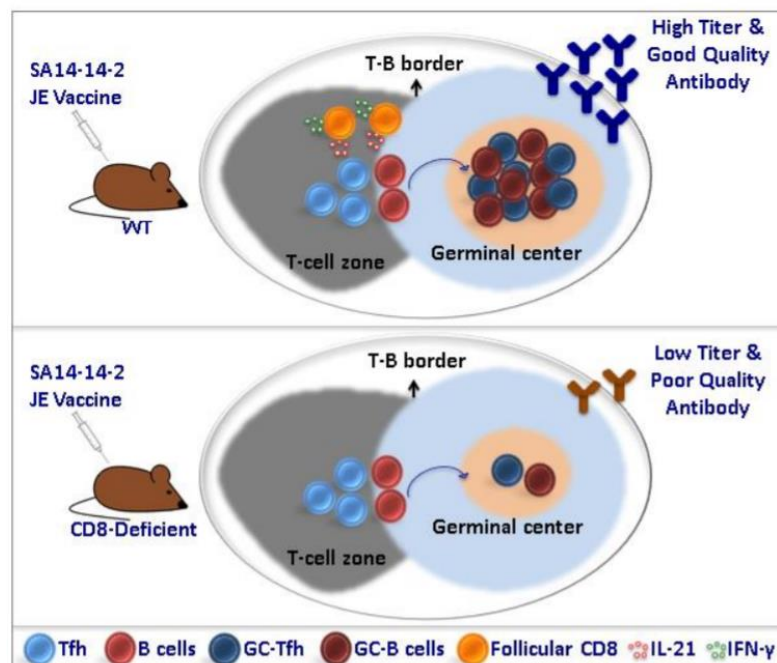


NII Scientists uncover an exceptional role of CD8⁺ T cells in shaping the protective antibody response to a human flavivirus vaccine

In a new study, coming up in European Journal of Immunology, the team of scientists at BDT's National Institute of Immunology (NII), New Delhi has shown that SA14-14-2 Japanese Encephalitis (JE) vaccine induced protective humoral immunity is largely dependent on CD4⁺ T cells and is augmented by CD8⁺ T cells. Although, SA14-14-2 vaccine-primed CD8⁺ T cells are not protective, they influence the overall process of the development of protective antibodies. The work performed in mice, is the first to implicate the CD8⁺ T cells in shaping the antibody response to a human vaccine.



This probably means that an ideal vaccine should synchronize both the CD8⁺ T cells and Tfh cells to achieve higher magnitude and good quality of protective antibodies' says Nimesh Gupta, Ph.D., who led the study.

The Intergovernmental Panel on Climate Change (IPCC) emphasize the research on vector borne diseases as main objectives of future research on human health. The mosquito-borne flaviviruses have been the major concern. Now with the expansion of mosquito vectors due to urbanisation and global warming, people in many countries are at higher risk to get infection by these deadly viruses.

It would be better if we develop a vaccine that can confer protection against multiple flaviviruses like JE virus, West Nile virus and Zika virus'says Nimesh Gupta. Flaviviruses show a high degree of sequence homology, which could be targeted while developing a multi-virus vaccine. This could happen if we know what cellular determinants need to be exactly pulled to get the ideal antibody responses.

For this study, the team utilized animal models to understand the mechanism of protective immunity conferred by the SA14-14-2 vaccine. In a series of virus challenge studies, study show that CD4+ T-cells alone, but not CD8+ T-cells, are sufficient to confer vaccine-mediated protection. However, the CD4-mediated protection was potentiated in the presence of vaccine-primed CD8+ T cells. The microanatomical structures 'germinal centers' in the secondary lymphoid organs, where the antibody response and memory is conceived, were thoroughly investigated by the team after the single dose immunization. By using CD8-deficient mice or by removing the CD8+ T cells during the immune response to this vaccine, researchers show that both the protective traits of CD4+ T cells and the quality of antibody response to the vaccine are impaired in absence of CD8+ T cells. The team further demonstrates that this is mainly due to the impaired differentiation of GC-Tfh cells, a specialized CD4+ T-cell subset crucial for GC development, leading to the poor germinal center response to the vaccine.

This is an exciting cellular interplay underlying the potent protective antibody responses. To understand if this cellular interplay could be generalized, we are studying the individual simmunized with SA14142 vaccine and also extending our observation to other live attenuated vaccines' says Nimesh Gupta, who is heading the Vaccine Immunology Laboratory.

The world is awaiting an ideal vaccine to fight against the ongoing Coronavirus pandemic. It may be useful to explore if synchronizing the Tfh-cell and CD8 T-cell response could help in inducing the potent protective antibodiesbyaSARS-CoV-2 vaccine.

The study titled 'CD8+ T cells are crucial for humoral immunity establishment by SA14-14-2 live attenuated Japanese encephalitis vaccine' also authored by Anurag Kalia and Mona Agrawal of Vaccine Immunology Lab was supported by the grants from the Department of Biotechnology and the institutional funds from the National Institute of Immunology, India.

Future vaccines may be rationalized for precisely balancing the CD8+ T cells and Tfh cells interplay to exert potent protective antibody response.

Japanese encephalitis is the leading cause of acute encephalitis in Asia and the western pacific region with more than 68,000 clinical cases reported annually. With the case fatality rate of 30% and the permanent neurologic or psychiatric sequelae in 30–50% of patients, JE has been most dreaded flavivirus encephalitis.

There is no anti-viral treatment available for JE but it's a vaccine preventable disease. Several inactivated preparations are in use as the traveler's vaccines. The SA14-14-2 live attenuated JE vaccine has been included in national immunization programs of JE affected countries. However, the protective immunity conferred by this historical vaccine wanes with time. Lack of understanding on how this historical vaccine works has been a limitation in development of superior vaccines and in revising the immunization policies in endemic regions.

The risk is rising with continuously expanding JEV geographical range and recently circulating new virus genotypes that can affect all age groups. This calls for a timely development of an effective vaccine that can prevent from JEV and related flaviviruses ideally in a 'One Life One Dose' regimen.

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