

PROFILE: MANUEL ELKIN PATARROYO

The Man Who Would Conquer Malaria

The turn-of-the-century stone building is rotting inside, floorboards dusty and dilapidated, pigeons roosting in the eaves. There are no windows in the moldy sills, and weeds are thriving—even this structure in the middle of Bogotá, Colombia, suggests the jungle is not so very far away. “This is how my buildings always come,” says Manuel Elkin Patarroyo, proud of the efforts that have transformed other nearby structures into a charming enclave, complete with gardens, that recall the Pasteur Institute in Paris—a similarity that delights Patarroyo, because he says that it irritates his rivals there.

Once restored, this addition to the Institute of Immunology at the San Juan de Dios Hospital will permit Patarroyo to expand his research empire and to begin mass-producing the source of his fame and his controversy: the malaria vaccine SPf66. But the immunologist does not want to dally in the ruined building and talk about whether the

world is going to want such vast quantities of the compound. The day is slipping away, it’s already 10 o’clock in the morning, and there are labs to dash through and years of work to review.

Patarroyo has a talent for transforming more than architecture. In the decade since he appeared on the international immunology scene, he has ridden innumerable highs and lows. Currently, in the eyes of many researchers, he is down again—this time for good. The most recent trial of SPf66 (published in the *Lancet* in September) failed: Thai children given several inoculations were no more protected than those given placebo. This finding follows a 1995 study of young children in the Gambia that also found the vaccine ineffective.

But Patarroyo has rebounded before. And anyway, to his mind no such thing as a down period exists—no matter what the studies find. His spirit is irrepressible, as is his belief that he does not have to answer his critics, that all will be made clear eventually. “I don’t care. They cannot touch me. It is their problem,” he states emphatically. “My enthusiasm will not leave me for a minute. The opposite! They don’t know what a favor they do me.”

Then he is off again, dashing through another lab and sliding down the length of a hall to answer a telephone. In rapid succession, he gives a tour of the molecular modeling room, the place where work on tuberculosis and on leishmaniasis is being conducted, and the “peptideria,” where the synthesized peptides that form the basis of the malaria vaccine are stored. He also points out myriad other labs and the entrance to the restricted area where SPf66 is made. “I usually arrive at eight in the morning, and I leave at 10 P.M., Saturdays included. It is not unusual for me, because it is as I want it to be,” he says, pausing in front of a mural, one of the many works given to the institute by famous Latin American artists. “If you are doing what you want and what you like, you do not feel a tension. My wife and my family are used to that.”

A group of his colleagues passes at that moment, and Patarroyo ruffles their hair, slaps them on the back, teases them. They laugh and joke with him. He explains—still for a moment against the swirling, colorful backdrop of “A Sense of Immunology,” by Colombian painter Gustavo Zalamea—that he sets up competitions in order to get work done more quickly. He has promised trips to Cartagena, a beautiful city on the coast, or seats at one of the Nobel ceremony dinners if his researchers finish projects ahead of schedule. “But I tell them, ‘You son of a gun, if you want to go the Nobel, you have to buy a tuxedo, because we are not going to be underdeveloped,’” he laughs.

Patarroyo refers often to his position as a Third World scientist in the First World research community. Yet he is in a very privileged situation. In Colombia, Patarroyo is a national hero; according to a magazine poll, his popularity exceeds that of his good friend, author Gabriel García Márquez. His funding is guaranteed by the government, as is his access to a large population of owl monkeys, some of the only animals that can serve as hosts for the malaria parasites that plague humans. Unlike many researchers whose finances are linked to their results and to being politic, Patarroyo really is free to ignore his critics.

He is not free, however, to ignore the realities of life in Colombia—where numerous guerrilla groups vie for power, where the drug trade bleeds into every



STEPHEN FERRY/Gamma Liaison

activity and where the magic realism of García Márquez can seem prosaic. This summer one of Patarroyo's shipments of white powder—that would be SPf66—was replaced with vials of a quite different white powder. And a few years ago Patarroyo and his family encountered guerrillas on a drive home to Bogotá from some pre-Columbian ruins. "I was captured for five hours because they wanted to talk to me," Patarroyo says, making light of the experience, his voice perhaps more quiet than he realizes.

But what makes him most happy about his notoriety, Patarroyo continues quickly, is that young Colombians are becoming interested in science. Another poll pronounced that 67 percent of the nation's kids want to be scientists. "What other success could I claim better than that one? To have brought into this country a consciousness," Patarroyo exclaims. "So for the children, rather than being Maradonas [the Argentine soccer great] or rock stars, no! They want to be scientists, and I think that is very important in our country."

Patarroyo himself had a very particular vision as a youth, as he tells it: "It was when I was 11, really, that I liked chemistry so much. And my dream was always to make chemically synthesized vaccines." His parents were both business people and wanted their children to be the same; they ended up with five physicians, one nurse and one child psychologist among their progeny. Although Patarroyo opposed his parents' business values, he acknowledges that his father gave him a firm sense that whatever he did, he must be useful to humankind.

He left his hometown of Ataco, in the Tolima region, to attend medical school in Bogotá. He says that he was a mediocre medical student and that it was not until his internship at San Juan de Dios that he understood what science was about. "It was so beautiful to me to save lives," he muses. "I wanted to make vaccines because I wanted to be useful."

In the late 1960s Patarroyo went abroad—something he encourages his researchers to do. After a short stint in virology at Yale University in 1968, Patarroyo worked in immunology at the Rockefeller University for several years. He then returned to Colombia, where he studied various infectious diseases until a colleague urged him to change his focus. "He said I was an idiot, that I was working on a problem that was not as important as malaria. Then he gave me the statistics," Patarroyo recounts as

he drives carefully but quickly through the Bogotá traffic to a traditional Colombian restaurant. Every year as many as 500 million people contract malaria; between 1.5 and three million of them, mostly children, die. Treatment of the disease is tricky, because strains of the parasite in many regions have become resistant to the principal drug, chloroquine, and the alternative, Lariam, increasingly appears to be highly toxic.

Patarroyo's approach to developing a malaria vaccine was unusual. Instead of creating it from dead or weakened strains of the malaria parasite, he synthesized peptides identical to those used by the most virulent strain, *Plasmodi-*

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um falciparum. At the time of Patarroyo's initial experiments, few immunologists thought manufactured peptides could produce a strong immune response. Patarroyo nonetheless tested various peptides for their ability to produce antibodies in monkeys and settled on four: one used by the parasite during its larval stage and three used by the mature parasite to bind to and infect red blood cells. In 1987 he reported that vaccination protected 50 percent of the monkeys. Controversy subsequently flared up when investigators could not replicate the results; Patarroyo claims they used a different compound.

Pausing in the middle of his lunch, Patarroyo starts to sketch a timeline on a yellow pad, marking the dates of his papers. Right after his first success, he fell into his first quagmire. "I made a mistake because of my ignorance in epidemiology," he explains. He decided to vaccinate Colombians but did not set up a double-blind study. He was roasted by the scientific community for his methodology and for the ethics of moving so quickly to human trials.

As other results were reported over the years—the vaccine was consistently safe but proved inconsistently protective—the community continued to divide. "He has always been a very intense personality, provoking strong emotions," notes Hans Wigzell, head of the Karolinska Institute in Stockholm. "I have been very impressed by his capacity to press on. His science is like brute force."

Wigzell cautions that even early on Patarroyo "had the feeling that people didn't understand him. So this is not something that has just popped up. Personally, I like him."

Even though most studies found the vaccine benefited only about 30 to 40 percent of patients, many in public health were delighted: 30 percent of 500 million is still a great deal. SPf66 was held to a different standard than other vaccines because of the peculiarities of malaria: even people who have developed natural immunity to the parasite often lose it. As major trials in Colombia and then in Tanzania bolstered the 30 percent or so figure, it seemed as though Patarroyo was vindicated. In 1995 he donated the rights to the vaccine to the World Health Organization.

Then came the Gambia and Thailand. Although some immunologists maintain they are not ready to give up on SPf66, they are frustrated by the variability of the results. "There has got to be some way of evaluating why it is or it is not working," comments Louis Miller of the U.S. National Institutes of Health.

Patarroyo notes that there may be reasons for the inconsistencies: very young children's immune systems, such as those of the six- to 11-month-olds inoculated in the Gambia, are different from those of adults; the vaccine used in Thailand may not have been identical to SPf66; genetic variability determines immune responses. But, he adds, he is uninterested in point-counterpoint. He just wants to keep going, studying ways of improving the vaccine and of developing others. That is the credo of the institute, he insists: "It is the search for the essence of things. It is not that we are going to develop a malaria vaccine. It is that we want to develop a methodology. Really to make vaccines." Then Patarroyo hints that his new research will illuminate why SPf66 seems so mercurial.

Whatever he may have in the wings, SPf66 remains the only malaria vaccine in trials, and his work, confounding and controversial, has enlivened the field. As for Patarroyo, he seems thrilled as always to be a scientist, thrilled to be directing his laboratory and thrilled to be free to think and transform. "We are really privileged, scientists," he says, skipping up the stairs to his office a little more slowly than usual because of lunch. "We get to have intellectual development! How many get to have that? Most people have to do things they don't like." —Marguerite Holloway