happy hypoxia, Strayer says. There are other possibilities. Recent imaging of a hypoxic patient showed "almost waxy-looking film all around the lungs," Caputo says. "I don't know what is actually going on pathophysiologically down there."

Caputo says this hypoxia is likely stressing a body already straining to battle the virus. What to do about it is prompting debate. An emerging view is that doctors should avoid aggressive treatment they've been trained to offer in other settings. Luciano Gattinoni, a guest professor in intensive care at the University of Göttingen Medical Center, is wary of what he calls a "Pavlovian response" to COVID-19 hypoxia, in which doctors may swoop in to inflate lungs with ventilators or high-pressure oxygen even when patients seem comfortable. Those measures, Gattinoni wrote online in *JAMA* on 24 April, could harm lungs that are inflating on their own but may be needed if patients aren't helped by noninvasive treatment.

Simpler interventions, he and others say, are important. Strayer, Caputo, and their collaborator Richard Levitan, a physician at Littleton Regional Healthcare in New Hampshire, who spent time treating COVID-19 patients in a New York City emergency room, offered patients supplemental oxygen and also flipped them on their belly, an approach traditionally used for people on ventilators, which can open the lower lungs. Last month in *Academic Emergency Medicine*, they reported that among 50 patients with low oxygen saturation, switching to a prone position raised average saturation significantly. However, 13 of the patients weren't helped for long and needed intubation within 24 hours.

Doctors are uncertain about the value of detecting low oxygen saturation early using inexpensive devices called pulse oximeters at home. Is home monitoring "going to prevent all bad outcomes in COVID? Absolutely not," says Levitan, who wrote a 20 April op-ed in *The New York Times* arguing that early hypoxia can rapidly progress to pneumonia and death. "If we were able to detect them when they were less sick, they'd do better." Negri tells her patients to monitor their oxygen saturation and visit the hospital if it drops to 93% or below. At that point, she considers blood thinners and other therapy.

No one, however, has studied whether early detection of hypoxia might head off bad outcomes. Some physicians believe pulse oximeters are best used with a doctor's guidance, perhaps through telemedicine. With many COVID-19 patients frightened to visit a hospital and arriving only when their symptoms have dangerously advanced, doctors also wonder whether home monitoring could hasten treatment—and whether, for some, that could make all the difference. ■

Sinovac Biotech has created a vaccine by growing the novel coronavirus in Vero monkey cells and inactivating it.

PHOTO: XINHUA/ALAMY STOCK PHOTO

BIOMEDICINE

COVID-19 shot protects monkeys

Vaccine from Chinese firm uses old-fashioned "killed" virus

By **Jon Cohen**

For the first time, one of the many COVID-19 vaccines in development has protected an animal, rhesus macaques, from the new coronavirus. The vaccine, an old-fashioned formulation consisting of a chemically inactivated version of the virus, produced no obvious side effects in the monkeys; human trials began on 16 April. And encouraging monkey results for other vaccines are close behind.

Researchers from Sinovac Biotech, a privately held Beijing-based company, gave two different doses of their COVID-19 vaccine to a total of eight rhesus macaques. Three weeks later, the group introduced SARS-CoV-2, the virus that causes COVID-19, into the monkeys' lungs. None developed a full-blown infection, and the monkeys given the highest dose of vaccine had the best response: Seven days after the animals received the virus, researchers could not detect it in their pharynx or lungs. Some of the lower dosed animals had a "viral blip" but also appeared to have controlled the infection, the Sinovac team reports in a paper published on 19 April on the preprint server bioRxiv.

In contrast, four control animals developed high levels of viral RNA and severe pneumonia. The results "give us a lot of confidence" that the vaccine will work in humans, says Meng Weining, Sinovac's senior director for overseas regulatory affairs.

"This is old school but it might work. What I like most is that many vaccine producers, also in lower–middle-income countries, could make such a vaccine," says Florian Krammer, a virologist at the Icahn School of Medicine at Mount Sinai.

But Douglas Reed of the University of Pittsburgh, who is developing and testing COVID-19 vaccines in monkeys, says the number of animals was too small to yield statistically significant results. In a manuscript in preparation, his team also raises concerns about the way the Sinovac team grew the stock of novel coronavirus used to challenge the animals, which may have evolved differences from the strains that infect humans. What's more, the monkeys are not a perfect model for COVID-19 as they don't develop some symptoms that kill many humans.

The study did address worries that partial protection by a vaccine could be dangerous. Earlier animal experiments with vaccines against the related coronaviruses that cause severe acute respiratory syndrome and Middle East respiratory syndrome had found that low antibody levels could lead to aberrant immune responses, enhancing the infection and damaging their lungs. But the Sinovac team did not find any evidence of lung damage in vaccinated animals that produced relatively low levels of antibodies, which "lessens the

concern about vaccine enhancement," Reed says. "More work needs to be done, though."

To check the possibility that SARS-CoV-2 variants might thwart a vaccine, the Sinovac researchers mixed antibodies taken from monkeys, rats, and mice given their vaccine with strains of the virus isolated from patients in China, Italy, Switzerland, Spain, and the United Kingdom. The antibodies potently "neutralized" all the strains, which are "widely scattered on the phylogenic tree," the researchers noted.

"This provides strong evidence that the virus is not mutating in a way that would make it resistant to a #COVID19 vaccine," tweeted immunologist Mark Slifka of Oregon Health & Science University. "Good to know."

An experimental vaccine made by the University of Oxford has also shown promise, although the data have not yet been published. Vincent Munster and his team at the Rocky Mountain Laboratories gave six monkeys the vaccine, which contains a gene for the surface protein of SARS-CoV-2 stitched into a harmless adenovirus that infects chimpanzees. Four weeks later, the researchers challenged the vaccinated animals and six controls. Seven days later, the vaccinated animals had a much stronger reduction of virus in their lower respiratory tracts than the controls. "The preliminary results look promising," Munster says. "People just have to be patient."

Sinovac recently started phase I human trials of its vaccine in Jiangsu province, north of Shanghai, which aim to gauge safety and immune responses in 144 volunteers. The company hopes to start phase II studies by mid-May that will assess the same endpoints but will enroll more than 1000 people.

If all goes well, Meng says, Sinovac will launch phase III efficacy trials that compare the vaccine with a placebo in thousands of people. Because of the low level of transmission now occurring in China, the company may run additional trials in harder hit countries. "We can't put all our eggs in one basket," Meng says. Sinovac may also ask regulatory agencies in China and elsewhere for emergency authorization to give the vaccine to those at high risk of becoming infected, such as customs agents and police officers.

According to the World Health Organization, the Oxford vaccine and five others had entered human trials as of 26 April, and 82 candidates were in development. Most use versions of the SARS-CoV-2 surface protein, rather than whole, killed virus. Meng says how a vaccine is made will not ultimately matter. "In this pandemic situation, the most important thing is to make a vaccine, no matter what kind of vaccine it is, that's safe and effective as soon as possible." ■

SCIENTIFIC COMMUNITY

Scientists discover upsides of virtual meetings

As the COVID-19 pandemic pushes conferences online, audiences grow

By **Michael Price**

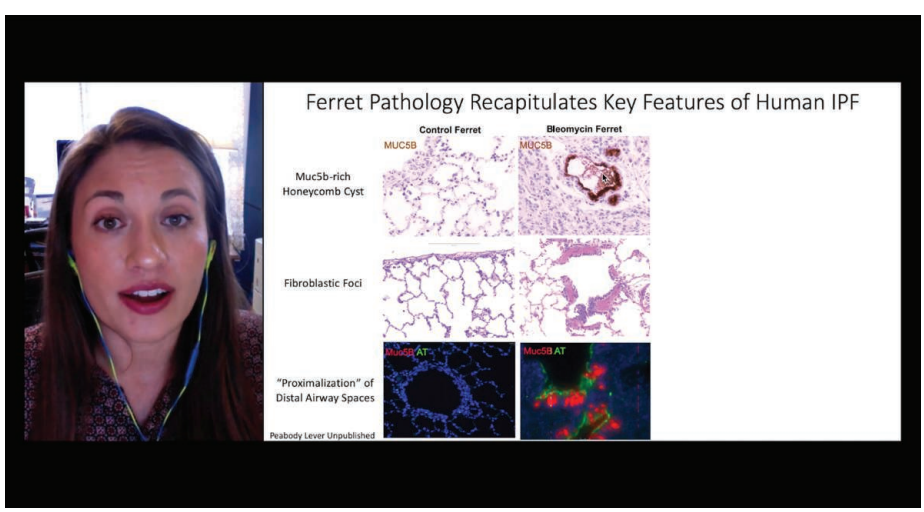
Biochemist Kathleen Prosser wasn't planning to present her research at a conference this spring. But when COVID-19 caused organizers to cancel a series of local chemistry meetings across Canada—called Inorganic Discussion Weekends—and offer a virtual alternative, she signed up to give a talk. Prosser, a Canadian citizen who is a postdoc at the University of California (UC), San Diego, figured she'd be talking mostly to fellow Canadians. But by going virtual, she gained an international audience. The day after her talk she heard from a chemist in Australia, asking for more details and hinting at a future collaboration. "The time zone difference would not have allowed them to see it live, but they watched it [afterward]," she says.

As the novel coronavirus outbreak shutters businesses and disrupts everyday life for billions around the globe, massive annual conferences and small society meetings alike have moved online. The new format poses numerous technical and organizational challenges, but it also offers opportunities—for reaching wider audiences, reducing the carbon footprint of meeting travel, and improving diversity and equity. For some meetings, the shift may be permanent.

The scientific community is "making lemonade out of lemons," Prosser says. "It's taking [a situation] that's really quite horrible and providing people a way to connect in spite of it all."

In many ways, virtual conferences offer a better experience, says Russ Altman, associate director of the Stanford Institute for Human-Centered Artificial Intelligence (AI). Altman's institute had planned an inperson conference in April, but COVID-19 forced organizers to scuttle it. In its place, they threw together a virtual conference to discuss how AI can help scientists fight the ongoing pandemic. The event was a smashing success, Altman says. The original conference—meant to focus on how AI intersects with neuroscience and psychology—would have drawn a few hundred attendees, but 30,000 people tuned in to the online version.

Altman says the virtual environment allowed moderators to better control the flow of discussion and questions from the audience. By privately messaging one another behind the scenes, they were able to discuss how a session was going and make adjustments in real time. "For example, we had one panelist who we thought was contributing a little bit too much," he says. The moderators responded by using private messages to encourage others to speak, and they made a mutual decision to ask questions designed to draw comment from other, less vocal pan-



Jacelyn Peabody Lever of the University of Alabama goes virtual for the American Physician Scientists Association.

PHOTO: AMERICAN PHYSICIAN SCIENTISTS ASSOCIATION/YOUTUBE/CC-BY/JACELYN PEABODY LEVER/LABORATORY OF STEVEN ROWE AT UAB

COVID-19 shot protects monkeys

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Science **368** (6490), 456-457.
DOI: 10.1126/science.368.6490.456