of cellular accessory molecules in replication; the immunologic and virologic events controlling primary infection and formation of the latent reservoirs; development of *in vitro* and *ex vivo* assays to monitor virus growth, immune responses, and reservoir status during HIV disease; animal models; and genetic analysis of host factors that modulate viral infection or disease progression. These grants serve as a source of new knowledge that fuels the discovery of new drugs and vaccine concepts.

To further stimulate the pursuit of new ideas, DAIDS funds a number of targeted programs, such as the Innovation Grants for AIDS Research Program, which provides limited funds for 2 years to help advance novel ideas that lack extensive preliminary data. The Novel HIV Therapies: Integrated Preclinical/Clinical Program is another example of how DAIDS supports the discovery, development, and evaluation of innovative HIV treatment concepts through multidisciplinary research and formal corporate partnering.

The Centers for AIDS Research (CFAR) program, also supported by DAIDS, provides administrative and resource support and emphasizes the importance of translational research and collaborations between basic and clinical investigators.

To assist the research community, NIAID supports the NIH AIDS Research and Reference Reagent Program, which is now in its 16th year of operation. The reagent program continues to provide the scientific community worldwide with a critical and unique resource for biologics and chemicals.

The Division's basic research efforts have yielded significant scientific information about the basic biology of HIV and the immune response to HIV infection. For example, DAIDS-funded investigators have identified the critical steps of how HIV uses the host machinery to enter and exit the cell, as well as the existence of multiple, persistent HIV reservoirs even with the use of highly active antiretroviral therapy (HAART). Although much has been learned in recent years, questions remain about the molecular interactions involved in the regulation of HIV expression and replication and about why the host immune response is not fully effective in controlling the infection. Information about how the virus attacks the body and how the body defends itself is critical to providing additional targets against which therapeutic interventions and vaccines can be directed.

### **Therapeutics**

The Division's therapeutics research program supports the discovery and development of effective therapies for HIV/AIDS and associated complications and co-infections by facilitating and expediting research on highly promising candidate agents and novel therapeutic concepts. Through strategic planning and funding, DAIDS supports research on potential new cellular and viral therapeutic targets, enhanced formulations of existing agents, and treatment regimens to

improve adherence, minimize toxicities, and impede emergence of resistance. In addition, the Division supports research on approaches to restore the immune system, to protect uninfected cells, and to improve assays to measure pathogen load and host immunity. Investigations include basic research and drug discovery, preclinical development of candidate therapeutics including therapeutic vaccine research, and advanced clinical testing in humans. The evaluation of new drugs and therapeutic agents in people is a critical aspect of therapeutic research. These clinical studies define new agents that are effective against HIV and its associated complications and clarify how best to use these drugs. Human testing of anti-HIV therapeutics is carried out in three large DAIDS-sponsored clinical trials networks: the Adult AIDS Clinical Trials Group (AACTG) (<http://aactg.s-3.com>), the Pediatric AIDS Clinical Trials Group (PACTG) (<http://pactg.s-3.com>), and the Terry Bein Community Programs for Clinical Research on AIDS (CPCRA) ([www.cpcra.org](http://www.cpcra.org)). In addition, research on acute HIV infection is conducted through the Acute HIV Infection and Early Disease Research Program (<http://aiedrp.org>). All of these DAIDS-supported clinical trials networks, especially the AACTG, are expanding their capabilities to conduct clinical trials in resource-poor developing countries. DAIDS also supports a large multicenter clinical trial titled Evaluation of Subcutaneous Proleukin in a Randomized International Trial (ESPRIT) to evaluate the effectiveness of interleukin-2 (IL-2) in maintaining immune function in addition to anti-HIV therapy and the impact of IL-2 on HIV disease progression.

DAIDS-sponsored therapeutics research has already had a dramatic impact on our understanding of the pathogenesis and clinical management of HIV infection over the past decade. Studies conducted by DAIDS-funded clinical trials research networks have (1) helped to define national and international guidelines for the treatment of primary HIV infection and associated opportunistic infections as well as prophylactic regimens for these secondary infections, (2) identified biological markers, such as CD4+ counts, and viral load for predicting a drug's effectiveness and disease progression, and (3) demonstrated the use of antiretroviral drugs for preventing mother-to-child transmission (MTCT) of HIV.

Studies have shown that HAART regimens, including reverse transcriptase and potent protease inhibitors, are capable of suppressing HIV viral load to undetectable levels in many infected individuals and partially restoring immune function. Such regimens have had a dramatic impact on HIV mortality in this country. Nonetheless, treatment failures occur as a result of the development of resistance to or noncompliance with these complicated and often toxic regimens. Moreover, damage to the immune system is incompletely reversed. To address these issues, DAIDS conducts studies of various treatment strategies in HIV-infected people with progressive disease and multidrug-resistant virus. For example, one study (CPCRA 064) evaluated the use of structured treatment interruption in this subset of HIV-infected individuals. In addition, there is an ongoing, urgent need for new therapeutic agents and regimens, new ways to boost immunity, and ways to rebuild and replace immunity lost to HIV infection. Toward that

end, DAIDS-funded research led to discovery of a therapeutic agent from a new class of anti-HIV drugs, known as fusion inhibitors, which was recently approved by the Food and Drug Administration. Early data suggest, however, that the development of resistance will continue to be a problem as new agents are introduced into HAART regimens, necessitating the need for continued research in this area.

### ***Vaccine and Prevention Research***

The development of safe and effective vaccine and nonvaccine strategies for the prevention of HIV infection and AIDS is a high priority of NIAID. DAIDS supports all phases of the discovery and development of preventive HIV vaccines, including basic research, preclinical testing, and human clinical testing of candidate HIV vaccines.

Vaccine research and development is supported through an extensive portfolio of investigator-initiated research in basic virology, immunology, and microbiology.

In addition, several DAIDS programs support the interface of preclinical and clinical research. These resources stimulate the development of new vaccine concepts and ensure a rational, deliberate process for moving concepts through to clinical trials. Among the vaccine research programs supported by DAIDS that encourage development along various stages of the vaccine pipeline are the Innovation Grants for Approaches in HIV Vaccine Research Program, which encourages novel and innovative concepts in vaccine discovery and development; the HIV Vaccine Research and Design Program (HIVRAD), which supports

concepts that have evolved beyond early testing and “matured” innovation grants; and the Integrated Preclinical/Clinical AIDS Vaccine Development Program (IPCAVD), which supports the iterative processes of vaccine concept refinement and testing. Through this program, research groups investigate promising vaccine concepts that are amenable to product development and are likely to lead to preliminary studies in humans. In addition, HIV Vaccine Design and Development Teams (HVDDT), consisting of consortia of scientists from industry and/or academia, identify specific promising vaccine concepts amenable to targeted development.

Clinical evaluations in humans provide the only way of determining whether a vaccine candidate could trigger a safe and effective anti-HIV response in people. NIAID-supported clinical trials of preventive HIV vaccines are carried out in the HIV Vaccine Trials Network (HVTN) ([www.hvtn.org](http://www.hvtn.org)). HVTN conducts all phases of clinical trials to determine the safety, immunogenicity, and efficacy of candidate preventive HIV vaccines. As HVTN concludes its fourth year, it has made progress towards its goal of developing and conducting a comprehensive HIV vaccine clinical research agenda that addresses the scientific and public health needs and builds on scientific opportunities in the field of HIV vaccine research. HVTN has undergone significant expansion to support international trials, instituted highly functioning protocol development teams, developed new vaccine concepts and advanced new protocols, reorganized laboratory programs, and developed an extensive training program. (Additional HVTN information is located in the Vaccine Research and Development

section of Selected Scientific Areas of Research on page 139.)

DAIDS also supports research on other biomedical and behavioral approaches to prevent the spread of HIV/AIDS. These approaches include drugs or vaccines that prevent MTCT of HIV, microbicides for preventing sexual transmission of HIV, interventions that reduce behaviors that expose people to HIV, programs to reduce intravenous drug abuse, measures to control other sexually transmitted diseases, and antiretroviral therapies to reduce the spread of HIV from infected people to their partners. NIAID-supported prevention clinical trials are centered in the HIV Prevention Trials Network (HPTN) ([www.hptn.org](http://www.hptn.org)). HPTN, formed in 2000 with additional support from the National Institute of Child Health and Human Development, the National Institute of Mental Health, and the National Institute on Drug Abuse, is a global, multicenter network dedicated to nonvaccine prevention research. Additional HPTN information is located in the AIDS section on page 42.

The Division's comprehensive vaccine and prevention program has led to a number of significant scientific advances in vaccine and prevention research. In the past, NIAID-supported researchers have improved the ability of vaccines to induce an antibody response by modifying the envelope protein, further explained the envelope structure of HIV, advanced our understanding of the role of cellular responses in controlling HIV, developed improved assays for measuring cytotoxic T lymphocytes, developed new and better animal models for testing candidate vaccines, and evaluated promising candidates in animal and clinical studies.

To accelerate identification of effective vaccine candidates, future studies will address the significance of latently infected resting T cells, study immune responses induced by current vaccine candidates, and assess the impact of HIV and human leukocyte antigen diversity. With regard to other prevention research, new microbicides will be evaluated for their safety and ability to prevent the sexual transmission of HIV. Moreover, building on past research that identified an inexpensive regimen to reduce HIV transmission at birth, NIAID will continue to evaluate other practical regimens for preventing MTCT of HIV, especially during breastfeeding.

Lastly, because the majority of new infections are occurring in the developing world, NIAID's prevention and treatment research activities are conducted on a global scale. In fiscal year 2001, NIAID launched the Comprehensive International Program of Research on AIDS (CIPRA). CIPRA provides long-term support directly to developing countries to plan and implement a comprehensive HIV/AIDS prevention and research agenda relevant to their populations and to strengthen the infrastructure required to carry out this research. As their national research capacity grows, countries can seek renewable CIPRA funding for multidisciplinary research projects and/or clinical trials for HIV prevention and/or treatment. In the past year, CIPRA awarded seven planning and organizational grants to Argentina, Brazil, Egypt, Georgia, Kenya, Malaysia, and Mozambique and one large multiproject grant to Senegal. For more information, visit the Web site at [www.niaid.nih.gov/daids/cipra](http://www.niaid.nih.gov/daids/cipra).

## Major Programs and Networks

- Acute HIV Infection and Early Disease Research Program
- Adult AIDS Clinical Trials Group
- AIDS Research and Reference Reagent Program
- Centers for AIDS Research
- Comprehensive International Program of Research on AIDS
- HIV Prevention Trials Network
- HIV Vaccine Design and Development Teams
- HIV Vaccine Developmental Resources Contracts
- HIV Vaccine Research and Design Program
- HIV Vaccine Trials Network
- Innovation Grants for AIDS Research Program
- Innovation Grants for Approaches in HIV Vaccine Research Program
- Integrated Preclinical/Clinical AIDS Vaccine Development Program
- Integrated Preclinical/Clinical Program for HIV Topical Microbicides
- Laboratory Methods to Assess Responses to HIV Vaccine Candidates
- Liver and Pancreatic Disease in HIV Infection Program
- Microbicide Preclinical Development Program
- Multicenter AIDS Cohort Study
- National Cooperative Drug Discovery Groups—Opportunistic Infections
- New Technologies for HIV and HIV Vaccine-Related Research Program
- Novel HIV Therapies: Integrated Preclinical/Clinical Program
- Pediatric AIDS Clinical Trials Group
- Simian Vaccine Evaluation Units
- Terry Bein Community Programs for Clinical Research on AIDS
- Therapeutics Research on AIDS-Associated Opportunistic Infections and Malignancies Program
- Women and Infants Transmission Study
- Women’s Interagency HIV Study

## DIVISION OF ALLERGY, IMMUNOLOGY, AND TRANSPLANTATION

### Mission

The human immune system is composed of intricate networks of specialized cells, molecules, and organs that act together to defend the body against foreign invaders, such as viruses, bacteria, and fungi, that may cause disease. However, aberrant immune responses play a critical role in the development of immune-mediated diseases, which include asthma and allergic diseases, autoimmune disorders, primary immunodeficiencies, and rejection of transplanted solid organs, tissues, and cells. Collectively, these chronic diseases affect tens of millions of Americans, resulting in considerable morbidity, mortality, pain and suffering, and high medical costs. Immune-mediated diseases cross many clinical specialties, and knowledge of the immune system and its role in disease is increasingly important in the clinical management of patients with these disorders.

The past two decades of focused research on the immune system have resulted in major advances in understanding the mechanisms that underlie a range of immune-mediated diseases. These advances in conceptual understanding now provide realistic opportunities for improvement in the diagnosis, treatment, and prevention of many of these diseases. The Division of Allergy, Immunology, and Transplantation (DAIT) ([www.niaid.nih.gov/research/dait.htm](http://www.niaid.nih.gov/research/dait.htm)) promotes and supports a broad range of research that seeks to further our understanding of the immune mechanisms underlying immune-mediated diseases and to

translate this basic knowledge to clinical applications that will benefit individuals affected by these diseases. The ultimate goal of DAIT's research program is the development of effective approaches for the treatment and prevention of immune-mediated diseases.

The Division supports research initiated by individual investigators; multidisciplinary program projects that explore the mechanisms of immune-mediated diseases, transplantation immunology, and the basic biology of the immune system; clinical research programs to assess the safety and efficacy of new therapeutic approaches; and interdisciplinary cooperative research centers.

DAIT supports basic, preclinical, and clinical research to enhance our understanding of the causes of immune-mediated diseases and to apply this knowledge to the development of improved approaches to disease diagnosis, treatment, and prevention through demonstration and education research projects. DAIT evaluates the effectiveness of behavioral and educational interventions to promote health and prevent disease in defined populations.

DAIT's research programs are placing increasing emphasis on the preclinical and clinical development of new tolerogenic and immunomodulatory approaches for the treatment and prevention of transplant rejection, asthma and allergic diseases, and autoimmune diseases. Another area of program growth involves the application of emerging technologies to further our understanding of immunologic principles and to develop diagnostic and prognostic tools and biomarkers of disease activity and therapeutic effect.

## Scientific Areas of Focus

### ***Asthma and Allergic Diseases***

Allergic diseases, including asthma, are among the major causes of illness and disability in the United States. Studies to examine the causes, pathogenesis, diagnosis, treatment, and prevention of allergic diseases represent a major focus of DAIT's basic and clinical research portfolio. DAIT's national network of Asthma and Allergic Diseases Research Centers focuses on the underlying immune mechanisms involved in these disorders and on approaches to improve diagnosis and treatment. In fiscal year (FY) 2002, DAIT established the Inner-City Asthma Consortium: Immunologic Approaches to Reduce Asthma Severity, a network of basic scientists and clinical investigators to evaluate the efficacy of promising immune-based therapies to reduce asthma severity and prevent disease onset in inner-city children.

### ***Autoimmune Diseases***

DAIT supports a broad range of basic and clinical research programs in autoimmunity. Basic research focuses on understanding the genetics of autoimmunity, elucidating the mechanisms of self-tolerance, developing approaches to induce self-tolerance, and characterizing pathways of immune-mediated tissue destruction. Knowledge gained from basic studies provides the rationale for developing clinical tests to diagnose autoimmune diseases and novel treatments for ongoing disease.

### ***Basic and Clinical Immunology***

The Division's basic immunology investigations focus on the properties, interactions, and functions of immune system cells and the substances produced by those cells. Information generated through this research provides the knowledge base necessary to develop treatment and prevention strategies. To promote research on these fundamental aspects of immune system functioning, DAIT supports multidisciplinary program projects on the biology of the immune system, including the basic biology of the immune responses for vaccine research, transplantation immunology and chronic rejection, and autoimmunity. Clinical immunology studies focus on immune-mediated diseases, including autoimmune diseases, asthma and allergic diseases, acute and chronic transplant rejection, and immunodeficiencies. Research in these clinical areas is supported by program projects on mucosal immunity, autoimmune diseases, and methods of immune intervention. In FY 2003, the Division recompleted and expanded the Autoimmunity Centers of Excellence program, which conducts clinical trials of new immune-based therapies for autoimmune diseases and basic research to understand the causes of these diseases. In addition, support is provided for research on the causes and underlying immune mechanisms of various inherited immunodeficiency diseases, such as severe combined immunodeficiency disease. In FY 2003, the Division funded the Primary Immunodeficiency Research Consortium, which will help prioritize and coordinate research directions and develop new resources for the study of these comparatively rare disorders.

## ***Immune Tolerance***

Immune tolerance is a high priority for NIAID, and, as part of a broad-based, long-range plan to accelerate research in this important area, DAIT established the Immune Tolerance Network (ITN). ITN is an international consortium of more than 80 investigators in the United States, Canada, and Europe dedicated to the clinical evaluation of novel, tolerance-inducing therapies in autoimmune diseases, asthma and allergic diseases, and rejection of transplanted organs, tissues, and cells. The goal of these therapies is to “re-educate” the immune system to eliminate injurious immune responses and graft rejection while preserving protective immunity against infectious agents. ITN also conducts integrated studies on the underlying mechanisms of these approaches and develops and evaluates markers and assays to measure the induction, maintenance, and loss of tolerance in humans. More information about ITN is available on its Web site at [www.immunetolerance.org](http://www.immunetolerance.org).

## ***Transplantation***

The Division’s research in transplantation immunobiology is focused on understanding the mechanisms whereby the immune system recognizes and either accepts or rejects transplanted organs, tissues, and cells; developing preclinical models to evaluate promising therapies to prevent and treat graft rejection; conducting clinical trials of new therapeutic agents and approaches to improve graft survival and function; and understanding the pathogenesis of chronic graft failure and developing new treatments and preventive

strategies. Clinical research to evaluate new therapeutic approaches to improve kidney engraftment and survival is carried out through the Cooperative Clinical Trial in Pediatric Kidney Transplantation.

## **Primary Research Areas**

### ***Asthma and Allergic Diseases***

- Asthma and Allergic Diseases Research Centers
- Inner-City Asthma Consortium

### ***Autoimmune Diseases***

- Autoimmune Diseases Prevention Centers
- Autoimmunity Centers of Excellence

### ***Basic and Clinical Immunology***

- Human Immunology Centers of Excellence
- Hyperaccelerated Award/Mechanisms in Immunomodulation Trials
- Vaccine Immunology Basic Research Centers

### ***Immune Tolerance***

- Immune Tolerance Network
- Innovative Grants on Immune Tolerance
- Non-Human Primate Immune Tolerance Cooperative Study Group

### ***Transplantation***

- Cooperative Clinical Trial in Pediatric Kidney Transplantation
- Immunopathogenesis of Chronic Graft Rejection

## DIVISION OF MICROBIOLOGY AND INFECTIOUS DISEASES

### Mission

The Division of Microbiology and Infectious Diseases (DMID) supports extramural research to control and prevent diseases caused by virtually all human infectious agents except HIV. DMID supports a wide variety of projects spanning the spectrum from basic research through applied research, along with the development and clinical evaluation of new drugs, vaccines, and diagnostics. NIAID also funds projects to sequence the full genomes of a number of medically important microbes, which can be exploited in many ways, for example, to trace microbial evolution, to locate targets for vaccine and drug development, and to identify mutations that contribute to drug resistance.

Research areas in basic bacteriology and mycology include molecular structure and function, genetics, biochemical composition, and physiologic and biochemical processes. Studies on these pathogens extend basic insights to identify vaccine candidate antigens and drug targets and to examine mechanisms of infection, pathogenicity, and virulence. Areas of particular interest include streptococci, pneumonia, nosocomial (hospital-acquired) infections, fungal infections, antibiotic resistance, bacterial sexually transmitted infections (STIs), and bacterial diarrheas.

Research areas in virology include molecular structure and function, genetics, synthesis, and reproduction of viruses; characterization of viral proteins and nucleic acids; mechanisms of pathogenicity, latency, persistence, and reactivation; interactions with immune

systems; and vaccine development. Basic information is being used to combat important viral diseases such as influenza, herpes, congenital cytomegalovirus infection, hepatitis, and viral diarrheas.

Research on parasites involves the application of biochemical, genetic, and immunologic approaches. Studies of parasites are leading to the identification of protective and diagnostic antigens and to the development of more effective drugs. In addition, studies of arthropod vectors are aimed at controlling the transmission of important pathogens such as the malaria parasite.

One of the primary goals of the Division is to develop new and improved vaccines and strategies for vaccine delivery for the entire spectrum of infectious agents: bacteria, viruses, fungi, and parasites. Since 1981, DMID has supported a program for the accelerated development of new vaccines to direct advances in molecular biology, immunology, genetics, and epidemiology. An integral component of these efforts is vaccine safety, which is evaluated in every vaccine clinical trial sponsored by NIAID.

DMID also supports numerous efforts aimed at developing more effective diagnostic tools for infectious diseases. Examples include diagnostic tests for STIs and Lyme disease and the development of antimicrobial resistance markers.

Finally, DMID maintains a drug development program that supports research at three levels: drug discovery (accomplished by screening and by targeted molecular research), preclinical evaluation (in animal models of human infections), and clinical trials (evaluation of new therapies in humans).



































