

Amidst growing vaccine concerns, NIH sets up engine for answers

Infectious diseases, and, by extension, the vaccines against them, occupy a lofty spot on the totem pole of public health. In the US, many states have laws requiring certain vaccines. Perhaps not uncoincidentally, the US government maintains the National Vaccine Injury Compensation Program (VICP), which compensates individuals injured by the (albeit rare) side effects of vaccines, among them allergic reactions, seizures and chronic arthritis. The program has come into the spotlight in recent years as some parents have voiced concerns about the safety of various shots. Given all this, the US government has an extra incentive to ensure the safety and efficacy of immunizations.

To that aim, the US National Institutes of Health (NIH) is spearheading a five-year, \$100 million initiative to examine how the human immune system functions both at rest and after changes in response to infectious disease as well as to vaccination. The funds will be divided up among six research centers across the country.

Matthew Fenton, who heads the allergy branch in the immunology division of the National Institute for Allergy and Infectious Diseases (NIAID) in Bethesda, Maryland, says one of the main goals of the initiative is to “help develop vaccines that work better not only in the average healthy person but also in people with chronic health conditions.”

Bali Pulendran, an immunologist at Emory University in Atlanta and one of the recipients of the NIH funding, is working on a longitudinal trial involving three vaccines: the seasonal influenza vaccine, the pneumonia vaccine Pneumovax and the shingles vaccine Zostavax. He expects to follow at least 60 participants—half of them elderly—for up to a year after vaccination. From blood samples, they’ll conduct microarray tests to characterize gene expression profiles, as well as analyze CD8⁺ T cell counts and levels of signaling molecules known as cytokines involved in immunity. Traditional tests of vaccine efficacy have looked mostly at antibody production.

The application of more sophisticated technology excites Pulendran. “If people do this sort of thing with different vaccines, we can discern patterns of gene signatures that are predictive of certain type of response,” he says. This could lead to developing multiple strains of vaccine suited to a person’s age, health or particular genetic makeup.

Using gene signatures to predict vaccine response might also improve the efficiency



Injection of funds: Money allocated to understanding immunizations.

of vaccine production. “We really hope to be able to develop profiles or signatures that tell us about vaccine efficacy and safety so that we can shorten the length of time that’s needed to test various vaccine candidates,” says Fenton.

None of this would have been possible without new high-throughput technologies that allow scientists to analyze more than 50 cytokines at once from a given blood sample or without the supercomputers that allow researchers to crunch through massive amounts of information. Gregory Poland, a Mayo Clinic researcher in Rochester, Minnesota who will be using his grant money to focus on responses to the influenza vaccine, estimates that there will be about one terabyte of information collected from each person in his study.

Dissecting such a vast collection of information will help expand basic understanding of how the human immune system functions, which, according to some, is sadly lacking.

“We’ve had this strange bifurcation in immunology where all of the big discoveries have been made in inbred mice, with the assumption that they’ll trickle down to work with humans,” says Mark Davis, an immunologist at the Stanford University

School of Medicine in California and another recipient of the NIH funds. “A lot of people have tried valiantly, [to apply findings in mice to humans] but the experience has not been good.”

Mark Blaxill, an editor at *Age of Autism*, a popular website covering many aspects of autism, including purported links to vaccine programs, says that although the fact that the NIH is examining vaccine safety is a sign of progress, the initiative amounts to the NIH “trying to fine-tune recommendations for a program that they think is largely in good shape.” A really thorough examination of human immune responses to vaccines, he says, would examine unvaccinated populations against vaccinated ones—difficult to arrange, he concedes, but not impossible.

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Correction

In the print version of the August 2010 issue of *Nature Medicine*, the article entitled ‘Parse the salt, please’ (*Nat. Med.* **16**, 841, 2010) included an incorrect credit for the photo on page 842. The photo should have been credited to Kathy Groves, Leatherhead Food Research. The error did not appear in the HTML and PDF versions of the article.