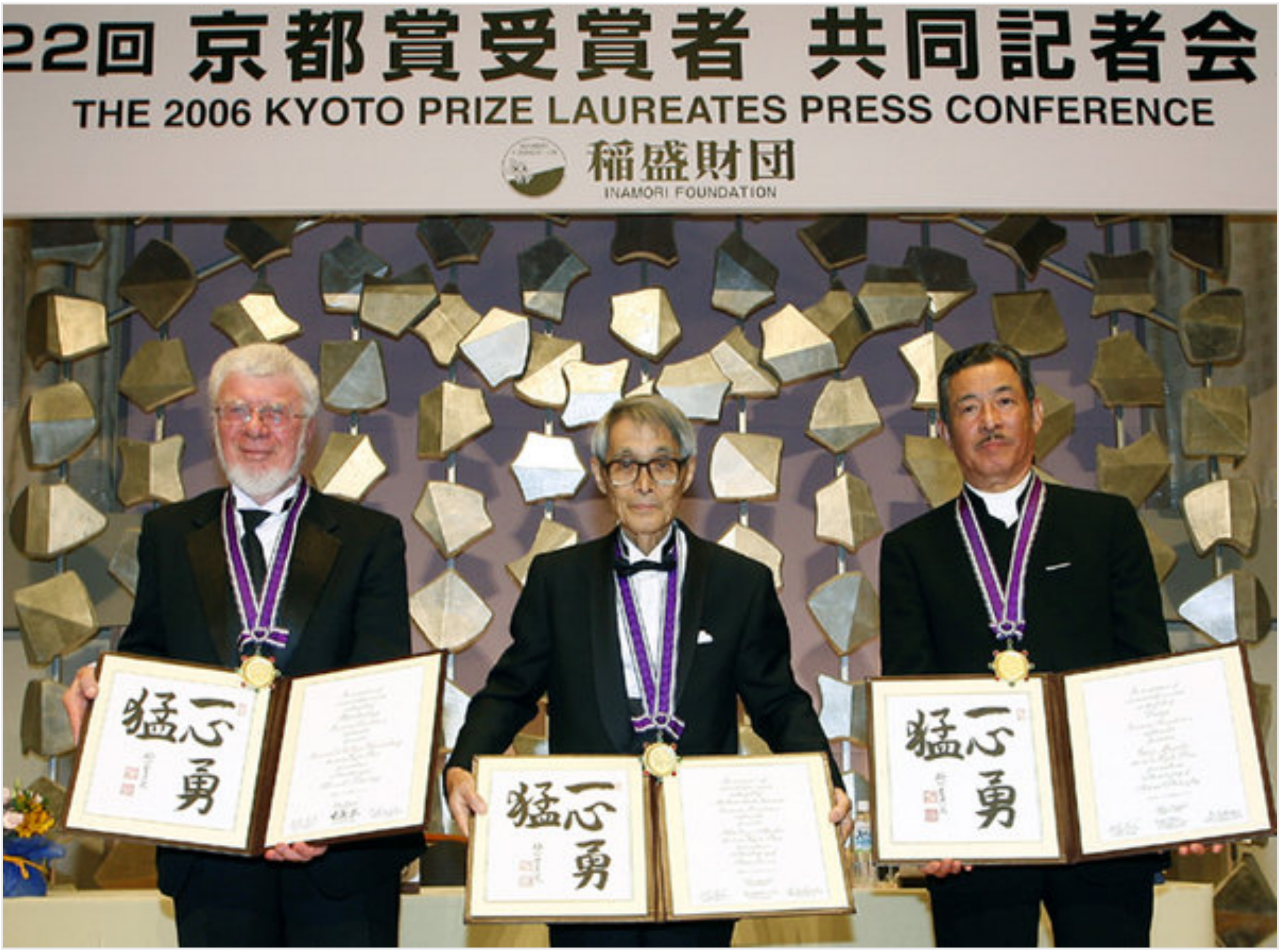
Leonard Herzenberg, 81, Immunologist Who Revolutionized Research, Dies



Leonard Herzenberg was in his lab at Stanford University one day in the early 1960s, laboriously counting cells under a microscope. His eyes hurt. “There’s got to be some kind of machine that can do this,” he remembered muttering.

He went on to develop precisely that — and in doing so helped revolutionize immunology, facilitate stem cell research and advance the treatment of cancer, H.I.V. infection and other illnesses.

Dr. Herzenberg, who died on Oct. 27 at 81 in Stanford, Calif., created a device that can pick out individual cells from a mass of trillions of them and then capture, sort and count them so they can be analyzed and used to fight disease.

Some likened his achievement to watching a parade of 10,000 men in drab suits, spotting the two wearing yellow ties and the three wearing pink ones, and then pulling the five out of line without anyone losing a step.

Today, more than 40,000 such devices are in operation around the world; virtually no significant medical lab is without one. In 2006, the Inamori Foundation presented Dr. Herzenberg with the Kyoto Prize, the Japanese equivalent of the Nobel Prize, in the category of advanced technology, calling his achievement “monumental.”

Dr. Irving Weissman, who was a student of Dr. Herzenberg’s and became one of the world’s leading stem cell researchers, said, “Without Len, tens of thousands of people now alive would not be.”

Dr. Herzenberg’s success was not his alone. At his side in the laboratory was Leonore Herzenberg, his wife of 60 years and a fellow researcher. “Len and Lee,” as everyone knew them, were known for holding brainstorming sessions with generations of young researchers, many of whom achieved international renown. Many of his most important papers listed her as an author.

“You can’t sort out which one did what,” Ms. Herzenberg said in an interview. “I swear it was magical.”

Leonard Herzenberg’s invention is called the fluorescence-activated cell sorter, known by the acronym FACS. (The generic name for it and similar devices is flow cytometer.) The FACS name was later trademarked by the medical devices manufacturer Becton, Dickinson & Company (also known as BD).

Dr. Herzenberg’s mission was always more medical than technical, although he liked fooling with gadgets. He used his cell sorter to become a leader in developing strains of antibodies — called monoclonal antibodies — that glom onto targeted viruses and bacteria.

He created the antibodies — large molecules made up of chains of amino acids — by introducing a specific germ to living tissue; the process prompted the body to form a multitude of antibodies geared specifically to attack that germ. He identified the antibodies by illuminating them with fluorescence — a process developed in the 1940s

— enabling him to capture and clone white blood cells that were making specific antibodies.

The technique permitted the creation of large numbers of pure, identical antibodies, which could be used for purposes as minute and delicate as plucking out exceedingly rare stem cells for study.

Dr. Herzenberg gave away the hybrid cloned cells that create pure, identical antibodies — a generosity rare in today's legalistic, profit-hungry scientific world — and they continue to be widely used.

His cell sorter, too, remains in wide use. Susan O. Sharrow, a biochemist with the National Cancer Institute, said in an email that the FACS "remains the gold standard" for such devices.

Leonard Arthur Herzenberg was born on Nov. 5, 1931, in the Flatbush section of Brooklyn, where he grew up. His father, William, was a clothing salesman; his mother, the former Ann Seidlitz, a legal secretary. Leonard read science books in elementary school and was doing experiments in his basement by high school.

He met Leonore Alderstein when they were students at Brooklyn College. At the time, he was nearing graduation; she, at 17, still had a few years to go. They decided to marry when both had graduated. Mr. Herzenberg, who had studied chemistry and biology, received his degree in 1952 and was accepted to continue his studies at the California Institute of Technology. The couple parted, but not for long. Loneliness and the weight of phone bills won out, and they married in 1953.

"Our parents thought we were too young, too innocent, too poor and too crazy," Ms. Herzenberg wrote in The Annual Review of Immunology in 2004. "They were probably right."

In California, Ms. Herzenberg took courses at Pomona College and was allowed to audit graduate courses at Caltech. (It did not admit women then.) Also allowed to take tests, she got A's, she said.

She was with Dr. Herzenberg at virtually every stage of his career — when he did postdoctoral research at the Pasteur Institute in Paris; when he was the first appointment to Stanford's new genetics department in 1959. Indeed, most of their waking life was in the lab. She wrote papers on her own and papers with him, including some on the cell sorter.

She never earned a college degree, but the University of Paris later named Ms. Herzenberg a doctor for her mountain of published work, and Stanford made her a full research professor.

"I am the equivalent of American Ph.D. ten times over," she said.

In the early 1980s, the couple helped develop a blend of mouse and human antibodies that were acceptable to human immune systems. Royalties from the patent stand as the most profitable ever for Stanford. They also jointly supported human rights, education and health endeavors. A recipient of many awards, Dr. Herzenberg donated much of his prize money, including the $445,000 that came with the Kyoto award, to these initiatives.

Dr. Herzenberg died of complications of a stroke, his wife said.

In addition to her, he is survived by his daughters Jana Herzen and Berri H. Michel; his sons Eric and Michael; and four grandchildren.

Dr. Herzenberg's idea for the FACS, which he named, evolved from his realization, shared by many, that microscopes were incapable of meeting the high-volume demands of minute biological research. He heard about work being done at the Los Alamos National Laboratory in New Mexico by Mack J. Fulwyler on a device to sort particles in mouse lungs resulting from atomic bomb fallout. The Fulwyler device was the original cytometer, according to J. Paul Robinson, a Purdue University professor who has documented the technology's history. Dr. Fulwyler gave Dr. Herzenberg his design plans.

By 1969, working with Stanford engineers and financing by the National Cancer Institute, Dr. Herzenberg had come up with his improved version of Dr. Fulwyler's cytometer. Three years later, the Stanford team produced an even more sophisticated one, a laser-powered model using fluorescence. Similar inventions emerged in this period, including one created by Dr. Wolfgang Göhde in Germany in 1968, the first patented cytometer to use fluorescence.

But Dr. Herzenberg's device ended up leading the pack because, as it evolved, it could address some of biology's most complex problems, said Dr. Howard M. Shapiro, another expert in the field. Emphasizing that success has many fathers, Dr. Shapiro said that Dr. Herzenberg most clearly "passes the paternity test."

This article has been revised to reflect the following correction:

Correction: November 11, 2013

An earlier version of this obituary contained several errors. Antibodies are large molecules made up of chains of amino acids, not "armies of protein cells." Dr. Herzenberg developed a process to capture and clone white blood cells that were making specific antibodies, not the antibodies themselves. And he gave away hybrid cloned cells, not living antibodies.