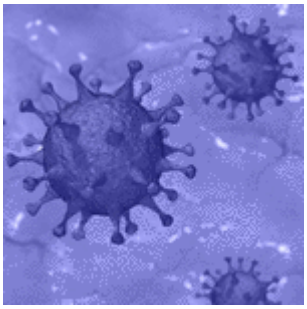
# Where did SARS-CoV-2 come from?



In previous zoonotic coronavirus events (SARS and MERS), near-identical strains of the virus were found in animal intermediate hosts (Cui, Li and Shi, 2019); however, a near-identical strain of SARS-CoV-2 has yet to be found in animals. The genome sequence of SARS-CoV-2 has highest similarity (96.3%) to that of Bat_SL-CoV_RaTG13, which was derived from a bat (Lam et al, 2020; Liu, Chen and Chen, 2019). However, can the origin of SARS-CoV-2 be explained solely by the evolution of a single virus? Li, et. al. (2020) provide preliminary insights into the complex evolutionary history of SARS-CoV-2.

Despite its similarity, CoV_RaTG13 has two notable genomic differences from SARS-CoV-2, indicating that the bat-derived virus cannot fully account for the novel SARS-CoV-2 virus: (i) the beginning region of SARS-CoV-2 ORF1a is more similar to that of Bat_SL-CoV_ZXC21 and Bat_SL-CoV_ZC45 (other bat-derived viruses); (ii) the ACE2 receptor binding motif located in the spike protein of SARS-CoV-2 is most similar to that of Pan_SL-CoV_GD (pangolin-derived virus) and is thought to be functionally similar. This is in contrast to the receptor-binding motif of CoV_RaTG13, which is considerably different and likely unable to facilitate infection of human cells. In addition, within this domain, the furin cleavage site of SARS-CoV-2 contains a unique insertion and likely increases the efficacy of spike glycoprotein cleavage (Walls, et al. 2020).

Furthermore, genome-wide comparisons by Li and colleagues

identified that SARS-CoV-2, CoV_RaTG13, and pangolin-derived viruses, each have genomic regions under similarly constrained negative selection – independent of the host – suggesting inter-species transmission. This further identifies Pan_SL-CoV_GD (as well as CoV_RaTG13) as a genomic contributor to the human SARS-CoV-2. Additionally, recombination detection analysis across divergent coronaviruses suggest that recombination events occur in bat-derived coronaviruses and that multiple recombination events between a variety of viruses contributed to the evolution of SARS-CoV-2.

The strong negative selection among human, pangolin, and bat coronaviruses in addition to the recombination occurring between bat coronaviruses results in the 'perfect storm' and provides an opportunity for coronaviruses to effectively adapt to new hosts, including humans. Settings such as animal markets are at risk of facilitating the recombination of highly divergent viruses, ultimately producing viruses with unique gene combinations and the ability to spread rapidly between humans.

**References:**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