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News Beyond Our Pages

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The NIAID, a component of the NIH, conducts and supports basic and applied research to understand, identify, treat, and prevent infectious and immune-mediated diseases better, including asthma and allergy. The NIAID supports allergic disease research through both investigator-initiated research grants and solicited research programs (see reviewE1). These programs have yielded major advances in the field of allergic disease over the past several decades. Although current and projected budget constraints for the NIH have created substantial challenges, numerous additional opportunities exist for even more notable scientific and medical advances.

Each year, the NIAID sponsors funding initiatives relevant to allergic disease research. Initiative development is guided by several factors, including public health needs, scientific opportunities, and the imperative to develop new research areas, such as attracting new investigators to an emerging field. In fiscal year 2007, the NIAID provided ~$114 million to support extramural research on asthma and allergic diseases and substantially larger sums for research on fundamental immunology that may ultimately prove relevant to our understanding and management of asthma and allergic diseases. Funding directed specifically toward asthma and allergic diseases included ~ 170 investigator-initiated R-series (R01, R21, and so forth) grants. Here we summarize some of the key NIAID-supported initiatives in asthma and allergic diseases.

Allergen and T-Cell Reagent Resources for the Study of Allergic Diseases

The NIAID developed this new program in response to a 2005 NIAID-sponsored workshop on the

future of immunotherapy. The subject matter experts who attended the workshop recognized a great need to identify and characterize allergen-specific T-cell epitopes for use in the development of novel immune-based therapeutics, including those that may induce immune tolerance against clinically important allergens. The goal of this program is to identify and characterize novel allergen-specific T-cell epitopes that activate both effector and regulatory T-cell subsets. We expect that this initiative will contribute significantly to our understanding of the mechanisms that underlie allergic disease and will lead to the development of new peptide-based immunotherapies. Epitopes identified by the investigators supported through this 2007 funding initiative will be deposited in the publicly accessible NIAID Immune Epitope Database and Analysis Resource (http://www.immuneepitope.org/home.do).

Asthma and Allergic Diseases Cooperative Research Centers

The NIAID established the first Asthma and Allergic Diseases Centers in 1971, and the program is now in its fourth decade of continuous funding. The Asthma and Allergic Diseases Cooperative Research Centers have been responsible for many important basic science discoveries and clinical advances in the fields of asthma and allergy and have trained many of today's academic leaders in these fields. The program currently supports 15 centers located throughout the United States. These centers conduct basic and clinical research on the mechanisms, diagnosis, management, and prevention of asthma and allergic diseases. Several of the centers are preparing to launch clinical studies, including the study of anti-IgE on airway responsiveness to allergen challenge, interaction of endotoxin-induced and allergen-induced inflammation on airway physiology, penicillin desensitization and its effects on mast cells, the interaction between allergen-induced chronic hyperplastic eosinophilic airway disease and asthma, the effect of nasal provocation with atmospheric particulate matter on allergic sensitization, and the use of oral immunotherapy to treat cow's milk allergy.

Consortium of Food Allergy Research

The NIAID established the Consortium of Food Allergy Research in 2005 to study the natural history of food allergy and develop new approaches to treat and prevent food allergies. The consortium is currently conducting an observational study in young children at high risk of developing peanut allergy. This study will correlate biologic markers and immunologic changes associated with the development of peanut allergy and the resolution of egg and cow's milk allergy. Another study is evaluating the capacity of oral egg administration in children with egg allergy to induce immune tolerance to this food. The consortium is also developing a clinical trial of sublingual immunotherapy for peanut allergy, as well as a “first-in-man” mucosal immunotherapy clinical trial that will attempt to induce T-cell tolerance in subjects with peanut allergy using recombinant and genetically modified peanut allergen proteins, administered rectally within killed *Escherichia coli*.

Exploratory Investigations in Food Allergy

Cosponsored by the NIAID, the Food Allergy and Anaphylaxis Network, the Food Allergy Project, and the United States Environmental Protection Agency, this initiative will support innovative exploratory and developmental research on the mechanisms of food allergy and associated comorbid conditions, including atopic dermatitis, asthma, and eosinophilic gastroenteritis, using *ex vivo* specimens from human subjects or animal models of food allergy. One important goal of this initiative is to attract additional investigators to the field of food allergy research. The NIAID expects to award grants under this initiative in mid-2008.

Atopic Dermatitis and Vaccinia Immunization Network

The NIAID established the Atopic Dermatitis and Vaccinia Immunization Network (ADVN) in 2004 with the goal of reducing the risk of eczema vaccinatum, a potentially life-threatening complication of immunization with smallpox vaccine. Eczema vaccinatum occurs almost exclusively in persons with atopic dermatitis (AD). Smallpox vaccination in the United States was halted in 1972 because of the eradication of smallpox, but the ADVN was launched because of the potential use of smallpox as an agent of bioterrorism and the possibility of vaccinating large numbers of people with vaccinia. The ADVN includes both clinical studies and studies in mouse models of AD. ADVN investigators have shown that subjects with AD have diminished cutaneous innate immune responses. Moreover, subsets of patients with AD with a history of eczema herpeticum have been found to have a more profound defect in their capacity to mount an innate immune response. Lessons learned from studies of patients with eczema herpeticum are expected to provide important information about the risk of eczema vaccinatum in persons with AD.

Inner-City Asthma Consortium

Since 1991, the NIAID has funded research on asthma in inner-city areas with the goal of improving the treatment of children living in environments where the prevalence and severity of asthma is particularly high. The current program, recompeted in fiscal year 2002, consists of 10 academic clinical centers, an administrative center, and a statistical and data coordinating center. The goals of the Inner-City Asthma Consortium are to evaluate the safety and efficacy of promising immune-based therapies to reduce the severity of asthma and prevent disease onset, to investigate the mechanisms of action of immune-based therapies developed to treat this disease, and to develop diagnostic and prognostic biomarkers. Recently completed and ongoing clinical studies include (1) evaluation of the use of exhaled nitric oxide as a biomarker to supplement a guidelines-based approach to the treatment of children with asthma, (2) a clinical trial of the effectiveness of anti-IgE therapy in children with asthma, (3) a phase I study of sublingual cockroach immunotherapy, and (4) a birth cohort study of children at high risk of developing asthma with the goal of identifying immunologic characteristics that will predict the development and the severity of asthma at a later age.

Immune Tolerance Network

First funded in 1999 and renewed in 2007, the Immune Tolerance Network (ITN) is an international consortium of investigators in the United States, Canada, Europe, and Australia dedicated to the development and evaluation of novel, tolerance-inducing therapies in immune-mediated disorders, including asthma and allergic disease. The ITN recently completed a proof-of-principle clinical trial using a recombinant ragweed allergen chemically conjugated to immunostimulatory DNA to treat allergic rhinitis.E2 Just 6 injections of this allergen-DNA conjugate, given to patients with ragweed allergy before seasonal exposure to ragweed pollen, markedly reduced rhinitis symptoms during both that year's and the following year's ragweed seasons. An ongoing ITN clinical trial is testing whether regular consumption of a peanut snack by high-risk children enrolled between 4 and 10 months of age will prevent the later development of peanut allergy.

Future directions

We anticipate the field of allergic disease research will continue to advance during the next several years, creating new scientific opportunities for discovery. Areas of growing research interest include the use of adjuvants to modify immune responses; evaluation of new mucosal routes of administration for immunotherapy, particularly in previously intractable conditions such as food allergy; birth cohort and prevention studies; discovery, validation, and use of biomarkers to predict and guide the treatment of allergic diseases; and defining the interrelationship between innate and adaptive immunity in allergic responses.

Career challenges in the current period of constrained funding

The NIAID initiated and renewed many of the aforementioned solicited research programs during periods of substantial growth in the NIH budget. The past several years have seen no net growth in the NIAID budget, prompting the institute to redirect some resources from new or renewal solicited programs to support the institute's pay line for investigator-initiated grants. It is unfortunate that the current budgetary constraints have occurred at a time of great progress and substantial achievements in the field of immunology (see reviewE3). Low NIH grant pay lines and success rates have the potential to affect the morale deeply of both new and established investigators, and to discourage young physicians and scientists-in-training from considering careers in the biomedical sciences. However, it is important to note that NIH support for biomedical research historically has rebounded after periods of fiscal constraint. The NIH already has instituted measures to preserve funding of key initiatives and to maintain support for investigator-initiated research. Some institutes, including the NIAID, also provide a special pay line for new investigators.

In these difficult times, we believe that academic investigators and trainees should routinely seek advice from colleagues and mentors who can critically evaluate their data and research plans to prepare highly competitive research grant applications. The NIAID is especially committed to supporting the needs of young investigators. In October 2007, the NIAID held a New Investigators Workshop on the NIH campus in Bethesda, Md. This 2-day workshop provided first-time recipients of R01 and R21 research grants with interactive lectures and group discussions aimed at strengthening the skills that new investigators need to be successful. This workshop also provided attendees with opportunities to meet their designated NIAID program and grants management officials. We encourage investigators at all stages in their careers to regularly contact their Program Officers, Scientific Review Officers, and Grants Management Specialists with grant-related questions. Slide presentations from the 2007 NIAID New Investigators Workshop can be downloaded from the following address: http://www3.niaid.nih.gov/about/organization/dait/NewInvestigatorWorkshop/.

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