Scientists identify molecular biomarkers of vaccine immunity

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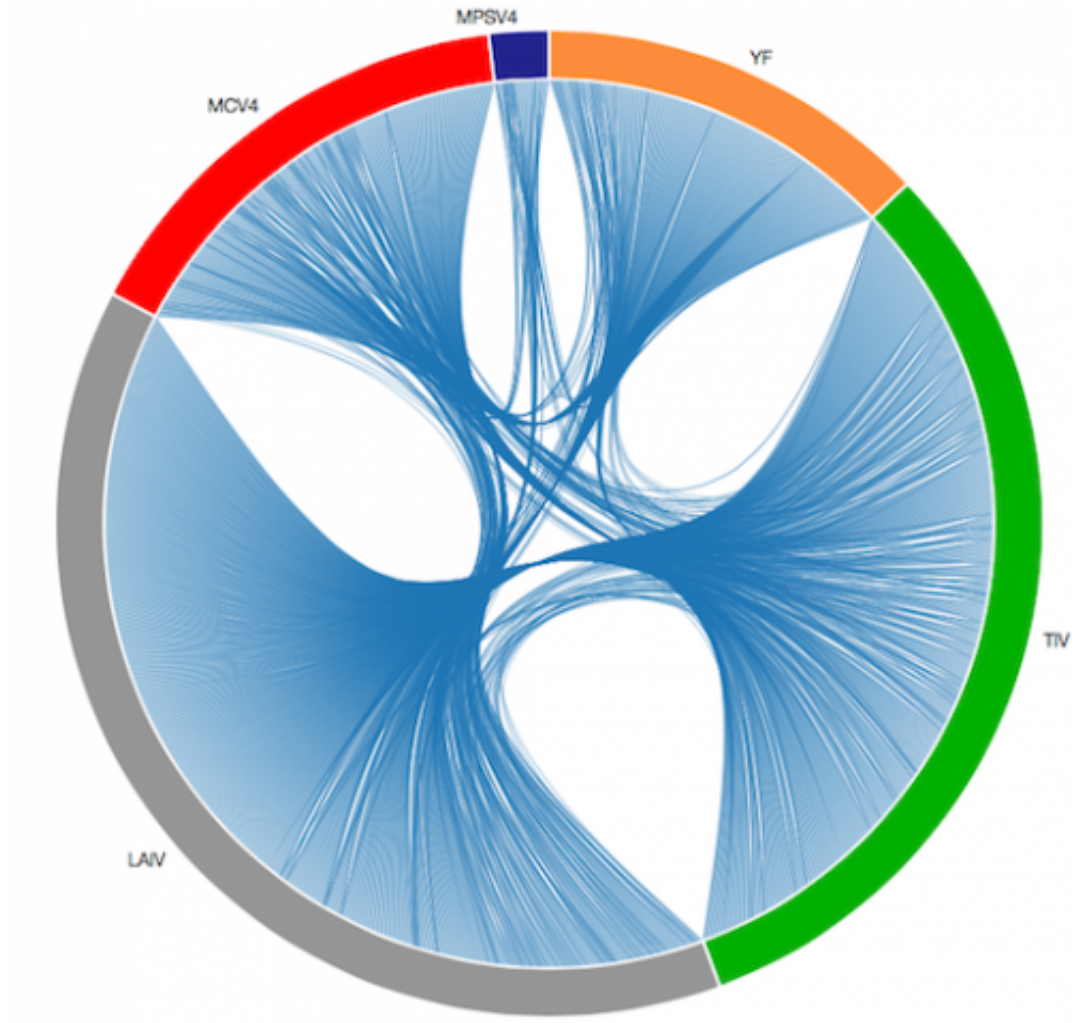

This is a representation of genes activated by five different vaccines in human volunteers' immune systems. The vaccines are: MPSV4 and MCV4 (meningococcal), YF (yellow fever), LAIV (live attenuated influenza) and TIV (trivalent inactivated influenza). Defining the patterns associated with successful immune responses will help researchers design better vaccines. Credit: Emory

Testing the efficacy of vaccines in clinical trials takes years, even decades. Yet challenging infections like HIV, malaria and dengue are striking today. To speed up vaccine testing, scientists at the Emory Vaccine Center have established a goal of creating a "vaccine gene chip."

This device could read the activity of all the genes in the genome in white blood cells within a few days of administration of a test vaccine. Reading such "molecular signatures" would rapidly help predict the ability of that vaccine to stimulate the immune system and protect against disease.

Now scientists led by Bali Pulendran, PhD have taken an important step toward making such a chip, by comparing the molecular signatures induced by five very different vaccines in the immune systems of human volunteers. The results are published online in *Nature Immunology*.

Pulendran, senior author of the paper, is Charles Howard Candler professor of pathology and laboratory medicine at Emory University School of Medicine and a researcher at Yerkes National Primate Research Center. Co-first authors of the paper are postdoctoral fellow Shuzhao Li, PhD, assistant professor of infectious diseases Nadine Rouphael, MD, and postdoc Sai Duraisingham, PhD.

Two of the vaccines they tested in the current study are aimed at stimulating immunity against *Neisseria meningitidis*, a bacterium that can cause life-threatening meningitis or sepsis.

Researchers immunized 30 healthy volunteers with two different types

of meningococcal vaccines, now-standard MCV4 or an older version, MPSV4. They surveyed the activity levels of human genes in blood samples from the volunteers, and compared the patterns against previous results they obtained while investigating responses to yellow fever and the seasonal flu vaccines.

Pulendran, whose lab had pioneered the use of such a "systems" approach to predicting vaccine immunity in previous studies using the yellow fever and seasonal flu vaccines, says his team was asking whether there are universal molecular signatures of vaccine effectiveness that were capable of predicting antibody responses to any vaccine.

"Our results suggest that gene expression predictors of antibody response are unlikely to be 'universal', but are dependent on the type of vaccine," he says.

For example, similar signatures correlated with the antibody responses against the carbohydrate components of the two meningococcal vaccines, while a different signature correlated with recall antibody responses such as that to the seasonal flu vaccine.

"These results represent a first small step towards identifying molecular signatures that might predict immunity to different types of vaccines, but clearly more comparative work is needed to define robust and predictors of immunity that may be common to a broader range of vaccines," he says.

To fully analyze the gene activation responses against meningitis and compare them to other vaccine response data, Pulendran and his colleagues had to build gene networks that were customized for immunology called "Blood Transcription Modules." These resources are available to other scientists to use and share.

Despite its nascent state, the field has already begun to offer unexpected insights about the workings of the immune system. Recent work published in *Science* from Pulendran's lab has demonstrated an unappreciated link between immunity to vaccines and the cells' ancient starvation response, using a systems approach to study immunity to the yellow fever vaccine.

The MPSV4 vaccine, available since the 1970s, contains the polysaccharide outer coating of the bacterium. MCV4 was the first of several meningococcal conjugate vaccines introduced in the last decade. MCV4 links the polysaccharide coating with a toxin protein from diphtheria bacteria. MCV4 is preferred for children, adolescents and younger adults, while MPSV4 is used in adults over 55. Both are different in form from yellow fever (live attenuated virus) and influenza (live attenuated or inactivated virus) vaccines.

More information: S. Li et al. Molecular signatures of antibody responses derived from a systems biological study of 5 human vaccines. *Nature Imm*. DOI: 10.1038/ni.2789 (2013).

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