

When the faster-spreading and more virulent COVID-19 mutant came to my home town, it shook up everyone. Here's an explainer of what it foreshadows



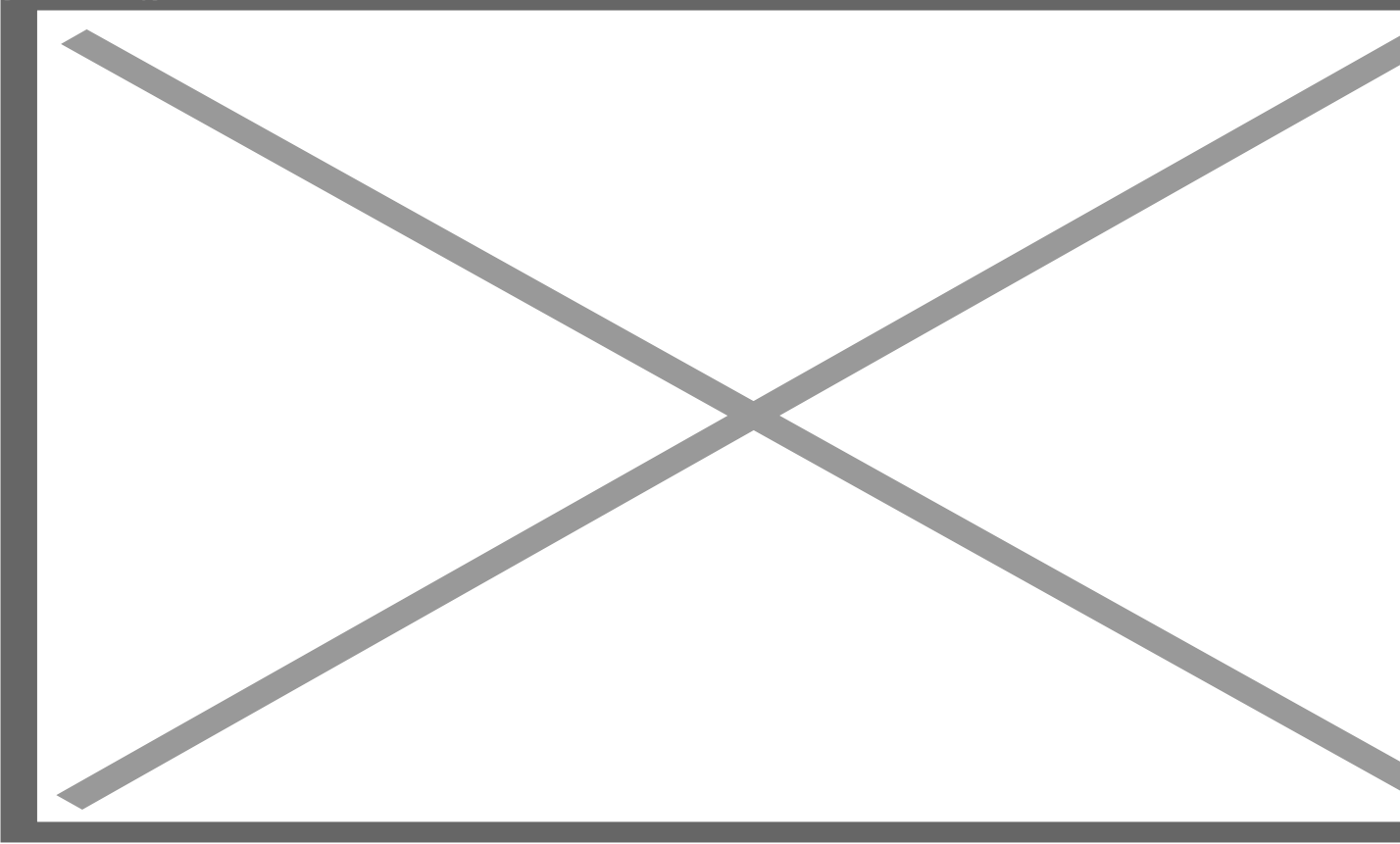
When a new variant of the COVID-19 virus appeared in the UK as 2020 drew to a close, I didn't think it would show up a half hour's drive from my home in the somewhat remote village in upstate New York soon after. The first cases were near Denver and in San Diego, and then traced to a jewelry store on Broadway in Saratoga Springs. My husband and I felt rather insulated and isolated here, hours from New York City.

The legacy of Caffè Lena

Earlier this year, I received an email from the executive director of [Caffè Lena](#), the oldest coffeehouse in the US. Don McLean debuted "American Pie" there, Arlo Guthrie first tried out "Alice's Restaurant," and Bob Dylan and many others have commanded the iconic tiny stage in the small, homey establishment that opened in [1960](#).

The café is now in "Safe Mode," with even the fabulous online events it has held throughout the pandemic too risky to record. The one-month shutdown follows the death January 12 from COVID of [Matt McCabe](#), owner of Saratoga Guitar and frequent performer at the coffeehouse. The opening image captures his final show, in December.

Image not found or type unknown



Matt McCabe plays his last set at Caffe Lena in December. He passed away from COVID on January 1.
Credit: Sarah Craig

The last time my husband and I had been to Saratoga was to dine outside Hattie's Chicken, next door to Caffe Lena. It was that fabulously warm wonderful November Saturday when the election results were in and we felt the first faint glimmers of hope return. We watched as a few musicians hauled their instruments up the steps of the recently-refurbished Caffe. I don't know whether Matt McCabe had the new variant of SARS-CoV-2. But now that Caffe Lena is stopping online broadcasts, I'll have more time to write, so thought I'd explain the confusing distinctions that have made a scary pathogen even scarier: mutants, variants, and strains.

What exactly are the new guises of SARS-CoV-2? And where did they come from?

A quick science lesson

Nucleic acids – DNA and RNA – are long strings of building blocks that impart meaning. Triplets of DNA or RNA bases encode the amino acids that link into proteins, and proteins underlie traits.

The sequences of nucleic acids can change, when the molecules copy themselves, like perpetuating a typo in a document. Not all changes to RNA or DNA affect the encoded protein, but if they do, they can

alter the corresponding trait. For a virus, that might be ease of transmission to a new host, strength of binding to receptors dotting the host's cells, or hiding from the immune response.

Once a mutation happens, two major factors – a founder effect and natural selection – influence the trajectory of its spread. Both can unfold at once, as is the case for SARS-CoV-2 right now.

Chance and selection fuel change

A founder effect is when a mutation or mutations arrive at a new location through chance sampling. That's how the UK variant ended up in Saratoga Springs.

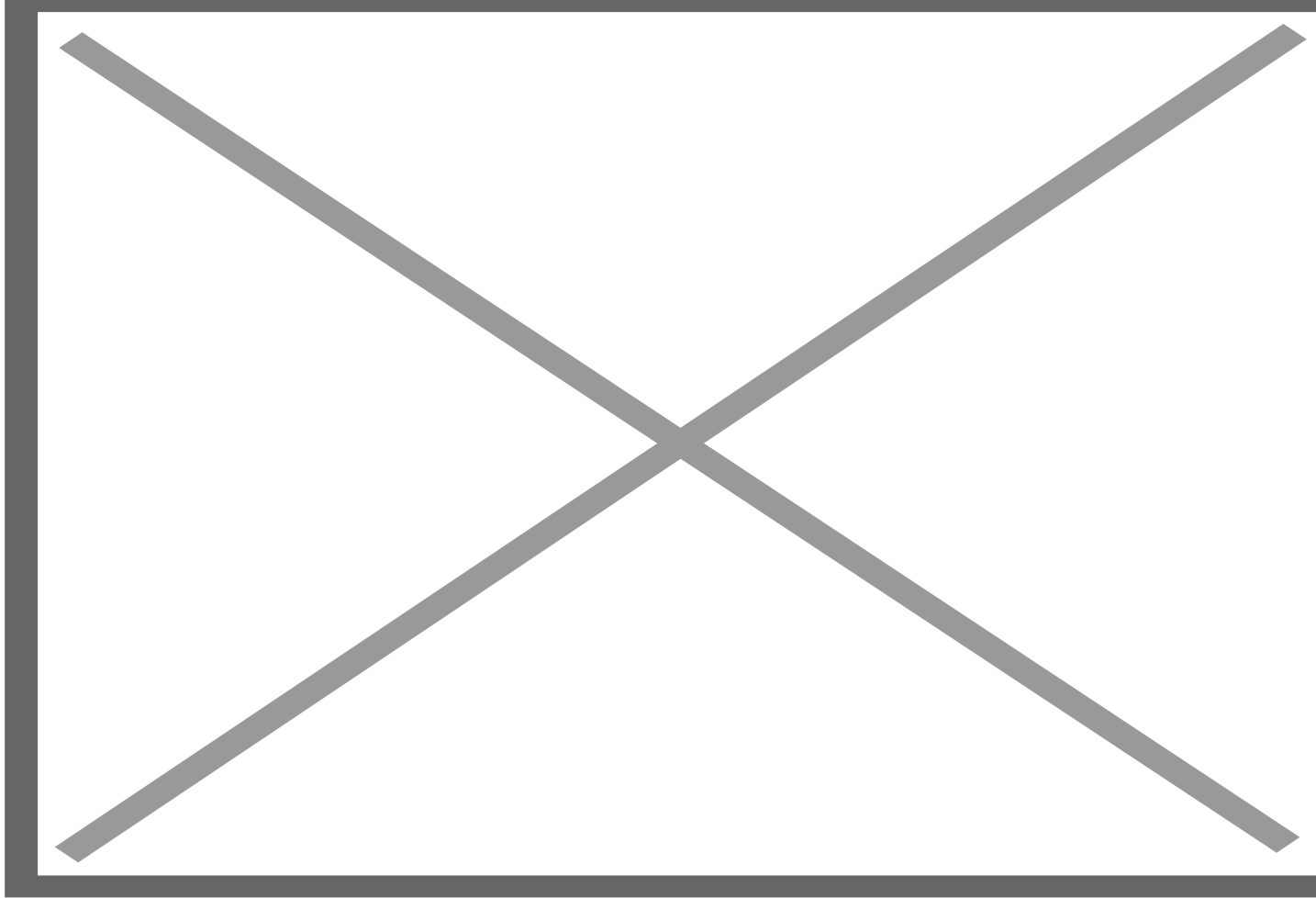
Several variants of the virus were circulating in the UK during the fall, genomic surveillance just beginning to pick them up, when a man unwittingly got on a plane and headed for Albany. A few days later, he was shopping for a Christmas gift at the jewelry store on Broadway in Saratoga Springs, and became the first person to harbor the new UK variant in New York state. Might he have, perhaps circuitously, infected Matt McCabe?

A founder effect can deliver a novel viral variant on a smaller scale than an airplane, too. A person might harbor several versions of SARS-CoV-2, yet only one jumps to another person in a sneeze or cough.

Soon after founder effects brought new variants here, natural selection unfolded too. It's survival of the fittest: if a new mutation benefits the virus, it persists.

The UK variant, called [B.1.1.7](#), consists of several mutations that enable viruses to copy themselves 71% faster, spread from host-to-host more readily, and bind more tenaciously to our cells.

Image not found or type unknown



Credit: New York Times

Mutations, variants, and strains, oh my!

New versions of SARS-CoV-2 differ genetically, but the degrees of difference are confusing. Here's clarification:

- A *mutation* substitutes one type of RNA base for another at a single place in the 30,000-base viral genome. If the change alters the encoded amino acid in a way that changes the virus's action, natural selection can favor it. To a geneticist, "gene mutation" and "gene variant" are synonymous.
- A *variant* to an epidemiologist is broader, meaning the viral genome has something different, arising from one or more mutations. B.1.1.7 harbors nine mutations in the spike protein gene alone, the part that the immune response "sees."
- A *strain* is even broader, denoting a variant that has a telltale observable or measurable trait or behavior. A new strain may emerge from gene interactions.

It's hard to keep up with the ever-mutating virus, and I can't describe them all in one post. But here's a description of three new faces of the virus that have dominated newsfeeds: D614G, a mink mutation, and B.1.1.7.

“D” versus “G” virus

The first notable COVID mutant, called D614G, popped up in several parts of Europe by early March, and then hopped planes to the US. Because it [spreads more readily](#) than whatever it mutated from, it's taken over. D614G may have seeded Europe from China in January through a founder effect, but once there, it likely spread, fast, under powerful natural selection.

“The mutation was concerning because it looked like something new was taking over in multiple places. In evolution, that's a strong clue that it might confer an advantage for the virus, that natural selection is at play,” said Adam Luring, of the University of Michigan Division of Infectious Diseases in a [JAMA webinar](#) January 2. Modeling and cell experiments indicated natural selection rather than a series of founder effects.

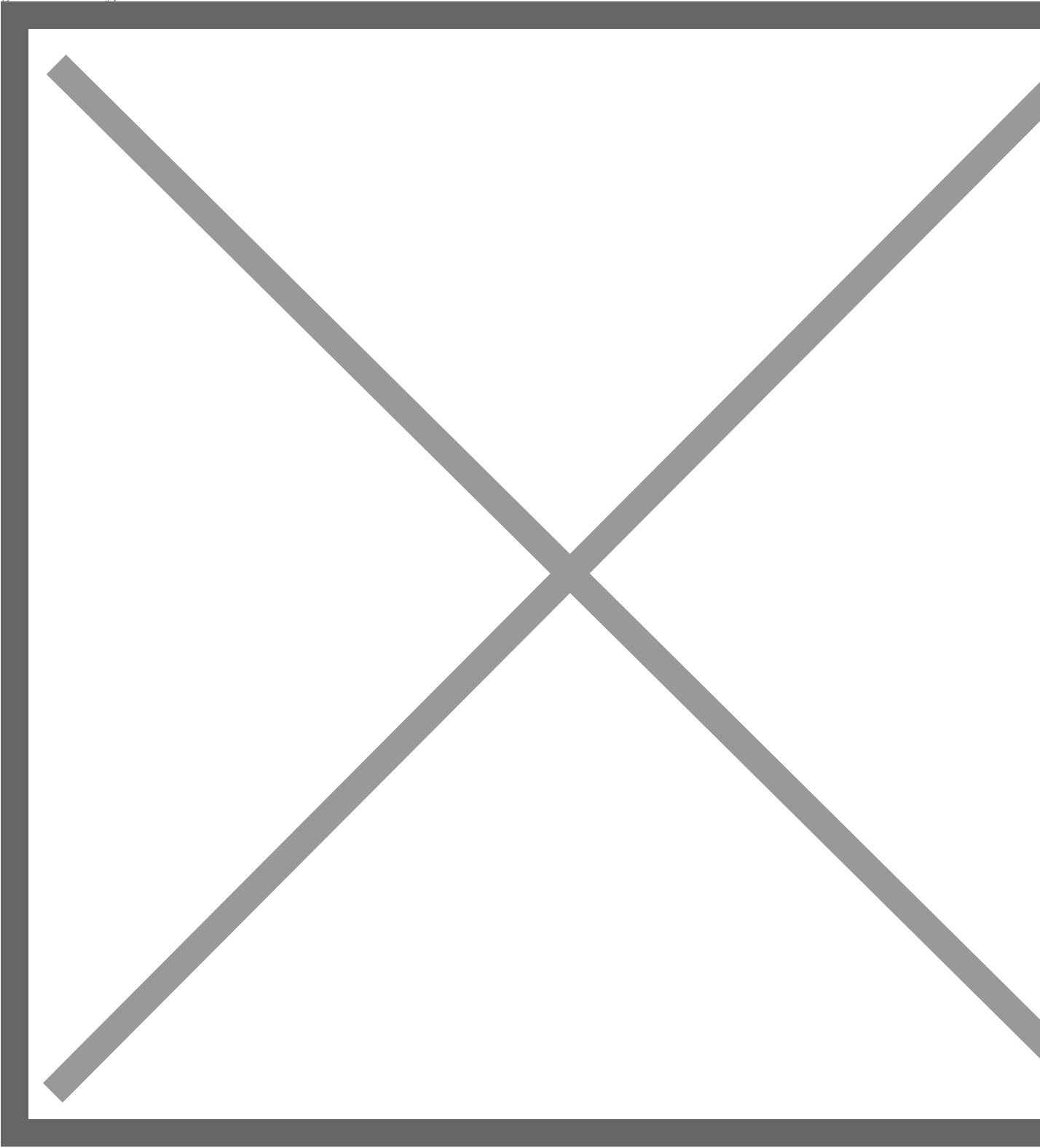
Anthony Fauci added perspective on D614G. “RNA viruses mutate, that's been known forever. The overwhelming majority of mutations are without any functional significance. Every once in awhile, we get one that is,” and that's the case for the single amino acid change at position 614 in the spike, the part of the virus that binds to ACE2 receptors on many human cell types. While the mutation spreads more easily and binds tighter to receptors, the antibodies that the vaccines elicit do attack it, he reassured. But spreading more easily means more opportunities to mutate.

What D614G enables the virus to do is a little like strengthening the tailhook of a fighter plane, making it better able to latch onto a cable on the deck of an aircraft carrier. The mutation affects a specific spot in the spike, where its “receptor binding domain” intersects a loop of amino acids that reverberates like a trap door. Once a spike grabs on, a second part of it clamps down onto the cell membrane and pushes the virus through. We're infected.

Here's what “D614G” means in [biochemical shorthand](#): a single RNA base change corresponding to the 614th of 1277 amino acids that comprise the spike. The mutation alters an aspartic acid (“D”) to a glycine (“G”). (Biochemistry convention represents each of the 20 amino acids with a single letter.)

The jargon behind D614G is abbreviated further to the “D” and “G” strains of the virus. D is the slowpoke, while newbie G copies itself more readily, boosting a person's viral load so that denser clouds of virus are exhaled.

Image not found or type unknown



Credit: Bette Korber/Cell

But the D614G mutation may eventually exert greater significance in terms of epidemiology. A viral variant that passes to more people (ups the “R naught” value) elevates the percentage of a population that must become immune (through infection or vaccination) to achieve herd immunity. I’ll save that for another post.

The mink mutation

Next came minks. [Reports](#) from the Netherlands in the spring, and in Denmark in June with autumn resurgence, pointed to mink farms. Human workers may have initially given the virus to the minks, which then returned the favor, in changed form.

The mink mutation also alters the spike protein, and is dubbed N453Y – a change from tyrosine to phenylalanine at amino acid position 453. Studies on people who’ve recovered from COVID show that sometimes their antibodies aren’t as able to neutralize [the new version of the virus](#), while the spikes bind more strongly to our receptors.

“The change is modest, so I don’t think it will compromise vaccines. But the big concern is a virus established in another host species where it can evolve and spill back into humans,” Lauring said. That’s why many countries are culling minks.

The UK and South African variants

The evolutionary tree diagrams that depict relationships of related species, like hippos, whales, pigs, and peccaries, are also used to track changes in viral genomes. The trees are derived from comparing DNA or RNA sequences, sometimes using mutation rates to estimate times of divergence from shared ancestors.

I think of evolutionary trees when my laptop freezes and I have to rescue the document from every time I’d hit “save.” I compare all the versions that suddenly overlap on my screen to deduce the order, from first draft to most recent.

Researchers similarly upload new SARS-CoV-2 genome sequences to the database [GISAID](#), where bioinformatics tools convert the data into branches, called lineages or phylogenies, of evolutionary trees. (See [COVID Genomes Paint Portrait of an Evolving Pathogen](#), here at *DNA Science*.)

[B.1.1.7](#) harbors a “signature” of 14 mutations. The most notable is N501Y (asparagine changed to tyrosine at position 501).

Blasting through the UK and South Africa and beyond with astonishing speed, N501Y clearly has an advantage – that’s natural selection at work, not a slower founder effect. The fact that N501Y arose independently in the UK and South Africa also points to natural selection. “This virus grows faster and it started later, and has spread rapidly, doing a lot better than its cousins. We should pay attention,” warned Lauring.

Follow the latest news and policy debates on sustainable agriculture, biomedicine, and other 'disruptive' innovations. Subscribe to our newsletter.

[SIGN UP](#)

The UK variant has probably been more widespread here and we didn't know it simply because we weren't looking. "The UK has a massive operation. They sequence 10% of all SAR-COV-2 tests; in the US, we sequence probably way less than 0.5%. Other countries that also don't do a lot of sequencing are now finding it because they're looking harder for it now," Lauring said.

Although B.1.1.7 doesn't make people sicker, its more rapid spread means that more people will become infected – and the sheer numbers will send more patients to already overburdened hospitals. It's déjà vu all over again from D614G.

Preliminary studies from [South Africa](#), where people who've been sick are becoming [reinfect](#)ed with the new variant bearing the N501Y mutation, indicate that the natural immune response isn't making sufficient neutralizing antibodies. Vaccines are likely to offer better protection because they're designed to coax the body to make a wider array of antibodies, tackling spikes at several points and from several angles. But if vaccine efficacy is even slightly lower than expected from testing before the new variants arrived, that'll raise requirements for herd immunity.

Coda

The battle of humanity against the novel coronavirus seems never-ending. Evolutionary trees reveal that SARS-CoV-2 jumped to us from bats only recently – so its genome is still adapting to our bodies. The virus is a moving target.

January 20, New York's governor Andrew Cuomo addressed the future of the changeling virus. As he reported two more cases of B.1.1.7 from Saratoga Springs, he said "it is just a matter of time" and "a matter of probability" until we will face a more deadly or vaccine-resistance coronavirus. Next week I'm writing about a machine learning algorithm that predicts mutations.

Meanwhile, what must we do, before nature attenuates SARS-CoV-2 into just another cause of the common cold? That could be years from now. Continue with the tried-and-true, if uncomfortable, public health measures – social distancing, hand-washing, and wearing masks.

Ricki Lewis has a PhD in genetics and is a science writer and author of several human genetics books. She is an adjunct professor for the Alden March Bioethics Institute at Albany Medical College. Follow her at her [website](#) or Twitter [@rickilewis](#)