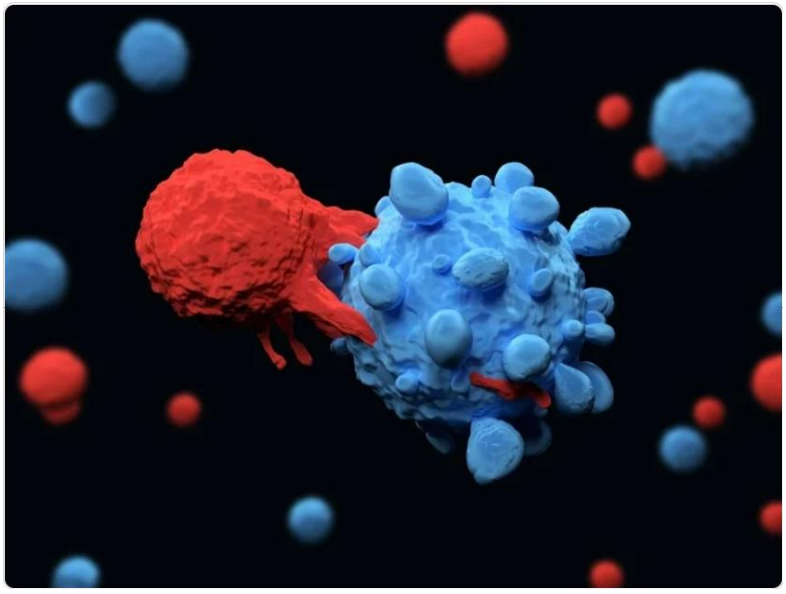
During the Absence of Neutralizing Antibodies, a Third Vaccination with a Single T Cell Epitope Protects Against SARS-CoV-2 Infection

The Coronavirus disease 2019 (COVID-19) pandemic, which has been caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), remains a global health emergency. Therefore, understanding the mechanisms and impact of booster vaccinations could immensely facilitate decisions concerning vaccination programs.

In a new study, scientists showed in a mice model that three doses of the same synthetic peptide vaccine, eliciting an exclusive CD8+ T cell response against one SARS-CoV-2 Spike epitope, protected against lethal SARS-CoV-2 infection, in the absence of neutralizing antibodies. Researchers also showed that the third dose resulted in superior generation of effector-memory T cells in the circulation and tissue-resident memory T (TRM) cells.



Introduction

Vaccines elicit neutralizing antibodies against the spike protein of SARS-CoV-2, but the antibodies decline over time. Furthermore, SARS-CoV-2 mutation rates are high, and certain mutations in its spike protein can evade vaccine-induced immune responses. Some high-risk groups, including transplant recipients, auto-immune disease patients who are on selected immunosuppressive regimens, etc., have lower humoral and cellular immunity after vaccination. Increasingly, third vaccinations are being given to solid organ transplant recipients as standard care.

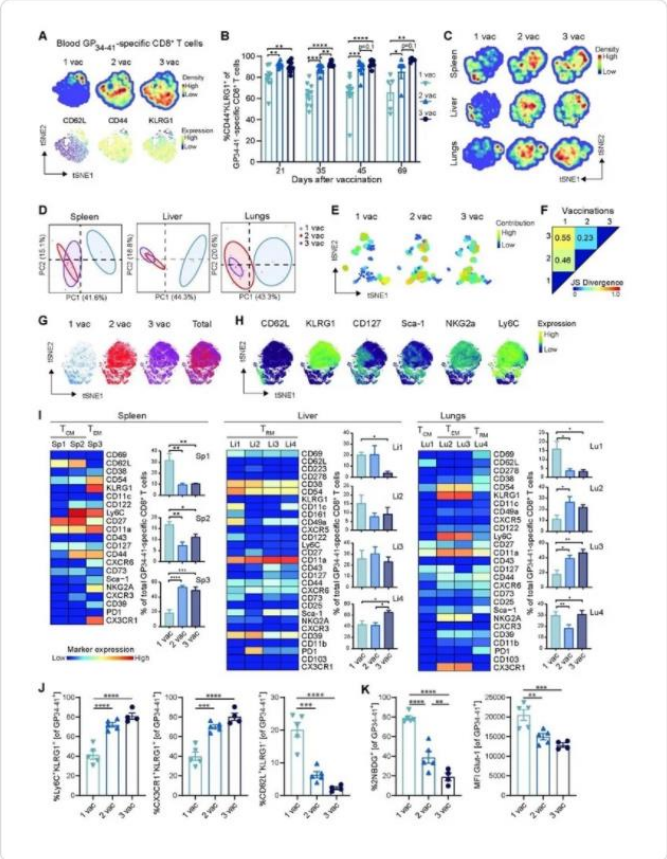
Booster vaccinations have so far shown promising results, but concerns remain regarding the risk groups mentioned above. In addition, these booster vaccinations may result in enhanced T cell responses, which should contribute to the control of SARS-CoV-2. Previous research has shown that T cells can mediate protection by themselves against SARS-CoV-1, but their efficacy against SARS-CoV-2 is unclear. Therefore, in the current study, researchers investigated the capacity of single B cell and T cell epitope-containing peptide vaccines to elicit protection against SARS-CoV-2 infection. To this end, they used the K18-hACE2 transgenic mouse model.

Findings

The study revealed that only a third vaccination with a long peptide harboring a single T cell epitope provided full protection. The authors claimed that this is the first study to demonstrate that vaccine-elicited CD8+ T-cells can protect against SARS-CoV-2 without the help of virus-specific CD4+ helper T cells or neutralizing antibodies. They, however, stressed the administration of the vaccine in a booster setting requiring at least two boosters.

These results are highly relevant in the light of current deliberations on a third vaccine, as the current vaccines elicit virus-specific T cells. Besides, the results could also guide the development of T-cell-focused vaccines. The latter would greatly benefit risk groups, such as patients with leukemia, autoimmune diseases, etc., who have impaired antibody responses and may rely on T cell-eliciting vaccines for protection.

An important fact to note is that the DNA vaccine platform used was highly efficient in generating neutralizing antibodies. As a result, it provided protection against SARS-CoV-2 infection. The results highlighted the inferiority of the antibody responses to single linear B cell epitopes. However, it was not possible to exclude the possibility that single linear B cell epitopes might exist that could elicit neutralizing antibodies. In scenarios where antibodies mediate protection by other mechanisms, the B cell-SLP platform may be quite valuable. Scientists stated that the addition of CpG and IFA as adjuvants and the insertion of a CD4+ T helper cell epitope to the linear B cell epitope vaccine was found to be extremely important to derive antibody responses.



More in-depth studies revealed that a third vaccination not only resulted in the superior generation of CD8+ T_{EM} cells in circulation but also of CD8+ T_{RM} cells in the liver and lungs. This result aligns with another recent human study, which showed that a third vaccination in kidney transplant recipients

led to increased circulating polyfunctional CD4+ T cells. Future research could analyze whether a third dose of the mRNA vaccine in healthy individuals is also associated with increased T cell immunity.

Scientists highlighted that the increase of T_{EM} and T_{RM} cells in the lungs post the third vaccination might be critical as the lungs are the primary entry point for SARS-CoV-2. Moreover, the efficient formation of the TRM cells in the liver, mainly observed after the third vaccination, could contribute to protection as these cells have superior potential to differentiate into ex-T_{RM} cells.

Conclusion

The current study showed that a third vaccination with a synthetic vaccine containing a single CD8+ T cell epitope results in protection against SARS-CoV-2, which could be attributed to an improved quantitative and qualitative CD8+ T cell response after the third vaccination. This is highlighted by greater numbers of virus-specific TEM and TRM cells with polyfunctional cytokine capacity.

Source:

https://www.news-medical.net/news/20211220/Booster-shots-improve-CD82b-T-cell-response-to-SARS-CoV-2-in-animal-model.aspx