Selected Science Advances, 2009

The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases. In the past year, NIAID has conducted and supported many basic and clinical research studies that have improved our understanding of disease and advanced the quest for new treatments and prevention strategies. Some of the most exciting discoveries are highlighted below.

Flu's Achilles' heel: Scientists identify proteins that neutralize multiple strains of seasonal and pandemic flu viruses

Two independent research teams supported by NIAID have discovered a common Achilles' heel in a wide range of seasonal and pandemic influenza A viruses. The pair of studies found a small family of infection-fighting proteins, or human antibodies, that neutralize various influenza A virus subtypes by attaching to these viruses in the same place. This common attachment site provides a constant region of the flu virus for scientists to target in an effort to develop a so-called universal flu vaccine. Such a vaccine would overcome the annual struggle to make the seasonal flu vaccine match next year's circulating flu strains and might help curtail the transmission of emerging pandemic influenza viruses as well. Lab-made human monoclonal antibodies based on the neutralizing antibodies identified also might be made relatively quickly and potentially could be used in combination with antiviral drugs to prevent or treat the flu during an influenza outbreak or pandemic.

Experimental cytomegalovirus vaccine shows promise

Every year, approximately 8,000 infants in the United States develop severe hearing, mental, or motor impairments after becoming infected with cytomegalovirus (CMV) while still in the womb. A vaccine to prevent congenital CMV infection has long been a public health priority, but has proved elusive. An NIAID-supported clinical trial enrolled 441 CMV-negative women to receive either an experimental CMV vaccine or a placebo. Women who received the vaccine were half as likely as woman who did not to later become infected with CMV. While larger studies are needed to confirm the possible effectiveness of this or any other CMV vaccine at preventing congenital CMV infection, the results do give rise to optimism that such a vaccine may be closer.

Male circumcision helps prevent HSV-2 and HPV infection

Medical circumcision can help heterosexual men significantly reduce their risk of acquiring two common sexually transmitted infections—herpes simplex virus type 2 (HSV-2), the cause of genital herpes, and human papillomavirus (HPV), which can cause cancer and genital warts. The findings build upon earlier NIAID-funded clinical research, which found that circumcision decreases a man's risk of acquiring HIV infection through heterosexual intercourse by more than 60 percent. The new study is based on two clinical trials at sites in Uganda involving 3,393 uncircumcised men between the ages of 15 and 49. Overall, researchers found that circumcision reduced the men's risk of HSV-2 infection by 28 percent and reduced HPV prevalence by 35 percent. Circumcision did not, however, affect the incidence of syphilis.

Pre-exposure prophylaxis as HIV prevention could yield substantial benefits, mathematical model finds

Providing antiretroviral drugs to people who are not infected with HIV but who are at high risk of infection—an investigational approach known as pre-exposure prophylaxis (PrEP)—could substantially reduce their lifetime risk of HIV infection and could be as cost-effective as other widely recommended public health and medical interventions, according to a mathematical model developed by NIAID grantees at Yale University. As a basis for their model, the researchers assumed 1) PrEP is 50 percent effective; 2) the target population is American men who have sex with men who are on average 34 years of age; 3) 1.6 percent of this population becomes newly infected with HIV annually; and 4) the antiretroviral drugs (tenofovir and emtricitabine) cost $9,000 annually. Within these parameters, the model predicts PrEP would cut the lifetime risk of HIV

infection from 44 percent to 25 percent. The model predicted that PrEP in this hypothetical setting would not be cost effective under current U.S. standards. However, the researchers assert that by changing the model's assumptions, for instance incrementally increasing the protective effect of PrEP, decreasing the drug costs, or targeting a higher risk population, PrEP could be a cost-effective approach to HIV prevention.

Memory B cells provide insight into HIV-specific neutralizing antibodies

Many researchers believe that a vaccine to prevent HIV infection must stimulate the body to make neutralizing antibodies, infection-fighting proteins that in the case of HIV prevent the virus from infecting immune cells. Using state-of-the-art technology, researchers at NIAID's Vaccine Research Center for the first time are now examining how neutralizing antibodies develop during natural HIV infection, which could provide key clues to developing an effective HIV vaccine. By collecting antibody-producing memory B cells from HIV-infected individuals and incubating the cells with a specially flagged protein from the outer shell of an HIV virus particle, the HIV-specific cells bind to the protein, enabling researchers to identify the cells and isolate and store them. For each of the HIV-specific memory B cells, a pioneering technique is then used to express the genes that code for HIV-specific antibodies, and assays are used to help scientists determine which of the antibodies can effectively neutralize HIV.

Adaptive features in innate immune cells

Natural killer (NK) cells are a type of white blood cell traditionally thought to be part of the innate, or inborn, immune system. Cells of the innate immune system provide a rapid, nonspecific response when exposed to a microbe for the first time. They do not expand or contract in number after exposure to a microbe, and behave as if they had never seen the microbe the next time they are exposed. This is in contrast to cells of the adaptive immune system that increase and decrease in number during an infection and, having seen the microbe once, retain a memory of the specific infection and are able to respond more efficiently the second time around. Recently, two groups of NIAID-supported investigators showed that NK cells may have features of adaptive immune cells. The first team observed that NK cells from mice exposed to a virus increased in number during the response to the initial infection and then contracted in number after the infection was cleared. Some virus-specific "memory" NK cells remained in circulation, and their number increased more rapidly after a second infection. The second team showed that activating NK cells with signaling molecules, called cytokines, led to stronger NK responses upon each subsequent exposure. Taken together, these two studies indicate that NK cells have never-before realized features of adaptive immune cells and thus could be considered novel targets for future vaccine development.

Scientists identify biomarkers of kidney transplant tolerance

NIAID-supported investigators have found that microRNAs (miRNAs), which are small pieces of nucleic acids that regulate gene expression, can determine the health and function of transplanted kidneys. In this study, investigators looked at expression patterns of several miRNAs in biopsies from kidney transplant patients. Patients undergoing acute rejection had different patterns of expression compared with those seen in recipients with normal functioning transplants. In addition, when they compared the miRNA levels in the kidney biopsies to those measured in white blood cells of the same patients, the patterns were similar. These results suggest that measuring miRNA levels in a kidney recipient's blood may be useful for diagnosing rejection and predicting how well a transplant is functioning—thereby avoiding the need for a kidney biopsy—and also may be useful for tailoring medications to the needs of individual patients.

Nonimmune cells contribute to the immune response to airborne allergens

In this mouse study, NIAID-supported scientists discovered that when special sensors called Toll-like receptors (TLRs)—which dot the surface of epithelial cells that line the lungs—detect the presence of airborne allergens, the sensors activate immune cells. The researchers observed that a particular TLR, TLR4, was sensitive to bacteria and dust mites. Previously, it was unclear whether TLRs on nonimmune epithelial cells at mucosal surfaces such as those in the lungs were involved in antigen sensing, or if it was TLRs found on immune cells in these areas that were critical to these allergic responses. The research team observed that TLR4 on airway epithelial cells, not on immune cells, helped induce the initial immune response to allergens in the lungs. The new results suggest that targeting TLRs may be a research avenue for developing novel treatments for allergic diseases such as asthma.

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