

(b)(3):50 USC 3024(i); Sec. 1.4(c); Sec. 1.4(e)

(U) Emergence of a new virus prompts immediate comparison of the genetic sequence to sequences of other known viruses. This can provide initial indications of important characteristics, such as transmissibility and virulence, if the new virus is a close match to other viruses for which these properties are known. These analyses also can elucidate the evolutionary history of the virus, and suggest the non-human species the virus emerged from or passed through on its way to humans.

(U) In the case of SARS-CoV-2, the evolutionary history remains unclear, despite ongoing investigations by many skilled laboratories. The closest relative of the virus was reported by Chinese researchers in bats, which host hundreds or thousands of coronaviruses, including some capable of infecting humans (such as ones related to the viruses that cause Ebola, SARS, and MERS). However, it is now well-established that the genome sequences in key parts of SARS-CoV-2 differ substantially from this related bat virus. For example, the SARS-CoV-2 spike protein, which mediates attachment to host cells, contains a furin cleavage site between the S1 and S2 domains, encoded by a 12-base pair insertion. This site is not found in the related bat virus or in any SARS-related coronaviruses (Beta 2 coronaviruses; although it is likely that only a small proportion of all bat coronaviruses have been characterized). The presence of this site is expected to increase infectivity in the human respiratory tract and other tissues, and thereby promote more efficient spread in human populations than other SARS-related coronaviruses.

(U) SARS-CoV-2 is an RNA virus. While viruses with RNA genomes accumulate mutations at a higher rate than DNA viruses, these mutations are generally single-nucleotide changes, additions, or deletions. Larger insertions, such as the 12-base pair insertion that encodes the furin cleavage site in SARS-CoV-2, generally are not seen to arise all at once.

(U) Larger genomic segments can arise naturally through recombination, when two viral genomes infecting the same cell exchange genetic material (as occurs, for example, when a novel influenza strain arises through exchange of genetic material between two strains, which may derive from different host species). The insertion encoding the furin site in SARS-CoV-2 could have occurred during co-infection of a non-human host by two different coronaviruses—one related to the bat coronavirus that is the closest known relative of SARS-CoV-2, and another coronavirus (not yet identified) with unique characteristics found in the SARS-CoV-2 spike protein.

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