

NIAID-SUPPORTED REPOSITORIES

NIAID's intramural and extramural researchers have developed an ample supply of resources and reagents that are used by scientists worldwide for basic research, applied research to develop therapeutics and vaccines, and commercialization. These resources include peptides, cell lines, monoclonal antibodies, viral vectors, and animal models.

Division of Acquired Immunodeficiency Syndrome (DAIDS)

NIH AIDS Research and Reference Reagent Program

The NIH AIDS Research and Reference Reagent Program acquires and distributes state-of-the-art reagents for AIDS-related research and makes these reagents available to qualified investigators throughout the world. It has grown significantly during the past 16 years and now has more than 5,200 reagents for public distribution. The AIDS Research and Reference Reagent Program also encourages and facilitates technology transfer through workshops, publication of methods, and provision of standardized panels and protocols; facilitates commercial development of reagents; and participates as an AIDS Collaborating Center of the World Health Organization (WHO).

The reagent program has immortalized and expanded white blood cells from more than 7,000 specimens from DAIDS-supported cohort studies of HIV-infected people, including the Multicenter AIDS Cohort Study, Women's Interagency HIV Study, and Women and Infants Transmission Study. These preserved cells will provide a source of DNA for future studies of genetic factors in HIV disease. By making these specimens available to the scientific community, DAIDS fosters collaboration among scientific investigators to promote further progress in the detection, treatment, and prevention of HIV

disease. More than 2,400 scientific publications have resulted, in part, from the use of reagents supplied by the NIH AIDS Reagent Program. To date, scientists from the United States and 65 foreign countries have been registered to receive reagents. In 2004 alone, more than 14,000 vials of reagents were distributed.

In 2003, the reagent program contract jump started the acquisition and distribution of urgently needed quality-controlled reagents for research on biodefense and emerging infectious disease agents such as anthrax and SARS.

Additional information is available at www.aidsreagent.org.

Vaccine Reagent Resource

Through the Vaccine Reagent Resource, DAIDS provides resources for the production or procurement of reagents essential for vaccine studies conducted by the HIV Vaccine Trials Network and the Simian Vaccine Evaluation Units, as well as other priority vaccine studies. These resources also provide for the quality assurance/control testing of reagents. Additional information is available at <http://www.niaid.nih.gov/daids/vaccine/reagentres.htm>.

Human HIV Specimens

Research on HIV transmission and disease progression patterns greatly benefits from a centralized system for receiving, cataloging, storing, and distributing samples collected from various well-characterized cohorts of HIV-infected individuals. NIAID provides state-of-the-art storage and computerized inventory management of specimens from domestic and international HIV epidemiology studies, HIV therapeutic and vaccine trials, and other prevention research studies through its central repositories.

Division of Allergy, Immunology, and Transplantation (DAIT)

Multiple Autoimmune Disease Genetics Consortium (MADGC)

Different autoimmune diseases are often found within a single family, suggesting common genetic contributions to the diseases. MADGC is a repository of genetic and clinical data and specimens from families in which two or more individuals are affected by two or more distinct autoimmune diseases. This repository provides well-characterized materials for use in research aimed at identifying the genes involved in autoimmune diseases. MADGC began enrolling families in May 2000. Additional information is available at www.madgc.org.

North American Rheumatoid Arthritis Consortium (NARAC)

NARAC is a collaborative registry and repository of information on families with rheumatoid arthritis. The NARAC database contains information on 902 families, encompassing 1,522 patient visits. Of the 902 families, data for more than half have been validated, including 600 affected sibling pairs. The family registry and the repository samples should facilitate the characterization of the genes underlying susceptibility to rheumatoid arthritis and are available to all investigators. More information can be found at www.naracdata.org. This registry is cosponsored by the National Institute of Arthritis and Musculoskeletal and Skin Diseases and the Arthritis Foundation.

Primary Immunodeficiency Diseases Registry (PIDR)

PIDR was established by NIAID to maintain clinical information on patients in the United States affected by primary immunodeficiency diseases. For each disease, the registry collects information on the natural course of the disease, including early and late complications, effects of therapy, and causes of death. The diseases included in the registry are chronic

granulomatous disease, hyper-IgM syndrome, severe combined immunodeficiency disease, X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, common variable immunodeficiency, leukocyte-adhesion deficiency, and DiGeorge syndrome. Researchers may apply to the registry to request contact information for physicians who are caring for primary immunodeficiency disease patients. In 2003, a repository also was established. The repository will contain cell lines and DNA from patients with primary immunodeficiency diseases. Researchers may apply to the repository for access to this material. For PIDR-related information see http://www.primaryimmune.org/med_programs/pid_registry.htm.

National MHC Tetramer Core Facility

In FY 1998, NIAID established a contract facility to provide researchers with peptide-major histocompatibility complex (MHC) tetrameric molecules for analyzing antigen-specific T cell responses. Because T cells are central to virtually all immune responses, this technology is applicable to studies in many areas including basic immune mechanisms, infectious diseases, vaccination, autoimmunity, transplant rejection, and tumor therapy. By centralizing the production of these tetramers, individual, defined peptide-MHC molecules can be produced economically and can be made available to investigators at greatly reduced expense. The MHC tetramer core facility is located at Emory University in Atlanta, Georgia, under the direction of Dr. John Altman.

Division of Intramural Research (DIR)

Transgenic and Gene-Targeted Mice Repository

DIR, in collaboration with DAIT, supports facilities for the acquisition, breeding, and distribution of transgenic and gene-targeted (knockout) mice, which are mice that are genetically engineered to serve as animal models for human diseases that do not occur

in nonhuman species. The repository provides these mice to both intramural and extramural investigators through the NIAID/Taconic exchange programs for use in research and for development of clinical therapies in various infectious and immunologic diseases.

Division of Microbiology and Infectious Diseases (DMID)

Global Health

Malaria Research and Reference Reagent Repository (MR4)

The malaria repository was established to acquire, produce, and distribute malaria research reagents, reference materials, and other information to qualified investigators throughout the world. A major component of the program is the quality control of reagents, standardization of protocols, and exploration of new technologies. International workshops and training sessions will be organized to stimulate and support both laboratory-based and field-based research. The long-term goal of the repository program is to promote technology transfer as well as to facilitate research leading to commercial development of reagents for malaria diagnostics, prevention, and treatment. NIAID established the repository in support of the Multilateral Initiative on Malaria, a research capacity-strengthening program in partnership with other national and international organizations. Additional information is available at www.malaria.mr4.org.

Tuberculosis Research Materials and Vaccine Testing

Mycobacterium tuberculosis (*M.tb*), the organism responsible for tuberculosis (TB), is difficult and time-consuming to grow and, because it is transmitted via aerosols, should be studied only in appropriate biohazard facilities. DMID funds a repository to provide *M.tb*-derived materials to qualified TB investigators worldwide in basic and clinical research areas, allowing work to begin quickly and eliminating the need for

these investigators to have their own biohazard facilities. DMID also supports the screening of potential anti-TB vaccine candidates, which are provided by individual researchers, in established small-animal, low-dose, aerosol-challenge models. Additional information is available at www.cvmb.colostate.edu/microbiology/tb/top.htm.

Leprosy Research Support and Armadillo Colony

Despite the availability of multidrug regimens to cure leprosy, leprosy has remained a problem worldwide. A major obstacle in leprosy research is the fact that *Mycobacterium leprae*, the organism responsible for leprosy, cannot be cultured in laboratory media and therefore has to be propagated in animals. To help alleviate this problem, DMID supports the maintenance of an armadillo colony, one of the best animal model systems of *M. leprae* infection and disease. DMID also funds a repository of viable *M. leprae* and purified, defined reagents derived from *M. leprae*, which are available to researchers worldwide. Additional information is available at www.cvmb.colostate.edu/mip/leprosy/index.html.

Schistosomiasis and Filariasis Research Repositories

For more than 30 years, NIAID contracts have supported two helminth resources that serve the research community. The Schistosome Resource Center (www.schisto-resource.org) is maintained by the Biomedical Research Institute (Dr. Fred Lewis, Principal Investigator), and the Filaria Resource Center is maintained by the University of Georgia (Dr. John McCall, Principal Investigator). Investigators worldwide can obtain schistosome or filaria life stages for research or teaching purposes. Selected materials, including molecular and genomic reagents, are made available to biochemists, immunologists, vector biologists, and others who cannot reasonably maintain their own life cycles due to lack of space, time, funding, or requisite expertise. Investigators can obtain parasites, vectors, and mammalian hosts free of charge, excluding shipping costs. In

addition to fostering schistosomiasis and filarial research, these two NIAID resources serve as valuable backup facilities for investigators who have experienced problems with their own established life cycles.

Pneumococcal Reference Laboratory

This laboratory provides reference and resource services and expertise to facilitate the evaluation of improved pneumococcal vaccines and other bacterial respiratory pathogens. A major objective is to establish a consensus assay and to improve and modify procedures for measuring antibody activity to pneumococci. The laboratory also provides radiolabeled polyribosylribose phosphate (PRP) and/or suitably derivatized PRP and purified PRP to laboratories for the performance of *Haemophilus influenzae* type B assays and for calibration of immunodiagnostic assays.

Viral Infections

Repository for Biological Reagents and Reference Standards

This repository stores and distributes serological and microbiological reagents for use as reference standards and for research in infectious and immunologic diseases. As a WHO Collaborating Center for Antiviral Drugs and Interferon, this NIAID repository is responsible for the storage and worldwide distribution of WHO international interferon standards and reference reagents.

***In Vitro* Antiviral Screening Program**

NIAID maintains a screening program to provide *in vitro* screens for evaluation of potential antiviral agents for inhibitory activity against herpesviruses (herpes simplex viruses 1 and 2, varicella-zoster virus, Epstein-Barr virus, cytomegalovirus, human herpesvirus 6 and 8), orthopoxviruses (vaccinia and cowpox), respiratory viruses (influenza A, influenza B, parainfluenza, respiratory syncytial virus, measles, rhinoviruses, adenoviruses, and severe acute respiratory syndrome coronavirus), viral

hemorrhagic fevers and encephalitic viruses (Venezulean equine encephalitis, Pichinde, Punta Toro, yellow fever, West Nile virus, and dengue fever), hepatitis B and C, BK virus, and papillomaviruses. These *in vitro* screens provide selective indexes of potential compounds, thus providing early information to guide selection and prioritization. Active compounds can then be evaluated against several virus strains and for assessment of pharmacologic properties.

World Reference Center for Emerging Viruses and Arboviruses

NIAID maintains the World Reference Center for Emerging Viruses and Arboviruses at the University of Texas Medical Branch at Galveston. The Center has reference virus sera and seed lots of various virus strains, which can be distributed to qualified researchers and facilities. Although focused primarily on arthropod-borne and rodent-borne viruses, other viral reagents are also available. This international program involves characterizing viruses transmitted to people and animals by mosquitoes and other arthropod vectors or animal hosts and researching the epidemiology of arboviruses and emerging viruses in the United States and in other countries. Center activities include (1) virus identification and characterization; (2) investigation and diagnosis of disease outbreaks; (3) preparation and distribution of certified virus stocks and reagents to qualified investigators/facilities; (4) development of new animal models of arboviral and other emerging diseases and studies of arboviral pathogenesis; (5) training of professional and technical personnel from any region of the world in arbovirus techniques; and (6) dissemination of information on arbovirus taxonomy, diagnostic techniques, and disease outbreaks. Because of the reference center's extensive virus reference collection, unique diagnostic capabilities, and contact with virologists and public health laboratories throughout the world, it plays an important role in the global surveillance network for emerging viral diseases.

Biodefense and Emerging Infectious Diseases

The Network on Antimicrobial Resistance in *Staphylococcus aureus* (NARSA)

NARSA is a multidisciplinary international network of basic scientists, clinical microbiologists, and clinical investigators that focuses on *S. aureus* and other staphylococcal species that exhibit antimicrobial resistance. NARSA is responsible for tracking and procuring staphylococcal isolates (including *S. aureus* and the coagulase-negative staphylococci) with reduced susceptibility to vancomycin (minimum inhibiting concentrations > 4 mg/ml) for inclusion in a central repository. A central repository of these isolates provides a standardized source of isolates for investigative studies. The strains collected for the NARSA repository are readily available to researchers. The well-characterized isolates collected and stored in the centralized NARSA repository, together with the registry database to which they are linked, provide the general scientific community with a valuable research resource for multidisciplinary investigation. Additional information is available at <http://www.narsa.net/content/default.jsp>.

In Vitro and Animal Models for Emerging Infectious Diseases and Biodefense

The *In Vitro* and Animal Models for Emerging Infectious Diseases and Biodefense Program provides a broad range of preclinical developmental resources for product development and clinical testing. The areas of this contract include *in vitro* screening for antimicrobial activity, clinical isolate panels for selected bacterial pathogens, small animal models, nonhuman primate models and studies, safety/toxicology and immunogenicity testing for vaccines, and safety/toxicology and pharmacology testing for therapeutics.

Biodefense and Emerging Infectious Diseases Research Resources Program

The Biodefense and Emerging Infectious Diseases Research Resource Program acquires, authenticates, stores, and distributes state-of-the-art research and reference reagents and standardized panels to the scientific community. This resource, funded in 2003, includes the capability to validate, expand, and produce biological agents including cell lines, clones, proteins, monoclonal and polyclonal antibodies, and diagnostic reagents and tools. The acquisition of NIAID Category A priority pathogens and reagents for research on these threat agents is a high priority.

Network for Large-Scale Sequencing of Microbial Genomes

NIAID has established a state-of-the-art, high-throughput DNA sequencing center that can rapidly sequence genomes of microbes and invertebrate vectors of infectious diseases. Data will be released in a timely, publicly accessible manner, with preliminary information about open reading frames and the annotation of gene function provided to the research community.

Pathogen Functional Genomics Resource Center (PFGRC)

PFGRC is a centralized facility that provides the research community with resources necessary to conduct functional genomics research on human pathogens and invertebrate vectors. PFGRC provides scientists with microarrays, genotyping, bioinformatics, and a repository for clone access and other reagents. In addition, PFGRC has the capability to train scientists in the latest techniques in functional genomics and development of emerging genomic technologies. Additional information is available at <http://pfgrc.tigr.org>.