



Leonard A Herzenberg 1931–2013

Garry P Nolan

On 27 October 2013, just a week before his 82nd birthday, Leonard (Len) A. Herzenberg passed away from complications due to a stroke. Joining him during his final hours was Leonore (Lee) A. Herzenberg, his wife and scientific partner for nearly his entire research career. He is survived by Lee and his children Jana, Berri, John and Rick. He leaves a research community indebted to his service to the public's benefit, and he leaves hundreds of thousands of patients, and more, who have benefitted from his brilliant contributions to immunology and translational medicine.

Who today can imagine modern immunology without cell sorting or fluorescence-labeled antibodies? How would simple blood profiling be done? How could the extraordinary intricacies of lineages and sublineages of the immune system be delineated, or the diversity of cell types in a tumor be understood? How could the discoveries that HIV-1 specifically attacks CD4⁺ T cells and that the onset of AIDS is caused by the loss of such cells have been made? Len's discoveries grew an industry and drove innovation via application of the tools he developed that eventually reached far beyond immunologists to the international biomedical research community.

Len, who grew up in Brooklyn, New York, finished his Ph.D. at the California Institute of Technology in 1955, moved to the Pasteur Institut to work with Nobel Prize winner Jacques Monod, then returned to the US after his postdoctoral fellowship to work at the US National Institutes of Health. In 1959, Len moved to Stanford University to initiate work on mammalian cells that would later lead to the revolution in cellular analysis for which Len is best known. Although it is just one of his many achievements, his seminal contribution is, of course, the fluorescence-activated cell sorter and the amazing research culture it engendered. In the very same basement where Nobel Prize winner Josh Lederberg had a team developing an automated laboratory for the Viking Lander to search for life on Mars, Len Herzenberg was developing his 'space-age' cell sorter. Len would often remark how critical it was to the development of fluorescence-activated cell sorting to have not only the support of Lederberg but also the intellectual environment the Viking engineering teams provided—space age, indeed!

A key moment in Len's career was a sabbatical in César Milstein's laboratory at Cambridge University in 1975. Len had heard of César's advances in the creation of monoclonal antibodies. Len saw in this a means to overcome several impediments inherent to polyclonal antibody reagents—Milstein's advances offered the possibility of a limitless supply of specific antibodies to which fluorophores could be readily conjugated. Upon returning from England, Len fulfilled his vision by generating many of the first monoclonal reagents to surface proteins of the immune system. Armed with such distinctive tools, Len 'married' them to fluorophores and fluorescence-activated cell

sorting and the 'modern age' of immunology arrived, the principles of which are still relevant today. It is to Len's everlasting credit that the absolute rule of his laboratory was to share any reagents developed under a 'no questions asked, no limitations imposed' policy—open-access science in the making.

The data-management solutions taking root in the Herzenberg laboratory under the leadership of Lee Herzenberg formed a forerunner to the bioinformatics revolution taking place today. As 'Len and Lee', they led an extraordinarily diverse and intermingled team that not only built the instruments that tabulated the expression and correlations of critical proteins from thousands to millions of cells per experiment but also spent endless hours pondering immunological mechanisms or arguing about how to develop intuitive representations of the deeply phenotypic data to provide a vision on how best to ask the next questions.

One of the most amazing qualities of the Herzenberg 'brand' of science was treating the laboratory team as family. The Herzenberg laboratory merged seamlessly with the Herzenberg household. Laboratory meetings led to invitations to dine with visiting scientists and to cooking family-style dinners at the Herzenberg homestead where, inevitably, discussions would move to the Bohemian-style den at the back of the house, a luxurious room filled with pillows and low-slung seats. Visiting luminaries from the field of immunology would be feted and science would be discussed until the very wee hours. Very little was considered 'off topic'. Trips were planned to the beach just over the Santa Cruz Mountains to collect seaweed from which phycoerythrin was purified back at Stanford to refresh precious laboratory supplies; new instruments and ideas would be vetted; and deals would be made with key industry executives. Len would sit offering opinions from his chair while Lee and the guests discussed the events of the day. Sometimes Len was thought to be sound asleep in his chair only to interject when somebody said something that roused him and the conversation would start afresh.

Leonard Herzenberg was not just about answers to important questions—he was a man who framed the answer as a window to new possibilities. He was an extraordinary innovator, a teacher, a man who cared deeply for his family, and a scientist who treated his colleagues and competitors as an extended family. His humanity was marked by his early unabashed commitment to rights for black and gay minorities, his vigilant exercise of free speech during the anti-war movements of the 1960s and 1970s and his stunning philanthropy that gave back the financial benefits of his accomplishments to the communities he cherished. No one could ever meet Len and walk away without remembering the connection he made. And for many he knew well, and many who never even met him, Len Herzenberg changed their lives in ways that would only make him smile.

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