New modular vaccine design combines best of existing vaccine technologies

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A new method of vaccine design, called the Multiple Antigen Presentation System (MAPS), may result in vaccines that bring together the benefits of whole-cell and acellular or defined subunit vaccination. The method, pioneered by researchers at Boston Children's Hospital, permits rapid construction of new vaccines that activate mulitple arms of the immune system simultaneously against one or more pathogens, generating robust immune protection with a lower risk of adverse effects.

As reported by Fan Zhang, PhD, Ying-Jie Lu, PhD, and Richard Malley, MD, from Boston Children's Division of Infectious Disease, in the *Proceedings of the National Academy of Sciences* on July 29, the method could speed development of new vaccines for a range of globally serious pathogens, or infectious agents.

Broadly speaking, the vaccines available today fall into two categories: whole-cell vaccines, which rely on weakened or killed bacteria or viruses; and acellular or subunit vaccines, which include a limited number of antigens—portions of a pathogen that trigger an immune response. Both approaches have advantages and disadvantages.

"Whole-cell vaccines elicit a broad range of immune responses, often just as an infection would, but can cause side effects and are hard to standardize," said Malley. "Acellular vaccines can provide good early immunity with less risk of side effects, but the immune responses they induce wane with time."

The MAPS method may allow vaccine developers to take a middle ground, where they can link multiple protein and polysaccharide (sugar) antigens from one or more pathogens together in a modular fashion, much as one would connect Lego blocks.

The resulting complex—which resembles a scaffold of polysaccharides studded with proteins—can stimulate both antibody and T-cell responses simultaneously much like whole-cell vaccines, resulting in stronger immunity to the source pathogen(s). However, because the composition of a MAPS vaccine is well defined and based on the use of isolated antigens (as one would find with an acellular vaccine) the risk of side effects should be greatly reduced.

For instance, mice injected with a MAPS vaccine combining proteins from tuberculosis (TB) and polysaccharides from Streptococcus pneumoniae (pneumococcus) mounted vigorous antibody and T-cell responses against TB, whereas those vaccinated with TB protein antigens alone mounted only an antibody response.

Similarly, 90 percent of mice given a MAPS-based vaccine containing multiple pneumococcal polysaccharide and protein antigens were protected from a lethal pneumococcus infection, mounting strong antibody and T-cell responses against the bacteria. By contrast, 30 percent of mice vaccinated with the same antigens in an unbound state survived the same challenge.

"The MAPS technology gives you the advantages of: whole-cell vaccines while being much more deliberate about which antigens you include; doing it in a quantitative and precise way; and including a number of antigens so as to try to replicate the effectiveness of whole-cell vaccination," Malley explained. "The immunogenicity of these constructs is greater than the sum of their parts, somewhat because they are presented to the host as particles."

The system relies on the interactions of two compounds, biotin and rhizavidin, rather than covalent binding as is used in most of the current conjugate vaccines. To build a MAPS vaccine, biotin is bound to the polysaccharide(s) of choice and rhizavidin to the protein(s). The biotin and rhizavidin then bind together through an affinity interaction analogous to Velcro. The construction process is highly efficient, significantly reducing the time and cost of vaccine development and production.

While his team's initial work has focused on bacterial pathogens, Malley believes the technology could impact vaccine development for a broad range of pathogens, in particular those of importance in the developing world. "Technically, one could construct MAPS vaccines for viruses, parasites, even cancer antigens," he said. "And the modularity is such that one could include antigens from multiple pathogens into the same vaccine, allowing the development of combinatorial vaccines much more efficiently."

More information: Multiple antigen-presenting system (MAPS) to induce comprehensive B- and T-cell immunity, www.pnas.org/cgi/doi/10.1073/pnas.1307228110

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