

## Science eLetters (<https://www.science.org/doi/10.1126/science.abp8715>)

Commentary on:

The Huanan Seafood Wholesale Market in Wuhan was the early epicenter of the COVID-19 pandemic. Worobey M., et al. (2022), *Science*, 337 (6609) 951-959

Oct. 29, 2022

### **SARS-CoV-2 origin is still unknown**

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In their article, Worobey et al. [1] confirm that the Huanan market served as an early superspreading event for COVID-19, but provide no definitive evidence that SARS-CoV-2 was first transmitted to humans from wildlife sold there. Out of the 457 animals (18 species) tested from the market, all were negative [2].

Although Worobey et al. date the first potential market-associated case to November 2019, wastewater surveillance and retrospective analysis of human samples raise the possibility that the

virus may have been spreading in France, Brazil and Italy in September–November 2019 [3]. Details about the first official human cases unconnected to the market are still unclear [4–6].

Worobey et al. examine SARS-CoV-2 positive environmental samples at the market, collected in January 2020 [2]. These samples are probably of human origin because the corresponding published sequences are identical to the ones found in patients [2]. Since the earliest detected cases at the market occupied stalls too dispersed for their direct contamination from 1–2 animal sources [7] and appear to be due to human-to-human transmissions outside of stalls, analysis of spatial distribution of positive samples is not relevant to infer the place of the first animal contamination. In fact, what the Worobey et al. density risk map may locate is the epicenter of a superspreading event, an area in the market's southwest where public toilets and a closed Mahjong room are found.

The distribution of human positive cases at the market is consistent with both a zoonotic introduction that would have occurred several weeks before the first cases were detected, and an introduction of the virus to the market by an externally infected person.

Worobey et al. situate the epicenter of earliest cases to a district that also includes the Wuhan Center for Disease Control laboratory, which conducts field and laboratory research on bat viruses [8] and which moved into a new location only 500 meters from the market on 2 December 2019, something they do not mention. The authors do not consider the possibility that this laboratory could be the site of the initial human case, but acknowledge that “upstream events” and “exact circumstances” remain “obscure”.

Although it may be challenging to distinguish an accidental infection during laboratory or field work from one that occurred between an animal and a market vendor, retrospective analyses of 2019 human samples available inside and outside China could prove informative to uncover upstream events.

In summary, the Huanan market can be considered as the epicenter of an early superspreader event but it is not possible to conclude that it was the entry point of SARS-CoV-2 into the human population. It is not yet clear how exactly SARS-CoV-2 originated. All hypotheses need to be investigated, including the possibility of a lab accident, as recently summarized in the SAGO committee report [9] and in the Lancet commission report [10].

## References

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Note: The views expressed here are those of the authors and not necessarily those of their respective institutions.

VCO and FG received funding from the "Who I am?" Labex to elucidate the proximal origins of the SARS-CoV-2 virus.

CDB has received a writer's fee from the United Nations Environment Programme for the forthcoming report "Covid-19: a warning".

RHE has received consulting fees on SARS-CoV-2 and the COVID-19 pandemic and receives funding from the National Institutes of Health and Janssen under grants and contracts unrelated to SARS-CoV-2 and the COVID-19 pandemic.

NP receives funding from the National Institutes of Health for vaccine research including COVID-19.

Competing interests for RAB, JMC, ED, JPD, HK, BK, ML, SM, MR, GT, NP: None declared.