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bioRxiv posts many COVID19-related papers. A reminder: they have not been formally peer-reviewed and should not guide health-related behavior or be reported in the press as conclusive.

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Posted December 13, 2020.

New Results

## SARS-CoV-2 RNA reverse-transcribed and integrated into the human genome

Liguo Zhang, Alexsia Richards, Andrew Khalil, Emile Wogram, Haiting Ma, Richard A. Young, Rudolf Jaenisch

doi: <https://doi.org/10.1101/2020.12.12.422516>

This article is a preprint and has not been certified by peer review [what does this mean?].

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### Summary

Prolonged SARS-CoV-2 RNA shedding and

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these patients most commonly are non-infectious<sup>1-14</sup>. Here we investigated the possibility that SARS-CoV-2 RNAs can be reverse-transcribed and integrated into the human genome and that transcription of the integrated sequences might account for PCR-positive tests. In support of this hypothesis, we found chimeric transcripts consisting of viral fused to cellular sequences in published data sets of SARS-CoV-2 infected cultured cells and primary cells of patients, consistent with the transcription of viral sequences integrated into the genome. To experimentally corroborate the possibility of viral retro-integration, we describe evidence that SARS-CoV-2 RNAs can be reverse transcribed in human cells by reverse transcriptase (RT) from LINE-1 elements or by HIV-1 RT, and that these DNA sequences can be integrated into the cell genome and subsequently be transcribed. Human endogenous LINE-1 expression was induced upon SARS-CoV-2 infection or by cytokine exposure in cultured cells, suggesting a molecular mechanism for SARS-CoV-2 retro-integration in patients. This novel feature of SARS-CoV-2 infection may explain why patients

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and suggests a new aspect of RNA virus replication.

### Competing Interest Statement

The authors have declared no competing interest.

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### Zoology

\* The Clinical Trials and Epidemiology subject categories are now closed to new submissions following the completion of bioRxiv's clinical research pilot project and launch of the dedicated health sciences server medRxiv (submit.medrxiv.org). New papers that report results of Clinical Trials must now be submitted to medRxiv. Most new Epidemiology papers also should be submitted to medRxiv, but if a paper contains no health-related information, authors may choose to submit it to another bioRxiv subject category (e.g., Genetics or Microbiology).

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