

1993

Zena Werb

Zena Werb was born in Europe in 1945 and survived the last months of World War II. Before the war, her father taught physics and mathematics and immigrated together with Werb and her mother to Canada in 1948.

Werb grew up on a farm where her academic father taught himself about agriculture. She entered the University of Toronto in 1962 and initially intended to study geology. At Toronto, she studied with J. Tuzo Wilson, who was a leading proponent of continental drift theories. However, as the only woman student, Werb was not allowed on a summer field course with the other students. Sensing that life sciences would be more inviting to women, Werb changed her field and graduated from Toronto in 1966, majoring in Biochemistry and Physiology.

Werb began her graduate studies at Rockefeller University, studying under Zanvil Cohn. She chose Rockefeller because of the flexibility of its program and freedom the University allowed its students to choose their research projects. It was in Cohn's laboratory that Werb began to focus her interest in cell biology. The years at Rockefeller were pivotal in her development as a cell biologist. Werb had learned a great deal about cells, membranes, and lipids, but wanted to study protein chemistry.

After her training, Werb sought to study science overseas. She was recommended for postdoctoral studies in the laboratory of John Dingle at the Strangeways Research Laboratory in Cambridge, England, because of the work being done there in protein chemistry. Following completion of her postdoc there, she continued in the Strangeways laboratory as a research scientist in tissue physiology.

By 1975, Werb was ready to return to the United States, where she initially became a Visiting Assistant Professor at Dartmouth Medical School. She moved to the University of California, San Francisco, in 1976, where she has remained, since 1983 a full professor in the School of Medicine.

Werb's early career concentrated on the cell biology of the macrophage. She discovered that macrophages had distinct receptors for cholesterol-rich lipoproteins, and were involved in cholesterol and cholesterol-ester loading and in cholesterol excretion. She also described the dynamics of plasma membranes in macrophages following phagocytosis. Her lab was one of the first to utilize quick-freeze deep-etch technology along with transmission electron microscopy to investigate clathrin and membrane structure during phagocytosis. She has remained fascinated by these cells, exploring their secreted products that are involved in the inflammatory response and tissue repair.

Werb's major interest over the past twenty years has been on the extracellular matrix. According to Caroline Damsky, a colleague at UCSF, Werb is now "acknowledged internationally as a pioneer in the important field of tissue and extracellular matrix remodeling." She became attracted to extracellular matrix remodeling because this

process appeared to be fundamental for morphogenesis and growth during development, for physiological processes such as involution and tissue repair, and in diseases such as tumor metastasis and arthritis. Early in her studies, she found that fibroblasts secreted extracellular matrix degrading enzymes of the metalloproteinase class in inactive precursor forms. The quest for understanding the regulation of these proteinases, particularly collagenase, led to discoveries in activation cascade pathways of gene regulation and insights into physiological functions. Along the way, Werb's lab described new members of what is now a multigene family of enzymes, including metalloelastase and stromelysin. Werb's laboratory hypothesized that cell shape, as dictated by the actin cytoskeleton, regulated cellular gene expression, particularly the metalloproteinase genes. This hypothesis linked the cytoskeleton to signaling systems that controlled cell behavior, particularly with respect to cell adhesion and extracellular matrix. In the past five years this hypothesis has been refined to incorporate the extracellular matrix receptors, particularly the integrins as key signaling machines in biological control.

The basic premise behind Werb's current work in her laboratory is that the extracellular matrix is not only structural, but informational, controlling cell phenotype. From this emphasis on extracellular matrix remodeling, Werb developed an interest in the first invasive event in mammalian development, implantation, and from this an ever-increasing fascination with the regulation of development. Current work in Werb's laboratory is divided between mammalian development and extracellular matrix turnover and signalling.

Werb credits much of the success of her lab to the talented students and postdocs she has recruited over the years. But, as Damsky points out, Werb "provides superb training for graduate students and postdocs." Susan Fisher, another colleague at UCSF, describes Werb as having "an incredible mix of brains and brawn, and no scientific problem is too tough for her to handle." Fisher says that Werb "has been extremely generous with her knowledge in the laboratory and that her greatest accomplishment as a scientist is to get right to the heart of a problem and to be able to use any technique, some of which she has developed herself."

Werb feels that the next decade in cell biology will require investigators to integrate knowledge of functions at the cellular level with the complex interactions that occur in tissues and organisms.

Werb's interaction with other scientists throughout the country and the world began as a graduate student when she attended her first ASCB Annual Meeting in 1970. It was held that year in San Diego and it was Werb's first visit to California. Since that time, Werb has played an active role in the ASCB, and at present serves on Council. She also served as Annual Meeting Program Chair in 1984, on the Editorial Board of the Journal of Cell Biology from 1983-1985, as Chair of the Publications Committee from 1990-1991, and on other committee and program assignments.

Werb was a Guggenheim Foundation Fellow from 1985-1986 and has won numerous other honors, awards, and fellowships. "She is an outstanding mentor and role model for

women at all levels of their careers, from graduate student to full professor" says Damsky.

In her limited free time, Werb enjoys classical music and modern jazz. She also enjoys cooking and insists that friends love her chocolate truffles, even if she refuses to eat them. Werb was also a potter until she developed an allergy to the mold that grows in clay. Fortunately, pollen does not affect her, so she can still enjoy growing orchids.