DNA test to predict odds of severe COVID-19 draws scrutiny

Relation between genes and risk is uncertain, skeptics say

By Jocelyn Kaiser

For people not yet vaccinated against COVID-19 or still nervous about venturing into crowds, the sales pitch may be alluring: Drool into a tube to provide your DNA and mail it off to see how likely you are to be among the 10% to 15% of people who will end up in the hospital or die from a SARS-CoV-2 infection. That’s the promise of a $175 test an Australian company launched last week in the United States. It combines genetic data with someone’s age, sex, and preexisting medical conditions to predict their risk of becoming extremely ill from COVID-19.

The firm developed its test using data on thousands of COVID-19 patients in the United Kingdom. It may be a forerunner of similar risk tests: An academic team has recently detailed a simpler genetic test to help determine how aggressively some people infected with SARS-CoV-2 should be treated.

Yet several genetics experts warn that how a person’s genes influence the course of COVID-19 remains too murky to deploy such risk assessments. “I think it’s premature to use a genetic test to predict a person’s likely COVID-19 severity. We don’t understand exactly what these genetic variants mean or how they affect disease,” says genetic epidemiologist Priya Duggal of Johns Hopkins University.

Duggal and others also suggest the company’s test might be pointless at a time when most people in the United States can get a highly effective COVID-19 vaccine and might even be a disincentive to get a shot. People should get vaccinated, stresses Richard Allman, chief scientific officer for Melbourne-based Genetic Technologies, the test’s developer. But he says the test could be useful before immunity develops and later, after it wanes.

The company drew on studies combining the genomes of thousands of COVID-19 patients for common DNA base differences called single nucleotide polymorphisms (SNPs). The genetic variants might influence a person’s resistance to the virus, for example, or susceptibility to a deadly immune overreaction. A global data-pooling effort called the COVID-19 Host Genetics Initiative has found tentative links between dozens of SNPs and a higher risk that an infected person will develop severe COVID-19—anywhere from a doubling to small increases, say from 15% risk to 16%.

Genetic Technologies incorporated seven of the SNPs into a test after evaluating candidate markers using the UK Biobank, a research database of mostly white U.K. residents age 50 to 84. The company compared about 2200 of the biobank’s participants who had been hospitalized for COVID-19 with 5400 who ended up with mild symptoms or no illness after an infection. The test also factors in COVID-19 risk factors such as being old, male, obese, or diabetic.

The SNP-based result is a “substantial improvement” in predictive power over using age and sex alone, the company concluded in a preprint in March. Whereas the average risk of severe disease from the coronavirus for a person 50 or older is 27%, it’s as low as 4% for some people over age 50, the company’s model suggests. For others, says Genetic Technologies biostatistician Gillian Dite, the risk is “really, really high”—as much as 98%, meaning an unvaccinated person infected by SARS-CoV-2 is almost guaranteed to develop severe COVID-19.

The test debuts in a regulatory gray zone, however. The Australian company and its U.S. partner, Infinity Biologix (IBX), did not seek U.S. Food and Drug Administration approval for validity because, Allman says, the test is not a direct-to-consumer product that requires the agency’s review. After a customer receives results from IBX’s federally approved labs, they can consult with a “telehealth” physician.

Several geneticists who reviewed the company’s preprint caution the test needs vetting in other, more diverse populations, and perhaps for new SARS-CoV-2 variants. “It’s a good start, but by no means is it calibrated or validated sufficiently to say this is a test I would take or my wife should take,” says cancer geneticist Stephen Chanock of the U.S. National Cancer Institute.

Dite says it has been difficult to find large data sets with clinical information on COVID-19 patients for additional validation, and the company went ahead “because of the importance of a rapid response to the pandemic.” The test asks whether someone is of non-European ancestry, which appears to increase the risk of severe COVID-19, so she believes it is relevant for U.S. minorities.

Members of the COVID-19 Host Genetics Initiative have proposed using just a single SNP on chromosome 3 to predict the risk of severe disease in infected people under age 60 who seek medical care; having one copy of this SNP elevates a person’s risk 2.6-fold, the group reported in a preprint in March. Even this single-SNP test may not quickly find medical use, says Massachusetts General Hospital physician-scientist Amit Khera. “There are almost no examples” of doctors or emergency room staff giving patients a rapid genetic test to guide treatment, he notes.

Still, many geneticists, including Chanock, who’s looking for genetic risk factors for COVID-19 himself, believe such tools are worth developing. But, he notes: “How and in what way a test like this is going to be useful is still very much an open question.”
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Science 372 (6547), 1139.
DOI: 10.1126/science.372.6547.1139