A Drug's Royalties May Ease Hunger

By Andrew Pollack

ERBITUX, the long-awaited and newly approved drug from ImClone Systems, could have an unexpected side effect. Besides helping American cancer patients, it may help feed the poor in Africa.

That is because some royalties from the drug's sales will go to its unsung co-inventor, Gordon H. Sato, a cell biologist and a member of the National Academy of Sciences who left a successful academic career to devote himself to producing food in the African desert. Even now, at the age of 76, Dr. Sato spends much of his time under the broiling sun in the drought-stricken nation of Eritrea, growing mangrove trees at the edge of the Red Sea.

"We're close to making a coastal village selfsufficient in food," he said in a telephone interview from Eritrea.

Dr. Sato says he has not paid much attention in recent years to Erbitux, which he worked on in the early 1980's and which some analysts and doctors say could become a major new treatment for colon cancer. He is only vaguely aware, he said, that the founder of ImClone, Samuel D. Waksal, is serving seven years in prison after pleading guilty to crimes including securities fraud for trying to dump stock in the company in late 2001 and that Martha Stewart had been on trial on charges related to her sale of ImClone stock at the same time.

But when the possibility of getting royalties was mentioned, Dr. Sato replied, "I hope so, because I'm running out of money here."



protruding from cell surfaces the way a key fits into an ignition, spurring the cells to grow. Cancer cells depend on this mechanism to grow wildly.

Dr. Sato and Dr. Mendelsohn decided to try to block the receptor for one of these growth-spurring agents, called epidermal growth factor. "We just thought, 'Let's stick a piece of chewing gum in our lock so the key can't get in,' " Dr. Mendelsohn said. Dr. Sato said he had been more interested in just studying the growth factor by stopping it from working.

Dr. Sato's researchers purified the receptor protein and injected it into mice, which treated it like an invading germ and made many antibodies to attack it. The antibody that stuck best to the receptor was called 225, after the number of the well in the laboratory plate in which it was found.

Years later, the antibody was changed to make it chimeric - part human, part mouse - to reduce the immune reactions in patients. After that, it was

In Africa, an unsung biologist is quietly tilling the fields



He said he had spent about a half-million dollars of his own money on the African work, which he named the Manzanar Project and is mostly financed by him.

Erbitux is most closely linked with Dr. John Mendelsohn, president of the M. D. Anderson Cancer Center in Houston. Dr. Mendelsohn's reputation rests largely on the development of the drug and related work in controlling cancer cell growth.

But the creation of what became Erbitux actually occurred in Dr. Sato's laboratory at the University of California at San Diego, where both he and Dr. Mendelsohn were professors.

Some of Dr. Sato's supporters say that because he is a self-effacing independent thinker with little interest in business, his contribution has been overlooked.

"I think most of Gordon's close associates feel that Gordon was the key intellect in those early days, the real driving force at the laboratory level," said Wallace L. McKeehan, a professor at Texas A&M University. But he and others said Dr. Sato tended to move on to new things and rarely discussed his role in developing Erbitux, which blocks a mechanism needed for cancer cell growth.

In the interview, Dr. Sato said he was irked only

called C225, by which it became widely known.

In 1983, the year the results were first published, Dr. Sato left San Diego to become director of the W. Alton Jones Cell Science Center in Lake Placid, N.Y. He stayed until 1992.

But even as he grew cells in dishes, he was experimenting with growing things on a larger scale in the desert. That interest started, he said, when he saw fellow Japanese-Americans growing food at Manzanar, the World War II internment camp in the California desert where he spent his high school years. After college, he worked as a gardener in Pasadena, Calif., then walked into the California Institute of Technology one day and applied to be a graduate student.

Around 1986, Dr. Sato said, he thought he could help alleviate Ethiopia's famine, which was primarily affecting the rebels who were trying to gain independence for Eritrea from Ethiopia.

Using money from a Japanese philanthropist, Dr. Sato brought clothing and water-purification equipment to the rebels. He dug ponds near the sea and filled them with seawater, then fertilized them so algae would grow and raised fish on the algae to provide high-protein food for the wounded.

Since Eritrea's independence in the early 1990's, Dr. Sato has been spending more than half of every year there, although he has cut back a bit since October, when he suffered a minor stroke. He also has a home in Wenham, Mass.

THE Manzanar Project has planted more than 600,000 mangrove trees along the Eritrean coast. The trees, which tolerate saltwater, grow naturally in some areas, but Dr. Sato is growing them in other areas by providing fertilizer. The leaves of the mangroves and the sun-dried seeds can be fed to livestock, which can in turn be eaten by people, he said.

by articles describing him as a member of Dr. Mendelsohn's team.

"The thing is, he was a member of my team," Dr. Sato said. "It was my team that developed the antibody and had the idea." Dr. Mendelsohn, he said, "came by the lab and got interested and joined in."

Dr. Mendelsohn said the early development was a joint effort. "There's no question his contribution was critical to this," he said.

But soon after the laboratory work was done, Dr. Sato left San Diego and moved on to other projects. It was Dr. Mendelsohn who turned the laboratory creation into a useful cancer treatment. He helped set up the first clinical trials, and he arranged to license the drug to ImClone, a struggling New York biotechnology company that, after missteps and scandals, finally won approval for it on Feb. 12 from the Food and Drug Administration.

THE patent on the antibody that became Erbitux, issued to the University of California, lists four inventors: Dr. Mendelsohn, Dr. Sato and two researchers in Dr. Sato's lab who did the grunt work - J. Denry Sato, who is Dr. Sato's son, and Tomoyuki Kawamoto, a postdoctoral researcher from Japan who died some years ago.

The inventors and the estate of Dr. Kawamoto will divide 42.5 percent of the university's proceeds from the patent, after legal fees are deducted, a university spokeswoman said.

The terms of the license are confidential, but the royalty rate is believed to be 1 percent. So if Erbitux sales reach the expected level of several hundred million dollars a year, Dr. Sato could receive several hundred thousand dollars a year. Royalty payments are set to end in mid-2007, when the patent expires, though the university will probably apply for an extension.

In the 1960's and 70's, Dr. Sato did pioneering work in figuring out how to grow cells in the laboratory using certain proteins called growth factors. These proteins fit into receptors

Some scientists have questioned the project, saying the ample use of fertilizer in the sea may damage coral reefs. Dr. Sato has argued that the fertilizer is applied bit by bit next to the mangroves, so that it does not spread.

In 2002, Dr. Sato won a Rolex Award for Enterprise, given by the watch company to people deemed visionaries. "Anybody who I've met who has seen his project says it's remarkable," said Haile Debas, the executive director of global health sciences at the University of California at San Francisco and a native of Eritrea. "He's just truly a remarkable human being," Dr. Debas added. "I'm humbled when I meet him."

Dr. Sato was involved in the formation of biotechnology companies like <u>Transkaryotic Therapies</u> and Hana Biologics. He is chairman of A&G Pharmaceutical of Columbia, Md., a company started by some of his former postdoctoral students after he gave them \$200,000 in seed money.

Dr. Sato said he had never tried to start companies but had just responded to requests for help. In some cases, his stakes in those companies have turned out to be valuable. "They'd give me stock, and I'm spending it here," he said.

Now, he said, that money is almost gone. Although he expressed no regrets about not sticking with Erbitux - "I've got too many things to do," he said - that work from long ago may help him with his current plan.

"I've got to buy fertilizers and devices for planting mangrove trees, and sheep and goats, and train the villagers," he said.