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# Vaccinomics: Scientists Are Devising Your Personal Vaccine

## A new breed of vaccine is being developed that will make possible immunizations tailored to your genetic profile. But how long will it be until your personalized booster shots are ready?

By Melinda Wenner Moyer

Our bodies defeat infections in part because our immune system's genes are many and diverse. This genetic heterogeneity, however, has a downside: it means that we each respond differently to vaccines. For example, compared with women men routinely produce fewer pathogen-fighting antibodies after vaccination, and in the last large U.S. measles outbreak in 1989 10 percent of previously vaccinated children were not protected. But these limitations could one day be overcome thanks to a push to replace one-size-fits-all vaccines with genetically "personalized" immunizations that are safe and effective for everyone.

The idea of tailored vaccines is hardly new. Gregory Poland, the head of the Mayo Clinic's Vaccine Research Group, has been working to unite the fields of genomics and vaccinology—what he calls "vaccinomics"—for 22 years, in part because he has never been fully pleased with the existing vaccine paradigm. "It is a population-based or public health–based approach and, within limits, it has served us well," he says. "But it is has also engendered an antivaccine movement, because there are people who have side effects."

The past decade has seen vaccinomics inch much closer to reality. With the completion of the first phase of the Human Genome Project in 2000, and the advent of sequencing technologies that can detect gene variations such as single nucleotide polymorphisms (SNPs), for the first time scientists have the tools in hand to find the key immune genes and genetic networks that play roles in vaccine response.

Poland envisions a future in which people can opt to have their genome sequences stored on chips in their health insurance cards. At the doctor's office, computers would scan the chips to determine whether the person's gene sequences have been linked to vaccine side effects or weak responses. Then the patient and physician "will pick and choose an individualized program that best fits his or her genetics," Poland explains.

To be sure, this scenario is likely decades away. But information gleaned from genomics could soon improve vaccines in subtle but effective ways. In a 2007 paper published in *The Journal of Allergy and Clinical Immunology* Poland and his colleagues reported that people who have mutations in a gene for a protein called SLAM produce 70 percent fewer antibodies after live measles inoculation than people without the mutation. Normal SLAM binds to a measles protein present in the vaccine, helping the body launch an immune response. Poland suspects that the mutation changes SLAM's shape so that it cannot bind the protein. If scientists could design a vaccine that did not depend on SLAM, Poland wrote, it would protect more of the population.

Genes could also predict who will suffer from adverse reactions. In a March 2009 study published in *Genes and Immunity*, researchers at the National Center for Computational Toxicology compared the genetic signatures of 16 people who experienced smallpox vaccine side effects, including fever, rashes and enlarged lymph nodes, to 45 people who did not. Using these data, the team built a diagnostic model that predicts who is likely to experience these problems based on sequence differences in a gene coding for an immune protein called interleukin-4 as well as variations in serum concentrations of three other immune proteins. If people were warned that they might experience adverse reactions to a particular vaccine, they could instead opt to receive other preventative treatments, such as antiviral medications.

One of the biggest challenges for vaccinomics is that it is extremely difficult to identify the genes responsible for vaccine responses. Humans have thousands of immune system genes, and they interact with one another in complex ways; some, for instance, control others. "You're trying to understand the simultaneous contribution of hundreds to

thousands of things happening at the same time," Poland says.

In addition, genetics is just part of the immune-response story. Poland and his colleagues have shown that genes are only responsible for 38.8 percent of the variation in the way people respond to the mumps vaccine virus and 45.7 percent of the disparity in how they respond to the rubella vaccine virus. What causes the rest is a mystery—environmental influences, perhaps, or differences in the amounts of protein being made from particular immune genes.

And even if scientists do put together all the pieces and find ways to develop genetically tailored vaccines, they will still have to "get these innovations out of the university setting, into the marketplace, and into the health care system," says Yann Joly, a lawyer and assistant professor in the Department of Human Genetics at McGill University in Montreal. Personalized vaccines might not be all that attractive to pharmaceutical companies, because introducing the genomic component will make manufacturing "even more complicated and less profitable," he says. "You also add a degree of uncertainty into it, because this is all new."

It is also possible that patients who are already wary of vaccines may be even more concerned about personalized inoculations, which have no public health track record as yet. "One hundred years from now we'll be much better at making pure and safer vaccines," says Paul Offit, director of the Vaccine Education Center at The Children's Hospital of Philadelphia. "I'm sure it will [initially] be met with the same level of distrust as is met with current science."

Poland, though, is optimistic. "There has been this deep schism between people who believe in vaccines and people who don't, and what's interesting is that both groups are highly attracted to this work we're doing," he says. What drives vaccine fears, he notes, is the knowledge that vaccines don't work for everyone and that they can, on rare occasions, cause serious side effects, such as Guillain–Barré syndrome, which develops in one out of every million people who receive the seasonal influenza vaccine. But with vaccinomics, "we'll actually be able to predict whether you need a vaccine, how many doses you need, and whether you're likely to have a serious side effect," he says. "The power of this—for human health—is undeniable."

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