The return of the "Mistigri" through the SARS-CoV-2 XBB.1.5 chimera that predominated in 2023

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Abstract

The number of SARS-CoV-2 recombinants identified during the pandemic has increased since the era of Omicron variants, but XBB.1.5 (or Omicron 23A) is the first lineage comprised of hybrid genomes to predominate at the country and global scales. Very interestingly, the XBB.1.5 recombinant, like the Marseille-4B subvariant (B.1.160/20A.EU2) and the pandemic variant B.1.1.7 (20I/Alpha) previously, has its ORF8 gene inactivated by a stop codon. XBB.1.5 was generated through two successive main events: a recombination between SARS-CoV-2 of lineages BA.2.10.1.1 (BJ.1) and BA.2 75.3.1.1.1 (BM.1.1.1) that generated the XBB (22F) lineage; then ORF8 gene inactivation by a stop codon. We further identified that a stop codon was present at 89 (74%) codons of the ORF8 gene in [?]1 of 15,222,404 genomes available in GISAID, and at 15 codons (12%) in [?]1,000 genomes. Thus, it is very likely that stop codons in ORF8 gene contributed on at least 3 occasions and independently during the SARS-CoV-2 pandemic to the evolutionary success of a lineage that became transiently predominant, most recently XBB.1.5. Such association of gene loss with evolutionary success, which suits the recently described Mistigri rule, is an important biological phenomenon very unknown in virology while largely described in cellular organisms.

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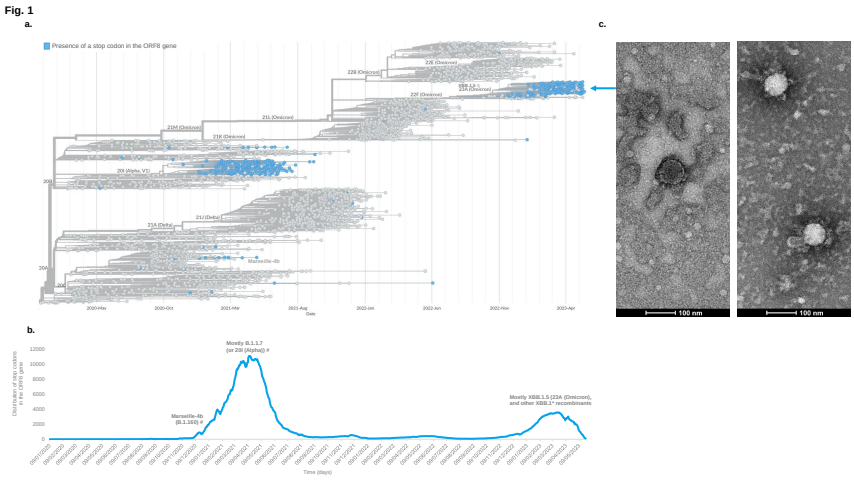

Fig. 2

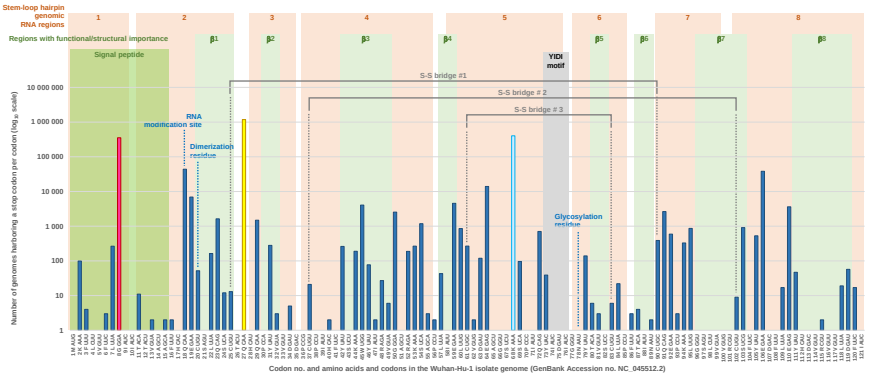

Fig. 3