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## 1999

### Philip Siekevitz

Phil Siekevitz claims to be "just a second generation founder" of the ASCB, but his association with its early leadership is unmistakable. Before becoming President of the Society in 1966, Siekevitz had collaborated with Van Potter and George Palade, both of whom served as President of the Society. The Rockefeller University, where Siekevitz is an emeritus professor, is the birthplace of the ASCB, so Siekevitz' history reflects that of the ASCB.

Siekevitz's birth in 1918 won his father, a Jewish immigrant dressmaker from South Philadelphia, a reprieve from World War I as a new parent. There, Siekevitz attended Olney High School and developed his early interest in biology.

Siekevitz was the first in his family to attend college, enrolling in the Philadelphia College of Pharmacy & Science. He chose that school because it was "cheap," and allowed him to live at home, even though he had to take two different buses – an hour each way – to get there. His primary interest even then was biochemistry. He wanted to go on to graduate school, but in his final year of college he was drafted into World War II; his effort to defer induction bought him just one year to graduate.

After graduating in 1942, Siekevitz entered the Army. His college chemistry credential led to his assignment to a Georgia decontamination unit to respond to chemical warfare attacks. He learned about chemical agents and how to decontaminate them, but "there wasn't much science to it. You might say we were just janitors." So Siekevitz requested a transfer, which resulted in his deployment as a lab technician to a San Bernardino, California Air Force supply base for the Pacific war. There, Siekevitz learned how to perform microscopic and chemical examinations. For this special skill, Siekevitz' service was extended by several months after the war to apply "the Wassermann test" for syphilis to returning troops.

After almost four years in the service, thanks to the GI Bill, Siekevitz was able to attend the University of California, Berkeley, whose biochemistry department was already highly regarded. Siekevitz was one of six entering the Ph.D. program in 1945.

Amino acid metabolism offered a succinct problem that Siekevitz was able to solve through the use of a nearby cyclotron source of C14, which could be used for metabolic studies. David Greenberg, who headed the biochemistry program at Berkeley, hired an organic chemist for this purpose, enabling Siekevitz to undertake his work on amino acid metabolism using a combination of biochemistry and autoradiography. Siekevitz and his Berkeley colleagues were among the earliest to use radioactive amino acids to study in vitro protein synthesis using cells and tissue slices. Greenberg, however, urged Siekevitz to concentrate on amino acid metabolism because this was a relatively unexplored field at the time. Siekevitz was able to finish his Ph.D. in three and a half years.

Returning to his interest in in vitro protein synthesis, Greenberg helped Siekevitz win one of the NIH's first post-doctoral fellowships in 1949 to work at Harvard's Massachusetts General Hospital under Paul Zameenik. Siekevitz and his new bride, Rebecca, who had studied library science at Berkeley, found a small apartment in Brookline, just a short trolley ride from Mass General. Siekevitz collaborated with Fritz Lipman's lab in mitochondrial biochemistry. While at Harvard, Siekevitz was among the first to use subcellular fractions, microsomes, mitochondria, and nuclei to look at protein synthesis. Prior to that, this type of work was done with whole homogenates or tissue slices. He included mitochondria in his in vitro system, which provided the ATP required for protein syntheses. The realization of the role of mitochondria led him to further work in the field.

In 1951 Siekevitz took a new oncology fellowship at the University of Wisconsin Madison for two reasons: Van R. Potter, a leader in mitochondrial metabolism, was there; and Siekevitz' wife was from Milwaukee where they had been married two years earlier. The Wisconsin years were productive for Siekevitz, professionally and personally: in addition to publishing seven papers in three years, two daughters, Ruth and Miriam, were born.

Just as Siekevitz was considering his next move, George Palade, having read Siekevitz' early work on in vitro protein synthesis, invited Siekevitz to come to work with him at Rockefeller. Siekevitz was delighted to join the prestigious scientists at the famous Rockefeller Institute and moved his family to New York in 1954. The laboratory he joined included modern cell biology founding fathers Keith Porter and Palade. George Pappas and Don Fawcett (later the ASCB's first President) were young investigators there. Monty Moses and Michael Watson arrived along with Siekevitz.

Siekevitz spent the next twenty years working with Palade. At first they studied the pancreas as a system for protein synthesis and secretion. Using the "Palade granules" (later named ribosomes), the small particles that are attached to the membranes of the ER, as means of identification of the ER, they

conclusively demonstrated that the microsomal fraction consists of fragments of the ER generated during tissue homogenization. Further work using radioactive amino acids showed first that the secretory enzymes of the pancreas were synthesized on the attached ribosomes, then transversed the ER membrane into the lumen of the ER, and appeared in the zymogen granules that are known to accumulate the enzymes before they are secreted into the lumen of the intestine.

Siekevitz then became interested in membranes and how they were formed. Inspired by a paper that showed that the liver microsomal enzyme glucose-6 phosphase was not present in the ER of liver cells at birth, Siekevitz decided to study other microsomal enzymes. He and his postdocs found that various microsomal enzymes had different time courses of appearance in the ER. They demonstrated that there is a turnover of enzymes in the ER, with each protein having a characteristic half-life. Siekevitz inferred the presence of a substructure where newly synthesized enzymes were deposited.

In 1974, Palade left Rockefeller for Yale. Siekevitz remained at "the Rock," changing focus to the study of membranes from the nervous system, first by trying to isolate the membranes at the synapse. As he was becoming convinced that this work was a dead-end, by chance Siekevitz discovered the postsynaptic density, a finding made a year earlier by Carl Cotman. Siekevitz determined that the density represented a separate subcellular structure that was attached to the post-synaptic membrane. For the next sixteen years, Siekevitz and his colleagues studied the postsynaptic density, determining which proteins, such as neurotransmitter receptors and ion channels, are attached to it. They found protein kinases there, as well as other enzymes, and began to unravel interactions between the many protein components of PSD.

One of Siekevitz's longtime friends and colleagues, David Sabatini, says that Siekevitz's "enthusiasm was infectious and he set a marvelous example with his own intense involvement in experiments, readiness to discuss novel ideas, and willingness to give his junior colleagues... freedom."

For his contributions, Siekevitz was elected to the National Academy of Sciences in 1975 and President of the New York Academy of Sciences in 1976.

Today, Siekevitz is retired from re-search and devotes much of his time to writing the history of cell biology at Rockefeller in anticipation of its 100th anniversary in 2001, tentatively entitled *The Origins of Modern Cell Biology*, with Carol Moberg. Siekevitz observes that Rockefeller's scientific strengths have evolved dramatically by those who have worked there – starting with virology and evolving into cell biology.

Siekevitz notes that the *Journal of Cell Biology* (originally *Biophysical and Biochemical Cytology*) was founded by the same scientists who founded the ASCB, and both the journal and the Society were based at Rockefeller. Siekevitz was also the editor of the first cell biology textbook in 1963, called *Cell Structure and Function*, printed in its third edition in 1991.

Siekevitz' contributions to the early development of the ASCB were many. Emma Shelton, Secretary of the Society from 1978-1981, recalls that in the beginning, the ASCB was very small and democratic. "Everyone went to the business meetings of the Society and Siekevitz had a comment on most issues. He was an ebullient character," says Shelton. The third ASCB Annual Meeting, in 1963, was held at the Commodore Hotel in New York City. Siekevitz served as a "one-man Local Arrangements Committee." A few years later, he attended the International Congress of Biochemistry in Stockholm, from which he brought home the idea of a poster session to the fledgling ASCB – now a staple of its meeting. At that same ASCB meeting, Siekevitz invited high school students to see the exhibits and some of the sessions. This was the origin of today's highly successful ASCB high school program. Siekevitz was also an early contributor to the Society's policy activity, having served as Chairman of what was then called the Science and Public Policy Committee. He advocated that the Society not limit its focus to NIH funding. (Paul Berg, the ASCB Public Policy Committee's current Chair, follows this philosophy today). Micheline Federman, a young student when she attended the first ASCB meeting, remembers that before Siekevitz, "I had never heard a scientist talk about the fact that we, the scientists, had a duty, an obligation, to educate the public who were after all funding us, about what we were doing."

While still in graduate school, Siekevitz wrote two "long-short" stories that were eventually published in a series called *New Directions*. He continues to write some fiction and has also written science and public policy articles for *The Nation*, *The New York Times* and *Nature*.

The Siekevitzs have been living in the same apartment building in Manhattan for thirty-three years. When they first arrived in New York with their young daughters, they lived in housing provided and subsidized by Rockefeller. Rebecca didn't like it, and jumped at the suggestion when George Pappas, then Keith Porter's postdoc, urged that the family move to Astoria, Queens, where he was. But when the Siekevitz girls enrolled in Hunter High School, the family moved back to Manhattan and never left. Their neighborhood, at 72nd & Broadway, was run-down in the early years, but over time has been gentrified. Rebecca worked for many years at the Metropolitan Museum of Art and for the New York Public Library, where she became the Head of Circulation for the Art Library. Ruth Siekevitz graduated from Clark University and stayed in the City, where she now works for the Avon Corporation. Miriam received her Ph.D. in Immunology at MIT. After graduate school she took postdocs in Germany and at the NIH before becoming a member of the immunology department at Mt. Sinai Medical Center. After a stint at a biotech company in California, she eventually left and enrolled in Stanford Law School.