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Press Release

Customized vaccine in a nasal spray format

HZI scientists investigate new approach to targeted activation and inhibition of defender cells

Scientists at the Helmholtz Centre for Infection Research (HZI) in Braunschweig, Germany, are currently investigating Alpha-GalCerPEG, a substance capable of activating target groups of cells that are part of the body's innate defense system. While many defense cells are activated by Alpha-GalCerPEG, T helper 17 (Th 17) cells are actually inhibited by it. Because uncontrolled activation of Th 17 cells can cause serious health problems, researchers are hopeful that they may be able to exploit Alpha-GalCerPEG's unique ability to inhibit these cells at will, when required, in a wide range of settings. As such, Th 17 cells are strongly activated by the intranasal application of vaccines. Alpha-GalCerPEG was shown to be effective at inhibiting Th 17 cells, even when administered intranasally as an adjuvant. These discoveries made by the Braunschweig researchers and published in the current issue of the scientific journal "PLoS ONE," shed new light on Alpha-GalCerPEG's considerable potential in the field of medicine.

Ideally, the entry of an infectious agent into a host organism will result in the activation and amplification of specific cells of the immune system capable of effectively protecting the host against the infectious agent. Vaccinations seek to mimic this effect in a controlled setting by purposely introducing attenuated pathogenic agents or their parts into a person's body in order to trigger an immunological response without producing the disease state or its associated symptoms. The goal is to establish an immunological memory against the specific pathogen. The nature of the pathogen determines which defense cells the body will ultimately make and the extent of cell activation. Immune stimulation can also wreak havoc in the body, for example in situations where cells hyper-react causing collateral damage to bystander cells or body tissues, thereby triggering an unchecked acute or chronic inflammatory response.

Th 17 cells, discovered only a few years ago, are integral to the body's innate ability to defend itself against many different pathogens. During the early stages of an inflammatory response, Th 17 cells act as vitally important antimicrobial "protection units." At times, however, Th 17 cells can steer the immune response in the wrong direction, which can result in states of chronic inflammation with tissue damage. Professor Carlos A. Guzmán, head of the Department of Vaccinology at the HZI Braunschweig, explains that for example "Th 17 cells have been implicated in the etiology of the arthritis observed following experimental infection with the bacterium Borrelia." In contrast, the stimulation of Th 17 cells seems to be important to achieve protection against other infections, such as tuberculosis.

Although, to date, our understanding of Th 17 cells is still – at best – rudimentary and even though these cells are probably more helpful than harmful by defending our bodies against infections, Guzmán is convinced that "in many instances, it would be ideal if we could just switch off the Th 17 cells whenever we wanted to, without compromising the jobs of the other defenders." While for vaccines that are administered intranasally proper measurement of the appropriate dose can prove difficult, the benefits, including for one the

ease of administration, beg for more work to be done in this area and represent an important part of Guzmán's research. “If you use a nasal spray to administer a vaccine, you eliminate the need for unpleasant injections," explains Guzmán. One major downside is that "with the nasal spray vaccine Th 17 cells always tend to become very strongly activated.” The ability to “switch off” the Th 17 cells through the addition of Alpha-GalCerPEG to the nasal spray may be the solution, where required.

“Alpha-GalCerPEG's mechanism of action has been pretty well characterized at this point, an important step towards its controlled medical application,” comments Sebastian Weissmann, a scientist on Guzmán’s team. “One of the goals of our lab is to develop an immunological toolbox, which would allow us to combine individual molecular building blocks to elicit a custom-tailored immune response by vaccination against specific pathogens. With Alpha-GalCerPEG we have found one novel, promising building block.”

Original Publication:

NKT Cell Stimulation with α-Galactosylceramide Results in a Block of Th17 Differentiation after Intranasal Immunization in Mice.
Beata M. Zygmunt, Sebastian F. Weissmann, Carlos A. Guzman
PLoS ONE
dx.plos.org/10.1371/journal.pone.0030382