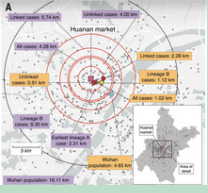


Where did SARS-CoV-2 come from?

01 Case Epidemiology



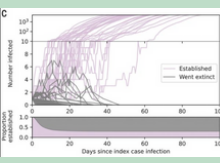
Hospitalizations and cases clustered around the Huanan market in Wuhan (WHO, 2021), both for epidemiologically linked and unlinked cases for the market (Worobey M, Science, 2021). That market link holds even when controlled for population density, age and ascertainment bias (Worobey et al., Science, 2022)

02 Natural genome

Table of Betacoronavirus Subgenus sequences from various regions including Serbia, Morocco, and Mexico.

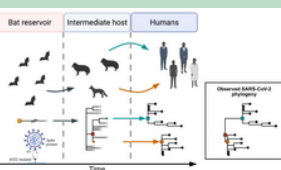
The SARS-CoV-2 genome shows many hallmarks of natural evolution, and no signs of genetic engineering or other manipulations (Anderson et al. Nature medicine, 2020 & Holmes et al., Cell, 2021 & Garry R, PNAS, 2022)

03 Multiple introductions



A single spillover (e.g. from a lab leak) would die out 70% of the time by itself. (Pekar et al., Science, 2021). Case history and simulations, phylogenetic clock and polytomies point to at least 2 separate successful introductions, and up to 15 total (Pekar et al., Science, 2022)

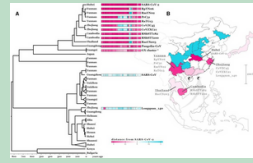
04 Two original lineages



Phylogenetic analysis showed that there were two separate lineages (Rambaut et al., Nature Microbiology, 2020) from the start of the outbreak, polytomies & lack of transitional genomes indicating multiple introductions from an animal population (Pekar et al., Science, 2022)

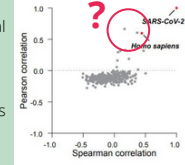
10 Recombination

The genome of SARS-CoV-2 is like a jigsaw puzzle with 27 pieces. All elements of its genome are found in nature (Zhou et al., Cell, 2021 & Temman et al., Nature, 2022) and the virus could have only come about through recombination in nature (on top of normal evolution & selection mechanism) (Lytras et al., Genome Biol Evol. 2022)



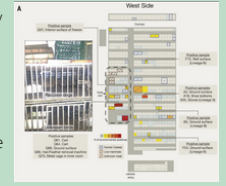
09 Environmental swabs

Sequencing of SARS-CoV-2 positive environmental samples have isolated animal sequences together with viral RNA (Liu, et al., Nature, 2023) Virus-positive swabs contained various wildlife genetic material, confirming previous photographic evidence of e.g raccoon dogs present (Worobey et al., Science, 2022)



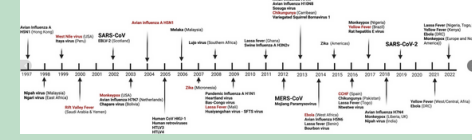
08 Animals at market

Investigations have shown that many SC2 susceptible animals had been sold at the Huanan market up until December 2019. (Xiao et al, Sci Reports, 2021 & Worobey et al., Science, 2022) Environmental samples cluster around shops where live animals were sold.



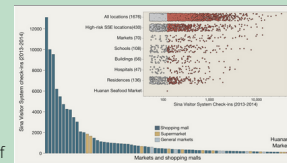
07 History

Zoonotic coronaviruses are common and have caused pandemics before (Cui et al., Nature Reviews Microbiology, 2018). SC2 shows many parallels to SARS-1 outbreak, including wildlife trade, time of year and Hubei farms link (Shi et al., Virus Research, 2007). All previous pandemics with an unknown pathogen were caused by zoonotic spillovers, which are common and present danger (Keusch et al., PNAS, 2022)



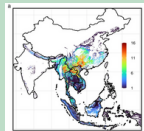
06 Outbreak site

All early cases cluster around a poorly visited market, a place unlikely to facilitate a human-to-human outbreak compared to restaurants, churches, stadiums that have been observed as amplifying events after introduction of SC2 in other cities (Worobey et al., Science, 2022). The market is also far away from the Wuhan Institute of Virology on the other side of the Yangtze river. (Holmes et al., Cell, 2021)



05 Hotspots

Bats & other animals carrying SC2r viruses have a wide range and are found in China (Zhou et al., Cell, 2021), Laos, Thailand (Wacharapluesadee et al., Nature communications, 2021) and other countries in South East Asia. Models suggest >60,000 CoV spillovers per year (Sanchez et al., Nature Communication, 2021)



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