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Scientist at Work/Kary Mullis; After the 'Eureka,' a Nobelist Drops Out

By NICHOLAS WADE

KARY MULLIS, Nobel laureate in chemistry, is jumping up and down at the kitchen table of his cabin, a place in the woods several miles beyond where the paved road ends. His large head and wiry body shake as if in rage. From his lips comes an angry buzzing sound.

He is imitating a swarm of yellow jackets, acting out an episode in which the wily insects ambushed him, inflicting five stings around the mouth, after he attacked their nest. He goes on to tell how he invented a brew, concocted in his kitchen blender, that eliminated the aggressors from his property for a season.

He feels somewhat the same way toward his former colleagues at the Cetus Corporation, where he invented the technique that won him the Nobel Prize. "None of those vultures had anything to do with it," he says emphatically. He is aggrieved that Cetus paid him a mere \$10,000 for the discovery but later sold it to Hoffmann-La Roche, owned by Roche Holding Ltd., for \$300 million.

His invention, known as the polymerase chain reaction or P.C.R., is used for amplifying chosen sections of DNA and has quickly become an essential tool for biologists, DNA forensics labs, and almost anyone else who needs to study the genetic material. Amplifying DNA, a requirement for most tests, used to be done in bacteria, a process that took weeks. With P.C.R., performed with chemicals in a test tube, the job takes a few hours.

Science has been just one of the keen interests in Dr. Mullis's life, competing with psychedelic drugs and women, although he is now happily married to his fourth wife, Nancy Cosgrove. His newest interest is writing. A book of essays, "Dancing Naked in the Mind Field," was published last month by Pantheon.

For those who would like to analyze creativity and sell it in bottles, Dr. Mullis would seem a promising subject. His invention is highly original and significant, virtually dividing biology into the two epochs of before P.C.R. and after P.C.R. Yet the Mullis formula for creativity, on closer inspection, is a brew probably somewhat unsuitable for general consumption.

One ingredient is unbounded self-confidence. "Part of it has to do with his ego and belief that he's much smarter than the people around him," said Dr. Corey Levenson, a former Cetus colleague now at Ilex Oncology in San Antonio. "Most people who launch into an unfamiliar area would first speak to recognized authorities and get all the background. Kary saw that as a waste of time. He figured it would take less time to do the experiments himself."

Dr. Mullis's friends speak of his physical as well as intellectual risk-taking. Dr. Frank McCormick, a cancer biologist at the University of California, San Francisco, recalls seeing Dr. Mullis in Aspen skiing down the center of an icy road through fast two-way traffic. "Mullis had a vision that he would die by crashing his head against a redwood tree. Hence he is fearless wherever there are no redwoods," Dr. McCormick said.

Along with lack of fear comes a lack of concern about people's opinions. In his new book Dr. Mullis describes episodes that others might keep private, such as the time he addressed the Empress of Japan as "sweetie" when being awarded the Japan prize, and how he was nearly arrested when he went to Stockholm for his Nobel Prize, for playing a laser beam from his hotel room at passers-by.

His fondness for the heterodox is evident in the account of a lecture he gave in April 1994 at a medical society conference in Toledo, Spain. "Just before the lecture, he told me he would not speak about the P.C.R. but would tell his ideas about AIDS not being caused by the H.I.V. virus," the ambushed president of the society, Dr. John F. Martin, wrote afterward in a letter to Nature.

"His only slides (on what he called 'his art') were photographs he had taken of naked women with colored lights projected on their bodies," Dr. Martin continued. "He accused science of being universally corrupt with widespread falsification of data to obtain grants. Finally he impugned the honesty of several named scientists working in the H.I.V. field."

Kary B. Mullis was born in 1944 in Lenoir, N.C., and grew up in South Carolina, where his father was a furniture salesman and his mother, who raised him after a separation, sold real estate. He trained as a chemist at the Georgia Institute of Technology and at the University of California at Berkeley. Then, shortly after getting his Ph.D., he dropped off the scientist's usual career path, first to write fiction and then, for two years, to manage a bakery.

It was a friend, Dr. Thomas J. White, who found him jobs back in science, first at the University of California, San Francisco, and then at Cetus in Emeryville, Calif., one of the first biotechnology companies. Dr. Mullis's job, essentially that of a technician, was to make short chains of DNA for other scientists. When machines became available to do the job, he had time on his hands for other pursuits.

Dr. Mullis has often described how the concept of P.C.R. came to him during a night drive along Highway 128 to his cabin in Anderson Valley. He was playing in his mind with a new way of analyzing mutations in DNA and suddenly realized that he had thought up instead a method of amplifying any DNA region of choice. Before the trip was over, Dr. Mullis has written, he was already savoring prospects of the Nobel Prize.

The night journey was made in 1983; the Nobel Prize came 10 years later. But by then Dr. Mullis had dropped out of full-time science again. He left Cetus in 1986, earning his living by consulting and lecturing. He has published no more scientific papers. The divine spark that kindled the idea of P.C.R. has not struck again.

"I like writing about biology, not doing it," Dr. Mullis says. "I don't want to go back to the lab myself and don't want to have people under my command. Fiction is my way around doing experiments."

He also enjoys giving lectures. "I love a microphone and a big crowd; I'm an entertainer, I guess."

Some of his agenda seems to have been selected with an eye to the shock value of adopting beliefs untypical of Nobel prize-winning scientists. He echoes the contrarian belief of the distinguished virologist Peter Duesberg that H.I.V. is not the cause of AIDS. He disputes the arguments that chlorofluorocarbons are depleting the ozone layer and that industrial waste gases may cause the climate to get hotter.

"Scientists are doing an awful lot of damage to the world in the name of helping it. I don't mind attacking my own fraternity because I am ashamed of it," Dr. Mullis says.

He jumps to his feet to swat a yellow jacket that has infiltrated the cabin.

Given his success as an independent thinker in chemistry, Dr. Mullis's challenges to other kinds of orthodoxy are not to be lightly dismissed. But the line between fact and entertainment in Dr. Mullis's world can be hard to discern. In his book he professes to believe in astrology, to have been rescued from a fatal accident by a person travelling in an astral plane, and to have conversed with an alien disguised as a raccoon.

Asked why people should accept his views on AIDS when he has no standing as a virologist, he replies, "I don't care, I'm on my vacation life here."

Vacation life? "I have a spiritual thing in me. After lots of tough lives I got a vacation." Is he speaking of reincarnation as a metaphor or the real thing? "I believe it," he says. "If reincarnation is a useful biological idea it is certain that somewhere in the universe it will happen."

Is it not awkward to accommodate reincarnation within the theory of evolution? "I don't think DNA is the whole thing even though I invented a cool way of playing with it," Dr. Mullis declares.

The invention of P.C.R. may well become a paradigm of scientific discovery because of its significance and because Dr. Mullis has described the eureka moment so graphically. But though the idea was central, proving it worked was also important. According to Dr. White, the friend who got him a job at Cetus and oversaw part of the development of P.C.R., the reduction of the idea to practice was done largely by others.

"Mullis as an experimentalist is sort of hit and miss," Dr. White said. "He got a lot of data but he was having personal problems and tended to do uncontrolled experiments, so it wasn't very convincing when he did get a result."

Even after a year, Dr. Mullis had not developed definitive proof of his concept, so Dr. White then enlisted another scientist. Within a few months, Dr. Randall Saiki, a rigorous experimentalist, produced data that convinced everyone at Cetus that the process worked, Dr. White said.

Dr. Mullis believes his colleagues tried to take credit for the invention away. Dr. White denies that, saying a plan to have Dr. Mullis author the first paper describing the theory of P.C.R. went awry because Dr. Mullis whiled away the summer creating fractal pictures on Cetus's computers instead of doing experiments.

By default, a paper by Dr. Saiki and other scientists on the applications of P.C.R. was published first. Dr. Mullis's own paper was rejected by the journals Nature and Science on the ground that it was not new.

"I feel he has never accepted responsibility for the course of how the publications came out," Dr. White said, noting that he and colleagues attempted to let scientists know Dr. Mullis was the inventor, such as having him describe the technique at an important conference.

Dr. White pays tribute to Dr. Mullis's fertile mind, describing how he came up with practical ways to improve P.C.R., such as the use of Taq polymerase, an enzyme made by bacteria that live at high temperatures. But managing his friend's creativity was not a carefree task.

"He's a hard person to know, hard not only on his spouses but on his friends," Dr. White said. "In the midst of being extremely charming, he could be extremely abusive." The two men are no longer close friends, but Dr. White, now vice president of Roche Molecular Systems in Alameda, Calif., owned by Roche Holding, said that Dr. Mullis was "a very unusual person, no doubt about it -- I am happy I knew him."

Dr. White's version of events is supported by Dr. Paul Rabinow, an anthropologist at the University of California at Berkeley, who made a study of Cetus at the time P.C.R. was invented. His book, "Making P.C.R.," was published in 1996. "Mullis is a brilliant, gifted guy who at Cetus found himself protected by a very steadfast character, Tom White," Dr. Rabinow said. "The one person who never said he wanted credit for P.C.R. was Tom White."

As for the monetary rewards for P.C.R., Dr. Mullis says in his book he was "plenty wrong" in his assumption that he would be amply rewarded by Cetus. His former colleagues consider he did not do too badly. He voluntarily quit the company in 1986 at a time when no commercial value had been established for P.C.R., and five years before its sale to Roche for \$300 million. "If the guy had been around five years later he would have been handsomely rewarded," Dr. White said. Dr. Levenson said: "Any invention you make is owned by the company. That's the deal."

Dr. Mullis has blazed through his friends' lives like a meteor, leaving so blinding a trail that few feel they see the core. "I don't know where creativity comes from," Dr. Levenson said. "He built his model of the universe to fit what he observed."

In Dr. Rabinow's view, Dr. Mullis is "a tinkerer, a bricoleur, he loves to play with things, he loves to try things out, he ignores people who say you can't do it." He adds, "He was an experimentalist not in the high scientific sense but the magician sense."

In Dr. Mullis's new profession, as author and lecturer, the magic is less evident. His book is amusingly written, but some of its viewpoints seem a little ad hoc, like a surprising attack on the Federal Reserve Board as a "tawdry sepsis."

Dr. Mullis repeats the words several times to savor their resonance. It's a good fighting phrase, but why apply it to the Federal Reserve? Dr. Mullis explains that with the Board's ability to intervene in currency markets its members have ample opportunity to profit from their inside knowledge. "If you can get around the law you do it, and Alan Greenspan is no different from Kary Mullis," he declares.

"But Kary, you're not dishonest," his wife protests. "With money I am," he says defiantly. The bottle of red wine at his side, full three hours ago, now stands empty. The yellow jackets are resuming their campaign. A mind that made a brilliant invention is wandering between sense and solipsism.