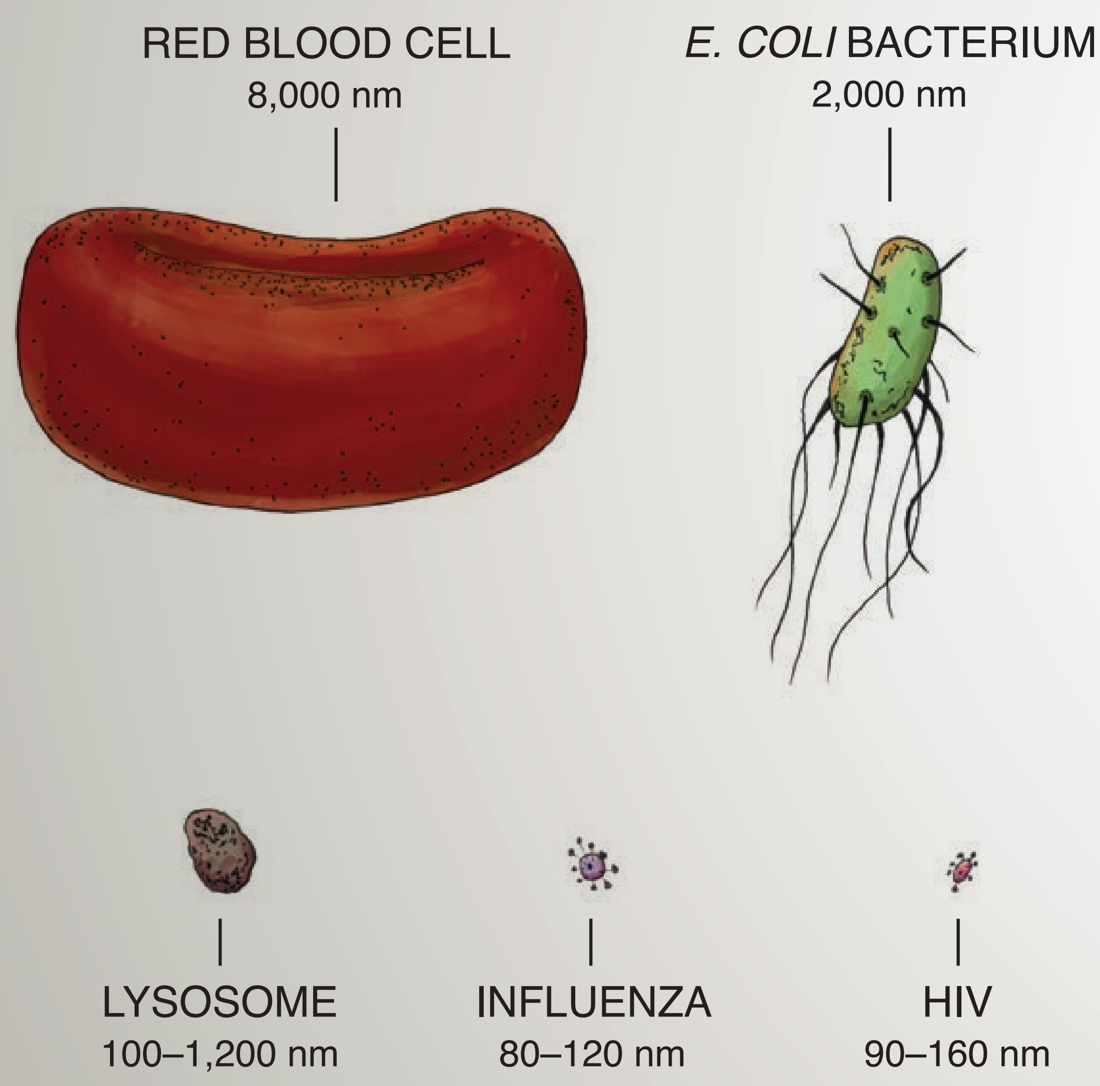
Caltech

AN EXCHANGE OF IDEAS

Caltech Scientists on COVID-19



In March, Caltech shuttered nearly all of its labs for the first time in the Institute's history. It was an act of social responsibility, a recognition of the need to help mitigate and respond to the COVID-19 pandemic.

At the same time, the Institute's community of researchers recognized that they each had an individual responsibility to respond. Over these past weeks and months, research teams both on and off campus have pivoted, shifting focus, resources, and even tools in an effort to address this challenge. They also are deepening the public's understanding and awareness of science so that citizens can make informed decisions in this time of unprecedented crisis.

This booklet captures a small collection of insights and stories from Caltech researchers who have unique perspectives on the COVID-19 pandemic. They provide critical understanding to a society that seeks reliable, straightforward sources of information and a rich exchange of ideas.

To learn more about Caltech's response to COVID-19, visit ***coronavirus.caltech.edu.*** *To learn about the science behind how viruses work and other important topics related to COVID-19, visit* ***scienceexchange.caltech.edu/coronavirus.***

Pandemics Past and Future

David Baltimore

No two pandemics are the same. Still, each has lessons to teach about the next. Nobel Laureate David Baltimore, Caltech president emeritus and Robert Andrews Millikan Professor of Biology, understands this better than most, having studied HIV during the height of the AIDS pandemic in the 1980s and 1990s.

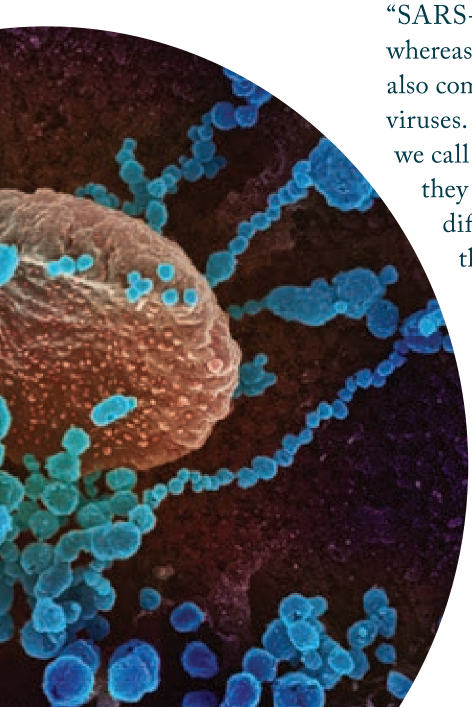
Today, as the novel coronavirus (called severe acute respiratory syndrome coronavirus 2, or SARS-CoV-2) causes the most destructive global pandemic since the peak of the AIDS pandemic, Baltimore provides a unique perspective on that public health crisis, the situation we face today, and how to prepare for the inevitable pandemics to come.

On initial reactions

"The start of our response to COVID-19 was very similar to our response to HIV. We tried to pigeonhole it as a disease of only certain people: Chinese people for COVID-19 or homosexuals for AIDS. We tried to ignore it. We knew, in the scientific community, that viruses don't only affect one group of people, that they spread to everybody. As soon as we knew COVID-19 was infectious, we knew it was going to spread everywhere in the world."

On HIV versus SARS-CoV-2

"SARS-CoV-2 is extremely infectious, whereas HIV is very poorly infectious. They also come from very different families of viruses. SARS-CoV-2 is a coronavirus. HIV we call a retrovirus or lentivirus. Although they are both viruses, they behave in very different ways. But they're similar in that they both came from animals. For HIV, it was monkeys, and for SARS-CoV-2, we think bats. They're both new to humans."



On preparation

"We've known what viral pandemics are for a long time, and we've just simply refused to put the resources into protecting ourselves. There are public health measures, there are surveillance method measures, there's the study of the spread of infectious agents, epidemiology. We need to build up our capabilities in all of those areas. We should be making vaccines against viruses that we don't know we're ever going to face in an epidemic form so that we have the experience, so that we have the fund of knowledge and the people who can respond very quickly. And we have to listen to science.

"We should have a cadre of public health people who are studying these problems continually or looking at all of the viruses in the natural world and are saying one by one, 'If this one got loose, what would we do?' and prepare ourselves. We can do all of that, and it's not actually enormously expensive, but it's something that has to be done by the public, not by commercial interests. That means there has to be money put aside for it.

"What we have done over my whole lifetime is: every time there is an epidemic, we say, 'Now we've got to study this and prepare ourselves for the next one.' And within a couple of years, that impetus is gone, the money has been reassigned to other problems, and we're not maintaining our surveillance of the natural world. We're not maintaining our capabilities in vaccine and drug development. And so we have to start all over again when the next disease comes along. And that's shortsighted."

"As soon as we knew COVID-19 was infectious, we knew it was going to spread everywhere in the world."

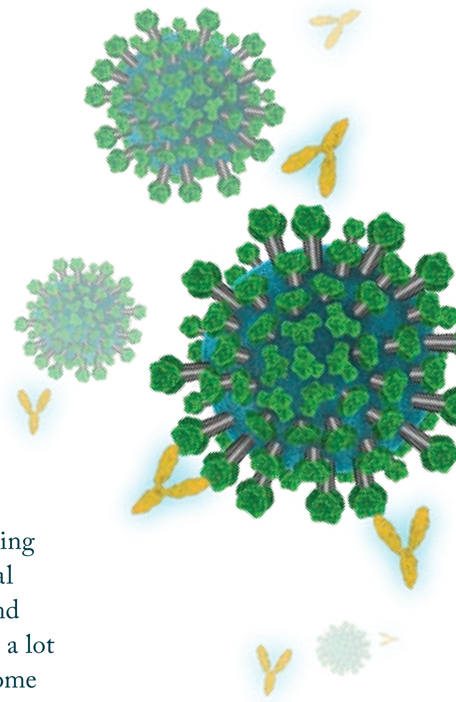
Pamela Bjorkman

Before the COVID-19 pandemic took hold, Pamela Bjorkman, the David Baltimore Professor of Biology and Bioengineering, primarily studied the immune system's response to the viruses that cause diseases such as AIDS and influenza. That background made Bjorkman and her laboratory colleagues especially well equipped to quickly turn their attention to SARS-CoV-2, the virus that causes COVID-19.

Today, Bjorkman's group is using electron microscopy to develop detailed three-dimensional structures of antibodies bound to the novel coronavirus spikes; these structures are allowing the researchers to study the atomic details of the interface between a virus and the cell it is trying to infect, an accomplishment that could lead to antibody-based therapies.

Bjorkman, who recently chaired Caltech's Public Understanding of Science Committee, is as committed to building an understanding of the science behind this public health crisis as she is to disarming the virus itself.

"As scientists, all of us need to be engaging with the public more because it's critical in our world that people trust science and understand what is going on."



On isolating antibodies

"Basically, the same techniques we were using to study HIV we can apply to COVID-19 because both viruses are enveloped viruses and they present a spike protein on the surface of the virus. Right now we're engaged in a collaboration with Michel Nussenzweig's lab at Rockefeller University, with whom we've worked for at least 10 years on anti-HIV antibodies, to isolate potential antibodies against SARS-CoV-2. When those antibodies have been identified, we can characterize them structurally. Once we know where the antibodies bind, we can understand how they bind, which ones are good, which ones are not so good, and so on.

"These sorts of structural studies are only possible at Caltech through support of facilities such as the Caltech Molecular Observatory, which allows researchers to solve structures by X-ray crystallography, and the Caltech Cryo-EM Center, where researchers can solve structures using cryo-electron microscopy."

On public misconceptions

"As scientists, all of us need to be engaging with the public more because it's critical in our world that people trust science and understand what is going on. There are a lot of misconceptions out there; I've seen some horrifying stuff on the web talking about the current COVID-19 crisis that's completely inaccurate scientifically. That's why I think, in general, that every scientist has an obligation to try to engage with the public. That would improve our world overall."

On information overload

"There is just a massive number of papers coming out. I've never seen anything like it. Every single day, there are at least 20 papers that I should read, and I just can't keep up. None of us can keep up with this. But that is wonderful. I'm hoping this will institute a new way of cooperating among scientists and then, in turn, create more public trust in science."

By the Numbers

Rob Phillips

For 20 years, Rob Phillips, Caltech's Fred and Nancy Morris Professor of Biophysics, Biology, and Physics, has grappled with the numerical characteristics of viruses.

In 2018, Phillips and his longtime collaborators Ron Milo and Yinon Bar-On made sweeping quantitative global estimates of how much biological matter there is on the planet, illustrating how humans have a disproportionate impact on our environment.

Now, with the global COVID-19 pandemic as a backdrop, Phillips and his team have turned this approach toward the study of the novel coronavirus behind the disease. In March, they published a paper in the journal *eLife* that lays out the key numbers behind COVID-19: the virus's average concentrations throughout the body, the stability of the virus on various surfaces, the infection rate, and more.

On the impetus to do this study

"One of the difficulties with research into SARS-CoV-2 is that there are so many different pieces of the puzzle: the survival of viruses on various surfaces, the structural biology of the spike protein on the virus's surface, electron microscopy of the structural elements of the virus, the cell biology of how the virus interacts with its host, and so on. There are people working on pieces of the overall puzzle, but they don't talk to each other, and their work is never put in one place.

"I've been pushing hard on a myriad of fronts since this crisis began to try to do something that will possibly make a difference. I have a coronavirus discussion group, and I taught a mini course on viruses; I have all these different threads that I've been trying to keep going. I've also had a 20-year love affair with the idea of trying to bring the sensibilities of physics to biology: having quantitative control over the facts of the subject and then trying to make predictions about the way biological processes will unfold.

"I realized in this situation that our team could really take stock of the literature and create a one-stop curated resource where people could find key numbers about the biology and infection process of SARS-CoV-2 all together in one place."

On what the numbers reveal

"The genetic data are quite interesting: SARS-CoV-2 is 50 percent genetically similar to the common cold coronavirus and 96 percent similar to coronaviruses in bats. These zoonotic viruses, ones that originate in animals and transfer to humans, are here to stay. They are a part of the human story.

"The data on the evolution of the virus and its mutation rate are going to give insights into the timescale over which the virus will change. Will there be a second wave of infections? Will it be seasonal?

"Something that makes it hard to get an overall handle on the infection rates is that there are also wide statistical variations in the data. Some people are much more infectious than others, with the viral loads harbored by different infected people showing a huge variation. It's a dynamic situation, so we're still getting a grasp on the numbers."

On the next set of questions

"There are a wide variety of fascinating questions that remain unanswered, ranging from what fraction of the viruses that emerge from an infected cell are infectious, to the number of viruses that are shed from such an infected cell, to the fraction of the population that is asymptomatic. The vast compendium of data now available with high spatial, temporal, and demographic resolution provides an opportunity to really drill down and figure out how this pandemic unfolded. This raises the hope that the next time such a pandemic arrives, and possibly even for this pandemic itself, if people are able to work fast enough, we will know much better how to think about how it will evolve and perhaps better how to react to it."

"There are so many different pieces of the puzzle."

Michael Alvarez

For two decades, Michael Alvarez, professor of political and computational social science, has been studying current voting technologies and election administration and procedures as co-director of the Caltech/MIT Voting Technology Project (VTP), a group formed in the aftermath of the controversial 2000 presidential election.

Alvarez and his colleagues in the VTP have pioneered new theories and methods to empirically test formal models of elections and voting behavior in order to develop ways to improve the current system. A tandem goal is to share what they learn with the public so that others can monitor voting records and political scientists can access data for their research.

A 2018 project led by Alvarez, in collaboration with the Orange County registrar of voters, evaluated more than 1.5 million voting records to assess election integrity. This spring, in the lead-up to Super Tuesday, Alvarez worked with colleagues and students to collect and analyze vast amounts of data on voter experience in both Orange County and Los Angeles County.

Alvarez is now turning his attention to this fall's presidential election and to the ways in which the COVID-19 pandemic might affect the processes and technologies on which the result of that election depends.

"We're going to do what we can to try to make sure that data are as accurate as possible."

On the November election

"This is obviously a big topic of concern at this point. It's unclear at this time exactly how we're going to run our elections this fall in California and how other states are going to conduct theirs. We've already seen a lot of controversy in Wisconsin in particular. And most recently in New Mexico as well, where they're having the same fights over whether the state should move entirely to voting by mail. I anticipate that that's the direction that we're going to take in California. Governor Newsom recently announced that all Californians will get a ballot in the mail, although there will also be some limited form of in-person voter services provided. Exactly what that looks like right now is difficult to know."

On working with the state and the county

"I've been working with the Secretary of State's office and with the county election officials throughout the state to try to help figure out what that plan would look like. We're doing all sorts of research focused on helping this effort. Let's just assume for a second that the scenario is that we have statewide voting by mail in November, that every voter is going to get a ballot in the mail and have the option to return that ballot. Well, that requires that the voter registration database that we have in California is as accurate as possible. We know from the work that we've been doing in Orange County and Los Angeles County recently that there are issues with the quality of the data that we currently have in the voter registration database. And so the research that we've been doing, in particular in Orange County and LA County, has been very helpful."

On the importance of high-quality data

"I think, at this point, in helping this conversation move forward, we're going to start working with data from the state voter registration database to try to ensure that data is as high quality and as accurate as possible so that every Californian gets that ballot in the mail and that there aren't multiple ballots being sent out or that people aren't on the rolls. We're going to do what we can to try to make sure that data are as accurate as possible."

On the follow-up

"When this election hits, we're going to be doing everything we possibly can to gather as much data as possible to study how it all works out and try to make sure that if it goes well, people can have confidence in the result. If it doesn't go well, we're going to try to be there so we can help diagnose what went wrong and try to help resolve it."

JPL Engineers

A new high-pressure ventilator developed by JPL engineers and tailored to treat COVID-19 patients was approved on April 30 by the Food and Drug Administration for use under the FDA's March 24 ventilator Emergency Use Authorization.

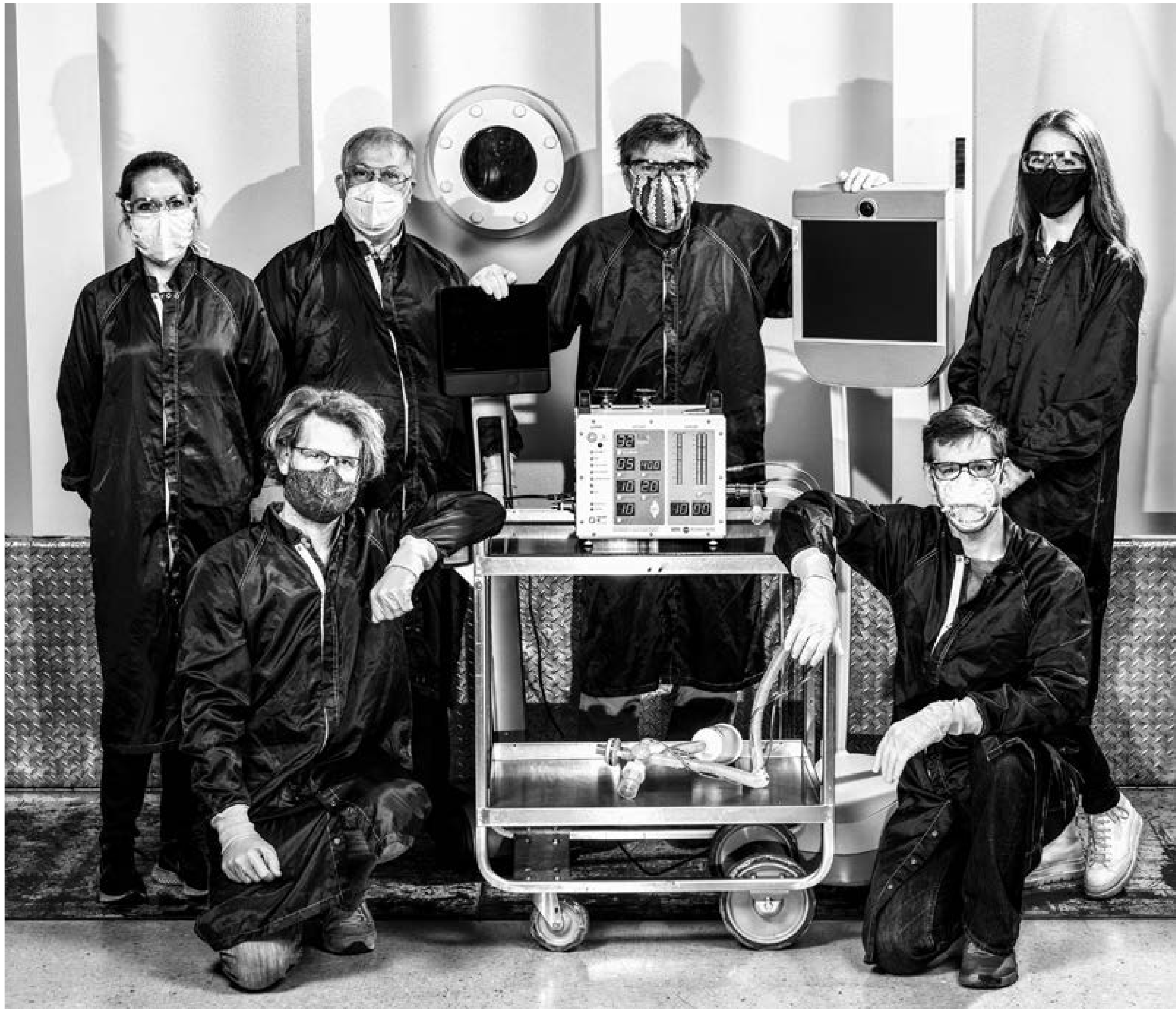
Called VITAL (Ventilator Intervention Technology Accessible Locally), the device was developed in an accelerated timeframe of 37 days to free up the nation's limited supply of traditional ventilators so they may be used on patients with the most severe COVID-19 symptoms.

VITAL can be built faster and maintained more easily than a traditional ventilator, and it is composed of far fewer parts, many of which are currently available to potential manufacturers through existing supply chains. Its flexible design means that it also can be modified for use in field hospitals being set up in convention centers, hotels, and other high-capacity facilities across the country and around the globe.

JPL engineer Stacey Boland (MS '01, PhD '05) served as the operations lead for the project, creating a communication pathway between engineers, designers, and visualization specialists with doctors, nurses, respiratory therapists, and intensivists (board-certified physicians providing special care for critically ill patients).

"We specialize in spacecraft, not medical-device manufacturing," says JPL director Michael Watkins. "But excellent engineering, rigorous testing, and rapid prototyping are some of our specialties. When people at JPL realized they might have what it takes to support the medical community and the broader community, they felt it was their duty to share their ingenuity, expertise, and drive."

The Office of Technology Transfer and Corporate Partnerships at Caltech (which manages JPL for NASA) is offering free licenses for VITAL to the commercial medical industry to facilitate the manufacture of the device.



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