ANNALS OF TECHNOLOGY

JONATHAN ROTHBERG'S RACE TO INVENT THE ULTIMATE RAPID AT-HOME COVID-19 TEST

The inventor and entrepreneur prophesies a future in which self-testing has become one more morning ritual between brushing our teeth and putting on a pot of coffee.

By Gideon Lewis-Kraus

August 29, 2020



While quarantining aboard his yacht, Rothberg has devoted himself to developing a diagnostic that is as fast, simple, and inexpensive as a home pregnancy test. Photograph by Jiajun Wang for The New Yorker

Save this story

On the morning of March 7th, the inventor and entrepreneur Jonathan Rothberg announced, on Twitter, that he'd been thinking through the possibility of "a low cost easy to manufacture home test kit for #Coronavirus." Attached to the tweet was a photo of a clean-swept desk before an orderly collection of curious desktop appliances, backlit, through a large picture window, by the sun's reflection in an azure surf. Rothberg lives and works in Connecticut, where his holdings include a biotech incubator, a vineyard, and a full-scale near-replica of Stonehenge, made of Norwegian granite and modified for celestial alignment with his children's birthdays, but for the moment he was at sea. He, his wife, and three of their five children had just arrived in the Bahamas, where they had planned to take the M/Y Gene Machine, their hundred-and-eighty-foot superyacht, on a spring-break cruise to Atlantis. Fortunately, the ship had been outfitted with Rothberg's demiurgic propensities in mind. One luxury broker and charter operator told me that Rothberg is venerated, in the small, gossipy world of superyacht owners, as "the mad scientist with his state-of-the-art lab." The broker continued, "It's well known in the industry that Rothberg does his best thinking on the ship, where his mind is clear and free of distractions."

Rothberg's "best thinking" generates new ideas at a berserk pace, often without regard for immediate feasibility, but his ambitions are warranted by a long history of unlikely successes. At various points in his career he's considered a return to academia; in each case he has found himself haunted by a practical problem of some personal urgency, and has relapsed into commercial enterprise. At fifty-seven, he presides over seven sibling companies, most of which are organized around the principle of scale: he likes to take existing technologies and make them faster, smaller, cheaper, and more readily available. His portable MRI sells for fifty thousand dollars, his home ultrasound for two thousand. He is most widely known, however, as a pioneer of "next-generation sequencing," a major advance in

the speed with which a genome could be read. The consequences of this breakthrough for personalized health, forensic investigation, and the study of human prehistory, to take only a few examples, have been breathtaking; in 2016, President Barack Obama bestowed upon him the National Medal of Technology and Innovation for his achievement.

Read *The New Yorker's* complete news coverage and analysis of the coronavirus pandemic.

Rothberg's original plan for 2020 had been to use one of his newer companies, Homodeus, to trawl for genetic evidence of "panspermia," the not entirely disreputable idea that life on earth arrived in the form of ancient space dust. But the problem of coronavirus testing—the need for reliable diagnosis of an unprecedented sweep—was a high-stakes contest of immediate appeal. Rothberg thought the team's background work in custom enzyme production was well suited to the contrivance of a COVID-19 diagnostic that did not rely on cumbersome and expensive machines. In February, Rothberg had been dumbstruck by the U.S. government's failure to marshal its resources in preparation for a comprehensive clinical-testing regime. He'd assumed that the people in charge would get their act together before long, but he swore to himself that he would face the next pandemic with a simple diagnostic platform of his own devising. By the time he boarded the Gene Machine, he felt that he could not afford to tarry.

The closest thing we have to a gold standard of pathogenic diagnosis is the polymerase chain reaction (PCR) method, which registers even trace amounts of the virus's nucleic acid. Such "molecular" tests can be calibrated for an unimprovable specificity: false positives are exceedingly rare. (Their sensitivity, or rate of false negatives, is less certain.) The process, however, is embedded in a vast infrastructure: labs depend on complex supply chains for materials and reagents, and samples must be collected and distributed throughout a network of depots for

processing. Optimizing this system requires a good deal of centralized coördination and oversight. Other countries rose to the occasion, and were able to use widespread PCR testing to track and manage their outbreaks. But, even if the U.S. government had acted with alacrity and competence, there are limits to what such a system can do. A streamlined operation might be able to complete thousands of tests at once, but trucks can only carry so many samples and move so quickly, and the turnaround time for a result is almost never less than a day.

Rothberg was not alone in his belief that America would continue to fail this test—and that a day's turnaround could still not guarantee a return to ordinary life. In university labs, small startups, and large life-sciences companies, researchers improvised, drawing upon a variety of techniques to compensate for the lack of national leadership. Rothberg told his core staff not to worry about competitors—he expected that most of them would be focussed on antibody tests, which can only diagnose in retrospect and have often proved untrustworthy, or antigen tests, which register the presence of viral proteins. These can be quick and inexpensive but aren't generally as accurate as molecular tests, which indicate not the presence of a viral proxy, like a protein, but of the virus itself. Rothberg's predictions were almost immediately confirmed: a small Massachusetts startup, E25Bio, soon announced that they had raised millions of dollars of venture capital, and anticipated approval for their fifteen-minute at-home antigen test within two months.

Our free daily newsletter delivers context, not clutter.

gideonlk@gmail.com

SIGN UP

By signing up, you agree to our user agreement (including class action waiver and arbitration provisions), and acknowledge our privacy policy.

Rothberg was committed to the development of a molecular nucleic-acid test as accurate as PCR, as fast and simple as a home pregnancy test, and as inexpensive as an antibody or antigen option. A standard PCR test normally costs about a hundred dollars, though the price is often subsidized; he wanted his available for ten. With such a device, Rothberg wrote on Twitter, "read-out would be in minutes - timer in App - read by camera in your smart phone. No other machines." Over the next forty-eight hours, Rothberg live-tweeted the creation of a new enterprise, tracing his "thought experiment" with a steady but haphazard accretion of technical detail, earnest self-promotion, and preëmptive networking. He tagged researchers at Yale and the University of Pennsylvania. By the end of the first day, he'd received an e-mail from a "great manufacturer." On day two, he reported that he'd made "some general progress on the sample collection." He asked his followers, in a poll, whether they thought he should continue, and, for reasons that were not fully clear, he tagged the Gates Foundation.

On March 9th, he convened, via Zoom, a handful of people, drawn from Homodeus and its kin companies, and told them he thought they could produce a device, secure the Food and Drug Administration's go-ahead, and ramp up to mass production in only three months. His optimism was, according to his employees, characteristic; Owen Kaye-Kauderer, a co-founder of Homodeus and one of the many bright, industrious twentysomethings with whom Rothberg regularly collaborates, told me that Rothberg's ideal company featured "one domain expert surrounded by seven kids who don't know that what they're trying to do can't be done." At the same time, Rothberg's suspicion that by the beginning of the summer there would still be an urgent need for his intervention betrayed a realism, even a pessimism, about the likelihood of a competent centralized response. His instincts also highlighted a fundamental distinction between those who coveted the hope that the pandemic might inspire a renewed commitment to collective action on a federal scale, and those who accepted as a fait accompli that America was a nation in which each looked after only his or her own. In another age or another society, a man of Rothberg's background and expertise—not only in

science and technology but in manufacturing, logistics, and sales—might have been summoned to help organize a public solution. As it was, he immediately began to write patents.

A few days later, his wife, Bonnie Gould Rothberg, a physician and epidemiologist, was recalled to her post at Yale New Haven Hospital. Rothberg told his eldest son, a Yale junior studying abroad in London, to pack his bags and head directly for Heathrow; the young man flew through Miami, picking up one of his cousins in transit, and joined his father and siblings on the Gene Machine. Rothberg's eldest daughter falls into a high-risk category—she takes immunosuppressant drugs—and nothing was safer than a naval quarantine. (The word itself is derived from the forty days of isolation imposed by the Venetian authorities on incoming ships.) Rothberg settled into dockside life in the Bahamian port of Albany with six children between the ages of nine and twenty-four, an eight-pound Pomeranian named Versace, a crew of about a dozen, and the hope that the F.D.A. would grant his test an emergency approval by June.

The various processes that comprise a regular molecular test—loosening the virus from the swab, cracking open the virus's protein shell to free the RNA inside, converting the viral RNA to DNA, and then amplifying that DNA to a detectable concentration—are normally done as a series of discrete steps, each at a different temperature, in a minimum of two test tubes. Rothberg wanted to abbreviate all of this commotion. It was clear to many scientists, Rothberg among them, that the best bet for a cut-rate but exacting diagnostic technology was "loop-mediated isothermal nucleic acid amplification" (LAMP), which was patented by a Japanese pharmaceutical company twenty years ago, and has primarily been used to meet diagnostic needs in low-resource places, for tropical diseases like Zika and dengue fever. In February, a company called New England Biolabs published a preprint of a LAMP-based COVID-19 protocol—not a test, per se, but a relatively simple lab procedure—that had been validated by Chinese collaborators

with patient samples from Wuhan. It was a promising advance, but Rothberg wanted to go further: to contain the entire mechanism in a single vial. Kaye-Kauderer told me that Rothberg's instructions to his team were "no pipetting, no nasopharyngeal swabs, no refrigerated enzymes, no liquid transfer—we had to keep the whole thing hermetically sealed, end to end." Christopher Mason, a geneticist at Weill Cornell, in New York, and a member of Homodeus's scientific advisory board, told me that such "one-pot solutions" are tricky—other scientists, he said, have tried and failed. Rothberg was known, however, for his intransigence in the face of technical challenges.

Rothberg was equally concerned with a host of smaller details. The long nasopharyngeal swabs used in most tests, for example, had been widely unavailable. Moreover, as Rothberg's wife told him over video chat, there was no way users would give themselves what felt like cranial defilements. Rothberg was reassured by a paper indicating that the virus could be reliably detected in the lower nostrils, and moved on to swab design. After a study by the Gates Foundation showed that swabs should be flocked, or tipped with tiny bristles, rather than spun on the model of a Q-tip, Rothberg's supply-chain managers—who were, as often as not, also his engineers—immediately began to negotiate with a Taiwanese vender to produce small flocked versions for their exclusive use. Another issue had to do with the LAMP process, which does not require the complex thermocycling of a PCR machine but does require some heat. Rothberg recognized that the average person was generally able to make tea, and his first thought was that the test tube could be placed into a cup of boiled water. The F.D.A. was open to innovative measures, but his team told him that miniature heaters were cheap enough to manufacture that it wasn't worth a regulatory provocation. With the exception of the heater, which Rothberg planned to do away with eventually, the design made good on everything he considered crucial.

After six weeks in the Caribbean and Florida, the Gene Machine began to head north, taking up a berth at a marina in Savannah, Georgia, where Rothberg could

more easily receive deliveries of the tools and matériel—3-D printers, for example, that worked with biocompatible resins—he required for prototyping. He had promised his youngest child, a nine-year-old, that they could spend the odd hours of the summer constructing a small hoverboard, and among the boxes disinfected and carted aboard each day were sets of ducted fans and microcontrollers. In late May, he told me that I was welcome to join the ship in port, as long as I was prepared to arrive by car rather than by plane. Though he had confidence in his prototypes, he stipulated that I get tested before I arrived. New York and New Jersey had the nation's highest confirmed caseloads at the time, but the dozens of testing sites I called advertised a three-to-five-day wait for results—if, that is, they accepted asymptomatic customers at all. In late March, President Trump had proclaimed that the approval of the country's first rapid-test kits, developed by Abbott Laboratories for use with their I.D. NOW machine, represented "a whole new ballgame." Almost twelve weeks into the New York metropolitan area's lockdown, however, the machine, which costs thousands of dollars, remained a scarce commodity. (A subsequent study, conducted by independent researchers at N.Y.U., indicated an accuracy of barely fifty per cent. Abbott said that the findings were "not consistent with other studies," and the White House continued to rely on them.) On June 1st, I visited a strip-mall clinic in the Meadowlands of New Jersey, one of the very few local venues to offer the service, and texted Rothberg a photo of my all-clear.

I stopped as little as possible on the thirteen-hour drive to Savannah, but it was difficult to miss the abrupt shift in rest-stop mask prevalence in the stretch between Richmond, Virginia, and Rocky Mount, North Carolina. The Gene Machine was moored at a distance from the other resting vessels, on the perimeter of a basin adjacent to the marina's active shipyard, where rusty fishing charters and stocky catamarans hung suspended in drydock. I stepped on a disinfectant mat, removed my shoes, and climbed the stairs to the main deck's exterior corridor. The superyacht's captain, Matt Gow, had been on board for the entirety of the

pandemic to date, and, unfamiliar with the radical revision of landed customs, extended his hand in greeting. Rothberg himself was more cautious, ushering me up to the breezy expanse of the sundeck, where we took our places opposite each other on long weatherproof settees and he gave drink orders to a uniformed crewmember wearing an unobtrusive headset. Rothberg is a tall, lanky, guilelessly charismatic man with a broad, wind-chapped face and a boyish mop of windblown brown hair. He lifted his clunky black wraparound sunglasses up and to the side, rested them askance on the frames of his prescription pair, and gestured to his marine habitat. Over the past six weeks, he'd left the boat only for short tours of the estuary, and for afternoon pedal-boarding for exercise in the tidal marshes. They'd seen dolphins and the occasional alligator. The shipyard was still for the day, and only the occasional police helicopter overhead broke the lush crepuscular silence. The world and its crises felt keeningly distant.

Rothberg was impatient to begin his external monologue wherever his internal one had been interrupted, but there was one piece of business he wanted to take care of first. In March, the entertainment mogul David Geffen provoked understandable ill will online when he posted to Instagram a photo of his own superyacht escape. "Isolated in the Grenadines avoiding the virus," he wrote. "I'm hoping everybody is staying safe." Rothberg insisted that his family's maritime isolation had been no sumptuous idyll; he had spent most of his time, when he wasn't petitioning his children for a moment of their attention, scanning the emerging literature for academic experts who could answer his questions as they arose. Whenever his wife was able to be home from the hospital for dinner, the children passed their mother's face in two dimensions around the table.

Rothberg was born in Connecticut, the second-youngest of seven siblings. His father, Henry Rothberg, had made a small fortune with the invention of a breakthrough form of adhesive for the installation of ceramic tile and stone. The family firm, Laticrete International, is now chaired by Rothberg's older brother David. Rothberg and his siblings describe an unruly but loving household; as Rothberg likes to put it, "My mother had seven only children." Henry had a

chemistry lab in the basement, and from an early age Jonathan pursued his own unsupervised experiments.

Rothberg was lost to his own dreamy agenda. He taught himself to write code on an early Texas Instruments minicomputer, then sold an inventory-management program to a local tire shop, but wasn't trusted with the house keys. He built a half-scale T. rex, attempted to shoot mice into outer space, and later counted cards at Atlantic City blackjack tables. He majored in chemical engineering at Carnegie Mellon, where he was the first person in the dorms with his own Apple computer. His close friend and first business partner, Greg Went, ferried him back to Connecticut for vacations. "Jonathan was just thinking out loud at all times, and not random thoughts but practical ones, so having him drive a car wasn't really a safe thing to do," he said.

Rothberg pursued a Ph.D. in biology at Yale. His doctoral adviser, Spyros Artavanis-Tsakonas, now an emeritus professor of cell biology at Harvard Medical School, described Rothberg to me as "perhaps the most original person I've met in my life, ever." Rothberg was an unusually wide-ranging and syncretic thinker, interested in the possibilities of "biotech" long before the word was in common circulation, and a businessman from his first day of grad school. When he was giving a talk in lab meetings, Artavanis-Tsakonas said, "he would have a little note at the bottom of the slide saying, 'This is proprietary information,' which was annoying to me but was also very funny." Artavanis-Tsakonas went on, "If he had an idea he would follow it up, not like many smart people in the lab who would think of something big, would start, and then with the first difficulty would let it go." Rothberg founded his first company, CuraGen, right out of grad school. It survived on a string of grants from government agencies, as well as from investments from his parents and siblings; his younger brother, Michael, gave him what amounted to his life savings at the time. The company's goal was to exploit the growing understanding of the human genome for novel therapeutics.

CuraGen went public, on the Nasdaq, in 1998. The following year, the bull market drove the share price from five dollars to two hundred and fifty in six months. His siblings could retire if they wanted to.

Rothberg married Gould, a graduate of Yale's medical and public-health programs, in 1995; in 1996, their first child, a daughter, was born with a condition that can cause seizures. In 1999, Rothberg and Gould had a son, who turned blue after birth and was rushed to the NICU. In times of distress, Rothberg soothes himself with engineering problems, and as he sat in the waiting room he fixated on the fact that there was no expeditious way to determine whether the baby's condition was genetic. He noticed a magazine cover celebrating the Pentium chip, and realized it should be possible to quicken genetic sequencing on the model of an integrated circuit. He spent his two weeks of paternity leave sketching out designs, and when he returned to CuraGen he formed a subsidiary company, 454 Life Sciences, to develop the idea. The result was the first major advance in genetic sequencing in the thirty years since the British biochemist and two-time Nobel laureate Frederick Sanger had published his own seminal method. The Human Genome Project—the first composite map of a human genome, which was completed in 2003—had taken thirteen years and cost about three billion dollars. In 2008, Rothberg and a research team used his technique to map and publish the first complete genome of a single individual, the geneticist James Watson. The project took four months and about a million dollars. The technology was also used, by a team in Leipzig, to sequence the first complete Neanderthal genome.

In the wake of the dot-com bust, CuraGen's stock price fell precipitously. The company's board, which saw Rothberg's high-speed-sequencing side hustle as more of a distraction than a valuable investment, fired him in 2005; 454 Life Sciences was sold off for a hundred and fifty-five million dollars, which Rothberg believed represented about a fifth of the subsidiary's actual value. In the next two

years, a rival startup called Illumina cornered the high-speed sequencing market. Illumina is now a fifty-billion-dollar enterprise.

Still, Illumina's sequencing machines were large and unwieldy—they often required special fortified floors for support—and sold for half a million dollars. It occurred to Rothberg, in his unplanned retirement, that he could put the entire process on a silicon chip and bring the price down by an order of magnitude. He worked on his next company, Ion Torrent, in "stealth mode" for two years. At a large biotech conference in February of 2010, during a keynote, he had his largest employee walk in from the back carrying in his arms a machine the size of a desktop printer. This new sequencer was limited, compared to its bulky predecessors, in the amount of DNA it could read at one time, but it cost only fifty thousand dollars, and promised to bring sequencing capability to labs and medical centers that couldn't otherwise have afforded it. Six months after its theatrical début, Ion Torrent was sold to Life Technologies for a total of about seven hundred and twenty-five million dollars. Rothberg bought a boat, he told me, as night fell on the marsh and the black water below was lit with the bright neon of the Gene Machine logo, and installed a high-backed throne on the bow of the sundeck—a reminder, he says, that things tend to work out in the end. His mind was in some Aegean port, and he didn't seem to notice the vicious clouds of stinging gnats. "I cruise into a new place," he said, "and think about how glad I was that I was fired."

Rothberg's biotech incubator, 4Catalyzer, originally encompassed four startups; last year, he added three more, including Homodeus. The endeavor, which includes a popular café named after his father and a garden named after his mother, has the feel of a personal micronation. Rothberg prides himself on his ability to identify and recruit talent from academia, finance, and the health-care industry, and in the process has essentially re-created his own jostling family under cover of startup cultivation. Each company also has a connection to his actual family. When Rothberg bought his eldest daughter a watch that was supposed to warn of seizures, it produced so many false alarms that he decided to throw it

away and start his own epilepsy firm. (He has also underwritten a variety of research labs and drug trials over the years, especially for rare diseases; the immunosuppressant that has left his daughter particularly vulnerable to COVID-19 emerged from a development program he and his wife funded twenty years ago.)

Rothberg has come, over time, to recognize his own administrative shortcomings, and for the COVID-19 project he hired some proven mercenaries for help. For financing, he brought in Emil Michael, best known for his role as the money man at Uber, and as C.E.O. he enlisted the aid of a high-ranking executive at a major Silicon Valley firm who preferred that his involvement not yet be a matter of public record, leaving Rothberg free to play a more expansive, oracular role. He prophesied a future in which his kits would be on sale at every Walgreens and CVS, a world in which self-testing has become one more morning ritual between brushing our teeth and putting on a pot of coffee. You might test all visitors to your home the way he tests all visitors to his boat. And, as he told his investors, their product had long-term post-pandemic potential: what he first called "COVID Detect" was quickly reimagined as Detect, a flexible diagnostic platform that could easily be retooled to identify cases of the flu, respiratory syncytial virus, and a variety of other maladies.

My arrival in Savannah coincided with the delivery of Rothberg's first manufactured prototypes. While he took videoconference meetings one day, I was joined on the sundeck by his intern, Isaac Bean, a self-taught molecular biologist and maker who'd answered a Twitter call for help, spoken to Rothberg an hour later, and driven from Colorado Springs to Savannah the next day. Bean and I sat at the bar and he opened the Homodeus app on his phone. While Rothberg's children worked out with kettlebells on yoga mats behind us, I took myself through the steps of the test: swirl the swab, which resembles a thin dental pick, in each nostril five times; submerge it into a microcentrifuge tube the size of a shark's tooth; replace the cap, which contains a single white "magic" bead—a set of

lyophilized, or freeze-dried, reagents—in an open cage structure, and shake until the bead's contents dissolve. Then I placed the tube in the small heater and clicked the timer, which was set for thirty minutes. As we sat and waited, Rothberg paced the length of the sundeck, discussing with his executive team the terms of the twenty-million-dollar financing round they'd just closed.

After thirty minutes, I withdrew the tube and pressed it into the chimney portion of what looked like a small plastic pipe; a hidden razor broke open the tube and the fluid made its way down a lateral-flow strip. A series of lines were supposed to indicate my status. My test failed to register a conclusive result. I had been around Rothberg's children, and the moment was tense. Rothberg came over to look into the problem, but Bean was already on his way downstairs to retrieve a set of replacement components that had been printed on the boat. We tried again; it came back negative.

In late July, some six weeks after I visited Rothberg, my wife and I feared that our three-year-old was showing symptoms of the virus. New York was long past its peak, but the testing situation was considerably worse than it had been during the spring; there were waiting times of nine or fourteen days. Rapid tests, which were still being conducted on Abbott's I.D. NOW machines, were few and far between, at least for most people; the only option seemed to be a pop-up center in a Bronx post office. Still, our pediatrician categorically recommended a lab test over a rapid one, the accuracy of which, in the wake of the N.Y.U. study, she did not trust. My wife, however, was nine months pregnant, and if there were even a chance our son was infectious we needed to take immediate steps. I disobeyed the doctor and drove our son to the Bronx. The line was hours long in sweltering sidewalk heat, and we were told that the center would almost certainly hit their daily capacity of a hundred and twenty-eight tests before we were called. We turned around and went to the pediatrician, where an instant test for strep came back positive.

What I had experienced in miniature was at the heart of a national debate about testing and public health. Delays in PCR tests had rendered their results pointless: a delay of even three days meant that infections were not being caught until the period of maximal contagion had already elapsed. There was, however, good-faith disagreement among experts about how to proceed. Faster PCR would be a tremendous help, but, so many months into the pandemic, any fantasy of national orchestration had been vacated, and by late July an alternative consensus had emerged in favor of widespread, frequent rapid testing.

Of primary importance was the apparently semantic difference between whether someone was "infected" versus whether they were "infectious." A PCR test can register the presence of an infection at such a vanishingly low "limit of detection"—the threshold at which a given test can reliably identify the presence of the virus—that it could return a positive result even before an individual is likely infectious. This might seem like a good thing, but there was an argument to be made that a test didn't need to catch an embryonic infection; it only needed to catch the onset, a day or two later, of infectiousness—which rapid tests could generally do. If a population were tested frequently enough, no carrier would be walking around undiagnosed for very long. Modellers at the University of Colorado Boulder and Harvard demonstrated in June that, depending on the prevalence in a community, testing everyone even twice a week would get the pandemic under control. The rollout of such a testing regime, according to Michael Mina, an epidemiologist at Harvard and a co-author of the study, "can effectively be akin to a vaccine that was introduced tomorrow." For this reason, many epidemiologists and public-health experts have pushed the F.D.A. to introduce separate regulatory tracks for "diagnostic" and "screening" purposes.

By July, it seemed as though the F.D.A. had come around to this way of thinking. The agency granted emergency-use authorizations (E.U.A.s) to the rapid point-of-care antigen tests produced by Quidel and by Becton, Dickinson & Company despite the fact that neither measured up to the PCR standard. But, to the chagrin of some experts, the agency continues to recommend against rapid testing for

asymptomatic individuals. (This week, President Trump announced a seven-hundred-and-fifty-million-dollar deal to buy a hundred and fifty million rapid antigen tests from Abbott Laboratories—intended, however, only for those who have shown symptoms.)

Rothberg, who is sensitive to the criticism that his own innovations are merely low-rent versions of better technologies, was determined in this case to make no compromises. His product would not only do away with the machines required by his competitors' antigen tests, it would approximate the diagnostic rigor of the PCR standard. The F.D.A.'s willingness to relax its benchmark for rapid tests was, he felt, irrelevant; he liked to quote the old Hebrew National slogan, "We answer to a higher authority." He spent the summer months of the slow regulatory process adrift along the Northeastern seaboard, working from moorings in Sag Harbor, Martha's Vineyard, and Guilford, Connecticut. He was sanguine enough about his test that he used the prototypes more than eleven hundred times on his boat in eleven weeks: his family and the crew were screened every day, and he sent drones to shore to ferry samples from prospective visitors. It wasn't until early August that his test gave a positive result in the wild: a replacement chef was prevented from coming onboard before he could expose everyone. They repeated the test with the same result, and Rothberg called in a favor with a friend and collaborator at Yale to line up an immediate PCR test, which confirmed the infection. "People who don't feel sick can't imagine they're sick, and that's the entire reason we're in this predicament," he said. "You can read this a hundred times, but it's a personal lesson in how insidious this thing is." Rothberg put the chef up in a motel for two weeks. He never developed symptoms.

When I met with Kaye-Kauderer in mid-August, in a coffee shop near his home in Brooklyn's Bushwick neighborhood, he had good news and bad news. The team had recently got very promising "preclinical" results: their test's sensitivity put them well within striking distance of the PCR standard. These findings, however,

were obtained in a controlled laboratory setting, and were based on "contrived" samples, an ambiguous term used to describe samples that had been rendered, by one process or another, more tractable. They were still at least a month away from formal validation trials with human patients and human noses. Moreover, the enzymes they needed were made by only about ten suitable venders in the world, and if a small company could even place an order the quotes came in high. As a result, they were going to have to price the kit at something like thirty-five dollars, at least initially, rather than ten. This wasn't the only concern. A newly discovered chemical problem was causing a high rate of invalid tests—that is, tests that registered the presence of neither viral nor human genetic material. The issue could be solved relatively easily with the introduction of a single additional step to dilute the sample, but Rothberg refused to add any complexity for the user.

More convoluted versions of the LAMP technique had, in the meantime, been deployed in dozens of places. Christopher Mason, the geneticist at Weill Cornell Medicine, had partnered with his brother, the mayor of Racine, Wisconsin, to test all of the city's employees out of an impromptu lab in the local firehouse, and others set up mobile labs in vans. Mason, who was running an open-access online LAMP research group, assumed that at least one of the dozen or so LAMP teams would hit upon a viable one-pot solution by the winter, if not sooner. Perhaps it would be Rothberg, who immediately came up with a few different potential fixes. But if Homodeus wanted to sell their kits into the large and lucrative university market, his team had very little time to get everything in order. Rothberg was unhappy about the setback, he told me, but he retained his sunny, page-a-day-calendar outlook: "The nature of developing stuff is you have to get up more than you get knocked down."

He reminded himself why he'd embarked on this course at the beginning. Just that morning, he'd been upset to hear that Purdue University, in Indiana, had suspended thirty-six students for attending a party. "You're telling me that the kids are responsible and not the school?" he said. "Come on. This makes me feel like,

my God, we've gotta get these out there—because if we test everybody it could be a pretty safe world."

Rothberg and I last spoke, in late August, over video chat; he was cruising back to New York, and, though he had Connecticut in sight to starboard and Long Island in sight to port, he didn't have a good satellite connection, and his inability to sit still left him a blurry smear on the screen. He was disquieted. For weeks, the team had been talking to various state governments, private colleges, large public-university systems, and major sports leagues. Their hope was that by late autumn their supply chains, which included around a dozen venders, most of them domestic, could be producing millions of units per month. But it still wasn't clear whether there was any practical way to test entire populations frequently enough to keep campuses, workplaces, and other congregate bodies open. With each passing week, the situation had grown increasingly dire. In mid-August, Stanford and Columbia announced that they were cancelling plans to resume in-class instruction. Other universities—U.N.C. and Notre Dame among them—opened briefly only to send their students back home. The nephew who'd stowed away on the Gene Machine in the spring had recently gone off to his freshman year in college, in Miami; within a week, there were infections on the two floors above him, and before he knew it he was isolated in a hotel room. Rothberg's two college-age children, both at Yale, had decided to take gap semesters, and were interning for his companies from the boat. "It agitates me that we messed up so badly," he said. "In so much time, we couldn't get anything done as a nation. That makes me feel really terrible—I just wanted kids to have a normal experience."

Absent a national plan, private institutions had been left to fend for themselves. Those with resources at their disposal had some options. The two-thousand-dollar machine that processed Quidel's thirty-dollar antigen test kits was backordered for the foreseeable future; it was being used for parties in the Hamptons and by concierge medical services. Large research universities had the expertise,

equipment, and authorization to do their own lab work. Elsewhere, it was understood that closure was a real possibility unless help arrived soon. Though some of Rothberg's earliest competitors had been held up—E25Bio, the Massachusetts company that expected an E.U.A. for their antigen test in April, had not yet achieved regulatory approval—there was no shortage of entrants to the field. Cue Health, a San Diego company that raised a hundred million dollars from institutional and strategic investors in June, had received an E.U.A. for their twenty-five-minute rapid point-of-care test. But their system also required costly devices, which could only process one sample at a time. Recently, the F.D.A. had granted approval to a saliva-based test developed at Yale, and Rothberg fielded half a dozen phone calls from friends who had the impression that the testing nightmare, and in turn the pandemic itself, was effectively over. Rothberg explained that the approval was not for a test but for yet another protocol: the spit could be collected at home or at the office, but it still had to be sent to a specialized lab for machine processing. Solutions of greater promise lay on the distant horizon. A California startup called Mammoth Biosciences had announced a partnership with GlaxoSmithKline to develop a CRISPR-based at-home test, but it seemed unlikely to appear before next year. Academic teams at Colorado State University and Columbia had also publicized auspicious approaches to rapid testing, the latter also based on LAMP technology, but their commercial partnerships remained in the early stages.

Although Rothberg had designed his kit for home diagnosis, he had been told early on that he should first pursue F.D.A. authorization for point-of-care use. Homodeus was not allowed to market their test until they had received an E.U.A., but they could nonetheless enter into preliminary discussions with interested parties. They aimed to deliver their first fifty thousand kits—a fraction of which, Kaye-Kauderer told me, they hoped to reserve for lower-resource communities—while it was still early in the semester.

Their test would require not only clinical validation data but usability trials. The Homodeus team had been invited to the campus of Roger Williams University,

which cleaves to a peninsular hillside in Bristol, Rhode Island, to conduct a pilot. The school's total population was only around six thousand—small enough, the school's testing task force believed, that it could adopt the sort of testing regime that Rothberg's kit would make possible. Students were expected to return to the campus in a week's time, and, despite the large white tent erected to replace indoor cafeteria dining, the expectant atmosphere was oddly normal.

The chair of the task force, Brian Wysor, a marine biologist who studies tropical seaweed and wore a mask patterned with red snails, told me that the goal was to make it to Thanksgiving; students would return home for the holiday and take their exams remotely. That was about as far ahead as they thought they could reasonably plan. For the time being, the university would be relying on a testing program set up by the Broad Institute, in Cambridge, to support institutions in the area. The school's events team had installed Plexiglas-protected card tables in the field house's cavernous gymnasium for sample collection; the effect was of a polling station in an unusually paranoid electoral district. The Broad Institute had provided label printers for the collected samples, which would be regularly dispatched by courier for the hour-long trip north to their lab. Results were expected within twenty-four hours, but the first tranches had been available in only eighteen.

Wysor nevertheless saw a world of difference between an eighteen- or twenty-four-hour turnaround time and the forty-five-minute result Homodeus could provide. Some of the dorm rooms had been set aside as isolation units; if the task force could instantly sequester an infectious student, they felt they stood a good chance of making it to November. To test six thousand people every three days with a thirty-five-dollar Homodeus test would cost four hundred and twenty thousand dollars per week. There were likely more economical solutions: Roger Williams could, for example, buy home-brew LAMP kits from New England Biolabs and set up its own lab on the Racine, Wisconsin, model. This method

could bring the cost of each test down to perhaps three or four dollars. But it would require a major investment in infrastructure and personnel. The promise of a self-administered test in a single tube was irresistibly seductive.

Ben Rosenbluth, a Homodeus co-founder and floppy-haired recent Yale grad who fell squarely into the category of "kids who don't know that what they're trying to do can't be done," had arrived early to conduct the pilot. The Homodeus kits—each encased in its own minimalist silver-foil packaging, like an extra-large Capri Sun juice pack—were complete, but the actual reagents had been replaced with dummy fluids. Koty Sharp, one of Wysor's colleagues in marine biology and a fellow-member of the task force, stood in for the health-services representative who would ultimately oversee the test's administration, and she and Rosenbluth "tested" three student volunteers.

The pilot demonstrated that what I'd done by myself with ease on the boat might prove less than straightforward when attempted en masse, and when Rosenbluth asked Sharp if she thought the test would suit their needs, she explained, with the patience and diplomacy of someone long accustomed to lab instruction, that she thought there was some work to be done before they'd be ready to roll it out on the order of fifteen hundred or three thousand students per day. It wasn't quite clear which steps of the process were best carried out by students and which required staff assistance. Some system would be required to link the students to their respective kits as they arrived, presumably after standing in an orderly line while observing social-distancing measures. They would collect their own samples under supervision, but would they manage the next steps on their own? A potentially infectious swab had to be handled, and eventually disposed of, in accordance with the proper biohazard protocols. The test tubes had to be shaken "vigorously" and then "flicked"—words that were not entirely self-explanatory—before being placed in the heater. Where would the students go to wait, and what would they do for that half hour? Then, once the test tubes had been withdrawn from the heater, returned to their original chimneys, and broken open to saturate the readout strip, their results had to be interpreted in no fewer than five minutes

and no more than ten—any shorter and the lines might not yet have appeared, any longer and the results were no longer valid. How would students be recalled from the waiting area for notification?

Homodeus was not a logistics consultancy, but no test was conducted in a vacuum, and every context presented its own complications. Rothberg, despite his general chutzpah, acknowledged that different people in different communities at different times and in different places will have different needs. There would never be such a thing as "the COVID test." "Remember those late-night infomercials for a knife that could do anything—the guy cuts down a tree with it outside and then goes to work in his kitchen?" he said. "Tests aren't going to be like that, and we're going to need antibody and antigen tests for population-level control. Our own nucleic-acid tests are going to complement lab tests where you want that accuracy—when you have a child with an immune deficiency, or when you have a pregnant wife. I liked having a nucleic-acid test before I brought someone onto my boat, for example, where the attack rate would've been horrible."

Rothberg's vision for a shelf of silver Detect kits in every CVS was nevertheless intact, and over the blurry course of our video chat he lurched back and forth between disillusion with the country and pride in his company. His optimism was abiding: his test, with its single vial, would work as advertised. "Let's get a lot of these out there by Thanksgiving," he said. "Let's let people see their families for the holiday." The pessimism was taken for granted: if people like him weren't going to save you, who would?

A previous version of this piece incorrectly described test specificity and sensitivity.

More on the Coronavirus

- To protect American lives and revive the economy, Donald Trump and Jared Kushner should listen to Anthony Fauci rather than trash him.
- We should look to students to conceive of appropriate school-reopening plans. It is not too late to ask what they really want.
- A pregnant pediatrician on what children need during the crisis.
- Trump is helping tycoons who have donated to his reëlection campaign exploit the pandemic to maximize profits.
- Meet the high-finance mogul in charge of our economic recovery.
- The coronavirus is likely to reshape architecture. What kinds of space are we willing to live and work in now?



Gideon Lewis-Kraus is a staff writer at The New Yorker covering technology, academia, and books, among other topics. He is the author of the memoir "A Sense of Direction."

More: Coronavirus Health Care Technology Medicine Coronavirus Treatment and Testing

A smarter scroll.

Sign up for our free daily newsletter.

gideonlk@gmail.com

SIGN UP

By signing up, you agree to our user agreement (including class action waiver and arbitration provisions), and acknowledge our privacy policy.

READ MORE

Can Designer Mice Save Us from COVID-19?

How vials of frozen, genetically engineered rodent sperm, raced to a remote lab in Maine, produced a breed of critters that could help scientists find a treatment or a vaccine.

By Raffi Khatchadourian

Amid the Coronavirus Crisis, a Regimen for Reëntry

A four-part strategy of hygiene, distancing, screening, and masks will not return us to normal life. But, when signs indicate that the virus is under control, it could get people out of their homes and moving again.

By Atul Gawande

ANNALS OF MEDICINE

Is the Military Low-T?

New data suggest that a quarter of American servicemen may have low testosterone. That doesn't mean what Pete Hegseth thinks it does.

By Rachael Bedard

THE LEDE

What China's Vibe-Coding Capital Can Tell Us About the A.I. Boom

Tech workers have flocked to Liangzhu, a small town outside Hangzhou, looking to escape China's corporate culture and build their future with A.I.

By Afra Wang

THE LEDE

"An Unprecedented Case of Child Abuse"

In an L.A. criminal court, new details emerge about the mysterious couple who collected more than twenty babies through surrogacy.

By Ava Kofman

FICTION

"Appeasement, Ohio"

Sometimes a person has to be bold and trust that the person he's being bold to will rise to the occasion.

By George Saunders

THE WEEKEND ESSAY

My Year of O.C.D.

A simple e-mail or kitchen appliance could send me into a pit of anxiety. The only way out, I learned, was in.

By Andrew Lipstein

PERSONAL HISTORY

My Education on the Border of the Syrian War

In the last Turkish town on the road to Aleppo, jihadis and spies mixed with reporters trying to prove themselves.

By Ben Taub

BRAVE NEW WORLD DEPT.

We're Learning to Live with Waymos. It's Going Weird

A view from the back seat.

By Molly Fischer

ANNALS OF TECHNOLOGY

Computer Chips Are the Most Magnificent Things Humanity Has Ever Made

They power our phones, cars, dishwashers—and the A.I. systems that prop up the economy. They're also at the heart of fierce geopolitical rivalry.

By Gideon Lewis-Kraus

THE LEDE

The Humanism Driving the Anti-A.I. Movement

At the Pro-Human Assembly in Washington, D.C., attendees talked less about jobs and policy, and more about their philosophy of life.

By Becca Rothfeld

THE LEDE

There Is No A.I. "Race"

We're constantly told that Chinese advances would have catastrophic consequences. But the first to innovate is rarely the one who wins.

By Chang Che

Privacy Information