AN AUDIENCE WITH…

Anthony Fauci

Anthony S. Fauci, M.D. is the Director of the National Institute of Allergy and Infectious Diseases (NIAID), a division of the National Institutes of Health (NIH) in the United States. Before becoming Director of the NIAID in 1984, he was appointed Chief of the NIAID Laboratory of Immunoregulation in 1980, a position he still holds. Fauci serves as one of the key advisors to the White House and Department of Health and Human Services on global AIDS issues, and on initiatives to bolster medical and public health preparedness against emerging infectious disease threats, such as pandemic influenza. Through 2007, he received a series of high-profile awards, including the Lasker Award for Public Service.

What impact do you anticipate the recent halting of Merck's large-scale International HIV Vaccine trial to have on other HIV vaccine clinical trials?

I think the major impact will be that for more advanced trials — the Merck trial was Phase IIb and enrolled a substantial number of people — we will be much more attentive to the periodic examination of data. When the Merck trials' Drug and Safety Monitoring Board first looked at the trial data, to our surprise it showed futility in the major endpoints, namely acquisition of infection and level of viral set point. There was also a suggestion that vaccinated people with background immunity to the adenovirus vector had a greater susceptibility to acquiring HIV infection. Based on the latter observation it will be necessary for us to put a pause on vaccine studies that involve an adenovirus vector performed in populations who may be at risk for HIV infection. In addition, in the future we will look very carefully at the results on a more frequent basis. It is a sobering revelation that what we thought was a promising product actually failed the first time. It is not going to diminish our enthusiasm and support for vaccine research because we still need to keep the pipeline robust. But when we get into more advanced clinical trials in the future, it will be done with an added degree of caution.

What are the main challenges remaining for vaccine development and how might they be tackled?

The main challenge that remains, even before the Merck trial, is that we still do not know how to best elicit protective immunity against HIV. The development of vaccines against all other viruses and microorganisms exploits the way that the body naturally responds to an infection to induce protection. Unfortunately, with HIV, the body does not respond adequately to natural infection. For this reason, we have the astounding situation in which, of the tens of millions of people who have been infected, there isn't a single example of someone who has completely eliminated the virus from their body following established infection. So, the main challenge is to work out how to induce a truly protective response; it is not a logistical challenge, it is not a technical challenge, it is a scientific challenge.

Aside from directly targeting the virus and preventing its entry into a host cell, what other areas of research could lead to new therapies to control or eradicate HIV?

There are several areas — one is that we need to intensify research to better understand the mechanisms of viral resistance. Understanding the molecular basis of resistance and having a road map to rational drug design is one way that we can use our research to lead to new therapies. Also, we must not forget that we need to continue to try and develop approaches to reconstitute the immune response, namely immune-based therapy. In addition, the viral reservoirs still serve as the major stumbling block in trying to eradicate HIV, so we need to identify agents and different strategies to diminish the viral reservoirs.

In light of the experience from emerging pathogens such as SARS and West Nile virus, what has been learned that might help facilitate the rapid development of vaccines or drugs to combat such threats?

First, state-of-the-art, point-of-care diagnostics are absolutely critical. By point-of-care, I mean that someone will come in with a new disease, such as SARS or West Nile, and you can make the diagnosis while the patient is in your care. A major problem is when you have a diagnostic that takes days to weeks because you are collecting data but you don't know how to use it without the results. For all of these emerging diseases, we are striving for a molecularly based (such as a chip), point-of-care diagnostic.

Second, we need to utilize the extraordinary advances that have been made with our sequencing capabilities. Now, we can sequence a new microorganism or virus literally within a day, whereas before it took months, if not a year, to do. We have the capability with the exquisitely sensitive molecular techniques to get enough sequence information from a specimen to determine what class of pathogen is causing an illness.

NIAID has identified promising candidates for the treatment of influenza, malaria and* Mycobacterium tuberculosis *that are being developed in partnership with industry sponsors. What are the main challenges for engaging with industry to bring these therapies to the clinic and how might these challenges be addressed?

When you are dealing with diagnostics, therapeutics or vaccines for these types of diseases, they do not necessarily kindle a lot of interest among the stockholders of a drug company, primarily because investment in a drug or vaccine for the developing world may not yield a profit margin and will probably have to be sold at a low price. So, they will be reluctant to approve the enormous investment that it takes for the development of a vaccine, drug or diagnostic. What the federal government, through the NIH, has been trying to do is to ameliorate some of the risks at the front end of the process. We have been making major investments in biomedical research for concept development as well as the early clinical trials that lead to product development so that the risk of failure is shared greatly by the federal government. Once you get something, either a concept or an early trial that looks like it almost certainly is going to be a success, it is more likely that companies will then make substantial investments to develop the product.