

The COVID-19 virus may not insert genetic material into human DNA, research shows

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The virus that caused COVID-19 likely does not integrate its genetic material into the human genome, research says. Although throughout human history there have been viruses capable of integrating their genetic material into human genes, this new study found that the COVID-19 virus, which is known to scientists as SARS-CoV-2, lacks the molecular machinery to integrate its RNA into human DNA. "Our work does not support the claim that SARS-CoV-2 fuses or integrates into human genomes," says Purdue scientist and co-lead author Majid Kazemian, pictured here. Credit: Rebecca

The virus that causes COVID-19, which scientists refer to as SARS-CoV-2, likely does not integrate its genetic material into the genes of humans, according to a study published in the *Journal of Virology*.

A separate study recently reported the virus's genetic material was found to have integrated into human DNA in cells in petri dishes. But the scientists conducting the newer research now say that result was most likely caused by genetic artifacts in the testing.

Majid Kazemian, a Purdue University assistant professor of biochemistry and computer science and one of the three co-lead authors on the research study, said that this finding has two

important implications.

"Relatively little is known about why some individuals persistently test positive for the virus even long after clearing the infection. This is important because it's not clear whether such individuals have been re-infected or whether they continue to be infectious to others. So-called 'human genome invasion' by SARS-CoV-2 has been suggested as an explanation for this observation, but our data do not support this case.

"If the virus was able to integrate its genetic material into the human genome, that could have meant that any other mRNA could do the same. But because we have shown that this is not supported by current data, this should allay any concerns about the safety of mRNA vaccines, he said."

It is possible for the genetic material of some viruses to be incorporated into the DNA of humans and other animals, resulting in what scientists call "chimeric events." Human DNA contains approximately 100,000 pieces of DNA from viruses that our species have accumulated over millions of years of evolution. In total, this lost-and-found DNA from viruses makes up a bit less than 10% of the genetic material in our cells.

Recent scientific journal articles have claimed that the SARS-CoV-2 virus can also cause these chimeric events. Even before this new research team conducted experiments showing this was not the case, the researchers suspected it was unlikely, said Dr. Ben Afzali, an Earl Stadtman Investigator of the National Institutes of Health's National Institute of Diabetes and Digestive and Kidney Diseases and a co-lead author on the study.

"While an earlier study suggested that, in cells infected with SARS-CoV-2, genetic material from the virus copied and pasted itself into human DNA, our group thought this seemed unlikely," Afzali said. "SARS-CoV-2, like HIV, has its genetic material in



the form of RNA but, unlike HIV, does not have the machinery to convert the RNA into DNA. SARS-CoV-2 is unlikely to paste itself into the genome and coronaviruses, in general, does not go near human DNA. As our study shows, we find it highly improbable that SARS-CoV-2 could integrate into the human genome."

Christiane Wobus, associate professor of microbiology and immunology at the University of Michigan Medical School, also a co-lead author on the study, said that although the collective understanding of RNA viruses is that integration of SARS-CoV-2 into the human genome would be very unlikely, it was important to examine the question.

"Unexpected findings in science—when confirmed independently—lead to paradigm shifts and propel fields forward. Therefore, it is good to be openminded and examine unexpected results carefully, which I believe we did in our study," she said. "However, we did not find conclusive evidence for SARS-CoV-2 integration, but instead showed that during the RNA sequencing methodology, chimeras are produced at a very low level as an artifact of the laboratory technique."

To examine the proposed integration event, the researchers developed a novel technique in which they extracted the genetic material from infected cells and then amplified or reproduced the genetic material 30-fold. If there were chimeric events in the host cell DNA, these bits of genetic material from SARS-CoV-2 should also increase 30 times. The data did not show this.

"We found the frequency of host-virus chimeric events was, in fact, not greater than background noise," Kazemian said. "When we enriched the SARS-CoV-2 sequences from the bulk RNA of infected cells, we found that the chimeric events are, in all likelihood, artifacts. Our work does not support the claim that SARS-CoV-2 fuses or integrates into human genomes."

More information: Bingyu Yan et al, Host-virus chimeric events in SARS-CoV2 infected cells are infrequent and artifactual, *Journal of Virology* (2021). DOI: 10.1128/JVI.00294-21

Liguo Zhang et al, Reverse-transcribed SARS-CoV-2 RNA can integrate into the genome of cultured human cells and can be expressed in patient-derived tissues, *Proceedings of the National Academy of Sciences* (2021). DOI: 10.1073/pnas.2105968118

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