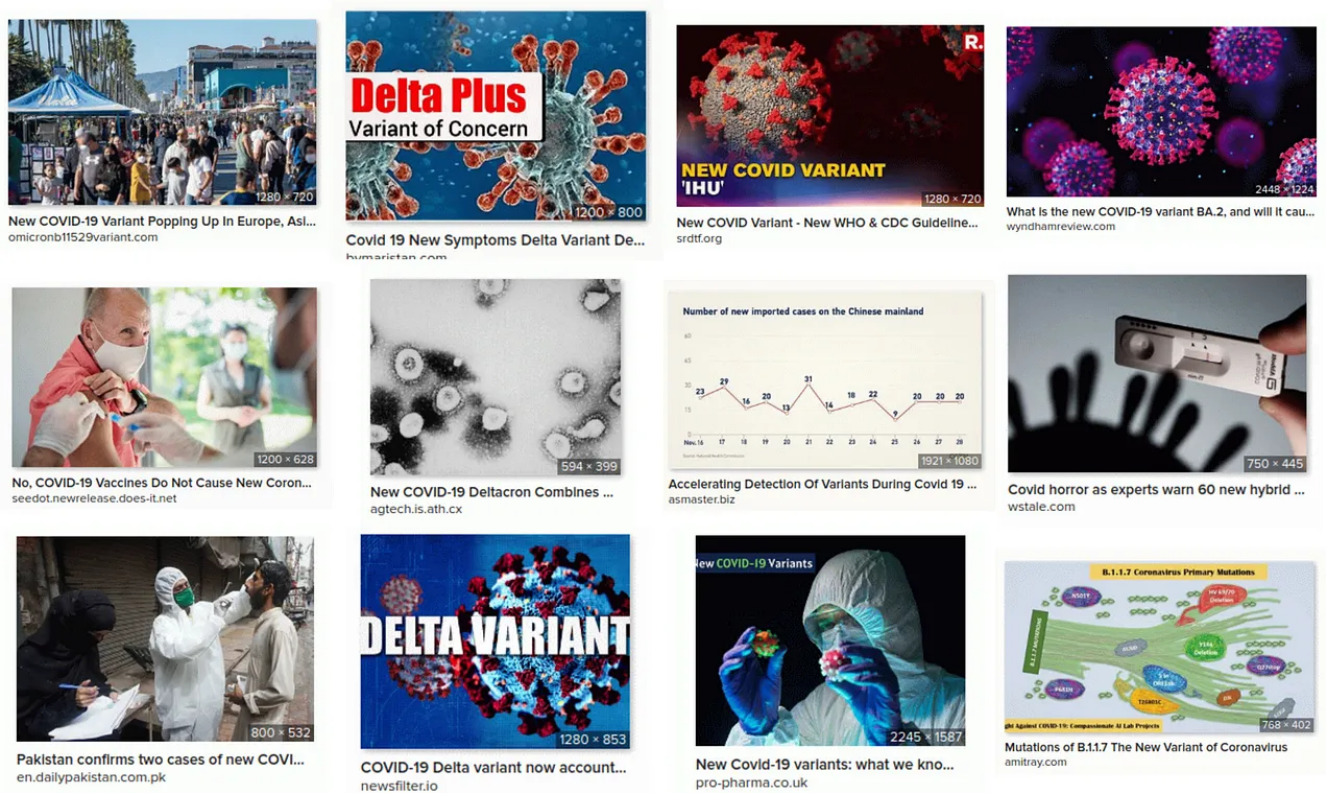
# Was Sars-Cov-2 DESIGNED to Spawn so Many Variants?

Ralph Baric Engineered Faster Mutating SARS Variant in 2010

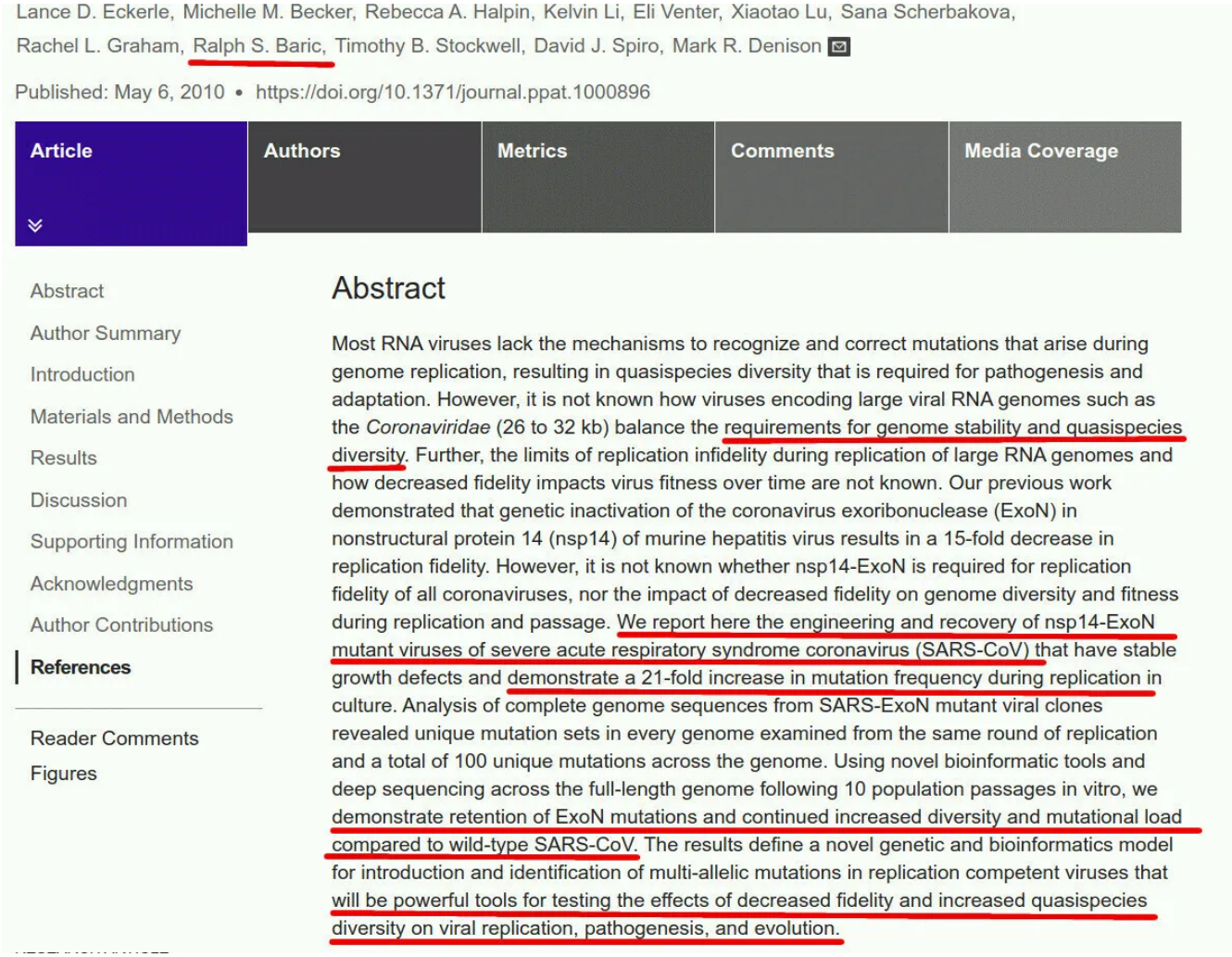
Igor Chudov
Mar 25



As new variants of Sars-Cov-2 keep appearing faster and faster, we have to ask **what makes the Sars-Cov-2 quasispecies mutate so fast, so much faster than the original Sars from 2003**, spawning endless new variants.




It turns out that science may have the answer for us! A well known genius scientist Ralph Baric published an interesting piece of research in 2010:



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Published: May 6, 2010 • https://doi.org/10.1371/journal.ppat.1000896

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## Abstract

Most RNA viruses lack the mechanisms to recognize and correct mutations that arise during genome replication, resulting in quasispecies diversity that is required for pathogenesis and adaptation. However, it is not known how viruses encoding large viral RNA genomes such as the *Coronaviridae* (26 to 32 kb) balance the requirements for genome stability and quasispecies diversity. Further, the limits of replication infidelity during replication of large RNA genomes and how decreased fidelity impacts virus fitness over time are not known. Our previous work demonstrated that genetic inactivation of the coronavirus exoribonuclease (ExoN) in nonstructural protein 14 (nsp14) of murine hepatitis virus results in a 15-fold decrease in replication fidelity. However, it is not known whether nsp14-ExoN is required for replication fidelity of all coronaviruses, nor the impact of decreased fidelity on genome diversity and fitness during replication and passage. We report here the engineering and recovery of nsp14-ExoN mutant viruses of severe acute respiratory syndrome coronavirus (SARS-CoV) that have stable growth defects and demonstrate a 21-fold increase in mutation frequency during replication in culture. Analysis of complete genome sequences from SARS-ExoN mutant viral clones revealed unique mutation sets in every genome examined from the same round of replication and a total of 100 unique mutations across the genome. Using novel bioinformatic tools and deep sequencing across the full-length genome following 10 population passages in vitro, we demonstrate retention of ExoN mutations and continued increased diversity and mutational load compared to wild-type SARS-CoV. The results define a novel genetic and bioinformatics model for introduction and identification of multi-allelic mutations in replication competent viruses that will be powerful tools for testing the effects of decreased fidelity and increased quasispecies diversity on viral replication, pathogenesis, and evolution.

Why is this 12 year old article so interesting? Because it shows how the leading Gain-of-Function researcher Ralph Baric was messing around with the SARS (the **original SARS of 2003**) virus in order to make it mutate faster and be able to spawn new variants at a greater rate.

Apparently, Ralph Baric was unhappy that the original Sars virus, while highly pathogenic, was not mutating fast enough. So he and his coauthors set out to make changes to the SARS virus to mutate faster!

Being brilliant researchers, they found a way to do it:

> We report here the **engineering and recovery of nsp14-ExoN mutant viruses of severe acute respiratory syndrome coronavirus (SARS-CoV)** that have stable growth defects and d**emonstrate a 21-fold increase in mutation**

> **frequency** during replication in culture.

> **Using novel bioinformatic tools** and deep sequencing across the full-length genome following **10 population passages in vitro**, we demonstrate **retention of ExoN mutations and continued increased diversity and mutational load compared to wild-type SARS-CoV.** The results define a **novel genetic and bioinformatics model for introduction and identification of multi-allelic mutations in replication competent viruses** that will be powerful tools for testing the effects of decreased fidelity and increased quasispecies diversity on viral replication, pathogenesis, and evolution.

> **Funding:** This work was supported by Public Health Service awards from the **National Institute of Allergy and Infectious Diseases**

To restate what they did in simple language: they used computer bioinformatic tools to find genetic changes required to make the virus mutate faster upon replication, thus allowing it to spawn more variants faster, while still remaining robust and replication competent.

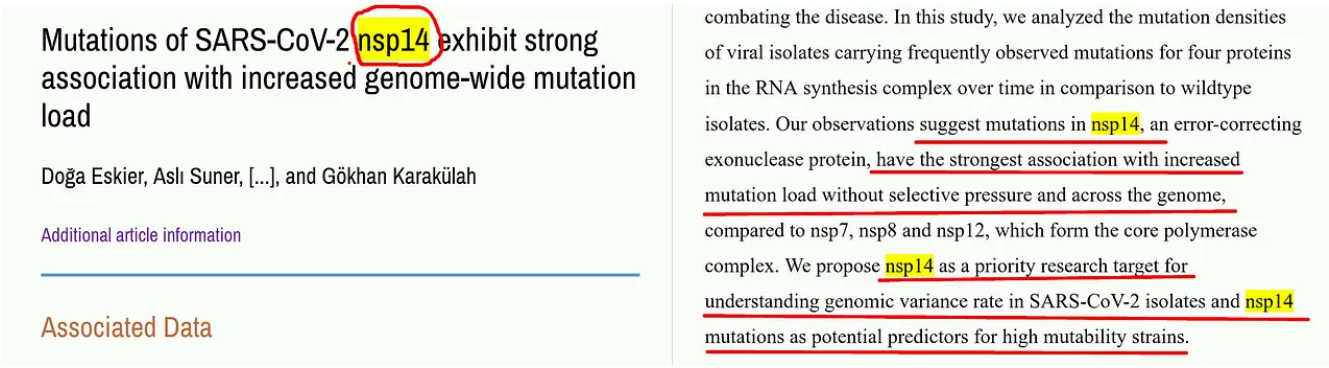
They found that so called “ExoN” mutations such as nsp14-ExoN, make the virus mutate 21 times faster, while keeping it replication competent (so that it is still able to replicate). They also passed it 10 times in-vitro as proof of concept, making sure that this mutant Sars variant indeed mutates 21 times faster to spawn even more variants.

Mind you, nsp14 is a “non-structural protein” that needs to be mutated to disable error correction and allow more mutations to appear during viral replication.

So what, you would say? Why should we care about this obscure protein?

# Sars-Cov-2 Mutates Faster Because of NSP14

Turns out that Sars-Cov-2 is also known to [mutate faster because of nsp14 mutations](#)...



Mutations of SARS-CoV-2 nsp14 exhibit strong association with increased genome-wide mutation load

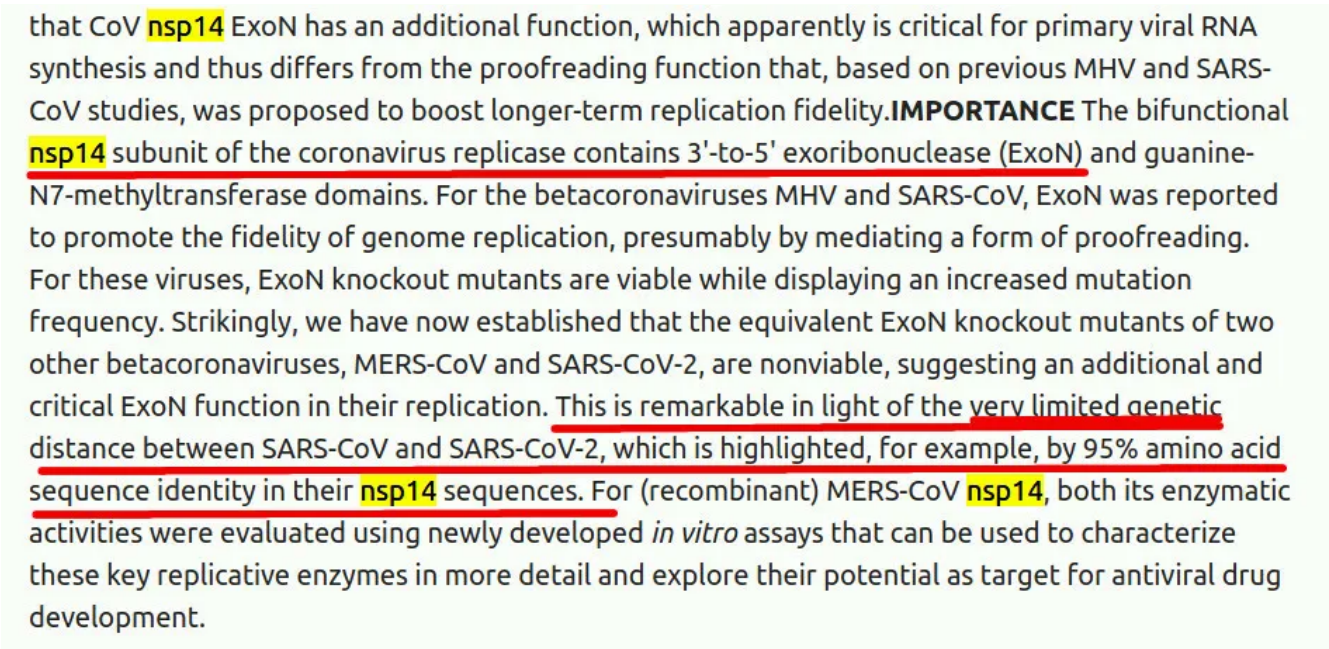
Doğa Eskier, Aslı Suner, [...], and Gökhan Karakülah

Additional article information

Associated Data

combating the disease. In this study, we analyzed the mutation densities of viral isolates carrying frequently observed mutations for four proteins in the RNA synthesis complex over time in comparison to wildtype isolates. Our observations suggest mutations in nsp14, an error-correcting exonuclease protein, have the strongest association with increased mutation load without selective pressure and across the genome, compared to nsp7, nsp8 and nsp12, which form the core polymerase complex. We propose nsp14 as a priority research target for understanding genomic variance rate in SARS-CoV-2 isolates and nsp14 mutations as potential predictors for high mutability strains.

... And Sars-Cov-2 [contains mutated Sars nsp14](#):



that CoV nsp14 ExoN has an additional function, which apparently is critical for primary viral RNA synthesis and thus differs from the proofreading function that, based on previous MHV and SARS-CoV studies, was proposed to boost longer-term replication fidelity.**IMPORTANCE** The bifunctional nsp14 subunit of the coronavirus replicase contains 3'-to-5' exoribonuclease (ExoN) and guanine-N7-methyltransferase domains. For the betacoronaviruses MHV and SARS-CoV, ExoN was reported to promote the fidelity of genome replication, presumably by mediating a form of proofreading. For these viruses, ExoN knockout mutants are viable while displaying an increased mutation frequency. Strikingly, we have now established that the equivalent ExoN knockout mutants of two other betacoronaviruses, MERS-CoV and SARS-CoV-2, are nonviable, suggesting an additional and critical ExoN function in their replication. This is remarkable in light of the very limited genetic distance between SARS-CoV and SARS-CoV-2, which is highlighted, for example, by 95% amino acid sequence identity in their nsp14 sequences. For (recombinant) MERS-CoV nsp14, both its enzymatic activities were evaluated using newly developed *in vitro* assays that can be used to characterize these key replicative enzymes in more detail and explore their potential as target for antiviral drug development.

So, Sars-Cov-2 contains a mutated nsp14 from SARS. How does it do in real life? Turns out, very well! nsp14 mutations [helped new variants to occur](#).

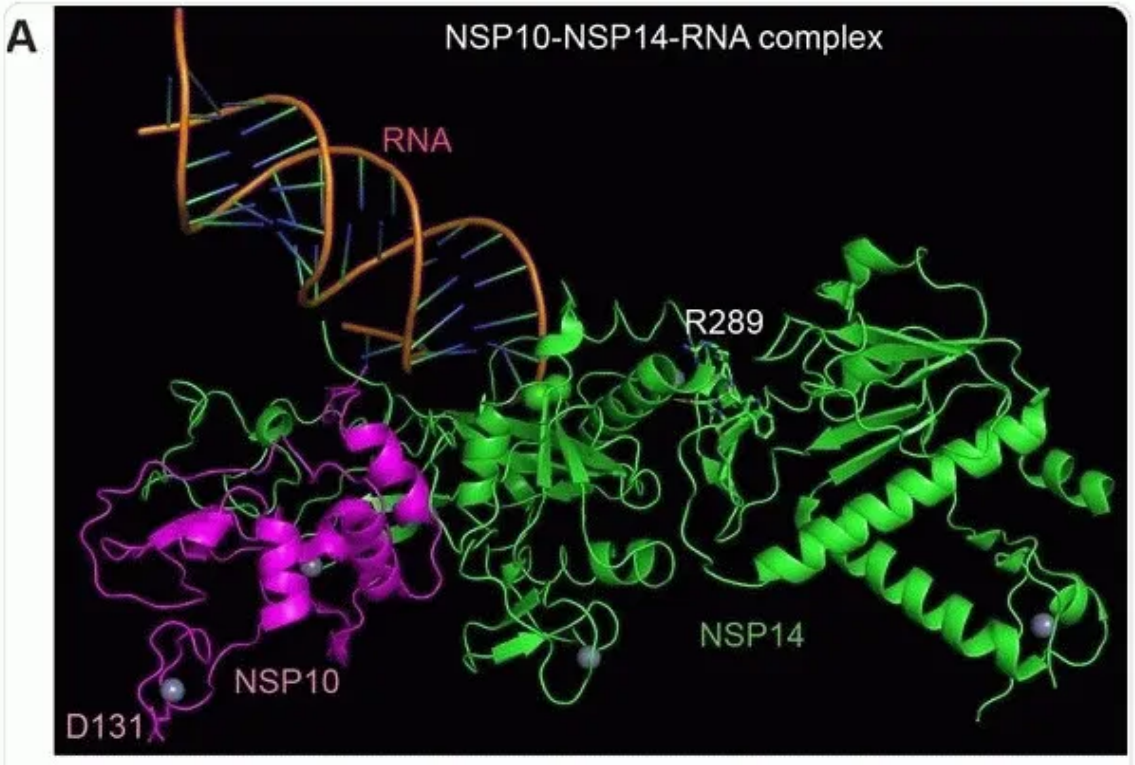
## Study findings

The examination of new SARS-CoV-2 genomes from these areas of the world led to the discovery of the BA.1.1 and BA.2 variants. Interestingly, these areas have witnessed the resurgence of COVID-19, despite previously good control. This indicates that the new mutations may have contributed to the rise in new cases in both countries.

Unlike the rest of the world, NZ reported its first Omicron case due to BA.1 on December 2021, and the first BA.1.1 only on the first day of 2022. Meanwhile, the rise in COVID-19 cases in NZ occurred from February 22, 2022, which leads to the postulate that during this period, viral evolution continued to occur.

This was facilitated by the occurrence of up to 70 mutations per viral genome, with BA.1.1 and BA.2 variants accounting for most cases, while BA.1 appeared to be fading out.

The new mutations were found in the non-structural protein (NSP)3, NSP10, and NSP14, all three of which are present in BA.1.1 genomes. The NSP10 mutation was found in more than 700 SARS-CoV-2 genomes; however, the NSP3 and NSP14 mutations do not occur together and affect different parts of the BA.1.1 genome.



# Nothing to See Here

This might be a pure coincidence: certain bats, sitting in the caves 1,000 km away from Wuhan, purely by chance decided to follow the suggestion of the 2010 Baric article and modified the nsp14 ExoN genes in order to make their virus mutate faster — just for fun.

We know the rest of the story: those bats also borrowed parts of the HIV genome, and parts of genetic code to make the NGVEGF peptide from Swine Flu of 2008. In addition, these bats illegally violated Moderna's patent and inserted a Moderna patented sequence into the key place of the Sars-Cov-2 virus as well, obviously without Moderna's permission.

I mean, why would Moderna give bats permission to use its patented code in Sars-Cov-2? There is no reason at all! The billions that Moderna made from Covid-19 vaccines, surely, are completely unrelated.

When done with the genetic modifications, those bats flew 1,000 km from their caves to Wuhan, China and started a global pandemic right in the "wet market" 2km away from the Wuhan Institute of Virology. All this is, of course, only a coincidence. There is nothing to see here. **Please move on, ignore it, and do NOT share this article!**

**18 replies by Igor Chudov and others**

**Pete Wiggin** Writes Wig Blog Mar 25 ♥ Liked by Igor Chudov

I postulated about a year ago was that the first gain of function mutation they would need is the mutation that makes it mutate faster...

...I had no idea the already did that in 2010

It is becoming more and more evident that America appears to be a nidus of infection...

We poisoned the World and were willing to do worse in Ukraine...

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**18 replies by Igor Chudov and others**

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