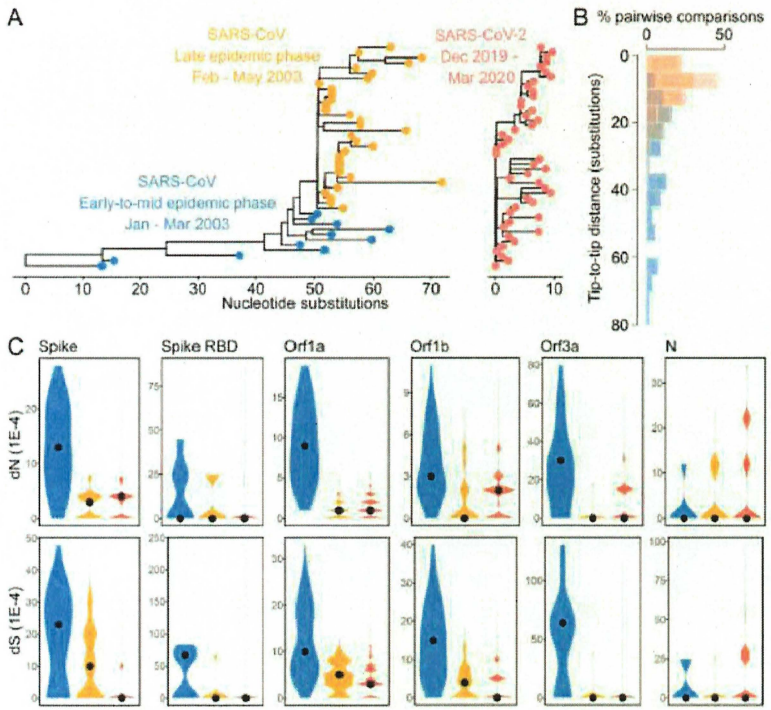
2

(b)(3):10 USC 424; (b)(6)

Informational Slides
29 JUNE 2020

(U) NOTABLE VIRUS FEATURES

(U) Adaptation to humans early in the outbreak: genomic evolution study

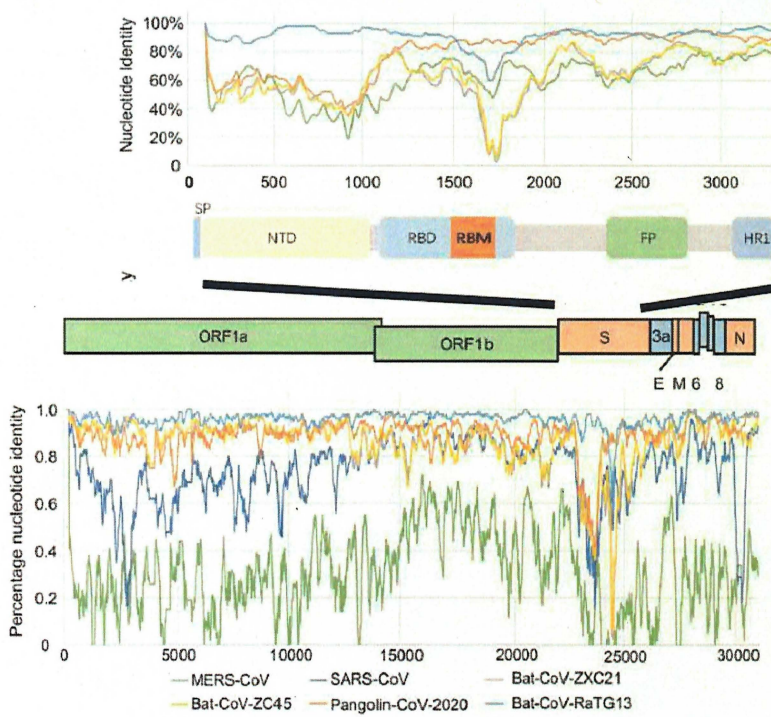


(U) "In a side-by-side comparison of evolutionary dynamics between the 2019/2020 SARS-CoV-2 and the 2003 SARS-CoV, we were surprised to find that SARS-CoV-2 resembles SARS-CoV in the late phase of the 2003 epidemic after SARS-CoV had developed several advantageous adaptations for human transmission. Our observations suggest that by the time SARS-CoV-2 was first detected in late 2019, it was already pre-adapted to human transmission to an extent similar to late epidemic SARS-CoV."

Zhan et al. SARS-CoV-2 is well adapted for humans. What does this mean for emergence? bioRxiv 2020.

(U) NOTABLE VIRUS FEATURES

(U) Similar to bat and pangolin coronaviruses in different regions



Liu et al. Are pangolins the intermediate host of the 2019 novel coronavirus (SARS-CoV-2)? PLoS Pathogens 2020.

(U) "In the region of nucleotides 1-914, Pangolin-CoV is more similar to Bat SARSr-CoV ZXC21 and Bat SARSr-CoV ZC45, while in the remaining part of the gene, Pangolin-CoV is more similar to SARS-CoV-2 and Bat-CoV-RaTG13 . . . In particular, the receptor-binding domain of the S protein of Pangolin-CoV has only one amino acid difference from that of SARS-CoV-2. Overall, these data indicate that SARS-CoV-2 might have originated as the recombination of a Pangolin-CoV-like virus with a Bat-CoV-RaTG13-like virus.

Xiao et al. Isolation of SARS-CoV-2-related coronavirus from Malayan pangolins. Nature 2020.

The following page is withheld citing (b)(3) 50 USC 3024(i), and is not provided.

(U) COULD A LAB HAVE MADE THE VIRUS?

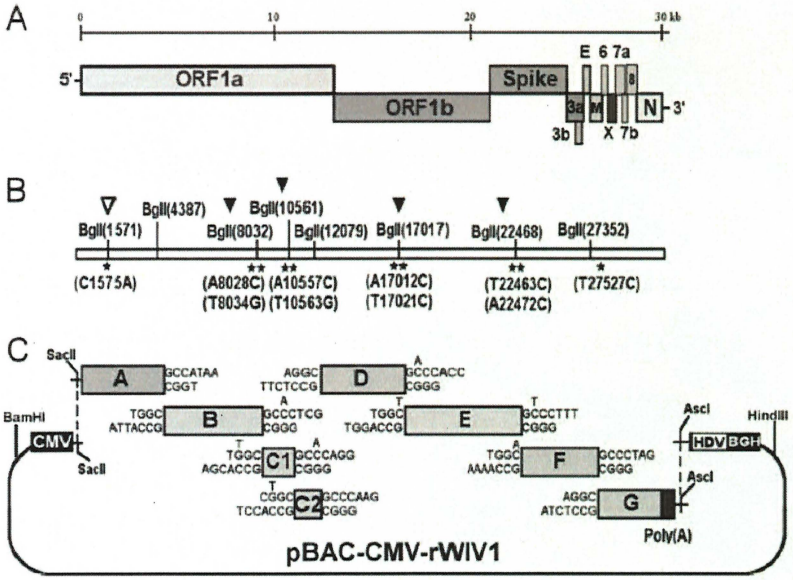
(U) "The Institute [Wuhan Institute of Virology] does not have the capability to design and synthesize a new coronavirus . . ."

(U) China Ministry of Foreign Affairs, press release 5 May 2020

The following page is withheld citing (b)(3) 50 USC 3024(i), and is not provided.

(U) PREVIOUS WIV RESEARCH IN RELATION TO SARS-COV-2

(U) Example: Method for synthesizing bat CoV WIV1 (reverse genetics system; 2016)



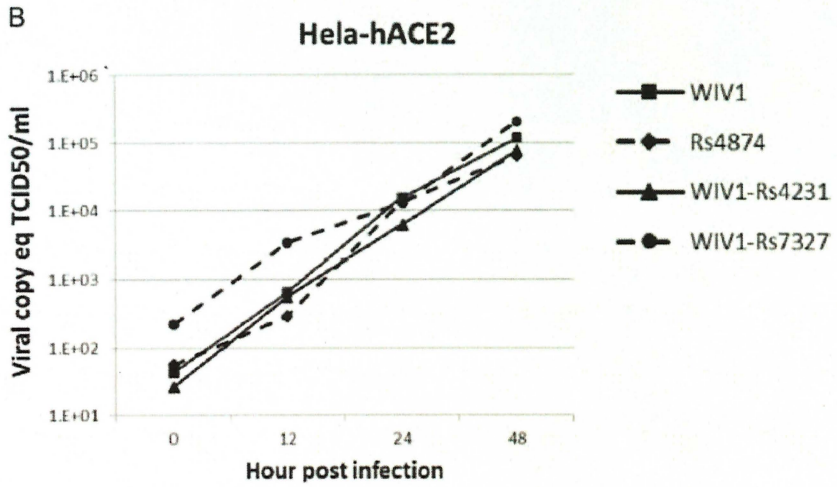
(U) "Strategy for construction of an infectious WIV1 BAC clone."

(U) "In this study, we have developed a fast and cost-effective method for reverse genetics of coronaviruses by combining two approaches developed by others. Our method allows the genomes of coronaviruses to be split into multiple fragments and inserted into a BAC plasmid with a single step . . . As the genomes can be divided into multiple short fragments, mutations can be introduced into individual fragments easily."

Zeng et al. Bat Severe Acute Respiratory Syndrome-Like Coronavirus WIV1 encodes an extra accessory protein, ORFX, involved in modulation of the host immune response. J Virol 2016.

(U) PREVIOUS WIV RESEARCH IN RELATION TO SARS-COV-2

(U) Example: Construction of chimeras with spike from new bat CoVs on WIV1 backbone, infection studies (2017)



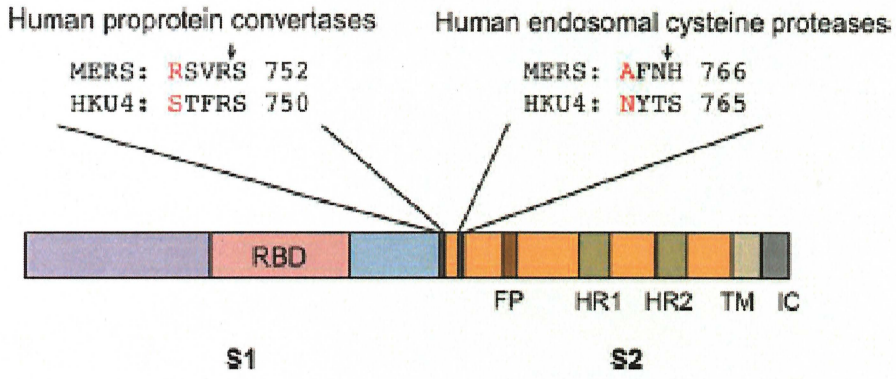
(U) Synthetic chimera infection of cells with human receptor.

(U) "In this cave, we have now obtained full-length genome sequences of additional 11 novel SARSr-CoVs from bats . . . Using the reverse genetics technique we previously developed for WIV1, we constructed a group of infectious bacterial artificial chromosome (BAC) clones with the backbone of WIV1 and variants of S genes from 8 different bat SARSr-CoVs."

Hu et al. Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insight into the origin of SARS coronavirus. PLoS Pathogens 2017.

(U) PREVIOUS WIV RESEARCH IN RELATION TO SARS-COV-2

(U) Example: Insertion of furin cleavage site enabling bat CoV (MERS-CoV progenitor) to infect human cells (2015)



(U) MERS-CoV and bat CoV HKU4 spike proteins.

(U) " . . . the two mutations adaptive to human cellular proteases transformed MERS-CoV spike from completely lacking to fully possessing the capacity to mediate viral entry into human cells, and thus they likely played the most critical role in the bat-to-human transmission of MERS-CoV, either directly or through intermediate hosts."

Yang et al. Two mutations were critical for bat-to-human transmission of Middle East Respiratory Syndrome coronavirus. J Virol 2015.