Keith R. Porter

1912–1997

BIOGRAPHICAL *Memoirs*

A Biographical Memoir by
Lee D. Peachey

©2013 National Academy of Sciences.
Any opinions expressed in this memoir are those of the author and do not necessarily reflect the views of the National Academy of Sciences.

NATIONAL ACADEMY OF SCIENCES

KEITH ROBERTS **PORTER**

June 11, 1912 – May 2, 1997

Elected to the NAS, 1964

By Lee D. Peachey

Keith Roberts Porter, a member of the National Academy of Sciences since 1964, died in Bryn Mawr, Pennsylvania, on May 2, 1997, at the age of 84. He was buried in the church cemetery in Pleasant Valley, Nova Scotia, near to where he was born and lived as a child. Interested in biology from an early age, he went on to do scientific research that justifiably earned him the title of being "The Father of Cell Biology." His many contributions to cell biology, along with those of the many graduate students, post-doctoral fellows, and other collaborators who worked with him at five universities, constitute a formidable body of achievement and often groundbreaking scientific advances that are hard to match.

If Porter was its father, then the mother of Cell Biology was the electron microscope. Porter was front and center in the 1940s when electron microscopes first were used in studies of cell structure. He developed many of the new specimen preparation methods that were necessary for the success of biological electron microscopy, and he pioneered their use in studies of many kinds of cells and cellular components. He was a founder of the Tissue Culture Society, of the American Society for Cell Biology, and of the journal that later became the *Journal of Cell Biology*. His manifold contributions have been recognized with many awards and honorary degrees. Because Porter's story is intimately tied to the story of the revolution in structural biology that followed the introduction of electron microscopy to studies of biological cells and tissues, it would not be possible to tell one of these stories without also telling the other.

Keith Porter was born in Yarmouth, Nova Scotia, on June 11, 1912, the third child and only son of Aaron Crosby Porter (1873–1949) and Josephine Roberts Porter (who died in 1953). He attended high school at the Yarmouth County Academy. After graduating

in 1930, he matriculated at Acadia University in Wolfville, Nova Scotia, where his activities included class government (senior treasurer), music (trumpet and assistant director of the school band), drama (stage manager), and chairmanship of the Undergraduate Biology Assembly, attesting to his interest in the arts, biology, and natural history, as well as to an early and life-long tendency to be a leader. He graduated in 1934 from Acadia with a bachelor of science degree in biology and chemistry, and he went to graduate school at Harvard University for master of arts (1935) and PhD (1938) degrees in biology, with his thesis research on frog development. Also in 1938, he married Katherine Elizabeth Lingley, a former classmate at Acadia. Elizabeth also was born in 1912, in Massachusetts, and had moved to Nova Scotia with her family when she was a young girl.

Keith Porter in 1934 at his graduation from Acadia University.

For one year after graduating from Harvard, Keith was a National Research Fellow in zoology at Princeton University, where he continued his study of frog development. He invented a method for producing androgenetic haploid frog embryos (genetically male parent only) by removing the maternal chromosomes from a fertilized egg "by means of a glass needle possessing a very fine but rigid point...inserted through the jelly capsule and into the cortex of the egg" and with "a slight upward motion" lifting all of the maternal chromosomes out of the egg, leaving "only the male chromatin present to influence the development which follows" (Porter 1939). The majority of these operated eggs began developing as haploid embryos with "practically perfect" development for 3 days. Then their development gradually became poor, and differences appeared among individuals. But almost all survived for 8-10 days as tadpoles with considerable differentiation of internal organs. Porter's new technique opened up the possibility that by using eggs and sperm from two morphologically distinct forms of frogs of the same species, he could separate the contributions of the (male) nucleus and the (female) cytoplasm in early development. But he didn't complete this work before he finished his year at Princeton.

In 1939, James B. Murphy was head of the Laboratory for Pathology and Bacteriology at the Rockefeller Institute for Medical Research in New York City. Porter knew of Murphy's work on cancer, as well as his belief that normal development and tumor-progression were related processes. Porter wrote to Murphy in June of 1939 inquiring about a position in his laboratory and suggesting that an embryologist, such as himself, should be well suited to study tumor development. Knowing of Porter's skills in working with isolated cells and developing tissues at Princeton, Murphy invited him to join his laboratory in September 1939 (Moberg 2012). He wanted Porter to use these skills to follow up on some work done by Albert Claude, a Belgian M.D. working in Murphy's laboratory. Claude had used highspeed centrifugation to concentrate a particulate agent in cell-free filtrates from chicken sarcoma tissue that Peyton Rous had shown, at Rockefeller in 1911, could transmit tumors to healthy chickens (Claude 1937). Claude also found that he could isolate similar particles from normal tissue using the same procedures, enforcing a possible relationship between normal development and malignant cell growth (Claude 1938).

At first, Murphy wanted Porter to investigate the ability of chemical carcinogens and cell fractions, such as Claude's particles, to lead to cancer when applied to chick embryonic membranes. Porter's early results in these experiments were not promising. In a report to Murphy in March 1941, Porter wrote that he was shifting his attention to a broader study of "the basic biological problems of growth and differentiation both as to extra and intra-cellular factors affecting these processes," and added, diplomatically, "Indirectly and at some future date such information may be essential to an explanation of the origin of tumorous growths." With Murphy's encouragement, Porter then returned to his earlier studies of nucleo-cytoplasmic relationships in developing frogs (Porter 1941).

This work was interrupted for part of the next two years after Keith and Elizabeth Porter were confined as patients in a tuberculosis sanatorium. True to form, Keith soon found his way into the hospital laboratory where diagnostic microscopy was carried out, and he began collaborating with Diran Yegian in a study of variations in the shapes and staining properties of cultured tubercle bacilli that had been observed earlier by light microscopy. Porter's microscopic re-examination of these presumed normal variants showed that the variation was due less to actual differences in the cells themselves than to artifacts caused by the mechanical and staining procedures used to prepare them for microscopy. This combination of careful microscopic observation and cautious questioning of reported observations would become a hallmark of Porter's scientific career.

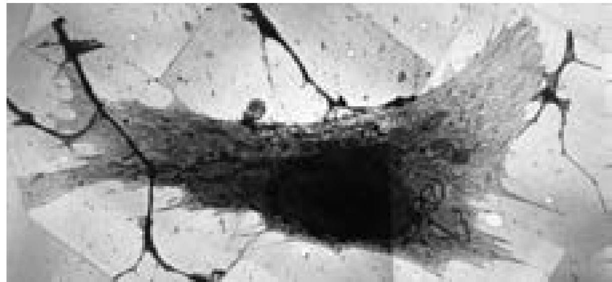
When Porter returned to Murphy's laboratory in 1943, he began to set up in vitro cultures of mouse cells and chick embryonic tissue, following a report from the National Cancer Institute describing a tissue culture method for studying chemical carcinogenesis. Porter found that tissue culture was difficult. There were few standards for culture conditions or culture media, and the results often were inconsistent. Little useful information came from these experiments. It was much like his earlier experiments with tubercle bacilli. Uncertain methodology led to uncertain results. However, the simultaneous presence of Claude's cell fractions and Porter's cell cultures in the Murphy laboratory unexpectedly led to a major revolution in cytology, triggered by the first use of an electron microscope to study these cells and cell fractions.

The background for this revolution had begun in Germany when Ernst Abbe showed that the smallest structural detail that could be seen in a light microscope was physically limited by the wavelength of light to about one-quarter of a micrometer (Abbe 1873). Claude estimated from his centrifuge data that his small particles fell below this limiting size, explaining why they could be detected as points of light in a dark-field microscope, but not imaged in the usual sense or their sizes measured. However, early in the 20th Century, physicists had discovered that beams of electrons have wave properties similar to those of light, but with much shorter wavelengths. That raised the possibility of a microscope using electrons in place of light, with a limiting resolution possibly hundreds of times smaller than Abbe's limit. Such electron microscopes, using magnetic coils as lenses, became available in Germany in 1939 and in the United States two years later. Early images of bacteria and viruses were little more than shadowy outlines of these tiny objects, but they demonstrated that electron microscopy indeed offered a significant improvement in resolution for studies of biological structure at a very fine level. It also became clear that much work on preparation methods would be needed before this potential could be realized with biological specimens, in part because of the damaging effects of the vacuum and intense radiation inside the electron microscope.

In 1943, Albert Gessler was the research director at the Interchemical Corporation in New York City and a man with broad interests. He had read an article in *Science* about Claude's frustration in trying to visualize his small particles, which by then were called microsomes, using light microscopy (Claude 1943). Gessler's research department had an RCA Model EMB electron microscope, the first in New York City, which was used to image commercial particulates such as paint pigments and abrasives, which also were too small for satisfactory imaging by light microscopy. Gessler contacted Claude and arranged for him to meet Ernest Fullam, who operated Interchemical's electron

Ernest Fullam at the RCA EMB electron microscope in 1941.

microscope. Fullam showed Claude how to put specimens onto thin plastic films stretched across small metal grids for introduction into the microscope, and told him they had to be completely dry to withstand the vacuum inside the microscope. Subsequently, Claude spread samples of two of his cell fractions on such grids and dried them, and late in 1944, he and Fullam recorded electron micrographs of these fractions. The images of the larger mitochondrial fraction showed the boundaries of the mitochondria more clearly than light microscopy ever could, and it even showed hints of internal structure never seen before within the mitochondria (Claude and Fullam 1945). One image in this paper, of the smaller microsome fraction, showed no such internal detail, but the profiles could be seen to be much smaller than those of mitochondria.



First image of a complete eukaryotic cell recorded using electron microscopy, July 1944.

Porter was with Claude and Fullam during one of their electron microscopy sessions. Porter was impressed by the unprecedented quality of the images of the tiny cell fractions, but he was concerned that there would be little hope for imaging anything as thick as a complete cell because of the limited penetrating power of the electron beam. However, he had noted that some of his cultured cells became extremely thin along their margins as they spread out on their substrates, suggesting that these cell margins might be thin enough for electron microscopy. Using some of his delicate skills from working with frog eggs and embryos, he mounted some

thinly spread cultured chick embryo fibroblasts, which had been grown on thin plastic films, onto electron microscope specimen grids, working underwater to avoid damaging surface tension effects on the delicate cells. He then briefly exposed the grids with the cells to vapors from osmium tetroxide to preserve them, and he dried them in air. In the evening of July 6, 1944, he and Fullam put these grids into the electron microscope. They located one whole cell that was lying over a single opening in the metal grid, where they could photograph it in its entirety on five glass plates. When these images were fitted together into a montage, the world had its first electron micrograph of a eukaryotic cell. The thick center portion of the cell, with its nucleus, appeared too dark to show any internal structure. But the margins of the cell, as Porter had hoped, were thin enough to clearly show intracellular structures that had never been seen before. In particular, he noted a reticular structure in the peripheral, or endoplasmic, regions of the cell. This new structure he named the endoplasmic reticulum, and it quickly became a subject for intensive study in many kinds of cells by Porter and others.

Porter had not forgotten Murphy's dream of identifying the source of tumors in chickens, or of the need to improve cell culture methods. The electron microscope had been a distraction from those efforts for two years, but in the end it became a source of new progress. In a report to Murphy (Porter 1947) he wrote:

> *The accumulated studies of the past two years make it clear beyond any doubt that cultured cells present unique possibilities for cytological studies with the electron microscope. Besides having the essential physical quality of thinness [compared to cells in tissues], they possess the valuable characteristic of wholeness [compared to cell fractions]. With the acquisition by cultured tissue cells of this tremendously important attribute, it becomes imperative to improve the procedures of culturing. That present culture methods are crude is a handicap. But this is probably only a temporary situation and with its correction the advantages of cultured cells will be greatly enhanced.*

Subsequently, Porter became a driving force for the improvement and standardization of tissue culture procedures and growth media. He pressed for the creation of a free-standing society, rather than a government agency, to promote freer and more expeditious activity in cell culture. As a result, the Tissue Culture Commission was founded in 1946, with Porter as its chairman and an international executive committee and

membership. In 1949, the Commission became the Tissue Culture Association and, under Porter's supervision, set up a centralized media testing and certification laboratory at the Sloane-Kettering Institute in New York, with support from the American Cancer Society and from two commercial laboratories willing to support this new and uncharted business. To correct what Porter perceived as a lack of people trained in the art of tissue culture, he also initiated a series of training courses, equipped their laboratories, and personally developed their training materials (Moberg 1996).

Eventually Porter's work with cells in culture led to results directly related to cancer. In a paper in 1947 with Claude and Edward Pickels, Porter reported success in culturing the Rous sarcoma in chicken cells and in visualizing "virus-like" particles in the cytoplasm of these cells using the electron microscope. They were cautious about saying that the identification of the particles as viruses was certain, writing only that they appeared "to possess properties commonly attributed to viruses" and noting that they were not present in normal cells, as Claude's microsomes had been. The next year, Porter and Helen Thompson observed virus-like particles on the surfaces of and inside mammary carcinoma cells of mice. These seminal studies led to the electron microscope becoming an important tool for the identification and study of viruses both in cells and in isolation. Other isolated cell components and extracellular fibrillar materials also were thin enough for electron microscopy. As examples, Porter and Sam Granick studied the structure of chloroplasts isolated from plant cells, and he and Parker Vanamee studied the solvation and reconstitution of fibrils of collagen, a key protein in the structure of connective tissue.

Even with these successes, it soon became clear that the electron microscope had limitations in biology. It had been used successfully for the examination of cell fractions, extracellular fibrils, and the thinly spread margins of whole cells, all of which were inherently thin. Even these had to be chemically preserved (fixed) to a much finer degree than had been required for light microscopy, and then they had to be dried. By comparison, light microscopy could be done on whole cells while they still were alive and functioning in their normal, aqueous environments. The comparison was not unlike a snapshot versus a movie. The only advantage of electron microscopy was its ability to resolve much, much smaller structural details. But the time was right for that. Biochemistry was beginning to provide more detailed information about specific proteins, carbohydrates, and lipids and their roles in animal and plant development, growth, and function. But if electron microscopy was to provide the structural framework for these results, it would need to be applied widely, including to whole cells and tissues. This meant that a lot of work on specimen preparation methods remained to be done.

For his part, Porter began to look for ways to cut appropriately thin slices of tissue samples for study by electron microscopy. Microtomes with steel knives had been used for many years to slice paraffin-embedded tissues into sections suitable for light microscopy, and sections as thin as a few micrometers were being cutroutinely. But section thicknesses less than about one tenth micrometer, as would be needed for electron microscopy, seemed out of reach. Some workers had modified existing microtomes toward this end, but with only limited success. Once again, focusing first on methods, Porter and Josef Blum, the head of the Rockefeller Institute machine shop, developed what became known as the Porter-Blum microtome. Other laboratories found better embedding materials, including epoxy resins. Knives made from broken glass were found to be sharper than steel knives, though less durable. More durable, diamond knives were developed by Humberto Fernandez-Moran in Venezuela, who sent an early one of these to Porter (Pease and Porter 1981). He cherished that knife, named it "Old Faithful," and personally used it for the rest of his career. By the 1950s, sectioning of tissues for electron microscopy became routine, and rapid progress followed in studies of the internal structure of many types of cells, especially the cytoplasm and its components. The nucleus, which had long attracted the most attention in cytology, took a back seat. The formerly bland "ground substance" of the cytoplasm was shown to contain many new kinds of organelles whose detailed structures were photographed, illustrated, described, and debated as they were examined in many types of cells from many species of animals and plants. A true revolution in the study of the structure of cells was beginning.

Albert Claude had returned to Belgium in 1949 to head a cancer institute, and James Murphy retired in 1950. In 1953, Herbert Gasser, the director of the Rockefeller Institute since 1935 and a man with great wisdom and vision, promoted Porter to associate member and put him in charge of a new Laboratory of Cytology, not limited to research on cancer. Porter was joined by George Palade, who had come to Rockefeller in 1946, and they shared the responsibility of developing this laboratory into a premier center for the study of cell fine structure. Scientists came from all over the world to learn the new methods of electron microscopy, and they took this knowledge back to their own laboratories as electron microscopy spread its reach. By 1954, Gasser had retired and Detlev Bronk became the new director of the Rockefeller Institute. In 1956, he promoted both Porter and Palade to full members and made them professors as well, after the Institute had transformed itself into a university and started to admit graduate students in 1955. Through the 1950s, Porter's own work at Rockefeller shifted its emphasis from technique development to application of the electron microscope to study

the structure of cells in tissues. In the period from 1954 to 1960 he published thirty research papers on a wide variety of cells, with several collaborators.

Established scientific societies and journals also got Keith Porter's attention during the 1950s. As one example, in 1953 Stanley Bennett and Porter published their studies of thin sections of chicken striated muscle cells in the *American Journal of Anatomy*. Beyond elucidating the form of the endoplasmic reticulum in striated muscle cells, that paper had an additional and beneficial effect on the publication of results from electron microscopy. Electron micrographs inherently contain many fine details, and it is important that the published versions of these images should adequately show these details, since they are the data upon which the scientific interpretations are based. The quality of reproduction of the micrographs in their 1953 muscle paper was a major disappointment to Porter and Bennett. In addition, a paper that Don Fawcett and Porter submitted in 1953 on the fine structure of ciliated cells to the *Journal of Experimental Medicine* was rejected, partly on the grounds that it was too morphological and not sufficiently medical. When Gasser heard of this, he suggested to Porter the creation of a new journal that would better serve the special needs of electron microscopists. Fawcett and Porter, not wanting to wait for a new journal, submitted their paper on cilia to the *Journal of Morphology*, which accepted and published it in 1954. Sadly, the quality of the published reproductions of the 8 plates with 32 micrographs in this important paper was almost as disappointing as that in the earlier paper in the *American Journal of Anatomy*.

With encouragement from Porter, Bennett wrote to Bronk making a strong case for a new journal, such as Gasser had suggested, with editorial policies and reproduction of illustrations suitable for electron microscopy. Bronk was convinced, and he convened a group of electron microscopists, including Porter and Fawcett, during a scientific meeting in Atlantic City in April of 1954, where he proposed that such a journal be published by the Rockefeller Press. The group gladly agreed and chose as its name: the *Journal of Biophysical and Biochemical Cytology*. Presumably, the adjectives were intended to encourage greater emphasis on the cytoplasm, where much of the cell's physical and chemical activities take place, rather than on genetic aspects of the nucleus and chromosomes, which had dominated cytology for decades. Thus the *JBBC* came into being, with its first issue in January of 1955. Many of the Atlantic City group sat on its first editorial board, and Porter was managing editor until 1964 (Porter and Bennett 1981). The reproduction of electron micrographs was of the highest quality, not from the start, but it improved after much careful monitoring and pressure from Porter. As a result of his urging, the Rockefeller Press adopted finer screening methods for engraving the plates,

a better grade of paper for printing micrographs, and even more careful attention to inking during the press run. In 1962, after cell biology had become a field unto itself, the name was changed to the *Journal of Cell Biology (JCB)*.

Keith Porter contributed in other ways to the spread of cell biology. He organized a "Conference on Tissue Fine Structure," which was held at Arden House in Harriman, New York, in January of 1956 and was attended by more than one hundred investigators. The proceedings were published as a supplemental issue in Volume 2 of the *JBBC*, providing to the world an outline and a progress report for cell biology. Many biological specimens that had been studied earlier by light microscopy were receiving a fresh look in electron microscopes. In 1960, Porter chaired the group of cell biologists that organized the American Society for Cell Biology, with encouragement from the Tissue Culture Association and the Cell Biology Study Section of the Public Health Service. The ASCB held its first meeting in Chicago in 1961 and continues to this day as a thriving institution with well-attended and energetic annual meetings.

Porter left Rockefeller in 1961, partly because of frustration with living in New York and partly from having to spend more time on administration than in the laboratory, and he moved to the Biological Laboratories at Harvard, which he chaired until 1967. The flurry of activity in the study of cell "fine structure" that had been released after 1945 continued unabated while he was at Harvard. The electron micrographs Porter published were of the highest quality, and his papers provided fresh information interpreted in a way that one began to recognize as uniquely Porter. He had an almost uncanny ability to look at static electron micrographs of cells and "see" what the cell was doing, or at least what it was equipped to do. Porter acknowledged that he had this talent, he was quite proud of it, and he didn't consider it in the least unscientific. He knew that functional conclusions drawn from static images are only hypotheses, not proven facts. But he also knew that these hypotheses were essential steps in discovering the true functions of cell structures, which in the end was the goal. Porter, and many of the best biological microscopists of that time and before, found ways to test their hypotheses, looking for similar features in other types of cells with similar functions, or by experimentally altering a cell's functional state and then looking for correlated changes in structure. Cell biology was becoming a dynamic field, studying dynamic activities of cells.

Among Porter's specific interests at Harvard was the study of microtubules in both plant and animal cells, done in collaboration with Myron Ledbetter, Lew Tilney, Dick McIntosh, Mark McNiven, and Breck Byers. Their results confirmed the common 9+2

pattern of microtubules in cilia of new kinds of cells and elucidated the roles that cytoplasmic microtubules play in the determination of cell shape and intracellular movements, such as the migration of cytoplasmic pigment granules in chromatophores of fish that adaptively change color to match their surroundings. There were studies of the uptake of proteins and lipids by cells with Tom Roth, of the T-tubular invaginations of the surface membranes in striated muscle cells with Clara Franzini-Armstrong, and of cytoplasmic filaments with Ian Buckley. Porter also began to develop an integrative view of cell fine structure, and wrote several reviews in this area (Porter 1961, 1963, 1966). With Mary Bonneville, he published *An Introduction to the Fine Structure of Cells and Tissues* in 1963. This popular atlas filled a gap left by textbooks of biology and histology that still illustrated only results from light microscopy. It had a set of typically superb, full-page electron micrographs, with brief descriptions of each and little general text material, so it was suitable as a supplement to the current texts. It had six English editions and was translated into German, Italian, French, and Spanish.

In 1968, after seven years at Harvard, Keith Porter moved to the University of Colorado at Boulder as professor and chairman of a new Department of Molecular, Cellular, and Developmental Biology. As much as he and Elizabeth had liked living in Cambridge, within walking distance of Harvard Square, and within two hours of their house in Woods Hole on Cape Cod, new challenges called to Porter. Colorado offered Keith a new environment housed in a new Biosciences Building, and Elizabeth quickly fell in love with Colorado. Keith was personally active in recruiting new faculty and getting support for them from within the University. His popularity in teaching won him a Teaching Recognition Award in his first year there. His research output at Colorado was prolific: more than 130 publications, half of them original research papers. He set an infectious example with his hard work and high productivity, and his department grew in size and developed a vigorous research and teaching environment. Early on, he set up a Laboratory for High Voltage Electron Microscopy as an NIH-funded national research resource. Its huge, 1000 kV high-voltage electron microscope (HVEM) had ten times the accelerating voltage of most electron microscopes, and this greatly increased its penetration though thick specimens and eased somewhat the longstanding requirement for very thin ones. Many scientists, including the present author, from the United States and other countries used the HVEM to study whole cells and sections of embedded tissues up to ten micrometers thick. By tilting the specimen slightly between two exposures and viewing the two images stereoscopically, Porter could visualize the full thickness of an intact cell in three dimensions, at the highest resolution. He must

have reflected back to the excitement of seeing that first whole cell in 1945, in images of much less quality by comparison.

The HVEM led to renewed interest in the cytomatrix, which earlier had been called the hyaloplasm or cytoplasmic ground substance. This part of the cell's cytoplasm fills the "empty" space between and around the so-called "formed elements" of the cell: the nuclei, mitochondria, granules, etc. It had little observable structure when viewed in the light microscope, though some of its physical properties suggested that it might be some kind of gel. It was difficult to see in thin sections in the electron microscope, since its structure was irregular and very much three-dimensional. In the HVEM, Porter, with John Wolosewick, Mark Ellisman, and Mark McNiven, saw it as a three-dimensional "microtrabecular" lattice and suggested that it somehow supports or contains the organelles of the cell, with the possible exception of the mitochondria. While details of this description were met with skepticism in some quarters, it did renew interest in this important and previously neglected part of the cell. As a logical extension of the three dimensionality of cells as seen in the HVEM, Porter also used the scanning electron microscope at Colorado to image the surfaces of cells in culture with Virginia Fonte, David Prescott, J. Frye, and G. J. Todaro.

Keith Porter, Ernest Fullam, and Albert Claude at a meeting in the 1980's.

Porter's interest in the bigger view of cell biology hadn't diminished at Colorado. He initiated the planning of the first International Congress of Cell Biology during the country's bicentennial year, hosted by the ASCB. It was held in Boston, in conjunction with the 16th annual meeting of the ASCB, with Porter as program chairman and the Congress office located in Boulder. The meeting, held September 5–10, 1976, was attended by about 4,000 participants from 41 countries and with 1,270 abstracts from contributors. Porter attended the gala reception dressed as Benjamin Franklin, in the spirit of the year.

The University of Colorado recognized Porter's contributions with the Robert L. Stearns Award for Distinguished Service in 1973. When he retired in 1982, at age 70, the university awarded him an honorary degree and renamed "his" building Porter Biosciences.

Keith Porter at the dedication of the Porter Biosciences Building in 1982.

The Wanderlust struck again in 1984, when Porter moved from Colorado to the University of Maryland Baltimore County in Catonsville to be the Wilson Elkins Distinguished Professor and Chairman of the Department of Biological Sciences. In addition to his duties as department chairman, he continued an active research program, his interests moving toward studies of living cells. Some of this work was in collaboration with his last graduate student at Colorado, Mark McNiven, and it extended earlier studies of microtubules and their role in the intracellular movement of pigment in chromatophores. That resulted in Porter's last scientific paper. It appeared in 1988 in Volume 106 of the *Journal of Cell Biology.*

Marilyn Farquhar, Keith Porter, Elizabeth Porter, Albert Claude, and George Palade at the Rockefeller University Commencement in 1976.

After four years in Maryland, Keith and Elizabeth moved to Pennsylvania, this time partly for personal reasons. They had no children and no family in this country, and my wife Helen and I had become very close to them over the previous thirty-two years. I had joined Keith's laboratory at Rockefeller in 1956, and he came to mine in 1988. His final academic position was as Research Professor in Biology at the University of Pennsylvania, where he shared a laboratory in the Biology Department with Clara Franzini-Armstrong and

President Jimmy Carter presenting Keith Porter with the National Medal of Science, 1977.

me. He continued his research, though at a somewhat reduced level, for several more years, maintaining an NIH grant for studies of cultured cells using a 400 kV electron microscope in our laboratory. He also taught a histology course, which was much praised and appreciated by its students. In his teaching, he never lost what Mary Bonneville once described as "his ability to peel away distracting detail in order to present the germinal center of the fruit" (Porter and Bonneville 1983).

Over his long career, Porter received many awards and prizes, including six awards shared with Albert Claude and/or George Palade from various organizations between 1962 and 1971. In addition to his election to the National Academy of Sciences in 1964, he was elected a member of the American Philosophical Society and of the American Academy of Arts and Sciences in 1977. He also received the Distinguished Scientist Award from the Electron Microscopy Society of America in 1975, the National Medal of Science from President Jimmy Carter in 1977, the first E. B. Wilson Award from the American Society for Cell Biology, and the Henry Gray Award from the American Association of Anatomists, both in 1981. He received honorary degrees from eleven universities in the United States, Canada, France, and Italy.

Keith Porter will long be remembered as an inventive and productive scientist with a prolific output, and as the founder of cell biology and a pioneer in that field in many ways. Literally hundreds of students and colleagues learned from him at close hand in his laboratories, many more were stimulated by his lectures and other presentations at scientific meetings and other venues, and countless others read and learned from his scientific publications, reviews, and occasional historical writings. Just as he moved easily from one subject to another in his own research, he gave people in his laboratory a lot of freedom in theirs. In some cases almost the only overlap between his own research and that of a colleague or visitor was the use of an electron microscope. He was generous in sharing his knowledge and ideas.

Porter worked hard and long hours in his laboratory, often staying, or returning after dinner, until well into the evening. His laboratories ran smoothly and efficiently. Importantly, I think, Porter had a special ability to judge people who came to the laboratory and to put them to a task that they were suited for, while challenging them to learn something new at the same time.

As one perhaps trivial example of this, when I joined Porter's laboratory in 1956 as his first graduate student, there still were two adult chickens in the animal facility, left from the earlier work on the Rous sarcoma. Since I was from "upstate" New York, and was thus a "farmboy," Porter asked me to deal with these chickens, which were no longer of any use. While I had never personally dispatched a chicken, I had seen it being done at my grandparents' farm, and I went to the animal facility and took care of the problem. From then on, I believe, there was very little either of us would not have done for the other.

Keith Porter helping the author with yard work at his house in the 1990s.

As the Father of Cell Biology, Keith Porter left behind a legacy of new ways to understand cell structure and function and the relationships between them. At its finest level, this structural scaffold now is beginning to provide molecular biologists and molecular geneticists with places to locate their vast profusion of specific molecules, revealing relationships between molecular structure and cell function. While Keith Porter never would have considered himself a molecular biologist, his pioneering contributions, along with those of Albert Claude, George Palade, and others who followed, have created an ultrastructural view of the cell into which new information on single molecules can be incorporated, the beginnings of true structural molecular biology. We now are in possession of a level of understanding of cell structure and cell function that no one, perhaps not even Porter himself, could have predicted on that fateful night of July 6, 1944, when that first cell showed him its face from the glowing fluorescent screen of an electron microscope. But Keith Porter was not someone who had only hopes for the future—he had expectations of it.

REFERENCES

Abbe, E. 1873. Beiträge zur Theorie des Mikroskops und der microskopischen Wahrnehmung. *Archiv für mikroscopische Anatomie* 9:413–468.

Claude, A. 1937. Properties of the causative agent of a chicken tumor. XIII. Sedimentation of the tumor agent, and separation from the associated inhibitor. *J Exp. Med.* 66:59–72.

Claude, A. 1938. A fraction from normal chick embryo similar to the tumor producing fraction of chicken tumor I. *Proc. Soc. Exp. Biol. Med.* 39:398–403.

Claude, A. 1943. The constitution of protoplasm. *Science* 97:451–456.

Claude, A. and E. F. Fullam. 1945. An electron microscope study of isolated mitochondria. *J. Exp. Med.* 81:51–62.

Fawcett, D. W. and K. R. Porter. 1954. A study of the fine structure of ciliated epithelia. *J. Morphol.* 94:221–281.

Moberg, C. L. 2012. *Entering an Unseen World. A Founding Laboratory and Origins of Modern Cell Biology* 1910–1974. New York: The Rockefeller University Press.

Moberg, C. L. 1996. Keith Porter and the founding of the Tissue Culture Association: A fiftieth anniversary tribute, 1946–1996. *In Vitro Cell. Dev. Biol.–Animal* 32:663–669.

Pease, D. C. and K. R. Porter. 1981. Electron Microscopy and Ultramicrotomy. *J. Cell Biol.* 91:287s–292s.

Porter, K. R. 1941. Unpublshed draft of an annual report to James Murphy. Porter Archives, Department of Biology, University of Pennsylvania, Philadelphia, PA.

Porter, K. R. 1947. Annual Report – 1947. Porter Archives, Department of Biology, University of Pennsylvania, Philadelphia, PA.

Porter, K. R. 1961. The sarcoplasmic reticulum: Its recent history and present status. *J. Biophysic. Biochem. Cytol.* (Suppl.) 10:219–226.

Porter, K. R. 1961. The endoplasmic reticulum: some current interpretations of its forms and functions. In *Biological Structure and Function, Volume 1*. Edited by T. W. Goodwin and O. Lindberg. pp. 127–155. New York: Academic Press.

Porter, K. R. 1966. Cytoplasmic microtubules and their functions. In *Principles of Biomolecular Organization*. Edited by G. E. W. Wolstenholme and M. O'Connor. pp. 308–345. London: J. & A. Churchill Ltd.

Porter, K. R. and H. S. Bennett. 1981. Introduction: Recollections on the Beginnings of *The Journal of Cell Biology*. *J. Cell Biol.* 91:suppl. vii–ix.

Porter, K. R. and M. A. Bonneville. 1963. *An Introduction to the Fine Structure of Cells and Tissues*. Philadelphia: Lea & Febiger.

Rous, P. 1911. A sarcoma of the fowl transmissible by an agent separable from tumor cells. *J. Exp. Med.* 13:233–246.

Yegian, D. and K. R. Porter. 1944. Some artifacts encountered in stained preparations of tubercle bacilli. I. Non-acid-fast forms arising from mechanical treatment. *J. Bacteriol.* 48:83–91.

SELECTED BIBLIOGRAPHY

1939 Androgenetic development of the egg of *Rana pipiens. Biol. Bull.* 77:233–257.

1941 Diploid and androgenetic haploid hybridization between two forms of *Rana pipiens, Schreber. Biol. Bull.* 80:238–264.

1945 With A. Claude and E. F. Fullam. A study of tissue culture cells by electron microscopy. *J. Exp. Med.* 81:233–246.

1947 With A. Claude and E. G. Pickels. Electron microscope study of chicken tumor cells. *Cancer Res.* 7:421–430.

With S. Granick. The structure of the spinach chloroplast as interpreted with the electron microscope. *Amer. J. Botany* 34:545–550.

1948 With H. P. Thompson. A particulate body associated with epithelial cells cultured from mammary carcinomas of mice of a milk-factor strain. *J. Exp. Med.* 88:15–24.

1951 With P. Vanamee. Observations with the electron microscope on the solvation and reconstitution of collagen. *J. Exp. Med.* 94:255–266.

1953 With J. Blum. A study in microtomy for electron microscopy. *Anat. Rec.*117, 685–710.

With H. S. Bennett. An electron microscope study of sectioned breast muscle of the domestic fowl. *Am. J. Anat.* 93:61–105.

1954 With G. E. Palade. Studies on the endoplasmic reticulum. I. Its identification in cells in situ. *J. Exp. Med*. 100:641–656.

1957 With G. E. Palade. Studies on the endoplasmic reticulum. III. Its form and distribution in striated muscle cells. *J. Biophys. Biochem. Cytol.* 3:269–300.

1960 With R. D. Machado. Studies on the endoplasmic reticulum. IV. Its form and differentiation during mitosis in cells of onion root tip. *J. Biophys. Biochem. Cytol.* 7:167–180.

With E. Yamada. Studies on the endoplasmic reticulum. V. Its form and differentiation in pigment cells of the frog retina. *J. Biophys. Biochem. Cytol.* 8:181–205.

1963 With M. C. Ledbetter. A "microtubule" in plant cell fine structure. *J. Cell Biol.* 19:239–250.

Diversity at the subcellular level and its significance. In *The Nature of Biological Diversity*. Edited by J. M. Allen. pp. 121–163. New York: McGraw-Hill Book Company, Inc.

1964 With M. C. Ledbetter. Morphology of microtubules in plant cells. *Science* 144:872–874.

With B. Byers. Oriented microtubules in elongating cells in the developing lens rudiment after induction. *Proc. Natl. Acad. Sci. U.S.A.* 52:1019–1099.

With T. F. Roth. Yolk protein uptake in the oocyte of the mosquito Aedes aegypti L. *J. Cell Biol.* 20:313–332.

With C. Franzini-Armstrong. Sarcolemmal invaginations constituting the T system in fish muscle fibers. *J. Cell Biol.* 22:675–696.

1965 With L. G. Tilney. Studies on microtubules in Heliozoa. I. The fine structure of Actinosphaerium nucleofilum (Barrett) with particular reference to the axial rod structure. *Protoplasma* 60:317–344.

1966 With D. Bickle and L. G. Tilney. Microtubules and pigment migration in the melanophores of Fundulus heteroclitus L. *Protoplasma* 61:322–345.

1967 With J. R. McIntosh. Microtubules in the spermatids of the domestic fowl. *J. Cell Biol.* 35:153–173.

1969 With J. R. Gibbons and L. G. Tilney. Microtubules in the formation and development of the primary mesenchyme in Arbacia punctulata. I. The distribution of microtubules. *J. Cell Biol.* 41:201–226.

With I. K. Buckley. Cytoplasmic fibrils in living cultured cells. *Protoplasma* 64:349–380.

1973 With V. G . Fonte. Observations on the topography of normal and cancer cell. *Scanning Electron Micros*. 3:683–688.

With D. Prescott and V. G. Fonte. Changes in surface morphology of Chinese hamster ovary cells during the cell cycle. *J. Cell Biol.* 57:815–836.

With G. J. Todaro and V. G. Fonte. A scanning electron microscope study of surface features of viral and spontaneous transformants of mouse Balb/3T3 cells. *J. Cell Biol.* 59:633–642.

1977 With H. R. Byers. Transformations in the structure of the cytoplasmic ground substance in erythrophores during pigment aggregation and dispersion. *J. Cell Biol.* 75:541–558.

1979 With J. J. Wolosewick. Microtrabecular lattice of the cytoplasmic ground substance. Artifact or reality. *J. Cell Biol.* 82:114–139.

1980 With M. H. Ellisman. Microtrabecular structure of the axoplasmic matrix: Visualization of cross-linking structures and their distribution. *J. Cell Biol.* 87:464–479.

1982 With M. A. McNiven. The cytoplast: A unit structure in chromatophores. *Cell* 29:23–32.

1988 With M. A. McNiven. Organization of microtubules in centrosome-free cytoplasm. *J. Cell Biol.* 106:1593–1605.

Published since 1877, *Biographical Memoirs* are brief biographies of deceased National Academy of Sciences members, written by those who knew them or their work. These biographies provide personal and scholarly views of America's most distinguished researchers and a biographical history of U.S. science. *Biographical Memoirs* are freely available online at www.nasonline.org/memoirs.