Decoding vaccination: Researchers reveal genetic underpinnings of response to measles vaccine

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Researchers at Mayo Clinic are hacking the genetic code that controls the human response to disease vaccination, and they are using this new cipher to answer many of the deep-seated questions that plague vaccinology, including why patients respond so differently to identical vaccines and how to minimize the side effects to vaccination.

Led by Gregory Poland, M.D., researchers in Mayo's Vaccine Research Group are publishing results of two genetic studies that identify mutations linked to immune response to the measles vaccine. They appear in the journal Vaccine.

"We are trying to understand, to the maximum extent possible, how a person's individual genetic makeup affects response to vaccination," says Dr. Poland.

These and similar studies will likely allow physicians to prescribe appropriate doses and timing of vaccines based on routine genetic screening blood tests in the near future. Longer-reaching implications of the vaccine group's work include the development of more effective vaccines and, perhaps someday, the ability to construct personalized vaccines.

"Vaccination is the single most important and far-reaching practice in medicine. By the time a child enters school in the United States, they have received upwards of 20 shots," says Dr. Poland. "In no other field of medicine do we do exactly the same thing to everyone — and we do it everywhere in the world."

Doctors and epidemiologists have long been puzzled about the genetic underpinnings to the fact that up to 10 percent of recipients fail to respond to the first dose of the measles vaccine, while another 10 percent generate extremely high levels of measles antibodies. The remaining 80 percent fall somewhere in the middle.

"We have found that two doses of the vaccine seem to be sufficient to immunize the vast majority of the population against measles, so we do it to everybody even though it's not technically necessary," says Dr. Poland. "If we could tell, based on a genetic test of every patient, who would need one dose and who might need two or three, imagine the implications not only for measles vaccines, but for every vaccine."

Millions of dollars could be saved by avoiding additional and unnecessary vaccine doses, not to mention the pain and suffering that could be spared by administering to young children the minimum number of shots necessary.

Early results published in Vaccine contain an exhaustive statistical analysis of the genes coding for the Human Leukocyte Antigen (HLA) system and other known cytokine/cytokine receptor genes. Dr. Poland's team was the first to single out all DNA base-pair mutations in these genes that have a measurable effect on the immune system's response to measles vaccination.

Any mutations found to play a role in the immune system response to the measles vaccine were identified and cataloged with the study subject's corresponding race.

Called SNPs (pronounced "snips"), these tiny genetic mutations represent the smallest possible change to a person's genetic code and offer clues to explaining why children of some racial and ethnic groups respond better to vaccination than other groups.

Ultimately, Dr. Poland and his team seek to assemble a comprehensive matrix of all the genetic mutations that affect immune response to vaccination on all of the roughly 30,000 human protein-coding genes. Such a library could direct physicians toward predicting exactly how individuals will respond to different vaccines.

"Imagine setting up an array of dominoes the size of a small city, and then depending on where you knock one over, predicting how the rest will fall," says Dr. Poland. "That is what we are trying to do in understanding how single genes, and networks of genes, control and determine our immune responses to vaccines — and, hence, whether we are protected or not."

Provided by Mayo Clinic

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