A vaccine against COVID-19 found to protect against infection and brain damage caused by the virus

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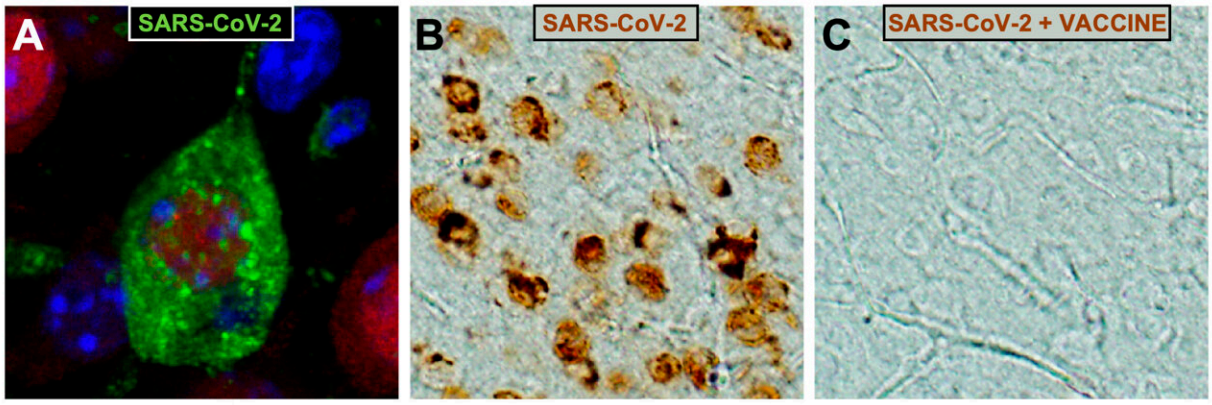

A) Neuron of the cerebral cortex infected with the SARS-CoV-2 coronavirus (viral particles in green). B and C) In B, cortical neurons infected by SARS-CoV-2 (in brown) and, in C, absence of infection in the same brain region of mice vaccinated with MVA-CoV2-S. Credit: IBiS

Although the pathology of the respiratory system is the main impact of COVID-19, many patients also manifest important neurological symptoms, such as loss of smell (anosmia), headaches, malaise, cognitive loss, epilepsy, ataxia and encephalopathy, among others.

However, this effect on the nervous system by the coronavirus has not been characterized in detail and it is unknown if the vaccines developed

against COVID-19 prevent the spread of SARS-CoV-2 to the central nervous system and confer protection against brain injury.

Now, using a mouse model susceptible to the SARS-CoV-2 coronavirus infection, a multidisciplinary team of Spanish researchers led by Dr. Javier Villadiego and Dr. Juan José Toledo-Aral (IBiS, CIBERNED and Department of Medical Physiology and Biophysics of the Faculty of Medicine of Seville) and Juan García-Arriaza (Department of Molecular and Cellular Biology of the CNB-CSIC, CIBERINFEC and PTI Global Health of CSIC), in collaboration with other groups from the University of Seville and the Spanish National Research Council (CSIC), demonstrate the ability of SARS-CoV-2 to infect different regions of the brain and to cause brain damage, and how the CNB-CSIC vaccine fully protects against infection of the brain.

These findings are published in *Nature Neuroscience*.

Researchers have studied the evolution of viral infection in different brain regions, noting that viral replication occurs mainly in neurons, producing neuropathological alterations such as neuronal loss, glial activation and vascular damage. "We have carried out a very detailed anatomo-pathological and molecular study of the brain regions and the types of cells that have been infected by the virus. It is remarkable how the virus infects different areas and mainly neurons," explains Javier Villadiego.

Once the pattern of infection in the brain by SARS-CoV-2 was established, the researchers evaluated the efficacy of the vaccine against COVID-19 developed at the CNB-CSIC. To do this, they immunized mice with one or two doses of the MVA-CoV2-S vaccine, based on the modified vaccinia virus Ankara (MVA) expressing the spike (S) protein of SARS-CoV-2, and analyzed the capability to protect against infection and damage to the brain.

"The results obtained were spectacular, demonstrating that even the administration of a single dose of the MVA-CoV2-S vaccine completely prevents SARS-CoV-2 infection in all brain regions studied and it prevents associated brain damage, even after a reinfection with the virus. This demonstrates the great efficacy and immunogenic power of the vaccine that induces sterilizing immunity in the brain," says Juan García-Arriaza.

These results reinforce previous data on the immunogenicity and efficacy of the MVA-CoV2-S vaccine in various animal models.

"We had previously shown in a series of publications that the MVA-CoV2-S vaccine that we developed at the CNB-CSIC induces in three animal models (mouse, hamster and macaque) a potent immune response of antibodies binding to the S protein of the virus and of neutralizing antibodies against different variants of concern of the virus, as well as T lymphocytes activation, essential markers for infection control," says Mariano Esteban, CNB-CSIC researcher involved in the study.

The results have important long-term implications for understanding the infection caused by SARS-CoV-2. "The data we have obtained on SARS-CoV-2 infection in the brain are compatible with the neurological pathology observed in patients with COVID-19," says José López-Barneo, IBiS researcher who participated in the publication.

"Our work is the first study of a vaccine that is 100% effective against brain damage caused by SARS-CoV-2 in a susceptible mouse, and the results obtained strongly suggest that the vaccine could prevent persistent COVID-19 observed in several people infected with SARS-CoV-2," says Juan José Toledo-Aral.

"The data provided in this study with complete inhibition of SARS-CoV-2 replication in the brain mediated by the MVA-CoV2-S vaccine,

together with previous studies published by the group and collaborators on the immunogenicity and efficacy of the vaccine against different variants of SARS-CoV-2, support phase I clinical trials with such a vaccine, or similar prototypes, to assess their safety and immunogenicity," the authors of the study emphasize.

More information: Javier Villadiego, Full protection from SARS-CoV-2 brain infection and damage in susceptible transgenic mice conferred by MVA-CoV2-S vaccine candidate, *Nature Neuroscience* (2023). DOI: 10.1038/s41593-022-01242-y. www.nature.com/articles/s41593-022-01242-y

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