Salim "Slim" Abdool Karim: Attacking AIDS in South Africa

Slim Abdool Karim joined the anti-apartheid movement as a boy in South Africa and has had the pleasure of watching the regime fall. Now he's set his sights on taking down AIDS.

When Karim met Nelson Mandela for the second time in 2000, he had his camera in tow, ready to capture a photo of him shaking the hand of his hero. Mandela later wrote the foreword to Karim and his wife's book, *HIV/AIDS in South Africa.*

Karim has witnessed the emergence and exponential growth of the AIDS epidemic in his country, along with the concurrent explosion of tuberculosis. To reverse the epidemic, he is following disease progression, testing treatments and prevention strategies (1), and deciding if and how they can be effective in resource-limited settings (2). By monitoring cytokines and T cell responses in the first weeks after infection, Karim has found that a more naive $CD8^+$ T cell response is better in the long run than a more differentiated response that includes a high frequency of memory T cells (3, 4). These studies also revealed that the initial magnitude of HIV-specific, IFN-γ–producing cells does not predict viral load at one year.

The issue of whether HIV causes AIDS is a scientific one that politicians shouldn't have been involved in.

By screening people with recent HIV infections, Karim has found that the majority of cytotoxic T cells recognize conserved domains in the Gag protein despite differences in host genetic backgrounds and HIV-1 subtypes. Thus host and viral diversity may not constrain the ability of a vaccine to elicit a universal response (5). Karim leads the Center for the AIDS Program of Research in South Africa (CAPRISA) and is an epidemiology professor at Columbia University in New York. And now that he's helped to convince the Howard Hughes Medical Institute (HHMI) to establish a new research center for HIV and TB in South Africa, he will be directing a research program there as well.

Who gave you the nickname Slim?
My schoolteacher. Under apartheid in South Africa, we had to take Afrikaans language classes, which I didn't like because I associated the language with racial oppression. My Afrikaans teacher once scolded me, "Jy dink jy is slim," which means, "You think you are so clever?" It stayed with me, as the Afrikaans word "slim," meaning clever, sounds like Salim. Plus, I was quite rotund then, so the name made [ironic] sense and it stuck.

Slim with his wife and collaborator, Quarraisha Abdool Karim.

Even as a boy you opposed apartheid?
Yes. I was born in Durban, the third largest city in South Africa, and at the age of 10, my family was forced to move out of our house and to an Indian township 25 kilometers south of the city. My mother was active in the anti-apartheid movement; she'd go to rallies and was part of the passive resistance. And so it sort of rubbed off on me. By the time I went to medical school I became involved in human rights and the anti-apartheid movement.

After medical school you came to Columbia University to do epidemiological research, but then returned to South Africa. Why?
In my heart of hearts, I'm South African. I feel I have a contribution to make here. It's hard to explain, but this is my country and the people here are amazing. It's the adversity that brings out their spirit and humanity despite the years of subjugation and indignity of racism.

WHAT WENT WRONG

How has the political situation in South Africa fueled the AIDS epidemic?
I think it's been a combination of our colonial history, the discovery of gold and diamonds, and the subsequent building up of the apartheid state (1). The migrant labor system destroyed family life by turning black tribesmen into laborers. Hundreds of thousands of black men were forced to move near the mines in order to work in white South Africa while their wives stayed behind in designated rural reserves. A man would then see his wife once or twice a year, and it became the norm for working men to also have what was called a town wife, who would see several men. This created a situation where family life was disrupted and diseases like syphilis and HIV could spread rapidly.

Later in the early nineties when it became clear that AIDS could be a huge heterosexual epidemic in addition to being a problem for hemophiliacs and gay men, the government was in the midst of dealing with what they called "swart gevaar," which literally translates to "the black threat." And the black threat was based on the fear that as the impoverished black population grew, whites were becoming a shrinking minority in South Africa. So when AIDS came around, their perspective was, well, if this disease wipes out blacks, then that takes care of the swart gevaar. And although they didn't broadcast this, the efforts of the apartheid government to control HIV were extremely minimal and not designed to have an impact.

In August, **The Lancet** *published manuscripts assessing the failure of the South African government to control the AIDS epidemic, and the new South African health minister, Aaron Motsoaledi, embraced the series. Why was this monumental?*
Interaction with government during the last few months has been almost surreal

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because we've just been through 10 years of having a difficult relationship with a minister of health, who saw science as something that challenged her perspectives rather than something that she could use to impact HIV.

Back in 2000, former president Thabo Mbeki had invited me and several other scientists to debate whether HIV causes AIDS. I participated in the debate, but it ended up causing a schism between politicians and the science community. Mbeki did not appreciate that the issue of whether HIV causes AIDS is a scientific one and that politicians shouldn't have been involved in it. That period was really the lowest point in my life. Despite everything I'd gone through under apartheid, this felt somehow lower. I felt like it undermined everything we had been working for.

So after having gone through this horrible period and finally having a minister who embraced the constructive criticisms in *The Lancet* series, well, I'm thrilled. We have to acknowledge that we've got a big problem on our hands before we can fix it.

And you know this new health minister personally, correct?

Yes! In fact, yesterday someone asked me if I ever imagined that my classmate in medical school—the only medical school for black students in the country at that time—would become the Minister of Health, and I said, "Imagine? Are you crazy? I never imagined there would be freedom in South Africa in my lifetime!"

Patients waiting at a TB clinic in Durban, where about 8,000 new cases of TB are treated each year.

RESEARCH IN REAL TIME

What will you be doing at HHMI's new center for HIV and TB?

We've got a range of studies planned. One of them is to learn how much of the TB resurgence we're seeing in patients with HIV is due to relapse. We need to understand relapse and reinfection because we need to devise strategies to stop the rapid spread of TB. Right now, we have nearly three quarters of a million patients on AIDS treatment. And these HIV-positive patients, with and without infectious TB, sit for hours in long queues in poorly ventilated, crowded rooms waiting for medical care—it's the perfect place to spread TB.

Are you involved in any clinical trials?

Several—two on HIV/TB treatment, two HIV prevention trials, and one on acute HIV infection. In one HIV/TB cotreatment trial, we've found that integrating TB treatment with antiretroviral treatment reduces mortality by 56%, potentially saving 10,000 lives in South Africa each year. In another trial, we are studying acute infection in sex workers. Before the trial began, my wife and I had been assisting sex workers in an intervention program to try and prevent HIV with education and condom distribution, so we were familiar with the community, enabling us to conduct studies with this hard-to-reach group. We had to screen over 700 sex workers to find the 245 that were HIV-negative. Once they volunteered for the study, we did everything in our power to convince them to use condoms and provided counseling. In fact, they appreciated coming into the clinic because they received high-quality health care from us. Despite this, we had an incredibly high incidence rate. And every time a woman was infected, the whole team felt that it was our failure. But still, in the earliest stages of their infection, we studied them in great detail. Our main interest was to better understand viral escape. What immune responses occur initially? What predicts whether you have a low virus set point?

And what have you learned thus far?

We've noticed that these women develop potent neutralizing antibodies after infection, but that they only neutralize a narrow spectrum of viruses. The problem is that there's high HIV diversity, and as each new antibody comes up to suppress the susceptible viral population, viruses that are not sensitive to the prevailing neutralizing antibodies become dominant. So you've got evolution in fast-forward, leading to viruses that are able to escape the immune response. We've been trying to understand why the body produces these antibodies that are so potent, yet so narrowly focused, by looking at neutralization sites on the viral envelope using chimeric viruses.

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We've also been looking at what happens to the cells in a woman's genital mucosa before and after infection. We want to see if there's a particular kind of immune response in the vagina that suppresses the systemic spread of the virus and leads to low viral loads. What we've found so far by looking at the cytokines obtained from vaginal washings of women pre- and post-infection is that you can predict what someone's HIV viral load set point will be. For example, we found that increased levels of cytokines IL-6, IL-10, and IL-12 p70 in the vagina are associated with HIV infection. The presence of genital inflammation not only increases the risk of infection but also leads to more severe $CD4^+$ T cell depletion immediately after infection (3).

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