

En Route to a “Functional Cure” for HIV

After four decades, what are the latest developments that raise hopes and expectations for a future functional cure?

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After four decades of human coexistence with HIV, what are the latest developments that raise hopes and expectations for a future “functional cure”? With this question in mind, data journalist Kelly Kiki, [reporting for iMedD Lab](#), traveled to New York City, visited Rockefeller University, and met with scientists, people living with HIV and participants in clinical trials. The interviews cover what science knows today, what modern research is looking for, and what the community anticipates.

Lying in a hospital bed with needles stuck in his arms, he seems to be in the midst of a bizarre bloodletting. It is his first leukapheresis, captured in the photographic frame of a Polaroid, placed almost in the center of a blank page. “March 8, 2019,” the accompanying handwritten caption reads. This is just one of the snapshots included in the dozens of identically structured pages of photographs that, along with various consent forms, medical test results and other documents, make up Logan Bellew’s impressively detailed personal archive—[photographic documentation](#) of his participation in a clinical trial to research a potential “functional cure” for HIV.

A photographer himself and exhibition production manager at the International Center of Photography in New York, he has meticulously organized and cataloged everything in a distinctive, heavy red binder. Holding it in his hand, he arrives at our appointment on a cold afternoon in late February 2024, on the campus of Rockefeller University on the Upper East Side of Manhattan. We sit in a small conference room in the campus’ first and most historic building, Founder’s Hall, next to the university’s research hospital, which Logan visited while participating in the 2019 clinical trial.

Arizona, Cyprus, the Red Binder

We casually browse through the red binder as we talk: he was a photography and art history student in Arizona, USA, in 2011 when a professor gave him the opportunity to spend the summer as a photographer on an excavation at Polis Chrysochous in Cyprus, where he would later have what he calls “a second life.”

The excavation was what initially took him to the island, but “then I started to become interested in what it’s like to be a queer person living in Cyprus. I rented a car, and I started going to other cities. And then I got invited back again in 2012, to photograph for the excavation again. I went out and started exploring a little bit more, making friends, and ultimately ended up having the encounter in which I seroconverted and became HIV positive. But I didn’t know it at the time.

About a month after I got back from Cyprus, I got very, very, very sick, so sick that I actually had to go to the emergency room [...] They did a strep test. It came back negative, but they said it looks like strep. ‘It’s probably a false negative.’ So, they sent me home with some antibiotics. And within two weeks I felt better [...] I noticed after I felt better that I had a bunch of lymph nodes, like behind my ears and in my neck, that had swelled during that time. Even after I started feeling better, they did not go away, they stayed swollen. I was thinking, maybe there’s something still wrong, but I didn’t really think anything of it at that time, until I went for a routine STI screening—I was getting tested every few months at that point” he recounts.

Eventually, in February 2013, he was diagnosed HIV positive. As he was in the process of preparing for graduate school and eventually moving to New Mexico for that purpose, it took him about a year to complete the insurance paperwork to begin treatment with antiretroviral drugs and very soon the virus was “down” to undetectable levels—where it has remained for the past ten years with consistent adherence to antiretroviral treatment (one pill a day).

After being diagnosed and beginning treatment, it was not long before he traveled back to Cyprus. He established ties with the island and has returned many times since. He is, after all, a long-time volunteer with the AIDS Solidarity Movement in Cyprus. His work there has been “extraordinarily rewarding” for him as well, he says, because it “has been an opportunity for me to sort of combat and fight against the forces of stigma and miseducation that caused me a lot of pain during the initial stages of my diagnosis.”

In 2019, a year in which his finances did not allow him to travel to Cyprus and spend his usual time there, he wondered how he could get involved and be active “in something regarding the progress of the movement of people living with HIV.” That’s when he was given the opportunity to participate in this clinical trial and experience what is now contained in the red binder.

It was a Phase Ib clinical trial (small human study) conducted at Rockefeller University Hospital and Massachusetts General Hospital in Boston, in which volunteers living with HIV were given seven doses of a combination of two broadly-neutralizing antibodies (bnAbs) over a 20-week period, either in addition to or during an interruption in their antiretroviral treatment. The goal was to determine how long the study participants’ viral load could be maintained at undetectable levels after treatment with the antibodies under investigation.

In Logan’s case, the fourth infusion was his last. On May 24, 2019, blood test results showed a detectable viral load, which increased further a week later. HIV was back with a so-called

“rebound”. According to study guidelines, this meant that he had to stop his antibody infusions and return to antiretroviral medication, which suppressed his viral load anew. “I was disappointed that I didn’t make it all the way through to the last infusion [...] I knew this was going to happen eventually, and they told me it would happen eventually. It was sort of like ‘you know, we’ll see how long it takes, essentially, that’s what we’re looking for right now’” says Logan, 35, who is now also one of the founding members of the [Community Advisory Board](#) (CAB) at Rockefeller University.

The results of this particular clinical trial [were published](#) in April 2022 in the journal Nature: among other findings, 13 of the 17 volunteers maintained viral suppression for at least 20 weeks without antiretroviral treatment, while two of the subjects who received all seven doses of antibodies maintained suppression after one year. The study concluded that “antibody administration affects the HIV-1 reservoir, but additional larger and longer studies will be required to define the precise effect of antibody immunotherapy on the reservoir.”

The HIV Reservoir

In the field of HIV research, if the vaccine is at one end (science is still far from an effective vaccine to prevent HIV), the “cure” is at the other end—which would mean either eradicating the virus completely or suppressing it so that it cannot replicate. But there are several reasons why it is difficult to achieve a true cure: the virus mutates frequently, and it also attacks the immune system itself, which it ultimately affects in two ways, by disguising itself and by weakening it.

At the same time, however, HIV has the unique ability to invade and integrate into the DNA of our cells. When the virus becomes part of the cell, it remains “silent”, hiding from the immune system. However, the cell continues to live and produce other similar cells, so the virus is not eradicated. This is the so-called “reservoir”. The usual standard HIV drugs, the antiretrovirals, prevent new cycles of infection by blocking the replication of the virus, but have no effect on the cells that already carry HIV, the “reservoir” of cells.

Broadly Neutralizing Antibodies

It is this reservoir of HIV that modern research is targeting, developing different types of strategies. Among the different approaches is immunotherapy, which includes different tools to activate different branches of the immune system. The antibodies belong under its umbrella. The Rockefeller University research team is focusing on broadly neutralizing antibodies—“broadly” meaning that they can recognize different types of HIV because they are able to identify parts of the virus that do not change. They are “neutralizing” because they prevent the virus from infecting new cells.

These are antibodies isolated from the white blood cells of people living with HIV and reproduced in the laboratory as monoclonal antibodies, which means that each dose contains “exactly the same antibody that you know a lot about its function, its potency, its breadth” explains Dr. Marina Caskey, Professor of Clinical Investigation and Physician at Rockefeller University, in a meeting

with us.

In addition to being one of the people behind the design of the research in which Logan Bellew participated, she has led a number of early phase clinical trials that have reinvigorated the field of HIV research. “We have done studies where someone with HIV was not in treatment and where we looked to see what those antibodies could do to their viral loads. We have done other studies where people came in on their ART, their HIV medication regimen, and they stayed on the regimen, but we gave the antibodies to see if, along with ART, we could decrease the number of infected cells, if we could have an effect on the reservoir. In other studies, we replace the HIV medication with the antibodies and these studies are called an Analytical Treatment Interruption (ATI)” says Dr. Caskey, describing some of the different clinical scenarios under investigation.

Speaking of antibodies, we couldn’t do without the reference scientist in the field, one of the people who discovered them, Dr. Michel Nussenzweig, Zanville A. Cohn and Ralph Steinman Professor, Investigator at the Howard Hughes Medical Institute, Senior Physician, Head of the Laboratory of Molecular Immunology at Rockefeller University. He also serves as Co-Director, responsible for Immunology, at the [Stavros Niarchos Foundation Institute for Global Infectious Disease Research](#) at Rockefeller University.

We met him in his office, next to the lab. Summarizing in simple terms what the scientific community seeks, Dr. Nussenzweig explains: “In cure research, what one tries to do is to get rid of the cells that are infected and that stay in people even when they’re taking medications. What we try to do in the lab right now is, in fact, work on both vaccine and the cure agenda –trying to understand where the virus is hiding, how it’s hiding. Our idea is that if we understand where it’s hiding and how it’s hiding, we might be able to get at it. And antibodies, we believe, are part of the solution to get to the cells that are hiding, identify them and have the immune system recognize them.”

Today, there are pharmaceutical companies that are testing antibodies to find long-term treatments: instead of taking one antiretroviral pill a day, for example, a person living with HIV could have an injection every six months. That “would be probably very good for some people, including people who forget to take their medicines, and teenagers and young adults. That would be exciting. But I think that just a chronic therapy is not enough. And really what I would like to see is one of these other two solutions, which would go much further in terms of public health” comments Dr. Nussenzweig.

A “Functional Cure” for HIV

What would be a cure in the case of HIV and what exactly is the achievement that science seeks and can offer to humanity is the big question –and perhaps a controversial issue. “You could define cure in many ways” says Dr. Nussenzweig, adding: “You could define it as completely getting rid of the virus. That’s unlikely for a number of reasons. But cure could also be remission –just like in cancer therapies, people go into remission and they don’t need drugs for a long time. I think that would be potentially achievable.”

Dr. Caskey will argue for her part: “In general, we think of cure as you get rid of something entirely. In HIV, we use the term cure more broadly. And that’s why there’s some criticism to using that word. But basically, we are talking about long term virologic suppression. So that means, if you were to measure the virus in the blood by the regular methods, you wouldn’t be able to measure it. And that has implications because we know that the person cannot progress in their infection to disease and someone who has an undetectable viral load or even a low viral load cannot transmit to another partner (editor’s note: reference to the revolutionary discovery, known as “[U=U](#)”, which has become a scientific assumption in recent years, that undetectable viral load equals untransmittable). So, viral suppression means you are preventing disease progression and you are preventing transmission. Long-term, viral suppression means long-term viral suppression without ART. And that is a ‘functional cure’.”

In New York City, just one block above Rockefeller University, is the Weill Cornell University School of Medicine. There, in his office, shortly after he has returned from the lab, we meet Dr. Brad Jones, Associate Professor in the University’s Department of Medicine, who also co-directs as principal investigator, in collaboration with Dr. Caskey, the [REACH](#) (Research Enterprise to Advance a Cure for HIV) project, funded by the U.S. National Institutes of Health (NIH), the principal federal agency for conducting and supporting medical research in the country.

Dr. Jones has been working on HIV research for almost 24 years—he has, in fact, dedicated his career to the field. By achieving a cure, we want “to free people from the burden of lifelong medication, so that there is a solution for those who are not on antiretroviral treatment or cannot adhere to it for various reasons,” he says.

Soon the conversation turns to antibodies: “If you would give these broadly neutralizing antibodies to someone every few months, that would start to look like a functional cure, right? People still need to get a treatment, but it’s not a drug therapy. Maybe there’s some advantages to that. And there’s also approaches where people are exploring ways to get the body to produce these broadly neutralizing antibodies on its own. So, instead of going in and getting an injection every few months, some cells in your body are making these probably neutralizing antibodies. And if we can achieve that, then that would look like a functional cure. On the other hand, antibodies in addition to what we call neutralizing, which block virus from infecting new cells, can also bind to infected cells and target them for killing by the immune system. Thus, the antibodies have these kind of two different effects. So, you can see from that angle how you can also use antibodies to go after classical cure.”

Focusing on remission, suppression of the virus, potentially without drugs (“functional cure”) versus an ideal cure (“classic cure”) is “a matter of passionate debates within the HIV advocacy community,” says 72-year-old Yves Gebhardt, a retiree working in the food service sector who has been a volunteer with the Manhattan HIV Care Network for more than twelve years and also a member of the Community Advisory Board at Rockefeller University.

In this “debate,” he presents his personal story: he moved from France to the U.S. in 1980 and was diagnosed with HIV in 2002. “I never thought that I would be positive, since I wasn’t basically

sexually active. I had sex maybe once or twice a year, and, therefore, never even thought of taking HIV test. When I developed a high fever, my then roommate sent me to the hospital and told me to get checked. And this is when they found out that I had stage four cancer (Hodgkin's lymphoma). And, then, the HIV diagnosis came at the same time. It was, of course, a tremendous moment. Actually, even the doctors were kind of puzzled and didn't know what to do, what to treat first. Should they start with HIV or should they start cancer treatment? So, they decided to do something totally, innovative at that time, I think: they started both treatments on the same day."

Within about seven or eight months "I was in what you call remission, which means some kind of a cure" he says, referring to the cancer. When he started his HIV antiretroviral treatment 22 years ago, he was given a three-drug regimen, with a total of eight pills, which he had to take twice a day—16 pills a day in total. It took him almost two years to get his viral load down to undetectable levels, where it has remained ever since –with his treatment today, for the past four or five years, limited to one pill a day.

"Everyone is familiar with remission when it comes to cancer. I have never been told that I was cured of cancer. So, a remission is fine with me. Would I prefer a total expelling of the invader? Yes, of course. But if it's not possible, or maybe it's not possible now, in the meantime, just stop him from doing anything. Neutralize him and, then, later kick him out. I'm good for that, too," Yves says.

Since the 1980s, when HIV was a death sentence, and since the 1990s, when first azidothymidine (known as AZT) and later triple antiretroviral regimens, which involved too many pills a day and too many side effects, humanity has come a long way. Today's antiretroviral regimens, often limited to one pill a day, ensure quality of life and also, if adhered to as prescribed with solid consistency, are able to keep the viral load undetectable –thus indirectly contributing to stopping the transmission of the virus. But even if HIV has turned into a chronic condition, the discovery of a functional cure is vital for a number of reasons, medical, practical and psychological.

Stigma and Freedom

Talking to community members, people living with HIV, you will hear about the psychological burden as the biggest problem of living with the virus today and the daily stress of not forgetting your medication –friends, family, cell phone, alarm clocks and the so-called "pill box", whatever is most convenient for each person is used as a daily reminder.

"Freedom," says 32-year-old David Turner, a writer and voice actor who has been living with HIV since 2017, in a one-word, disarming response to the question of what the discovery and availability of a treatment would mean to him. "Freedom from my thoughts," he adds, emotionally expressing that it would also mean a lot to all the people who have lost their lives to AIDS/HIV, that "their deaths wouldn't be in vain."

As we meet, at the end of February 2024, he is participating in a clinical trial being conducted at Rockefeller University Hospital and the National Institutes of Health Clinical Center in Bethesda, Maryland, which involves the intravenous administration of either the two monoclonal antibodies

that the Rockefeller University research team is working on or a placebo. This particular study is “double blind,” meaning that neither the research team nor the people taking part know what each of them has received. At the same time, participants continue their usual treatment as the study is designed to assess whether antibodies can have an effect on the HIV reservoir during viral suppression induced by antiretroviral treatment. Each participant will stay in the study for 20 months and the study, which will enroll approximately 100 people, will last three to four years.

“Anything that could help the betterment of people with HIV I would totally do [...] I want to be alive when we find a cure—even if I’m in my 60s or 70s” says David, who grew up in southern Louisiana and moved to New York in 2012. When he was diagnosed HIV positive, he was in a very bad state: he had been homeless, using drugs, and most of all, drinking too much alcohol and having unprotected sex. “Even if I had been negative the day when I finally tested positive, I probably would’ve been dead by now –maybe from an overdose. So, in one sense, HIV put my life back on track” he says today that he has completely changed his lifestyle: he takes care of his diet and his mental health, he doesn’t smoke, he doesn’t take drugs, he doesn’t drink alcohol.

But the stigma still hurts him: “I love living up here [editor’s note: in New York]. I can be black, gay and HIV positive without feeling like I’m in danger. I can’t do that back down South. And it’s funny, we live in the United States with so many different ideologies in one country” he comments. And then he continues: “I can never go back to my hometown again without getting some type of discrimination. When my grandmother died, I went down there for her funeral in 2021. No one would touch me. No one would shake my hand because I have HIV. They took my dad, my godmother, and hugged them. But they had nothing to do with me. They looked at me like I was a plague or something. So, the stigma and the bigotry is still here, is here in many of us in small towns. In cities like New York, New Orleans, Chicago, you’re not going to get too much discrimination from that, because pretty much everybody is like, they have their own shit, but down south in the small Christian towns...”

Female, Heterosexual, Long-Term Survivor, Minority

Community members will emphasize the need for accessibility and inclusion in any future treatment. “We all need an HIV cure for all—not only for white people, not only for rich people, not only for American people, not even for Western people. A cure that’s for everyone around the world. Anything else would not be correct” says Yves.

The question of a functional cure for all is directly linked to the representation of all in clinical trials. This issue is emphatically raised by [Ivy Arce](#), artist, creative designer, activist for over three decades and president of the board of directors of [Treatment Action Group](#). Although she makes it clear that “all this work that I do in terms of HIV, I have never gotten paid in my life and I refuse to get paid,” she stresses the need for decent and equitable financial rewards for women who testify to a lifetime of HIV experiences, for work needed on behalf of advocacy organizations to ensure that pre-exposure prophylaxis (PrEP) treatments are addressed and equally inclusive of women, and of course for their participation in research. “There’s very few positive women that are on the table [...] But diseases like that really affect women as well as men and they’re only studying

mostly men. I mean, the percentage of women in the clinical trial even for heart disease is so minimal” she says.

Ivy, now 60, was diagnosed HIV positive in 1990, just a few months after she moved to New York upon returning to the U.S. from Spain, where she had gone to work during her final year of studies in 1989 and contracted the virus. The timing of her diagnosis means, among other things, that she has experienced many situations from a position of minority or exclusion.

She managed to get tested at a time when “they didn’t test women” and the official narrative was that HIV threatened only gay men. At the age of 25, she found herself in positions where her then-job required her to turn in a period calendar and she couldn’t use the bathroom—because at a time when people were dying and people were deeply afraid of AIDS, “suddenly you have a (positive) woman who bleeds once a month.” She is the mother of two HIV negative boys, now aged 24 and 18. That is, she is part of the first generation that was able to plan, and practice, parenthood without transmission. Women “need to be paid, to be on this table” she says.

The under-representation of women with HIV in clinical trials is confirmed by Dr. Caskey: “Unfortunately, in our studies we haven’t done very well. Probably we have 10% or 20% women.” And she immediately explains that even if we take social considerations out of the equation, the representation of women in medical research is necessary not only because women make up a large proportion of the population living with HIV, but also because “even if you look at it biologically and immunologically, there are differences between men and women in terms of HIV persistence in HIV reservoirs. So, it is important that we study the spectrum of people who have HIV, and that includes not only the dichotomy of men and women, but also the trans people, because of changes in the hormones that may affect the reservoirs in ways that we don’t fully understand. So, it is important to be very inclusive.”

When asked why women are still an underrepresented or even unrecognized social group when it comes to HIV, she points to the family burdens that women have taken on, which can be a practical reason for not being able to participate in a clinical trial. But she will also note their disadvantaged position, abusive situations, or limited control over their daily lives, which can lead to either mistrust of research or less freedom of choice on what to do with their bodies.

The road to a future “cure” for HIV is not easy. However, the developments seem exciting. Although we are in the beginning, there has certainly been research progress, thanks to scientific commitment on the one hand and the determination of people to make themselves available for research on the other, thinking more or less of what Logan said towards the end of our meeting, just before we closed his red binder: “If I can, I will use my body, my virus, my blood cells to contribute to the treatment of someone else, or to the prevention of seroconversion to someone else in the future, or even just to free people from this stigma.”

Kelly Kiki is a data journalist and project manager at the non-profit journalism organization iMedD. She has been working in the media industry since 2007, and she was trained in data journalism at

the Lede program at the Columbia Journalism School in 2018.

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Correction: An earlier version of this article incorrectly listed Ivy Arce's title at Treatment Action Group.

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