**Stanford stem cell product, delayed for more than a decade, to be tested again**

*By Lisa M. Krieger*  06/14/2015 05:45:22 AM PDT



File: Stanford University Professor Irving Weissman, center. (AP Photo/Doug Mills)

STANFORD -- In the 1990s, Stanford's Irv Weissman created a unique way to grow and deliver blood stem cells to desperate patients with aggressive cancers, boosting survival rates.

But then the discovery itself died -- a victim of the heartbreaking economics of commercial stem-cell development, where the long and rocky road of research, especially in the field of "personalized medicine," often discourages investment.

Now, 10 years after the technique's sale and then abandonment by a biotech company, it is back in Weissman's hands. The goal, he said, is to finally resume his research to prove, once and for all, its effectiveness in patients with no other hope.

"I am frustrated by more than a decade of delay," said Weissman, who codirects the Stanford Institute for Stem Cell Biology and Regenerative Medicine. "But I'm delighted that medical need, rather than rapid profits, is now the primary criterion to translate our stem cell discoveries."

Weissman's discovery was a method to isolate, purify and transplant cells, called blood-forming stem cells. These are the cells deep in the marrow of our bones that generate the river of life -- red cells, white cells and platelets -- flowing through our arteries and veins. His goal is to use them to regenerate patients' blood-forming systems after high-dose chemotherapy.

A dose high enough to kill all tumor cells also kills these blood-forming stem cells -- and eventually the patient. But if the cells can be extracted from the patient's bone marrow before treatment, purged of cancer and then returned to the body after chemotherapy, they might be lifesaving. In essence, patients could rebuild their blood supply from scratch.

Excited by its promise, Weissman in 1987 co-founded a Palo Alto-based company called Systemix to commercialize this approach. And -- in an audacious and dramatic departure from traditional procedures -- he patented not only his technique, but also the stem cell itself.

In its initial small trial in women with advanced breast cancer at the Stanford University School of Medicine in the mid to late '90s, patients who received aggressive high-dose chemotherapy -- followed by Weissman's "rescue" with their own purified stem cells -- significantly boosted their chances of long-term survival. More than 12 years after treatment, 33 percent of the women with advanced metastatic breast cancer were still alive, compared with 7 percent of those who received a therapy that was not purified, according to a 2011 Stanford study.

Conventional medical opinion is that stem cell transplants coupled with high-dose chemotherapy don't work for patients with breast cancer, explained Dr. Judith Shizuru, the Stanford researcher who led the study. But when stem cells are purified to remove cancer cells, using Weissman's approach, outcomes improve, she said.

To get his innovation into the hands of a company large and prosperous enough to accelerate research, Weissman in 1991 sold a majority share of Systemix to Sandoz Pharma, the big Swiss drug and chemical company, for $392 million. A Lehman Bros. analysis forecast that Systemix would have nine approved cancer and AIDS therapies producing $1.9 billion in revenue by 2003.

"This takes us one step beyond traditional biotechnology," said Max Link, Sandoz chief executive at the time, announcing that the firm planned to market Weissman's approach.

Then Sandoz merged with Ciba-Geigy and became Novartis, which bought the remainder of Weissman's company for $76 million in 1997 -- and, with it, all patents.

It made Weissman an instant multimillionaire. But his recipe was put on the back burner. Meanwhile, despite Systemix's pioneering work, the share price of the company declined as it failed to produce a product. And then Weissman helplessly watched as Novartis canceled its stem cell program. "Even though we were in the middle of the clinical trials -- too early to have the results -- Novartis decided to shut them down," he said.

Novartis, which shuttered Systemix in 2000, explained that it ended the program because it couldn't produce blood stem cells in large enough numbers to develop a commercial market -- and it was not in the business of producing personalized "custom-made" therapies.

The company did not respond to repeated requests for an interview for this article.

Personalized medicine, in which treatments are tailored to each patient or even use the patient's own cells, holds great promise because of its precision. But it's a tough business because the cells can't be manufactured and mass-marketed like drugs.

"Progress in realizing the promise of personalized medicine has been slow and uneven," Harvard Professor of Management Practice Richard G. Hamermesh wrote in the Harvard Business Review, citing the slow adoption of Herceptin, the first targeted cancer drug aimed at patients whose tumors have specific genetic characteristics. And even after Herceptin was approved for patients with metastatic breast cancer, it took nine years for its use to shift to newly diagnosed patients.

Other personalized drugs, such as Pfizer's lung cancer drug Xalkori or GlaxoSmithKline's melanoma drugs Mekinist and Tafinlar, have much smaller markets than blockbusters like the antidepressant Prozac or cholesterol-lowering Lipitor.

Changing the business model "means moving from a grand-slam mentality -- creating a handful of drugs that can generate annual sales of $1 billion or more each -- to one that emphasizes singles, doubles, and occasional triples," wrote Hamermesh, who chairs the school's initiative to improve the effectiveness of leadership in health care organizations.

Weissman's travails also illustrate another challenge to quick profitability: It can take a long time to learn whether a stem cell therapy against cancer is truly effective.

And it's a cautionary lesson about selling out too soon.

"We think that there is an advantage to keeping it under the experience of the academic people who did the discovery, to translate it from bench to bedside with a higher probability of success, compared to commercial spinoff where you don't have control," said Dr. Maria Grazia Roncarolo, a stem cell expert brought to Stanford to lead efforts in fast-tracking stem cell therapy to patients.

"Once you prove efficacy, Big Pharma cannot put it on the shelf," she said. "But you need to prove efficacy before you give it away."

Weissman felt success slipping through his fingers.

"When we developed the method and isolated human blood-forming stem cells, we were on track to deliver cancer-free blood stem cells to patients with a variety of cancers, including metastatic and aggressive breast cancers, lymphoma patients and myeloma patients," he said.

In late 2000, Weissman and Shizuru convinced Novartis to license key technologies to his new company, Cellerant. But research funding was halted because of tepid investor interest.

"Well before the launch of the War on Cancer, the corporate profit motive has driven the cancer research agenda," said Karuna Jaggar, executive director of the Breast Cancer Action, a San Francisco-based patient advocacy group. "Time and again, history has shown that it is not only the possibility of saving lives but the potential of making money that has steered the research agenda toward some areas -- and away from others.

"As long we have a health care system that puts profits before patients we will always be at the mercy of corporations looking to make profits. Any new innovation needs to be evidence-based and proven safe and effective no matter what money is to or is not to be made," she said.

Now, a quarter-century after it was conceived, the technique is finally back in Weissman's hands at Stanford -- although Novartis still holds the patent.

At age 74, he is helping plan the study needed to more definitively prove its effectiveness -- and get it to desperately ill women.

"We will take it forward in a nonprofit setting," Weissman said.