With each new virus, we’ve scrambled for a new treatment. Our approach has been “one bug, one drug.”  Illustration by Christoph Niemann

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THE QUEST FOR A PANDEMIC PILL

Can we prepare antivirals to combat the next global crisis?

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In 1981, a young man visited Cedars-Sinai hospital, in Los Angeles, with shortness of breath and with curious purplish lesions on his skin. After reviewing biopsies and scans, a twenty-eight-year-old medical resident named David Ho found an odd fungal infection in the patient’s lungs and a rare cancer, Kaposi’s sarcoma. These conditions were both associated with immune deficiency, though nothing in the patient’s history explained why he would be in such a state. He was given antibiotics and discharged; not long after, he died. Over a few months, Ho and his colleagues saw five men with similar symptoms. They wrote up the cases and sent them to the Centers for Disease Control—the first report of what became known as AIDS.

Ho continued to explore the disease. “Some people were very concerned that I was so intrigued by those few cases at the very beginning of my career,” he told me. “‘Why would you want to devote your career to an esoteric disease?’” Particularly one that seemed mainly to afflict what was considered a fringe population—gay men. But Ho, who had emigrated from Taiwan when he was twelve, speaking no English, had an underdog mentality and would not be dissuaded.

He made several discoveries throughout the nineteen-eighties about H.I.V., the virus that causes AIDS, and in 1990, at the age of thirty-seven, he moved to New York to become the director of the Aaron Diamond AIDS Research Center. A year later, he received a call asking him to fly back to L.A. to test a very important patient. There, he confirmed that Earvin (Magic) Johnson was H.I.V.-positive. The following week, Johnson disclosed his condition and announced that he was retiring from the N.B.A. Ho has cared for him ever since. Johnson later said that he’d never thought AIDS would kill him, because Ho had assured him that better medicines were in the pipeline. In 1994, Ho found that a certain class of drugs could dramatically reduce the viral load in AIDS patients. But, within each infected individual, the virus evolved quickly, evading treatments. One drug was not enough. His team devised the idea of an AIDS “cocktail”—a combination of three or four drugs that, acting in concert, could corner the virus. In 1996, Time named Ho its Man of the Year.

In November, 2002, a novel disease broke out in China: severe acute respiratory syndrome, caused by a coronavirus called sars-CoV. Ho was asked by China’s top public-health officials to advise them.
“The most dramatic memory I have is going to Beijing, arriving in the late afternoon or early evening, and going to the hotel along the biggest avenue,” he recalled. “If you remember the Tiananmen incidents of many years ago, with the protester and the tank, that’s the boulevard. It has ten or twelve lanes. There was only the car that’s driving me and one ambulance for as far as one could see.”

He went on, “That’s when I got interested in coronaviruses, serving as a consultant and seeing the devastation firsthand in several cities throughout China.” Back in New York, Ho began investigating the coronavirus family. Some coronaviruses can produce lethal diseases, like sars; others are among the causes of the common cold. But, he said, “the sars epidemic ended in July of 2003. By the next year, there was hardly any interest. Funding for that area kind of dried up. So we simply dropped it and went on with our H.I.V. work.” In 2012, another coronavirus, mers-CoV, caused an outbreak in the Arabian Peninsula; Middle East respiratory syndrome, as it was called, sickened more than twenty-five hundred people and killed more than eight hundred. Ho followed it with interest, but this outbreak, too, passed quickly. Then, this past December, a disease with similar symptoms flared up in China and, within a month, was linked to another coronavirus, sars-CoV-2. Ho told me, “My Chinese heritage caused me to focus more on the news coming out of China in late December and early January. However, the experience with sars also put a pause on our natural reaction to jump in and get involved.” His attitude shifted when the story did. “It was the growing magnitude of the outbreak that told us, ‘Oh, we’d better think about getting into this,’ ” he said.

Ho was just setting up his lab at its new home, at Columbia University. He is friendly with Jack Ma, the founder of the e-commerce giant Alibaba, who asked how he could help. In February, Columbia announced that Ma’s foundation had awarded a $2.1-million grant to Ho and several Columbia colleagues to develop antiviral drugs. This project was prompted by the covid-19 crisis, but the mission goes beyond it; the researchers are thinking not only about the current pandemic but about future ones as well.

What will the next global pathogen be? “If you’d asked me that three or four months ago, I would have said influenza,” Ho told me, with a chuckle of dismay. For scientists, this isn’t just a thought experiment; it’s the sort of question that shapes years of research. Two years ago, a team at Johns Hopkins issued a report titled “The Characteristics of Pandemic Pathogens,” which was based on a
literature review, interviews with more than a hundred and twenty experts, and a meeting devoted to the issue. It grimly considered the possibilities.

Could bacteria do us in? Outbreaks of plague have wreaked havoc throughout history, but the development of effective antibiotics in the past century “took bacteria off the table as a global biological risk for the most part,” Amesh Adalja, a physician at Johns Hopkins and the report’s project director, told me. Bacteria can evolve, and develop drug resistance, but usually not quickly. How about fungi? They threaten some species, but don’t adapt well to warm-blooded hosts (and may have helped encourage the evolution of warm-bloodedness). Prions? These are responsible for mad-cow disease and its human variant, but are mostly avoidable by preventing food contamination and refraining from cannibalism. Protozoa? Malaria has killed perhaps half of all humans who have ever lived. But protozoa are typically transmitted by vectors such as mosquitoes and fleas, which are limited by climate and geography. Viruses, the report concluded, are the real menaces.

Not just any viruses, though. The likeliest candidates are those with a genome of RNA, which evolve faster than those with DNA. Viruses that spread before symptoms appear also have a considerable advantage. (The only infectious disease we’ve wiped out, smallpox, is not contagious during the incubation period.) And the most daunting are those transmitted by respiration, rather than by feces or bodily fluids, which can be controlled through sanitation. Viruses that can move between animals and humans are especially hard to manage. All in all, this character sketch gets us pretty close to identifying two classes of viral assailants: influenza and coronavirus.

None of our off-the-shelf treatments equip us for such a pandemic. If bacteria invade, there’s a long list of antibiotics you can try. Between ciprofloxacin and amoxicillin, we can treat dozens of different types of bacterial infection. For the roughly two hundred identified viruses that afflict us, there are approved treatments for only ten or so. And the antiviral drugs that exist tend to have narrow targets. Only a few have been approved for use against more than one disease. Many drugs that work on one virus don’t work on others within the same family; antivirals suited for some herpesviruses (such as the one that causes chicken pox and shingles) aren’t suited for others. Some antivirals can’t even treat different strains of the same virus.

And so every time a new virus appears we scramble for a new treatment. Our usual antiviral approach is, as researchers say, “one bug, one drug”; often, it’s no drug. Ho has spent forty years fighting the
AIDS epidemic, which has killed thirty million people and still kills nearly a million a year; he has seen three coronaviruses ambush us in the past two decades. Like many scientists, he's tired of being behind the ball. He'd like to see a penicillin for viruses—one pill, or, anyway, a mere handful—that will eliminate whatever ails us. He and his colleagues aim to have these next-generation drugs ready in time for the next pathogen. “We have to be proactive,” he told me. “We must not be in a position of playing catch-up ever again.”

Viruses are quite conniving for things that are not alive. A bacterium is a living cell that can survive and reproduce on its own. By contrast, a virion, or virus particle, can do nothing alone; it reproduces only by co-opting the cellular machinery of its host. Each virion consists of nothing more than a piece of DNA or RNA encased in protein, sometimes surrounded by a lipid membrane. When it gets itself sucked into a cell, it manipulates the host into building the proteins necessary for viral replication—in essence, turning it into a virus factory. Some of the proteins start to work on duplicating the virus's genome; others form a new viral coat. Those components get bundled into entirely new virions, produced by the thousands, which then pop out of the cell and make their way to other cells, within the same body or in a new one, happy to sail on the winds of a sneeze.

The fact that viruses have so few moving parts is one reason they are so hard to destroy without carpet-bombing the host organism. “They’re basically evolutionarily optimized to be minimalists, so there aren’t a lot of targets,” David Baker, a biochemist at the Howard Hughes Medical Institute, told me. The strategies employed against bacterial diseases are generally useless when it comes to viruses. Some antibiotics, including penicillin, interfere with proteins that form the cell walls of bacteria, causing the germs to burst open and die. (Viruses don’t have cell walls.) Other antibiotics interfere with bacterial ribosomes—tiny intracellular structures that manufacture proteins—or mess with an enzyme crucial to a bacterium’s metabolism. (Viruses have neither.) When a strain of virus does have an obvious vulnerability, there’s no guarantee that another strain will share it—an obstacle for crafting generalist antivirals. And viruses tend to mutate quickly and readily acquire drug resistance, as Ho found with H.I.V.

The most valuable weapon against viruses remains the vaccine—but vaccines (at least the kinds we’ve formulated so far) tend to work against only specific, identified viruses, and have to be taken before infection. Since they’re not effective for everyone, moreover, we’d want antivirals for acute treatment.
even if we had a vaccine in hand. And fast-mutating viruses, like influenza, present a moving target, which is why, by the time a new batch of flu vaccine is manufactured every year, it’s already outdated, powerless to fight much of what comes along. These limitations typically apply to antibody therapies as well: they tend to be specific to a single, already encountered virus, and can’t be stockpiled for use against new ones. That’s why Ho and his colleagues, like researchers elsewhere, are looking for molecular vulnerabilities in virus families, and ways to exploit them.

The earliest antivirals were discovered by means of empirical observation, and almost through happenstance. The first antiviral drug that came on the market, in the early nineteen-sixties, was a repurposed anti-cancer drug put to use as a topical treatment for a herpes infection that attacked the cornea. Another early drug, ribavirin, was developed in the nineteen-seventies, and worked against several DNA and RNA viruses, including those that cause pneumonia and hemorrhagic fever. The same decade also saw the development of acyclovir, which Ho called a “true breakthrough”; it inhibits the reproduction of a variety of herpesviruses. A series of advances came in the nineteen-eighties, in response to H.I.V. One history of antivirals, published in 1988, decried the toxicity and low efficacy of earlier drugs: “Two decades ago, antiviral therapy fell somewhere between cancer chemotherapeutic principles and folk medicine.” Today, with advances in genomic analysis and computer modelling, researchers hope to find drugs that are both stronger and broader in their effects. Different researchers are targeting viruses at different points, like generals probing for weak spots along an advancing front.

One afternoon in March, I was set to visit the lab of Alejandro Chavez, a frank and fast-talking pathologist and cell biologist at Columbia who is collaborating with Ho. (Their lab buildings are kitty-corner.) A few hours before our appointment, though, I got a message: the university had barred visitors. All nonessential employees had been sent home. Ho and Chavez could carry on with their work, since they were researching SARS-CoV-2, the virus that causes COVID-19, but I wouldn’t be allowed in. When I asked if Chavez would give me a virtual tour of the lab by FaceTime, he was skeptical. “It’s not gonna be that exciting, man,” he warned me. “You know what biology looks like. It’s like moving clear fluids from one thing to another. It’s not gonna blow your mind.” The lab, sparsely peopled, contained a dozen PCR machines—DNA-amplifiers, each about the size of a toaster oven—and shelves cluttered with supplies and glassware. Debbie Hong, a graduate student, was hunched over a lab bench, holding a pipette.
“It’s not like the movies, with lasers and lights and, like, crazy cells in green,” Chavez said as he panned his iPhone around his lab. “It’s all pretty benign-looking.”

Chavez’s antiviral research focuses on a particular type of protein involved in viral reproduction—a scissoring enzyme known as a protease. In normal cells, ribosomes read instructions encoded in RNA and make a batch of some specified protein. When a virus like SARS-CoV-2 presents itself to a ribosome, the intruder’s instructions are followed—making the particular proteins that the virus requires in order to replicate. But the ribosome delivers the batch of proteins all linked together in a long chain, a “polyprotein.” So both cells and viruses then slice up these polyproteins into the smaller pieces they need. It’s a little like what happens at a newspaper-printing plant, when a huge roll of paper spins through the press and then gets sliced up into individual broadsheets.

Cells and viruses both use proteases to do the slicing; for Chavez’s team, the challenge is to identify new compounds that will inhibit viral proteases without interfering with a human cell’s proteases. He’s planning to test about sixteen thousand drugs, taken mainly from three “libraries” of compounds, many of which have already been tested for safety in humans. “If you have some information on toxicity, it’s very helpful to advance the compound faster,” Chavez said, referring to the process of pharmaceutical development. Each library—a case filled with thousands of chemicals—is packed in dry ice and shipped from facilities elsewhere straight to the laboratory door.

In standard “high-throughput screening,” you might take a plate with three hundred and eighty-four wells, each three millimetres wide, and introduce into each well a tiny sample of the same viral protein—in this case, a particular protease—but a different drug candidate. It’s as if you were testing three hundred-odd insecticides against one kind of pest. But Chavez has devised a method that lets him study more than one viral protein at a time. In each well, he will place about twenty coronavirus proteases, plus about forty proteases from H.I.V., West Nile, dengue, Zika, and so on. “I can do as many as I want,” he said. “Why would I stop at coronavirus?” In effect, he’s testing an array of insecticides against a menagerie of pests—aphids, weevils, Japanese beetles—at once.

The innovation came naturally to Chavez. “My background was in building new technologies,” he said. “And so I was, like, ‘Oh, I think I have a clever trick. Let’s play around with it.’” He and Debbie Hong tried it. “We were, like, ‘Holy crap, there might be something here.’ And this is the opportune time to really apply it full scale.” The approach could speed the identification of chemicals with broad
effects—ones that work against an array of viral proteases, not just one. (The main protease used by the new coronavirus, researchers say, is similar to one used in picornaviruses, a family that includes poliovirus, the hepatitis-A virus, and the human rhinovirus.)

Chavez estimates that his multiplex project could take one or more years. “But if, at the end of that process, I could have a compound that I know works not only against the current strains but also on a lot of the future ones, that would be very useful to prevent this sort of event down the road,” he said. “Because it’s not a matter of if it’s gonna happen again—it’s simply a matter of when it’s gonna happen again.”

To replicate, viruses need to chop things up; they also need to glue things together. Proteases do the chopping. Another class of proteins, called polymerases, do the gluing. Interfere with the polymerases and you interfere with the assembly of the viral genome.

DNA and RNA molecules are strings of smaller molecules called nucleotides. A good way to stop polymerases from functioning, it turns out, is to supply decoy versions of these nucleotides. A virus is tricked into integrating these building blocks into its own genetic sequence. These nucleotide “analogues” are faulty parts; once they’ve been added to a chain of viral RNA, they effectively bring things to a halt. It’s as if you’d been assembling a toy train from a pile of cars and someone slipped in a car with no hitch on the back, ending the sequence prematurely. Human cells are generally good at detecting and avoiding such defective parts; viruses are more easily duped.

One pioneer in developing such polymerase inhibitors is Mark Denison, the director of the Division of Pediatric Infectious Diseases at Vanderbilt, who—remote learning being the new way of things—spent an hour and a half on the phone talking me through a PowerPoint presentation. Denison began studying viruses in 1984, working with Stanley Perlman, a microbiologist now at the University of Iowa. “I couldn’t spell ‘molecular biology,’ I couldn’t spell ‘pipette,’” Denison recalled, but Perlman took a chance on him. “I didn’t really understand how difficult the problem is, which is a good thing.” He persisted, with his wife occasionally nudging him back to the lab. “Ultimately, I started seeing the incredible, terrible beauty of viruses, and how unique their replication patterns were and how much we had to understand about them.”
Denison has been studying polymerases and nucleotide analogues for the past thirty years, and he points out that coming up with these decoys is especially challenging when dealing with coronaviruses. Unlike other viruses, coronaviruses are excellent proofreaders when it comes to reproducing their genome. Another small protein sits on top of the polymerase, checking its work as it goes down the RNA chain. “It’s like an autocorrect on your phone, if it worked well,” he said. Coronavirus genomes, which are about three times the size of the average RNA virus's, “are the biggest and baddest,” Denison said.

Still, he figured that there was a way to elude the proofreaders. In 2012, he cold-called Gilead, a pharmaceutical company with a specialty in antivirals, asking to try its hepatitis-C drug sofosbuvir. He recounted, “They said, ‘Well, no, you can’t. That’s our multibillion-dollar drug. We don’t know you.’ ” But they were open to collaboration, and sent Denison's lab a selection of other compounds. Denison and his team got to work testing them on a coronavirus called mouse-hepatitis virus, which is safe to work with because it doesn’t infect people. “To our shock, basically, the very first one we tried had activity against our model virus,” he told me. “And I thought we made a mistake, and then it worked again. So I wrote them back and said, ‘Umm, this looks like it works.’ They said, ‘Here’s sixty chemical modifications of that same drug.’ So we tested all sixty, and every single one was more active than the original compound. But one of them was really good. And they said, ‘Well, then, here’s the one we want you to work with.’ ” It turned out that this drug, called remdesivir, had been developed, without notable success, for use against Ebola.

This research helped Denison and his longtime collaborator Ralph Baric, a virologist at the University of North Carolina, land a large N.I.H. grant, in 2014, to study coronavirus drugs. Denison and Baric have been particularly excited about a small-molecule drug known as NHC. (It’s technically a nucleoside analogue—nucleosides lack the phosphorus group that nucleotides have.) This one also sneaks into a growing RNA chain, but, instead of halting construction immediately, it introduces mutations in subsequent copies. Denison says that NHC checks all the boxes: it inhibits multiple coronaviruses (including sars-CoV-2), has a high barrier to resistance, and protects mice that have been given the drug even before infection. Unlike remdesivir, which has to be infused intravenously, it can be taken orally, as a pill—an easier and cheaper way of administering a drug. (To be sure, neither NHC nor remdesivir has yet been shown to work in clinical trials.)
“Most people do extensive testing on one drug, then see if it works more broadly,” Denison said. “We took the opposite approach, which was: we don’t even want to work with a compound unless it works against every coronavirus we test, because we aren’t even worried about SARS and MERS as much as we are about the one that we don’t know about that’s going to come along.”

The usual goal with antivirals is to interfere with the virus, not the host. But some researchers have taken a seemingly counterintuitive approach, seeking to change the host environment in a way that makes it less congenial to viruses. With “host-targeted antivirals,” the aim is to disrupt certain processes in the human cells which are used for viral replication but—with luck—not for much else. Shirit Einav, a Stanford virologist who completed medical school in Israel before doing a residency in Boston, is one enthusiast of this strategy. Frustrated that some of her hepatitis-C patients were beyond the help of available treatments, she turned to research, spending five years looking for a way to target hepatitis C and studying a drug that looked promising. She became discouraged when she realized how narrow-bore it was. It worked against one strain of the virus but proved useless against others, and resistance to it quickly developed. “In the end, I realized how limited the scalability of this approach is,” she said. “That was actually how I then transitioned to the host-targeted approach.”

Host-targeted drugs, she believes, could have a broader application than other antiviral drugs. No matter which specific virus invades them, human cells have the same basic machinery. The challenge is typically to find a dosage high enough to bother the virus but not so high that it harms the host. It helps that our cells feature redundancy: if you interfere with one cellular protein that viruses depend on, the cell often has a backup for itself.

Where Chavez and Denison are targeting viral proteins, then, Einav focusses on host proteins—in particular, a class of enzymes that are co-opted by viruses to shuttle themselves inside invaded cells. A few years ago, she discovered two cellular enzymes required for viral infection and found that, in mice, two drugs that impair these enzymes reduced dengue and Ebola viral loads. In lab-grown cell cultures, they slowed the replication not only of dengue but also of other pathogens in the Flaviviridae family, such as West Nile and Zika. Einav’s collaborators are now testing these drugs on the new coronavirus. She’s hopeful, given that they’ve also shown promise against the virus that causes SARS. But she notes that they didn’t work for DNA viruses. An infinitely broad-spectrum antiviral, she
acknowledged, may be out of the question: “I don’t think it’s one for all, but it might be one for many.”

Other host-directed drugs are being tested for use against sars-CoV-2. A pancreatitis drug, camostat mesylate, inhibits a cellular enzyme that helps some viruses dock with cells, and was shown last month to work against the new coronavirus, at least in cell cultures. And, because the same enzyme is enlisted by other coronaviruses, like the ones that cause sars and mers, there’s hope that the drug might be effective against a range of these viruses. Chavez told me that if Einav’s compounds work in patients—always a big if—“I think it could be a jackpot. These are all interesting ideas. I think you really want a multipronged approach.”

At a moment like this, the urgency of such research is self-evident. But the market has not encouraged the development of drugs for use in acute infections. The big investment has been in drugs for chronic viral diseases, such as AIDS and hepatitis B. “If you start looking at acute viral infections”—which hit suddenly and kill you or pass on through—“it’s pretty gloomy,” Einav said of the financial prospects that pharmaceutical companies see. David Baker, of the Howard Hughes Medical Institute, noted that, although cancer drugs are also expensive to develop and bring to market, “there will always be people dying of cancer.” But pandemics arrive infrequently and don’t necessarily stay for long—characteristics that make them a commercial liability. “It’s one of those cases where a traditional market economy doesn’t work so well,” Adalja, of Johns Hopkins, said. “Suppose you made a sars antiviral in 2003,” after its 2002-03 run. “You would not have had a return on investment, because sars was gone.”

In 2014, Timothy Sheahan, a microbiologist now at the University of North Carolina and a collaborator of Denison’s, joined a group at GlaxoSmithKline working on broad-spectrum antivirals for respiratory infections. A year later, the project was shut down. “I gained insight into how pharma works and how hard it is to develop drugs that not only work but are safe,” he said. (He noted that many drugs that seem safe in animal models prove otherwise in human trials.) “Twenty years ago, most if not all Big Pharma companies probably had some antiviral-drug program. Now there aren’t many.” Jason McLellan, a molecular biologist at the University of Texas at Austin, pointed out that, of the six human coronaviruses known before the Wuhan outbreak, the two that caused sars and mers killed only a few thousand people combined, and the four others cause a common cold. “I’m not
sure you can fault companies for not doing a bunch of drug development on coronavirus,” he said.

Denison’s sense of the need for basic, noncommercial research makes him voluble in his gratitude to the N.I.H. “They’ve supported me doing this work for about thirty years,” he said. “And so I think this demonstrates the critical importance of doing fundamental research on every known human-virus family and understanding their mechanisms and their unique targets, because you just don’t know which family it’s going to come out of next.” All these researchers agreed on the importance of developing multiple broad-spectrum antivirals; all recognized that the private sector was unlikely to be a mainstay of support.

Last month, the Bill & Melinda Gates Foundation, Wellcome, and Mastercard pledged a hundred and twenty-five million dollars to the covid-19 Therapeutics Accelerator to help researchers, regulators, and manufacturers overcome some of the market impediments to drug development. Creating a new antiviral will cost much more than that, but funding from foundations, along with public institutions, can ease certain pain points—for instance, by making it possible to solicit compounds for a pandemic-drug library of candidates for screening. I asked Trevor Mundel, the Gates Foundation’s president of global health, how we might prepare for the next global contagion. Let’s say we had a drug that worked against a broad spectrum of coronaviruses, and maybe other viruses, too. Would we manufacture and stockpile billions of doses, just in case? Who would pay for that? He said that, if drugs with clear broad-spectrum potential came along, governments likely wouldn't need much convincing. At a minimum, countries might make tens of millions of doses available for health-care workers and other critical employees. But in the absence of truly broad-spectrum antivirals we might need twenty drugs that act on different components of infection. Then we’d need to stockpile all twenty.

Mundel, a former pharmaceutical executive trained in mathematics, highlighted two basic challenges when it comes to preparing antivirals for pandemics. “One rate-limiting factor is manufacturing. People find that a boring subject, but if you don’t get manufacturing right you can end up with nothing,” he said. “The other thing that is, of course, rate-limiting is clinical studies. And you saw how chaotic that can be with Ebola, and initially in China”—he was referring to the covid-19 pandemic. “There were a lot of studies being done that were not well designed or controlled. And we start to see that in other places as well: everybody’s jumping in with an observational study.”
A better platform for doing clinical studies would insure better data, but geography stands in the way. Because pandemics move fluidly across borders, ongoing studies like Gilead’s remdesivir trials in China risk running short on patients if an outbreak is contained in one location while flaring elsewhere. “You’ve got to have a global clinical study where you can shift around where you’re getting patients from,” Mundel told me. “And nobody has ever had that kind of clinical study that’s been global and could pull from different geographies as things pop up. So that’s what we’re trying to put in place.” Meanwhile, the World Health Organization has launched a multi-arm trial across many countries, with room to add more arms and countries. It’s called the Solidarity Trial.

On my call with David Ho, he led me on a FaceTime tour of his spartan office and sprawling lab spaces. Hanging in an atrium was a two-story tapestry depicting a double helix, which he’s had for twenty-five years. It was made by a man who helped design Ho’s previous lab space and who later died of AIDS. Down a hallway, Ho pointed through a window to a high-containment facility with PCR machines, centrifuges, incubators, and microscopes. Venturing inside this area requires head-to-toe protective gear.

Another room housed the lab’s most expensive machines, including one that makes cells fluoresce and one with a sign warning “CAUTION LASER IN USE.” (Chavez’s disclaimer notwithstanding, green cells and lasers aren’t just for movies.) The main lab was big and open, with the capacity for seventy-five researchers. That day, it was nearly empty. The “nonessential” people who had been sent home included AIDS researchers.

As he walked back to his office, the deserted corridors reminded me of Ho’s description of the empty boulevard in Beijing. Now at his desk, Ho reflected on negligence and hubris. “We as a society dropped the ball after sars,” he said. “Just because the virus went away, we naïvely thought, Well, you know, goodbye, coronaviruses.” There’s no reason, Ho said, to think that it will ever be possible to bid such a farewell: “This is the third coronavirus outbreak in two decades.” There is, undoubtedly, a fourth somewhere on the horizon, if a different RNA virus doesn’t encircle the world first. There is no way to predict what disease it will cause—it won’t be sars, or mers, or covid-19—but certain things will be the same. Masks will come out, streets will empty, fear will take hold. One thing might be different, if Ho and others like him have their way: there might be a therapeutic arsenal already in place.
“This one is teaching us the lesson that we should persist and come up with permanent solutions,” he said. “We need to persist until we find a broader solution. An outbreak due to this virus or some other viruses will surely come back.”

A GUIDE TO THE CORONAVIRUS

- How to practice **social distancing**, from responding to a sick housemate to the pros and cons of ordering food.
- How the **coronavirus behaves inside of a patient**.
- Can survivors help **cure the disease and rescue the economy**?
- What it means to **contain and mitigate** the coronavirus outbreak.
- The success of Hong Kong and Singapore in stemming the spread holds lessons for how to contain it in the United States.
- The coronavirus is **likely to spread for more than a year** before a vaccine is widely available.
- With each new virus, we've scrambled for a new treatment. Can we **prepare antivirals to combat the next global crisis**?
- How pandemics **have propelled public-health innovations, prefigured revolutions, and redrawn maps**.
- **What to read, watch, cook, and listen to under coronavirus quarantine**.

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