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Samuel Silverstein

One might compare biomedical research to climbing mountains. Samuel Silverstein, Chairman of the Department of Physiology and Cellular Biophysics at Columbia University's College of Physicians and Surgeons, could comment on the accuracy of the metaphor — he does both.

Silverstein's passion for science is matched by his interest and ability in mountaineering. In 1959 Silverstein and some of his young friends climbed, named, and mapped the Battle Range in the southern Selkirk mountains of British Columbia, Canada. In 1962, he was part of another pioneering expedition that made the first ascent of the southeast spur of Alaska's Mt. McKinley. Later, he participated in a National Geographic Society-National Science Foundation-American Alpine Club sponsored expedition to Antarctica. He and his fellow mountaineers made the first ascents of Antarctica's highest peaks. For this effort and achievement, then Chief Justice Earl Warren presented the team with a National Geographic Society medal. Silverstein is a former director of the American Alpine Club, an avid cross-country and alpine skier, and has written a number of articles on these expeditions. He sees many parallels between mountaineering and science: "mountains are an unknown frontier with a defined summit; science is a frontier without a summit."

Silverstein's professional career is less dangerous but just as interesting and challenging as his avocation. A native of New York City, he attended secondary school in Colorado Springs, Colorado and received an A.B. from Dartmouth College in 1958, where his interest in human organizations and earth science led him to major in government and minor in geology. Choosing "gallstones over moonstones," Silverstein received an M.D. from Albert Einstein College of Medicine in 1963.

In his second year at Einstein, an experimental pathology project dealing with lab membrane transport — and the influence and guidance of his mentor, the late Alex Novikoff — piqued his interest in cell biology and medical research. He received a Helen Hay Whitney Fellowship to pursue postdoctoral research in the Laboratory of Cell Biology led by George Palade at Rockefeller University. There, together with Samuel Dales, he showed that reoviruses uncoat in the lysosomes of their host cells. In 1971, Silverstein and his colleagues, George Acs and Judith Christman, identified the mode of replication of the double-stranded RNA genome of reoviruses.

From 1968-1974 Silverstein was a member of the faculty at Rockefeller University in the Laboratory of Cellular Physiology and Immunology. Describing his experiences there, Silverstein notes that Jim Hirsch and Zan Cohn created a very stimulating atmosphere, and Rene Dubos, although emeritus, always was available for a chat. "I have been fortunate," he says, "to have had outstanding mentors at Einstein and Rockefeller. That good fortune continues in my colleagues at Columbia."
At Rockefeller, Silverstein and Frank Griffin formulated a general concept of immune phagocytosis, which they termed the "zipper mechanism." Subsequent studies with Samuel Wright identified the membrane receptor for the cleaved third component of complement, C3bi, on human mononuclear phagocytes.

Silverstein, together with Marcus Horwitz, also received wide attention for their work on Legionnaire's Disease, demonstrating that Legionella pneumophila, the bacillus that causes the disease, like the bacteria that cause leprosy and tuberculosis, is a facultative intracellular pathogen.

Since moving to Columbia in 1984, Silverstein has continued work on the functions of plasma membrane receptors of macrophages, neutrophils, and platelets and has initiated several new projects. Along with Martha Furie and Ada Huang, he has developed a model for studying the permeability properties of monolayers of cultured endothelial cells. Together with Joel Swanson, he described the interconnected and tubular structure of macrophage lysosomes. Other ongoing work in Silverstein's laboratory includes discovery of a novel pathway for the intracellular sequestration and secretion of organic anions and antibiotics by macrophages together with Thomas Steinberg, Charles Cao, Harold Neu, and Deborah Rudin; the recognition that both facilitative and sodium-dependent glucose transporters provide a constitutive pathway for the transmembrane passage of water with John Loike, Jorge Fischbarg, and Suzanne Hickman; and the demonstration that neutrophils, macrophages, and platelets form protected extracellular compartments when they adhere to surfaces bearing extracellular matrix proteins, together with John Loike, Jeffrey Weitz, Roy Silverstein, Gary Matsueda, Edgar Haber, and Samuel Wright.

Silverstein's interest in science extends beyond his own lab. In addition to serving as Editor of the Journal of Cell Biology from 1978-1988 and as Chairman of the Journal's Editorial Board from 1979-1983, Silverstein founded the Columbia University Summer Research Program for High School Science Teachers, which differs from other summer research programs in that it requires a two-year commitment from participants. The program is designed to elevate the interest of high school students in science by providing high school science teachers with the opportunity to gain hands-on experience with the practice of science by working in university research laboratories. Silverstein's involvement with this program has convinced him that these experiences provide teachers with unique avenues for personal and professional growth, enhance their ability to communicate to their students the excitement of science, and aid them in providing encouragement and guidance to students who are considering careers in science or in the health professions. He points out that in addition to summer programs, there are many simple ways for universities to aid teachers. "Teachers often do not have access to good science libraries. We remedy this by providing teachers who participate in our program a Columbia library card," he said.

Silverstein also is enthusiastic about the prospects for improving medical education. As a leader of the Robert Wood Johnson Foundation's medical education project at Columbia, he is working both to increase student understanding of the "grand synthesis"
accomplished by modern cell and molecular biology, and to focus student attention on the needs of the whole human being. Silverstein is a firm believer in the need for better training in science. "Science is what we humans do best at this point in history," he said. "C.P. Snow wrote about the need for increased communication between the two cultures. Scientists are the principal creators of modern culture. I believe that in the next century those who are unprepared to understand science are likely to be viewed as uncultured."

A member of ASCB since 1964, Silverstein served as a Council Member from 1988-1991 and currently serves on both the Public Policy and Education Committees and as one of ASCB's two representatives to the FASEB Board of Directors. His involvement in public policy brought him in April 1992 to testify on behalf of ASCB to the House Appropriations Subcommittee on Labor, Health and Human Services. In his testimony, Silverstein advocated increased funding for NIH's investigator-initiated extramural grant program and for training grants for student researchers. Silverstein hopes the ASCB's efforts to build an effective grassroots network and expand the Congressional Biomedical Research Caucus will "cause Congress to give increased support to biomedical research and training."

Silverstein and his wife Jo Ann, a health policy analyst, have two children and live in New York.