SKA analysis calculated the impact of 6400 satellites, taking into account both direct signals and leakage called "side lobes."

The SKA team finds that satellite transmissions will lead to a 70% loss in sensitivity in the downlink band. If the number of satellites in megaconstellations reaches 100,000, as predicted by many, the entire band 5b would be unusable. SKA would lose its sensitivity to molecules such as glycine, a protein component. "If it was detected in a planetary system that was forming, that would be a very interesting piece of information," Diamond says. "This is a new area that SKA is opening up." The band could also contain the fingerprints of water molecules in distant galaxies, a tracer that cosmologists use to study how dark energy is accelerating the expansion of the universe.

Since 1959, ITU has protected a number of narrow frequency bands for astronomy. But in recent decades, digital receivers have allowed telescopes to "operate over the whole spectrum," Diamond says. "We've learned to coexist with transmitters," typically by excluding them from a radio quiet zone or siting telescopes in remote areas. But they have no control over transmitters flying overhead.

Radio astronomers want the satellite operators to turn off their transmitters, move to other bands, or point them away when they are flying over an observatory. Tony Beasley, director of the U.S. National Radio Astronomy Observatory, says they have been discussing these options with SpaceX. "In the next year or two, we will be doing tests where we're going to be trying to coordinate in real time, technically, with them." Beasley says this is a reflection of SpaceX's corporate culture: "They want to do cool stuff; they don't want to do any harm."

Other astronomers don't want to count on corporate goodwill. At the UNOOSA workshop, they pushed for two recommendations: that all future satellites in low-Earth orbit be designed to avoid beaming at radio telescopes and radio quiet zones, and that satellites control the leakage from their side lobes. Those recommendations, along with others that would protect optical observatories, will be debated next year in U.N. subcommittees before going to UNOOSA and, ultimately, the U.N. General Assembly for approval.

Beasley is philosophical about the situation. "SpaceX is legally transmitting inside one of their bands and there are going to be impacts for anyone trying to do radio astronomy," he says. "These spectrum allocations represent the goals and intent of society. We make [them] to enable commerce and to enable defense and all kinds of activities. We have to come to a solution that satisfies all these to some extent." ■

COVID-19

Found: genes that sway the course of the coronavirus

Host variants boost severity risk, may point to drug options

By **Jocelyn Kaiser**

It's one of the pandemic's puzzles: Most people infected by SARS-CoV-2 never feel sick, whereas others develop serious symptoms or even end up in an intensive care unit clinging to life. Age and preexisting conditions, such as obesity, account for much of the disparity. But geneticists have raced to see whether a person's DNA also explains why some get hit hard by the coronavirus, and they have uncovered tantalizing leads.

Now, a U.K. group studying more than 2200 COVID-19 patients has pinned down common gene variants that are linked to the most severe cases of the disease, and that point to existing drugs that could be repurposed to help. "It's really exciting. Each one provides a potential target" for treatment, says genetic epidemiologist Priya Duggal of Johns Hopkins University.

Kenneth Baillie of the University of Edinburgh, an intensive care physician and geneticist, led the new study, which he discussed on 2 October at an online meeting of a data-pooling effort called the COVID-19 Host Genetics Initiative. He's hoping the results, also posted as a preprint on medRxiv, will speed treatments, although he cautions that any clinical trial inspired by the findings should wait for the study's acceptance in a peer-reviewed journal. "Because the epidemic is progressing at such an alarming rate, even a few months of time saved will save lots of lives," Baillie says.

In a standard approach to finding genes that influence a condition, geneticists scan the DNA of large numbers of people for millions of marker sequences, looking for associations between specific markers and cases of the disease. In June, one such genome-wide association study in *The New England Journal of Medicine* (*NEJM*) found two "hits" linked to respiratory failure in 1600 Italian and Spanish COVID-19 patients: a marker within the *ABO* gene, which determines a person's blood type, and a stretch of chromosome 3 that holds a half-dozen genes. Those two links have also emerged in other groups' data, including some from the DNA testing company 23andMe.

The new study confirmed the chromosome 3 region's involvement. And because 74% of its patients were so sick that they needed invasive ventilation, it had the statistical strength to reveal other mark-

PHOTO: FABIO TEIXEIRA/ANADOLU AGENCY/GETTY IMAGES

A study of some of the sickest COVID-19 patients, such as those placed on ventilators, has identified gene variants that put people at greater risk of severe disease.

ers, elsewhere in the genome, linked to severe COVID-19. One find is a gene called *IFNAR2* that codes for a cell receptor for interferon, a powerful molecular messenger that rallies the immune defenses when a virus invades a cell. A variant of *IFNAR2* found in one in four Europeans raised the risk of severe COVID-19 by 30%. Baillie says the *IFNAR2* hit is "entirely complementary" to a finding reported in *Science* last month: Very rare mutations that disable *IFNAR2* and seven other interferon genes may explain about 4% of severe COVID-19 cases (25 September, p. 155). Both studies raise hopes for ongoing trials of interferons as a COVID-19 treatment.

A more surprising hit from the U.K. study points to *OAS* genes, which code for proteins that activate an enzyme that breaks down viral RNA. A change in one of those genes might impair this activation, allowing the virus to flourish. The U.K. data suggest there is a variant as common and influential on COVID-19 as the interferon genetic risk factor.

Other genes identified by Baillie's team could ramp up the inflammatory responses to lung damage triggered by SARS-CoV-2, reactions that can be lethal to some patients. One, *DPP9*, codes for an enzyme known to be involved in lung disease; another, *TYK2*, encodes a signaling protein involved in inflammation. Drugs that target those two genes' proteins are already in use—inhibitors of *DPP9*'s enzyme for diabetes and baricitinib, which blocks *TYK2*'s product, for arthritis. Baricitinib is in early clinical testing for COVID-19, and the new data could push it up the priority list, Baillie says.

The chromosome 3 region still stands out as the most powerful genetic actor: A single copy of the disease-associated variant more than doubles an infected person's odds of developing severe COVID-19. Evolutionary biologists reported last month in *Nature* that this suspicious region actually came from Neanderthals, through interbreeding with our species tens of thousands of years ago. It is now found in about 16% of Europeans and 50% of South Asians.

But the specific chromosome 3 gene or genes at play remain elusive. By analyzing gene activity data from normal lung tissue of people with and without the variant, the U.K. team homed in on *CCR2*, a gene that encodes a receptor for cytokine proteins that play a role in inflammation. But other data discussed at last week's meeting point to *SLC6Z20*, which codes for a protein that interacts with the main cell receptor used by SARS-CoV-2 to enter cells. "I don't think anyone at this point has a clear understanding of what are the underlying genes" for the chromosome 3 link, says Andrea Ganna of the University of Helsinki, who co-leads the COVID-19 Host Genetics Initiative.

The U.K. genetics study did not confirm that the *ABO* variants affect the odds of severe disease. Some studies looking directly at blood type, not genetic markers, have reported that type O blood protects against COVID-19, whereas A blood makes a person more vulnerable. It may be that blood type influences whether a person gets infected, but not how sick they get, says Stanford University geneticist Manuel Rivas. In any case, O blood offers at best modest protection. "There are a lot of people with O blood that have died of the disease. It doesn't really help you," says geneticist Andre Franke of the Christian-Albrecht University of Kiel, a co-leader of the *NEJM* study.

Researchers expect to pin down more COVID-19 risk genes—already, after folding in the U.K. data plumbed by Baillie's team, the COVID-19 Host Genetics Initiative has found another hit, a gene called *FOXP4* implicated in lung cancer. And in a new medRxiv preprint posted last week, the company Ancestry.com reports that a gene previously connected to the effects of the flu may also boost COVID-19 susceptibility only in men, who are more likely to die of the disease than women.

Geneticists have had little luck so far identifying gene variants that explain why COVID-19 has hit Black people in the United States and United Kingdom particularly hard. The chromosome 3 variant is absent in most people of African ancestry. Researchers suspect that socioeconomic factors and preexisting conditions may better explain the increased risks. But several projects, including Baillie's, are recruiting more people of non-European backgrounds to bolster their power to find COVID-19 gene links. And in an abstract for an online talk later this month at the American Society of Human Genetics annual meeting, the company Regeneron reports it has found a genome region that may raise the risk of severe disease mainly in people of African ancestry.

Even as more genetic risk factors are identified, their overall effect on infected people will be modest compared with other COVID-19 factors, Duggal says. But studies like the U.K. team's could help reveal the underlying biology of the disease and inspire better treatments. "I don't think genetics will lead us out of this. I think genetics may give us new opportunities," Duggal says. ■

Science's COVID-19 reporting is supported by the Pulitzer Center and the Heising-Simons Foundation.

VOICES OF THE PANDEMIC

The United Kingdom's mask crusader

Trisha Greenhalgh argues COVID-19 shows that health policy need not wait for perfect evidence

By **Ellen Ruppel Shell**

In May, when several prominent U.K. scientists pushed back against a Royal Society report recommending face masks to help control the spread of COVID-19, Trisha Greenhalgh was furious. The scientists argued there was insufficient support in the scientific literature for the efficacy of masks, and the U.K. government, following their lead, declined to mandate masks for the general public.

"The search for perfect evidence may be the enemy of good policy," Greenhalgh, a physician and expert in health care delivery at the University of Oxford, fumed in the *Boston Review*. "As with parachutes for jumping out of airplanes, it is time to act without waiting for randomized controlled trial evidence."

Greenhalgh is a firm believer in evidence-based medicine. She wrote a best-selling book on the topic, and her research has earned some of her nation's highest honors. But in recent years, she has grown critical of what she believes is the privileging of randomized controlled studies over clinical experience and close observation. COVID-19, she argues, has revealed the limits of evidence-based medicine—masks being a potent case in point.

"The real tension in public health is, in the absence of strong evidence, whether it's appropriate to take action," says Tom Inglesby, director of Johns Hopkins University's Center for Health Security. "And a large-scale intervention like masks is extremely difficult to study." Yet the limited evidence available suggested masks could reduce the amount of virus transmitted from one person to another by more than 90%. And that, Greenhalgh insists, should have been enough to motivate an inexpensive and largely risk-free public health intervention. "Hundreds of thousands of lives were lost before many governments introduced mandatory masking," she says.

Found: genes that sway the course of the coronavirus

Jocelyn Kaiser

Science **370** (6514), 275-276.
DOI: 10.1126/science.370.6514.275