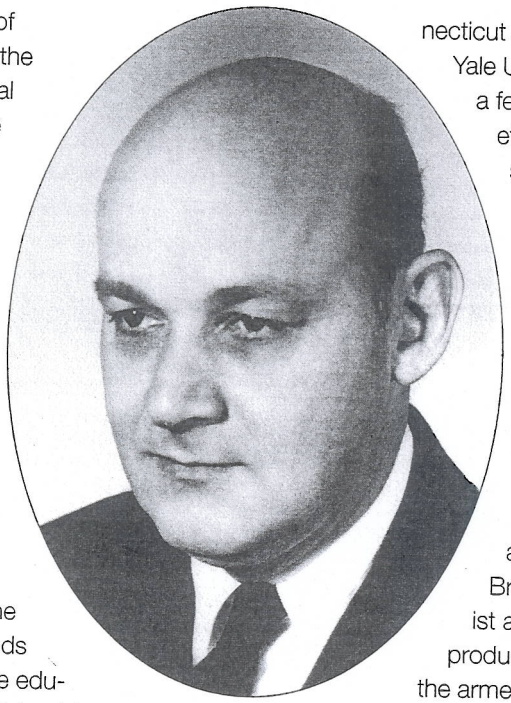
Retrospective: Emil L. Smith (1911–2009)

BY ROBERT L. HILL AND ALEXANDER N. GLAZER

Emil L. Smith, a longtime member of ASBMB and a former member of the *Journal of Biological Chemistry* Editorial Board, passed away on May 31 at the age of 97. He was among the pioneers in the study of protein structure and function from the very beginning of his graduate studies in 1931 and continued as a prominent contributor to these fields for almost 50 years.



Smith was born on July 5, 1911 in New York City, the son of Eastern European immigrants. The immigration officers on Ellis Island had given his father the name Smith. He attended public schools, and while in high school and college, he played the jazz saxophone with various dance bands well enough to pay in part for his college education. At age 16, he was admitted to Columbia University, where he chose a premedical curriculum. In his sophomore year, two gifted teachers sparked his interest in biology and chemistry. He received his bachelor's degree in 1931.

His choice of Selig Hecht as his Ph.D. advisor in the Laboratory of Biophysics at Columbia was remarkably discerning. Noblest George Wald, also a Ph.D. student with Hecht, described him as "one of the most vivid scientific figures of his time; a pioneer in the development of general physiology in this country; and for more than two decades a leader in his chosen field, the physiology of vision." Smith studied aspects of the visual response to flickered light and received his Ph.D. in biophysics in 1937. Other work that he initiated during his Ph.D. studies led to clear proof that chlorophyll in green plants is protein-bound.

Smith received a John Simon Guggenheim Fellowship to continue work on the chlorophyll-protein complex, and from 1938 to 1939, he worked with David Keilin at the Molteno Institute at Cambridge University, England. Forced to return to the United States by the outbreak of World War II, he finished his fellowship with Hubert B. Vickery at the Connecticut Agricultural Experimental Station at Yale University. From 1940 to 1942 he was a fellow with Max Bergmann at the Rockefeller Institute. Bergmann, the last student of Emil Fischer, was regarded as the most eminent protein chemist in the world. His contemporaries in Bergmann's group included William Stein, Stanford Moore, Joseph Fruton, Klaus Hoffman, and Paul Zamecnik, who became lifelong friends. This period set the research directions for his entire career.

From 1942 to 1946, he worked at E.R. Squibb and Sons in New Brunswick, NJ as a senior biochemist and biophysicist guiding mass-scale production of human plasma proteins for the armed forces. In 1946, he moved to the University of Utah College of Medicine as Associate Professor of Biochemistry, Associate Research Professor of Medicine, and head of the Laboratory for the Study of Hereditary and Metabolic Disorders. He was promoted to professor in 1950. Smith left Utah in 1963 to become the chairman of the Department of Biological Chemistry in the new School of Medicine at the University of California, Los Angeles, where he continued a productive research program until his retirement in 1979.

From 1946 to 1958, the main focus of the research in his group was on the characterization, specificity, and mechanism of action of peptidases. From 1958 onward, the focus shifted to the determination of the sequence of diverse proteins: papain, cytochromes *c*, subtilisins, histones, and glutamate dehydrogenases, in that order. These studies led to a stream of novel findings on post-translational modification of proteins and intriguing insights into molecular evolution and protein function that comparative protein sequence analyses could provide.

The textbook, *Principles of Biochemistry* (First Edition, 1954), which he co-authored with Abraham White, Philip Handler, and DeWitt Stetten, was a lifelong source of sat-

isfaction for Smith. Over 25 years, the book went through seven editions, the last of which was published in 1983.

Smith was very active in promoting international scientific cooperation. Most notably, in 1973, as chairman of the Committee for Scholarly Communication with Peoples' Republic of China, he led a delegation to negotiate in Peking the first exchange agreements between the U.S. and Chinese academies, a breakthrough that ended a long period during which there were no contacts between U.S. and Chinese scientists. During that visit, he met with Prime Minister Chou-En-lai, and a picture of the two was prominently displayed in Smith's UCLA office.

Smith received many honors for his scientific achievements, including a Guggenheim Fellowship (1938–1940), election to the National Academy of Sciences (1962), election to the American Academy of Arts and Sciences (1965), election to American Philosophical Society (1973), the Ciba Foundation Gold Medal (1968), and the Stein and Moore Award of the Protein Society (1987).

This is but a brief sketch of the career of a gifted, multidimensional individual. Several reflections offered below add to the picture. We offer our deepest sympathy to Smith's family.

I was an NIH postdoctoral fellow for two years with Emil Smith at the Metabolic Lab, and I remember him for his opinions in many things besides biochemistry, which he freely expressed in the lunchroom where he ate his brown bag lunch with all others in the lab. After a year or so, I decided to write a paper for submission to the Journal of Biological Chemistry *on my work on the proteolytic enzyme leucine amino peptidase. I thought that I could write reasonably well and after giving him the first draft of the paper, I found that he had revised it extensively and saw little of my prose on reading it. As it turned out, we wrote several papers together, and he effectively showed me how to write with clarity and accuracy on the work I had done. This was an invaluable experience that helped me throughout the rest of my career and (that) I could use to help my own students and fellows write acceptably for publication.*

Robert L. Hill
James B. Duke Professor of Biochemistry
Duke University

I did not know Emil Smith well, as he had long since retired when I came to the department in 1994. However one of his findings was embedded in the field of chromatin. That was the unusual and almost complete conservation between peas and cows of the histone H4 amino acid sequence. In other words, H4, a protein that helps form the nucleosomal building block of the chromosome, had hardly changed in some 2 billion years of evolution. This argued for the extreme importance of almost every amino acid of H4.

Subsequently, when we made even large H4 N-terminal deletions in yeast and found them to be viable, this surprised almost everyone in the field. But this allowed us to have viable strains with which to test H4 N terminus function. Two such functions were discovered in our lab. One is the role of the H4 N terminus as a binding site for heterochromatin proteins to control the expression of the silent mating loci. Another is the role of the H4 N-terminal acetylation sites in alleviating repression by the nucleosome. So I am pleased to have added a small chapter to the study of histone function, a study stimulated by the protein sequence analysis of histone H4 started by Emil Smith.

Michael Grunstein
Chair, Department of Biological Chemistry
University of California, Los Angeles

Emil Smith was one of the true pioneers in the development of protein chemistry, particularly in the immediate decades following WWII. He was a contemporary and colleague of the likes of Stein and Moore, Sanger, and Anfinsen and many others who developed and applied methods that allowed the determination of amino acid sequences on an ever-expanding scale. He worked on a variety of proteins, particularly proteases, cytochromes, histones, and dehydrogenases, and this work was instrumental in providing some of the earliest molecular evidence for Darwinian evolution.

He and his colleagues were also leaders in developing reagents for the chemical modification of proteins and in using these approaches as probes for protein structure-function relationships. They have remained valuable tools that are still used to evaluate three-dimensional structures and as adjuncts to various molecular biological manipulations. In fact, it was the appreciation of the molecular bases of protein function that came from Smith's work, and from many laboratories of the same time frame, that was indeed essential to the development of both structural and molecular biology.

In the latter stages of his active career, Smith played a major role in the founding of the Protein Society, and this remains a tangible legacy of his prominent place in the history of the development of protein chemistry as a central focus in biological research.

Ralph A. Bradshaw
Professor, Chemistry and Pharmaceutical Chemistry
Deputy Director, Mass Spectrometry Facility
University of California, San Francisco

One noontime, as a relatively young UCLA faculty member, I was walking back to campus from an errand in nearby Westwood Village. I ran into Emil Smith, headed the other way. He was the longtime chair of the medical school department of biological chemistry, always friendly to me, but with such a vast store of information that he shared forcefully with those around him, he could be scary. Emil smiled and asked, "What's new?" My mind raced. What bit of news could I possibly come up with that would be worthy of reporting to this intellect of a thousand detailed interests, always possessed of full knowledge about each of them?

With only a slight pause, I hit on it. "Lucy and I were just in London," I replied, "and saw a fascinating new play by Peter Shaffer called "Amadeus."" "Oh?" asked Emil, "What's it about?" "It's about Mozart," I said, "and his relationship with his contemporary composer Salieri, who was driven into hatred of Mozart by jealousy of his musical gifts." I started to fill in the plot, but Emil interrupted. Chortling, he said, "He stole it!" "Shaffer stole it?" I asked in disbelief. "Sure," answered Emil. "That was a play by Pushkin, written in 1830." I could only mumble, "It was?" "Yes," said Emil over his shoulder as he strode off, "and it was later made into an opera by Rimsky-Korsakov."

Crestfallen from my latest failed attempt to convey something new and worthwhile to Emil Smith, I walked on to my office. Then a few weeks later, I happened on The Complete Pushkin in my friend's bookshelf. I leafed through it and was not surprised to find a short play, "Mozart and Salieri," with some of the same elements as "Amadeus."

But what else should I have expected? In previous encounters I had heard Emil hold forth on topics as diverse as the fundamental change in European civilization brought about by the invention of the horseshoe and the misattribution of a cello concerto to Haydn. His interests extended to art, where he had amassed a magnificent collection of pre-Columbian statuettes, and an equally impressive house full of prints, including several of the most famous by Edward Hopper. In music, Emil knew the classical repertoire in detail and also loved jazz. He told me that he had paid for his schooling by playing saxophone in jazz bands, but I could never persuade him to give me a demonstration.

Emil possessed as retentive a memory as anyone I ever met, and it stayed with him until the end of his life. A few months before Emil's death, Dick Dickerson interviewed him about the history of the UCLA Molecular Biology Institute, in which Emil played an early role, including helping to recruit Paul Boyer as its director. In that interview, Emil was able to recall the precise day on which he first visited UCLA some 46 years before.

With Emil Smith's passing, we have lost a vast store of memories and as enthusiastic a raconteur as you could ever hope to encounter.

David Eisenberg
Investigator, Howard Hughes Medical Institute
Director UCLA-DOE Institute for Genomics and Proteomics Departments of Biological Chemistry and Chemistry & Biochemistry

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Robert L. Hill is James B. Duke Professor of Biochemistry at Duke University and can be reached at hill@biochem.duke.edu. Alexander N. Glazer is professor of the Graduate School Division of Biochemistry and Molecular Biology at the University of California, Berkeley, and can be reached at glazer@berkeley.edu.