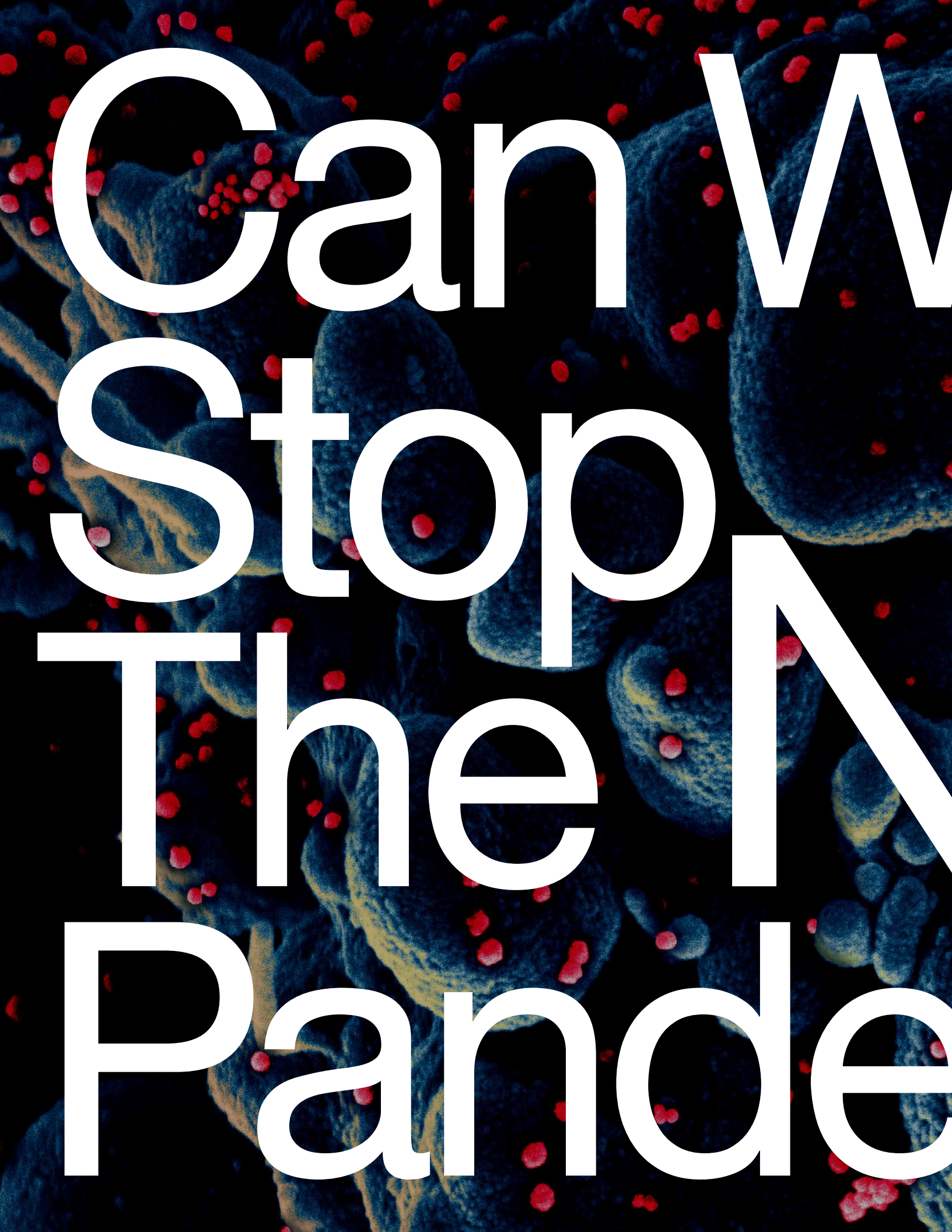
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Experts at NYU Langone's Vaccine Center and alumni mobilize to prevent the spread of infectious diseases

BY BARBARA BRODY

On The Front Lines

By this past March, as COVID-19 tightened its grip on the United States, New Yorkers deserted the normally bustling streets and subway platforms. Schools, restaurants, bars, and gyms were shuttered as panic about the virus set in. Grand Central Station and Times Square were suddenly eerily empty, even as many residents wondered how they would practice "social distancing" in a city that's home to 8.5 million people. Was the Big Apple the right place to be during a pandemic?

Mark J. Mulligan, MD, had no such doubts. He was exactly where he was supposed to be.

Dr. Mulligan, an internationally renowned infectious disease expert, joined NYU Langone Health nearly two years ago as director of the Division of Infectious Diseases and Immunology and inaugural director of the Vaccine Center at NYU Langone. "I think that New York City is the perfect place to have a vaccine center," says Dr. Mulligan. "When we do clinical translational research in human study participants, we always strive for diversity, and we have great diversity here."

Mark J. Mulligan, MD, Director, NYU Langone's Vaccine Center

Given the millions of international travelers flying into and out of three regional airports each year, New York City is also highly vulnerable to infectious disease outbreaks. Although that might make some people nervous, Dr. Mulligan considers it an opportunity to study and conquer some of the most challenging diseases of our time.

"It's not just coronavirus," says Dr. Mulligan. "We seem to be increasingly having these threats to human health through emerging or reemerging infectious pathogens like pandemic influenza, Ebola, Zika, and even measles."

As director of the Vaccine Center, Dr. Mulligan strives to fight these diseases as well as whatever new menace might be around the corner. "We want to be on the very cutting edge of research in combating infectious disease threats to public health," he says. The center is also committed to developing vaccines for non-contagious conditions, such as by developing immunotherapy for cancer. "We're interested in autoimmunity, vaccines for infectious diseases, and vaccine-related technologies. That's a part of our vision as well. We want to train the next generation of outstanding scientists and physician investigators," he adds.

Building on a Legacy

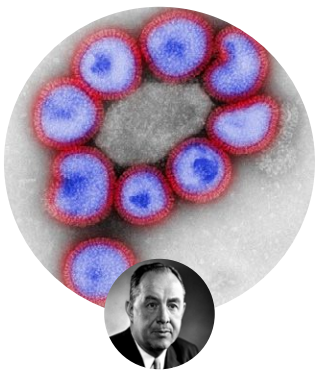
Of course, NYU Grossman School of Medicine has a long history of training pioneering doctors and researchers. Polio vaccine inventors Jonas Salk and Albert Sabin studied medicine at the School, as did Emil Gotschlich '59, who created the first meningitis vaccine, and Douglas Lowy '68, who played a critical role in the development of the HPV vaccine. Prominent faculty members have included Thomas Francis, the first person in the U.S. to isolate the influenza virus, as well as Ruth Nussenzweig, MD, PhD, Hon. '04, and Victor Nussenzweig, MD, PhD, Hon. '04.

"A lot of very fine work in immunology and virology at the very beginning of the HIV epidemic in the early 1980s happened here," says Dr. Mulligan. "Bellevue is a city hospital, but it's staffed by NYU Langone physicians, and the hospital is legendary for many developments in medicine, including infectious diseases going back all the way to … yellow fever, smallpox, and tuberculosis."

Today this impressive history continues both at NYU Langone Health and beyond as a vast network of alumni take what they've learned at the School and apply it to their work combating a variety of infectious diseases around the world.

NYU Langone's Legacy in Vaccine Discovery

Diphtheria, 1920s
William Park



Influenza, 1930s
Thomas Francis

Pneumococcal pneumonia, 1940s
Colin MacLeod

Thomas Francis Jr.: Fabian Bachrach, Wellcome Collection; Colin MacLeod: Image courtesy of The Lillian and Clarence de la Chapelle Medical Archives at NYU

The Newest Threat: COVID-19

When an infectious disease crisis hits, mobilizing quickly is essential. "Part of our vision and mission [at the Vaccine Center] is that we have in place processes so we can quickly respond to emerging threats," says Dr. Mulligan. By early 2020, even before COVID-19 had infected many in the U.S., the center had already launched novel coronavirus research and was aiming to develop medical countermeasures, including diagnostics, potential treatments, and vaccines.

By late February, the Vaccine Center had obtained stock of the virus from the Centers for Disease Control and Prevention, via the National Institutes of Health (NIH). Its staff were growing the virus in a high-containment BSL-3 laboratory, in collaboration with Meike Dittmann, PhD, assistant professor of microbiology, and preparing to test therapeutic candidates against it. Because IRB-approved protocols for specimen and data collection had long been in place—they're the same protocols used when studying influenza and other infections—researchers were able to forge ahead swiftly.

Around the same time, NYU Grossman School of Medicine alumnus Michel C. Nussenzweig '82, PhD, was at nearby Rockefeller University developing plans to clone COVID-19 antibodies in his lab. Dr. Nussenzweig, a professor at Rockefeller and a Howard Hughes Medical Institute Investigator, is a basic immunologist who invented a unique method of human antibody cloning. He is the son of vaccine pioneers Ruth and Victor Nussenzweig. Like his mother, Dr. Nussenzweig is a member of the National Academy of Medicine and the National Academy of Science.

"We've cloned antibodies to HIV, Zika, and hepatitis B, and the method we've used is definitely applicable to the coronavirus," he said in March. Step one—recruitment of infected volunteers from whom antibodies to COVID-19 could be obtained—was already underway.

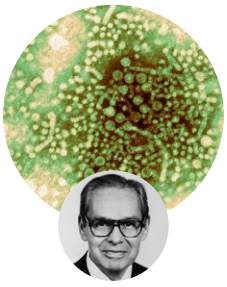
Elsewhere, at the Precision Vaccines Program at Boston Children's Hospital, alumnus Ofer Levy '97, PhD '96, was focusing on developing a coronavirus vaccine that would specifically target people 65 and older. At press time his group was collecting blood samples on senior volunteers and testing the efficacy of various adjuvants.

The Promise for HIV

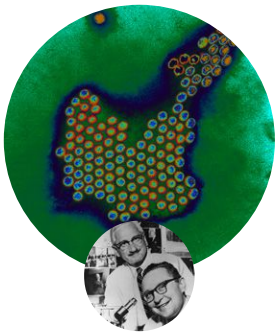
HIV treatment has advanced dramatically in the past few decades, and patients are living longer and better as a result. Yet there is still no cure, and infected patients must take a combination of antiretroviral drugs every single day—a regimen that is problematic in many parts of the developing world. Groundbreaking work by Dr. Nussenzweig aims to change the narrative.

For the past decade, Dr. Nussenzweig has been studying adaptive immunity, specifically the role of B lymphocytes and antibodies to HIV-1. His laboratory cloned antibodies from infected patients and discovered that a select group of "elite controllers" have immune systems that naturally produce broadly neutralizing antibodies that kill off the virus. Dr. Nussenzweig and his colleagues then produced two antibodies to HIV-1 for clinical testing.

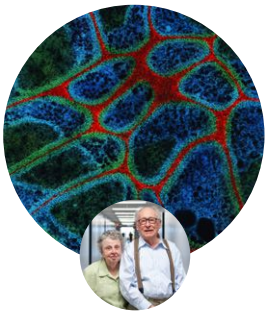
Michel C. Nussenzweig '82, PhD



Hepatitis B, 1950s
Saul Krugman



Polio, 1950s
Jonas E. Salk '39
Albert B. Sabin '31, BA (WSC '28)



Malaria, 1960s
Ruth S. Nussenzweig, MD, PhD, Hon. '04
Victor Nussenzweig, MD, PhD, Hon. '04

Tachi Yamada '71, in Ghana

The results so far have been impressive. Phase I and II clinical trials conducted at Rockefeller University have found that injecting these antibodies is safe and effective in suppressing the virus for several months.

"Antibodies have two ends: a side that's like a drug, which recognizes the virus, and another side, the constant domain, which interacts with the host's immune system and has the potential to clear the virus from the body or from infected cells," Dr. Nussenzweig explains. Unlike antiretroviral drugs that are currently on the market, these antibodies—if confirmed to be effective in subsequent clinical trials—would need to be administered only twice a year, he adds. He believes that this regimen has the potential to be used for HIV treatment as well as pre-exposure prophylaxis (PrEP).

In February, Rockefeller University entered into a licensing agreement with global pharmaceutical company Gilead Sciences to continue investigating the antibodies Dr. Nussenzweig discovered and attempt to develop them into new commercial therapeutics for HIV.

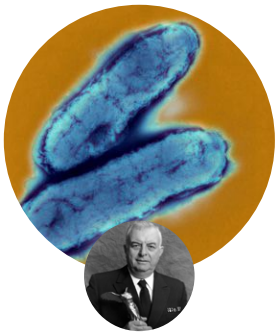
Respiratory Infection Protection

Respiratory syncytial virus (RSV) hasn't garnered as much media attention as coronavirus or HIV, yet the NIH estimates that it infects 64 million people globally and causes 160,000 deaths each year. NYU Grossman School of Medicine alumnus Tachi Yamada '71 is a gastroenterologist whose career has detoured into infectious disease work. When he served as president of the Bill & Melinda Gates Foundation Global Health Program, he tackled tuberculosis, HIV, malaria, and other infectious diseases, and he is keenly aware of the impact of RSV.

As chair and co-founder of Icosavax, a Seattle-based biotech startup, Dr. Yamada is committed to bringing an RSV vaccine to market. The company has already identified a lead candidate to target RSV called IVX-121. "We create completely synthetic proteins that resemble viruses," Dr. Yamada explains. "Two proteins come together in a test tube to form an icosahedral structure that resembles a virus, and on the surface you can put any protein—in this case, a viral antigen. That protein then can induce an immune response.

"Our initial product is a vaccine for respiratory syncytial virus, but we're considering how to apply that technology to other important infectious diseases," adds Dr. Yamada, who's also a venture partner at Frazier Healthcare Partners, a firm that invests in companies commercializing a variety of novel therapeutics. He estimates that Icosavax's RSV vaccine will be in clinical trials by the first quarter of 2021.

Meningitis, 1970s
Emil C. Gotschlich '59, BA (ARTS '55)



Hemophilus influenzae type b, 1980s
John Robbins '59, BA (WSC '56)

Human papillomavirus, 1990s
Douglas R. Lowy '68

Emil Gotschlich: Robert Reichert / The Rockefeller University; Douglas R. Lowy: Ernie Branson, National Cancer Institute

Considering that Icosavax has already obtained $51 million in funding from a series of private investors, Dr. Yamada's projection may very well be accurate. Yet research on many other infectious diseases is critically lagging, due to lack of funding and support from the government, he says.

In 2014, when Dr. Yamada was vice chair of the Council of the National Academy of Medicine, he served on a global commission convened by the academy to address global health risks. "The whole point of the report [created by the commission] was to outline the steps the world needed to take in order to be better prepared for the next pandemic," says Dr. Yamada.

Those steps contributed to the effort by the World Health Organization (WHO) to strengthen its mechanisms for pandemic preparedness. These changes have greatly enhanced its responses to the COVID-19 crisis. "When Ebola came, the WHO had no money and had very little ability to respond to the problem. This time I think the WHO very much took the leadership role, and has had some resources to be able to address the problem," says Dr. Yamada.

Around the same time, a group of private, philanthropic, and civil organizations formed the Coalition for Epidemic Preparedness Innovations (CEPI), a global alliance designed to stop epidemics by advancing vaccines. As of January 2020, CEPI had awarded funds jump-starting many initiatives aimed at developing vaccines that could prevent COVID-19. One such initiative led by a partnership between Moderna, a biotech company, and the NIH has already launched a clinical trial to test the first vaccine against this pandemic infection.

"Perhaps, to some degree, the world is better prepared today than it might have been five years ago," says Dr. Yamada. Still, the lack of adequate resources and infrastructure has been devastating. "The global impact of an infectious threat is far greater than the impact of a terrorist attack, yet the reality is that we spend $100 billion a year [in the U.S.] on homeland security and two or three times that on defense, and we don't spend even $1 billion on pandemic preparedness," Dr. Yamada laments.

"Pandemics are not one-off things," he continues. "They occur every two or three years. We've had H1N1, we've had Lassa fever, we've had Ebola, we've had MERS, we've had SARS, we've had Zika. Every two or three years, another major epidemic comes along, yet we are not organized or appropriately prepared for it. The world has to be better prepared for this kind of thing."

With additional reporting by Elizabeth Chute

Left to right: Ofer Levy '96, PhD; Sharon Levy '92, Res. '96; Elissa Weitzman, ScD, MSc; David J. Dowling, PhD

Can a Vaccine Prevent Opioid Overdose?

Opioid addiction might not technically be contagious, but it is one of the major health crises of our time. According to the National Institutes of Health (NIH), 128 Americans die every single day as a result of overdosing on opioids. One innovative approach that may save lives: a vaccine that prevents fentanyl overdoses.

In August 2019, the NIH awarded $2.3 million for a pilot project that's being led by NYU Grossman School of Medicine alumni Ofer Levy '97, PhD '96, and Sharon Levy '92, MPH, at Boston Children's Hospital. Dr. Ofer Levy is a vaccine researcher who directs the Precision Vaccines Program at the hospital; his wife, Dr. Sharon Levy, is board-certified in developmental/behavioral pediatrics and addiction medicine and is director of the Adolescent Substance Abuse Program at the hospital. Their goal is to create and test a vaccine that would induce antibodies in the body to block fentanyl from entering the brain, where it suppresses respiration and leads to fatalities.

Although Narcan (naloxone) is widely available as an antidote that can reverse an overdose, it's designed for one-time use and needs to be rapidly administered during an opioid overdose. A preventive vaccine would, at least in theory, create antibodies that would prevent fentanyl from getting to the brain and causing an overdose; it could offer protection for months or even years.

The vaccine would protect people exposed to fentanyl and might be particularly helpful for those accidentally exposed through another drug. "The patients I see often get exposed to fentanyl because it's contaminating some other drug like heroin or cocaine," Dr. Sharon Levy explains. "This isn't a stand-alone treatment. I see it as an additional layer of protection," she adds.

At the moment, Dr. Ofer Levy and his colleagues, including his key collaborator David J. Dowling, PhD, are focusing on testing the vaccine components as well as adjuvants designed to make it most effective. "We have a good lead on the antigen, and within two years we hope to identify the optimal adjuvant," he says. One particular challenge is that the vaccine needs to be tailored to the unique immune system of addicted individuals. "There are differences between the immune systems of opioid users and non-users," he explains.

Meanwhile, Dr. Sharon Levy's colleague Elissa Weitzman, ScD, MSc, is leading interviews with addicted teens to learn about whether they would be willing to take such a vaccine and whether they would fully understand what it can and cannot do. "We don't want them to think, 'I have the vaccine now, so I'm safe,' because that's not quite right," she says. The team is also hoping to home in on the best candidates to receive such a vaccine—which might turn out to be anyone who seeks treatment for opioid addiction.

Dr. Sharon Levy says that patients often decide they're ready for treatment and come into a clinic eager to begin but are told they can't immediately start medications that are commonly administered to aid withdrawal. "We need a little window of time; otherwise, the medication will make them sick," she explains. "This [vaccine] might be something we can use immediately; it might be a way in the door."