50 million doses by early next year.

Several other DNA vaccines are being developed against COVID-19, using a variety of antigens and delivery mechanisms. Two have entered late-stage trials: one by Japanese company AnGes, based in Osaka; the other, which Weiner helped to develop, by Inovio Pharmaceuticals in Plymouth Meeting, Pennsylvania.

More than half a dozen DNA vaccines for COVID-19 are in early-stage trials, including one by the South Korean biotech company GeneOne Life Science in Seoul, and another that Richmond is involved in, developed by the Thai firm BioNet in Bangkok.

But Richmond expects many more to emerge, targeting diseases for which there are currently no vaccines — from cytomegalovirus, which can be passed to babies during pregnancy, to respiratory syncytial virus. DNA vaccines are also being trialled or developed for influenza, human papillomavirus, HIV and Zika.

DNA vaccines can store lots of information, which means they can encode large proteins or even multiple proteins. Weiner says that gives them promise as anticancer vaccines, which he is exploring in his own research.

"It's a very exciting time for genetic technologies," he says.

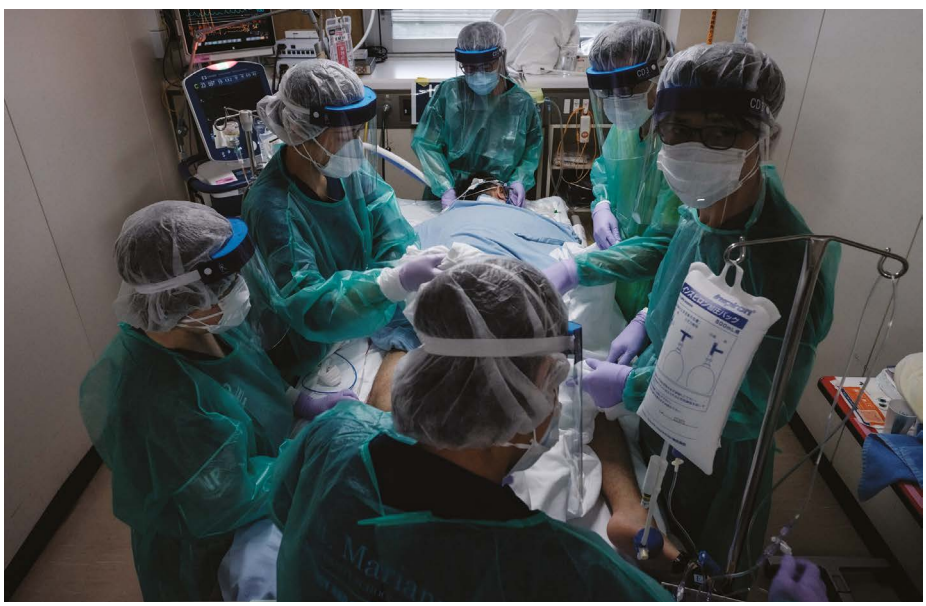
ROGUE ANTIBODIES LINKED TO DEATHS FROM SEVERE COVID

The self-targeting 'autoantibodies' attack blood proteins that play a key part in fighting infection.

By Diana Kwon

Antibodies that turn against elements of our own immune defences are a key driver of severe illness and death following SARS-CoV-2 infection in some people, according to a large international study. These rogue antibodies, known as autoantibodies, are also present in a small proportion of healthy, uninfected individuals — and their prevalence increases with age, which might help to explain why older people are at higher risk of severe COVID-19.

The findings, published on 19 August in *Science Immunology*[1], provide robust evidence to support an observation made by the same research team last October. Led by immunologist Jean-Laurent Casanova at the Rockefeller University in New York City, the researchers found that around 10% of people with severe COVID-19 had autoantibodies that attack and block high levels of type 1 interferons, protein molecules in the blood that have a crucial role in fighting off viral infections[2].



Physicians treat a person with COVID-19 at a hospital in Japan.

YASUYOSHI CHIBA/AFP VIA GETTY

"The initial report from last year was probably one of the most important papers in the pandemic," says Aaron Ring, an immunologist at the Yale School of Medicine in New Haven, Connecticut. "What they've done in this new study is really dig down to see just how common these antibodies are across the general population — and it turns out they're astonishingly prevalent."

The research team focused on detecting autoantibodies that could neutralize more physiologically relevant concentrations of interferons. They studied 3,595 people with severe COVID-19 from 38 countries. Overall, 13.6% of these people possessed autoantibodies, with the proportion ranging from 9.6% of those below the age of 40, up to 21% of those over 80. Autoantibodies were also present in 18% of people who had died of the disease.

Casanova and his colleagues suspected that these devious antibodies were a cause, rather than a consequence, of severe COVID-19. There were hints that this might be the case — the group had previously found that autoantibodies were present in around 4 in 1,000 healthy people whose samples had been collected before the pandemic[2]. The team also found that individuals with genetic mutations that disrupt the activity of type 1 interferons are at higher risk of life-threatening disease[3,4].

To examine this link further, the researchers hunted for autoantibodies in a massive collection of blood samples taken from almost 35,000 healthy people before the pandemic. They found that 0.18% of those aged between 18 and 69 had existing autoantibodies against type 1 interferon, and that this proportion increased with age: autoantibodies were present in around 1.1% of 70- to 79-year-olds, and 3.4% of those over the age of 80.

"There is a massive increase in prevalence" with age, Casanova says. "This largely explains the high risk of severe COVID in people in the elderly population." He adds that these findings have clear clinical implications, and suggests that hospitals should be checking patients for these autoantibodies, as well as mutations implicated in blocking type 1 interferons.

A sample of more than 30,000 people is "too big to ignore", according to Ring. He adds that researchers should now consider whether autoantibodies play a part in driving other infectious diseases. Ring's team has found evidence[5] of autoantibodies against various immune-system components in people with COVID-19, and he and his colleagues are now investigating further. "I suspect that we've just started scratching the surface," Ring says.

1. Bastard, P. *et al. Science Immunol.* **6**, eabl4340 (2021).
2. Bastard, P. *et al. Science* **370**, eabd4585 (2020).
3. Asano, T. *et al. Sci. Immunol.* **6**, eabl4348 (2021).
4. Zhang, Q. *et al. Science* **370**, eabd4570 (2020).
5. Wang, E. Y. *et al. Nature* **595**, 283–288 (2021).