Leonard Herzenberg

(1931–2013)

Immunologist who pioneered cell-sorting technology.

Leonard Herzenberg, together with his wife and scientific partner of more than 60 years, Leonore, transformed immunology. His accomplishments continue to influence every aspect of modern biological science.

Were it not for Herzenberg, researchers might still be waiting for fast, precise ways to count and sort cells. That task, now routine, is essential for working out how cancers and tissues grow, and for diagnosing certain diseases. Herzenberg also developed technologies to create monoclonal antibodies — lab-produced versions of the proteins used by the immune system to recognize dangerous cells and toxins. These are now deployed in laboratories for innumerable assays, and in humans for certain cancers, infections and inflammatory diseases.

Herzenberg, who died on 27 October aged 81, was born in New York City. After graduating in 1952 from Brooklyn College in New York, he began doctoral studies in genetics at the California Institute of Technology in Pasadena, joining a department that included seven future Nobel laureates. Among this auspicious group, Herzenberg blossomed scientifically and, along with Leonore, whom he had met at Brooklyn College, he also became politically active. Len and Lee, as they were known, worked with a chemist down the hall — Linus Pauling, who himself would go on to win two Nobel prizes — to start a local chapter of the Federation of American Scientists that worked to combat the insidious efforts of McCarthyism in the 1950s, among other goals.

After Len received his PhD, the Herzenbergs moved to Paris, where Len did a fellowship at the Pasteur Institute with biologist and Nobel laureate Jacques Monod. Discussions at lunch revolved alternately around bacterial genetics and the French Resistance. While abroad, Herzenberg was drafted into the US peacetime army. He arranged to serve in the Public Health Service and moved to Bethesda, Maryland, to join the lab of pathologist Harry Eagle at the US National Institutes of Health. Here, Herzenberg "carried a pipette rather than a gun" for his country. He helped to define the minimal components of the nutrient broth necessary to clone cells. More than a decade later, this enabled him to produce antibodies in cell culture, a technology that generates billions of dollars' worth of drugs and lab reagents.

In the 1960s, after moving to California to work at Stanford University, Herzenberg recognized the need for an automated, high-throughput method to enumerate and separate rare cells in a population of millions. Such technology could be used, for example, to explore whether individual immune cells made one or several kinds of antibodies, or to identify those producing antibodies capable of killing cancer cells.

Herzenberg formed a team of engineers and biologists to take a machine that sorted particles by size and enhance it with techniques to detect fluorescence and manipulate droplets. The result was modern flow cytometry — a way to count and separate viable cells in a stream of fluid lit by lasers that reveal fluorescent markers on the cells. Fluorescence-activated cell sorting (known as FACS) is now widely used in labs and hospitals. For instance, FACS can isolate fetal cells from maternal blood, which allows clinicians to perform genetic testing using a minimally invasive procedure. Remarkably, the fundamental aspects of FACS have not changed in the more than 40 years since its invention.

Another ubiquitous technology also owes its existence to the Herzenbergs. In 1976, on a sabbatical at the University of Cambridge, UK, the Herzenbergs worked with biochemist César Milstein on his technology to fuse cells. They created cell lines that produce made-to-order antibodies which attach to specific markers on cell surfaces.

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Len recognized the power of this technology to identify specific proteins and cell populations. Lee coined the term 'hybridoma' for a class of workhorse lab cells, a combination of an antibody-producing white blood cell and an immortal tumour cell.

Although Herzenberg's patents are among Stanford's highest earning, he believed that any scientific advance belonged to the people who had funded it; that is, to the public, whose taxes supported his grants. He asked co-inventors of flow cytometry to assign patent royalties back to the lab. He freely shared resources that his laboratory developed, providing researchers from other labs with reagents, cell lines, data and information, sometimes well before publication. This collaborative philosophy was appreciated by scientists worldwide. It also helped to accomplish his primary goal: more-rapid advances.

Throughout his career, Herzenberg was actively involved in sociopolitical causes. His early exposure to the dangers of the anti-intellectualism and misinformation of McCarthyism seeded a lifelong commitment to bringing rational thought to public discourse. He railed against proponents of eugenics and nuclear proliferation, and, in later years, against those who stigmatized people with HIV.

He also supported efforts to promote career opportunities and equality for women and minorities in science. The Herzenbergs established programmes to bring disadvantaged young people in California's San Francisco Bay Area to Stanford to learn about medical research. Lee continues this tradition of balancing outreach with scientific research.

Although Len is considered the father of modern flow cytometry, his contributions extend far beyond that. He was a great scientist, a great collaborator and a great mentor. ■

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