‘Pirola’ BA.2.86 may not be a ‘black swan’ event like Omicron, experts say. It’s what could spawn from it that has them worried

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Erin Prater

Highly mutated COVID strain “Pirola” BA.2.86 may not be a “black swan” event after all, introducing a viral plot twist in the pandemic like Delta and Omicron did nearly two years ago. But it’s not your garden-variety variant either, experts caution.

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Highly mutated COVID strain “Pirola” BA.2.86 may not be a “black swan” event after all, introducing a viral plot twist to the pandemic like Delta and Omicron did nearly two years ago.

But it’s not your garden-variety variant either. That’s according to experimental data released Thursday by leading variant researcher Yunlong Richard Cao, an assistant professor at Peking University’s Biomedical Pioneering Innovation Center in China. His lab performed experiments using a pseudovirus, a version of the variant created in a lab.

The good news: BA.2.86's ability to infect human hosts may be "much lower" than high-flying variant "Eris" EG.5—estimated to comprise more than a fifth of U.S. cases as of Sept. 1, according to the U.S. Centers for Disease Control and Prevention—and "Kraken" XBB.1.5, a former leading variant.

Lower infectivity could mean that BA.2.86 never truly takes off, according to Cao. Ironically, the variant's flaw may be due to some of the 30-plus mutations that separate it from other Omicron spawn—a handful of which actually work against the virus.

The not-so-great news: BA.2.86 features a greater number of mutations that help it rather than harm it. The formidable strain can "significantly escape" immunity from XBB variants from both vaccination and infection, Cao found.

Unfortunately, new COVID boosters, set for U.S. release later this month, were tailored to XBB.1.5—and how they will hold up against the highly mutated Omicron spawn is now more in question than ever.

"The updated vaccine's efficacy against BA.2.86 should be closely monitored," Cao wrote in a Thursday Twitter thread on his findings. "However, BA.2.86 may not prevail very fast due to its lower infectivity."

> Sharing some new experimental data on BA.2.86:
> 1) BA.2.86 is antigenically distinct compared to XBB.1.5.
> 2) BA.2.86 can significantly escape XBB-infection/vaccination induced antibodies.
> 3) However, the infectivity of BA.2.86 may be much lower than XBB.1.5 and EG.5.
> (1/n) pic.twitter.com/sJZ8ySKxMG
>
> — Yunlong Richard Cao (@yunlong_cao) August 31, 2023

New data released on Twitter Friday evening by Ben Murrell, a researcher at the Karolinska Institutet in Sweden, showed that blood samples taken citizens last week—presumably from individuals who had been infected with an XBB-family variant—performed better than it expected when it came to neutralizing BA.2.86.

The findings offer a more positive outlook for how new boosters might protect against the highly mutated variant, Dr. Eric Topol, a professor of molecular medicine at Scripps Research and founder and director of the Scripps Research Translational Institute, said in a Friday tweet.

> More good news about the BA.2.86 variant, from great work by the @karolinskainst team, adding to its low cell infectivity by @yunlong_cao's group report
> Some unanticipated cross-reactivity of XBB.1.5 antibodies, which forecasts better for the new booster https://t.co/VXIJEIhHsz
>
> — Eric Topol (@EricTopol) September 2, 2023

A new COVID standard-bearer?

We can, perhaps, breathe a collective sigh of relief—for the moment. But it's far from time to let our guard down, experts tell *Fortune.*

BA.2.86 may not be the next "Omicron event," fueling an unprecedented surge of cases, causing the makers of vaccines and therapeutics to scramble, and creating a new viral normal.

But one of its spawn could be.

"I'm more worried about its descendants," Ryan Gregory, a biology professor at the University of Guelph in Ontario, tells *Fortune*. He's been assigning "street names" to high-flying variants since the WHO stopped assigning new Greek letters to them. "It's a potential BA.2.86.1.5 that concerns me."

Gregory cites BA.2.75 and the original XBB variant as examples. Both were initially thought to be cause for concern but didn't make much of a splash. "It's their descendants that became dominant," he pointed out.

"Even if Pirola (BA.2.86) itself doesn't cause mass casualties, we don't want it as the new starting point for further evolution as the dominant variant."

Murrell agreed with Ryan, writing in a late Friday tweet that BA.2.86 "doesn't appear to be nearly as extreme a situation as the original emergence of Omicron." What's more, "our antibodies do not appear to be completely powerless against it."

"The fact, however, that another Omicron-like emergence event has occurred … should warn us against giving up our genomic surveillance infrastructure," he added.

A new variant that evolved in an immunocompromised person, as BA.2.86 is thought to have, is unlikely to immediately out-compete top COVID strains. Why? Contained within a single host, it had no need to develop increased transmissibility to win an evolutionary survival-of-the-fittest. Globally circulating variants, on the other hand, have had months to pick up new mutations and refine their ability to spread.

Once a highly mutated variant from a long-term infection escapes into the broader population, however, it's likely to begin its own process of refinement, Gregory said. And "the fact that Pirola has gained enough of a foothold to be evolving among hosts now means we need to be wary."

At this stage of COVID evolution, variants are evolving in tandem: picking up the same, or similar, sets of mutations due to evolutionary pressure. They're also combining with one another inside of individuals, who can pass those new variants to others. (An immunocompromised host is not needed to create a recombinant. Most any host will due.)

That means BA.2.86, which is highly immune-evasive but perhaps not the most skilled at spreading, could combine with another top COVID variant that is—and potentially wield both traits.

“It’s time to closely watch BA.2.86’s next steps,” Raj Rajnarayanan—assistant dean of research and associate professor at the New York Institute of Technology campus in Jonesboro, Ark., and a top COVID variant tracker—said in a Thursday tweet.

> Time to closely watch BA.2.86*'s next steps
>
> I recon it would try to pick other mutations including #FLip combo mutations (S:F456L/L455F) and/or recombination with top circulating XBB* (EG.5, FL.1.5.1 etc) to boost its infectivity, ACE2 binding affinity and other properties
>
> 2/n
>
> — Raj Rajnarayanan (@RajlabN) September 1, 2023

Already, there appear to be multiple subgroups of BA.2.86 forming.

“There is a reasonable chance it quickly optimizes and gains back some of that transmission ability,” Jay Weiland, a leading COVID modeler, told *Fortune* on Friday.

A closely watched phenomenon

As of Wednesday, 21 sequences of BA.2.86 had been reported, according to a Friday situation update from the World Health Organization. Five cases were reported in Europe, one in Africa, and one in the U.S. One infected individual had recently traveled to the Western Pacific region, where the variant has not yet been reported.

As of Friday morning, 28 cases had been reported globally, according to top variant tracker Mike Honey.

By Friday afternoon, that total had risen to 33.

A bulk of the identified cases have been identified in Denmark: 12, to be exact. The variant has also been spotted in Scotland, England, Portugal, Israel, France, Canada, and Gauteng and Mpumalanga in South Africa. In the U.S., it’s been identified in Virginia, Texas, Ohio, and Michigan.

Additionally, BA.2.86 has been detected in wastewater in multiple locations, including Switzerland, Thailand, Norway, and U.S. states Ohio, Michigan, and New York. But it’s impossible to say how many cases are behind each detection.

> Here's an animated map showing the spread of the new BA.2.86 "Pirola" variant.
>
> 23 samples have been reported so far, over 4 continents.
>
> Locations are approximate – typically country and state/province.
> 🧵 pic.twitter.com/nFRqpsA5g1
>
> — Mike Honey (@Mike_Honey_) August 30, 2023

So far, no deaths have been reported among cases, according to the WHO. As of last week, an elderly man in Europe was hospitalized with the strain, according to reports.

The WHO last month announced that it had declared BA.2.86 a “variant under monitoring,” the lowest of three levels of alert. Shortly thereafter, the CDC announced that it, too, was tracking the variant, and that it had been detected in the U.S.—in Michigan—in addition to Israel and Denmark, where it had first been reported earlier in the week. The next day, the U.K. Health Security Agency (HSA) said that the variant had been identified in England, and that it was “assessing the situation.”

Unlike most circulating variants, which evolved from Omicron spawn XBB, BA.2.86 is thought to have evolved from BA.2, a much earlier strain of Omicron that circulated in early 2022.

And it appears to be vastly different from its predecessors. So far, most widely circulating Omicron variants feature a small handful of mutations that make them slightly different from the last—usually a bit more transmissible. BA.2.86, on the other hand, features 30 or more mutations that separate it from other Omicron—mutations with the potential to make it considerably more immune-evasive, and able to more easily infect cells, according to Jesse Bloom, a computational biologist at Fred Hutch Cancer Center in Seattle and top variant tracker.

That makes BA.2.86 as different from other Omicron strains as the first Omicron was from the original strain of COVID found in Wuhan in 2019, Bloom asserts in a widely cited presentation he posted online.

Because of this, Pirola has the potential to become the next variant the WHO awards a Greek letter to—likely Pi, hence the nickname. Even if the international public health organization doesn’t award it a new moniker, it deserves one, because of the giant leap in viral evolution it represents, some experts say.

“What sets this one apart from the many other Omicron subvariants is that it exhibits a large number of mutations … far more than we usually see,” Gregory previously told *Fortune.*“It’s fairly likely it’s going undetected in some other countries.”

The fact that the cases are geographically dispersed, with no travel history, “suggests that there is established international transmission” that may have occurred only recently, the U.K. HSA said in its risk assessment. There may be a degree of community transmission in the U.K., it added.

The cases’ wide spread, and their significant similarities, suggest that growth could be rapid, Ryan Hisner—a top variant tracker who discovered the second and third identified cases, in Denmark—previously told *Fortune*.

But even if BA.2.86 does spread rapidly, it may not drive hospitalizations and deaths upward, Dr. Stuart Ray, vice chair of medicine for data integrity and analytics at Johns Hopkins’ Department of Medicine, points out.

Though the highly mutated variant is “quite divergent” from other known circulating strains, “it’s unclear whether it will have a significant effect on the number of severe cases or our management/prevention strategies,” he previously told *Fortune*.