Small molecule with high impact

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Researchers from the vaccinology and applied microbiology department at the Helmholtz Center for Infection Research in Braunschweig, Germany, have now found a new molecule with the capacity of improving responses to vaccines. The synthetic compound, the so-called c-di-IMP, might be more than just a potent vaccine enhancer. The scientists expect to create new vaccination strategies based on c-di-IMP. The group's results have now been published in the current issue of the scientific journal *Vaccine.*

The adjuvants present in vaccines have a bad reputation. For most people, they are only unnecessary compounds within a medicinal product. This is a misunderstanding since adjuvants have a critical impact on the success of a vaccination. In the best case scenario, one single vaccination shot would be now sufficient for conferring life-long protection.

Vaccines are one of the most powerful tools against infectious diseases. They protect against an infection by preventing the infection to arise. In a typical vaccine, attenuated or killed pathogens or just some of their sub-cellular components are injected into the body. The immune system responds to those foreign components, producing antibodies and/or killer cells, which are able to fight the pathogen, as well as memory cells. The latter recognize the true pathogen after host infection, thereby promoting a specific and rapid response able to prevent the establishment of a disease.

However, the immune system often reacts only weakly to the attenuated pathogens or their fragments present in a vaccine. Thus, partial or short-life protection is usually stimulated. The adjuvants by themselves do not trigger an immune reaction, but given as components of a vaccine, they modulate and enhance the immune responses elicited, thereby providing a stronger, early and long-lasting protection. While searching for new adjuvants, the vaccine researchers at the HZI have now found the molecule "c-di-IMP".

"This molecule leads to a strong immune response and it is significantly more effective than known adjuvants," says Rimma Libanova, who is examining the molecule in her PhD thesis. To investigate how it works, she vaccinated mice with a harmless protein, which acts as a foreign structure for the immune system of a mouse. Like during a vaccination against a virus or bacterium, an immune response starts against the protein - without the danger of a real infection. One group of mice received the vaccine with the enhancer molecule, the other without the additive. After 42 days, she analyzed the immune reaction of the mice to the foreign protein. "We found a strong immune reaction in mice that received the optimized vaccine. Furthermore, we measured the stimulation of important effector mechanisms, which are key for the success of a vaccination," says Thomas Ebensen, who is working with Rimma Libanova on the new enhancer. Until now, the researchers were only able to show the effect in mice - but they think one step further: "With this new adjuvant, we want to improve already existing vaccines, such as those against influenza or hepatitis. Maybe it also helps to create new vaccines using component that in the past did not promote efficient immune responses using known adjuvants."

"The molecule might also help us to develop new vaccination strategies," says Professor Carlos A. Guzmán, head of the "Vaccinology and Applied Microbiology" Department at the HZI. His department is working on an alternative to the "shot": the snuff vaccination. Here, the vaccine is taken as a nasal spray to work where most pathogens enter the body: at the mucosae. Guzmán highlights, "c-di-IMP enhances also local mucosal immune responses, representing a strong candidate for the implementation of such type of vaccines. This is very important because mucosal vaccines can prevent not only diseases, but also to block infections before they even take place, thereby protecting also non vaccinated contacts against disease."

More information: Libanova R, Ebensen T, Schulze K, Bruhn D, Norder M, Yevsa T, Morr M, Guzman CA. The member of the cyclic di-nucleotide family bis-(3', 5')-cyclic dimeric inosine monophosphate exerts potent activity as mucosal adjuvant. *Vaccine*, Volume 28, Issue 10, 2 March 2010, Pages 2249-2258, ISSN 0264-410X, DOI:10.1016/j.vaccine.2009.12.045

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