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Journal of Antivirals & Antiretrovirals

Perspective

An Overview on Coronavirus-Derived Broad-Spectrum Live-Attenuated SARS-CoV-2 Vaccines

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DESCRIPTION

The vaccinia virus used to treat smallpox, using SARS-CoV-2 related viruses from wild animals for live vaccines is an understudied but reliable strategy. The effectiveness of a live-attenuated vaccine made from the pangolin coronavirus GX_P2V was assessed in this study. We found that the attenuated mutant, GX_P2V(short_3UTR), significantly and persistently protected golden hamsters against SARS-CoV-2, especially after two treatments. Additionally, we demonstrate that GX_P2V(short_3UTR) and XBB.1.16 likely share neutralizing epitopes in sera from convalescents who received vaccination against the SARS-CoV-2 variant XBB.1.16. Additionally, it is demonstrate that the same sera from XBB.1.16 convalescents had much lower titers against the XBB.1.16 variation itself, pointing to an immune evasion tactic similar to a decoy that the highly immunogenic XBB.1.16 epitopes that cause cross-neutralizing antibodies may not be able to effectively neutralize the virus itself. Our research highlights the efficacy of GX_P2V (short_3UTR) as a live, broad-spectrum SARS-CoV-2 vaccine and reveals unique immune evasion mechanisms of the XBB.1.16 variant.

Sera from individuals and hamsters were obtained for this investigation in the manner previously described. The Fifth Medical Center, General Hospital of the Chinese PLA's ethical committee accepted this study, and all participants signed informed consent forms.

The American Type Culture Collection (ATCC) provided the Vero cells, which were obtained and grown in Roswell Park Memorial Institute (RPMI) 1640 medium (Gibco) supplemented with 10% fetal bovine serum.

FBS from Gibco, 1% penicillin and streptomycin from Gibco, and 37 degrees Celsius in an incubator with 5% CO_2. The absence of mycoplasma in the cell cultures was verified.

The pangolin coronavirus GX_P2V(short_3UTR) strain was passaged in Vero cells and kept at 80°C after being isolated from a lung-intestine mixed sample of a pangolin caught in anti-smuggling operations in 20172. This GX_P2V(short_3UTR) strain acquired two genomic mutations compared to the original strain derived from a lung-intestine mixed sample (GX/P2V/2017): an alanine to valine substitution in the nucleoprotein and a 104-nucleotide deletion in the hypervariable region of the 3'-terminus untranslated region4. In both *in vitro* and *in vivo* infection studies, this GX_P2V(short_3UTR) strain is significantly attenuated, enabling culture in a Biosafety Level 2 laboratory 4,11.

MT627325 is the GenBank entry number for the SARS-CoV-2 strain. and SARS-CoV-2 Omicron XBB.1.16 were isolated from a patient with laboratory-confirmed COVID-19 by passaging in Vero E6 cells (The sequence has been sequenced but not yet submitted, and it is compatible with EPI_ISL_17714261). The viral working stocks were grown, titrated, and stored right away at 80°C in Vero E6 cells. The Biosafety Level 3 facility served as the site for all SARS-CoV-2 research.

Utilizing the attenuated viruses found in wild animals as live vaccines is a viable method that is similar to the use of the vaccinia virus to vaccinate against smallpox given that SARS-CoV-2 related viruses have been detected in wild animals1-3. However, research on the SARS-CoV-2 vaccine continues to be under developed. In our earlier research, we produced the pangolin coronavirus GX_P2V and later discovered its naturally occurring variant at the 3'-UTR, often known as the short 3UTR (GX_P2V)4. Upon infection in golden hamsters, this mutant may induce cross-neutralizing antibodies against SARS-CoV-2 while being extremely attenuated. Interestingly, we found that patients who had received the wild-type SARS-CoV-2 vaccination may develop high-titer neutralizing antibodies against GX_P2V(short_3UTR) following breakthrough infections with the Omicron BF.7 variant.5. These findings highlight the potential of GX_P2V(short_3UTR) as a strong COVID-19 vaccination candidate. In the current work, we assessed the immunogenicity of GX_P2V(short_3UTR) and the immunity it provided in golden hamsters against both SARS-CoV-2 and the virus itself. Additionally, we quantified the neutralizing antibodies that are directed against XBB and GX_P2V (short_3UTR).1.16 among those who had already contracted the XBB and Omicron BF.7 viruses. variations of 1.16. Our research identifies GX_P2V(short_3UTR) as a top live vaccination.

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Received: 07-Aug-2023; Manuscript No. JAA-23-27496; **Editor assigned:** 09-Aug-2023, PreQc No. JAA-23-27496 (PQ); **Reviewed:** 30-Aug-2023, QC No. JAA-23-27496; **Revised:** 06-Sep-2023, Manuscript No. JAA-23-27496 (R); **Published:** 13-Sep-2023, DOI: 10.35248/1948-5964.23.15.288

Citation: Santos M (2023) An Overview on Coronavirus-Derived Broad-Spectrum Live-Attenuated SARS-CoV-2 Vaccines. J Antivir Antiretrovir. 15:288.

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