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COVAXIN ELICITS IMMUNE MEMORY TO VIRUS, STUDY FINDS

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The COVAXIN vaccine. File | Photo Credit: MURALI KUMAR K

A small study conducted on 71 individuals who received two doses of Covaxin found that the vaccine generates antibodies and easily detectable memory B cell and T cell responses in many recipients. The study has been posted on a preprint server *medRxiv.* Preprints are yet to be peer-reviewed and published in a scientific journal.

The multi-institutional research, which is led by a team of scientists from Delhi's National Institute of Immunology, found that immunological memory to the virus and the variants after full vaccination seemed to last up to six months in many individuals. The cellular immune responses in the form of memory B cells and memory T cells seen in most vaccinated people would mean that the immune system can respond swiftly and provide protection in case of a breakthrough infection.

"The study finds that both B cells and T cells develop well after Covaxin administration. This means that even though antibodies may decline with time, the memory compartment will be marshalled quickly in case of a future infection to limit virus multiplication and disease," virologist Dr. Shahid Jameel Director of the Trivedi School of Biosciences at Ashoka University says in an email.

The study also evaluated the cellular immune responses in 73 individuals who have been naturally infected but have not been vaccinated. The samples in the infection group were collected between November 2020 and January 2021, prior to the Delta variant surge in India.

The researchers first measured anti-spike antibodies in the plasma samples from vaccinated and recovered individuals. All vaccinated and recovered individuals had detectable anti-spike IgG antibodies; the IgG titer against the spike protein was not significantly different between the two groups.

The study has measured the RBD-specific memory B cells but not the spike-specific memory B cells.

"We did not measure the spike-specific memory B cells for this study. We are currently undertaking this study. The levels of spike-specific memory B cells may not be very different from the RBD-specific memory B cells but this has to be studied," Dr. Nimesh Gupta from NII and the corresponding author of the preprint says in an email.

"We have demonstrated that vaccine induces memory T cells in about 85% of the subjects. The T cell responses are largely preserved against the variants, including the Delta variant," Dr. Gupta adds. According to the preprint, there was about 1.3-fold reduction in the case of memory T cells against the beta variant, with no significant impact against the Delta variant.

"While antibody-based neutralisation is reduced with Alpha, Delta and Beta variants, the memory compartment is not adversely affected," says Dr. Jameel.

The quantity of memory T cells is comparable to that of natural infection, and the composition of

memory subsets is indicative of a long-term durability of vaccine-induced T cell responses, says the preprint.

The analyses are from four weeks post-second dose up to six months, the authors note this is sufficient to gather key information on persistence of immune memory. However, the durability of immune memory cannot be defined due to absence of the longitudinal follow-up.

“Being a killed whole virus vaccine, antibodies and T cells against other viral proteins are also expected. In this paper the authors show this for the nucleocapsid as well. However, this is often wrongly cited as an advantage of Covaxin. Since the nucleocapsid protein is inside the virus, antibodies or T cells against it have little value in protection,” says Dr. Jameel.

“While the data are useful, the conclusions that can be robustly based on them are limited at this stage for a number of reasons,” immunologist Dr. Satyajit Rath, formerly with NII says in an email to *The Hindu.*

According to Dr. Rath, a major issue with the study is that the numbers of people tested are quite modest. While 71 vaccinated people were tested for antibodies, only 39 of them were apparently tested for memory B cell and T cell responses. The naturally infected group size is even smaller at 27, he says.

“We should note that each individual has been tested only once, so there is no information about the time course of immunity in any given individual,” says Dr. Rath. “Further, both these groups are quite diverse in when they were either infected or vaccinated. On average, naturally infected people were tested over seven months after their illness, while vaccinated people were tested about four months after vaccination. This limits how much meaning we can ascribe to comparisons between the two groups. To add to this uncertainty, the people in each group also have a lot of variation about when they were either vaccinated or infected, further compounding this problem of limited comparability.”

Dr. Rath mentions another important limitation of the study with regard to the measurements made in people belonging to both groups. “The cell-based tests for immunity provide relative rather than absolute measurements in the absence of very painstaking efforts for standardisation,” he says. “This means that quantitative comparisons of the 'levels' of immunity shown by these measurements can be reliably made only within this study. The actual numbers of cellular immunity levels from this study cannot simply be compared to those from other studies elsewhere. This is not a limitation of this study alone, but simply the nature of these tests.”

Since testing was done only when symptoms were reported, the study does not allow exclusion of asymptomatic reinfections and breakthrough infections among the naturally infected and vaccinated groups, respectively. “This introduces a potential variable that remains unaccounted for,” Dr. Rath says.

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