Noel T. Keen

1940–2002

BIOGRAPHICAL *Memoirs*

A Biographical Memoir by
Brian Staskawicz,
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NATIONAL ACADEMY OF SCIENCES

NOEL T. **KEEN**

August 13, 1940–April 18, 2002

Elected to the NAS, 1997

By Brian Staskawicz, Alan Collmer, and Donald A. Cooksey

Noel T. Keen was a pioneer in the application of molecular techniques to the study of plant-pathogen interactions. He distinguished himself with many seminal contributions in the fields of biochemical and molecular plant pathology. He spent his entire academic career in the Department of Plant Pathology at the University of California, Riverside, where his major contributions involved decoding the biochemical and molecular basis of race specificity in plant pathogens and solving the 3-D structure of the bacterial enzyme pectate lyase C. Noel was always intrigued about why a particular pathogen caused disease on one plant host but was unable to cause disease on a closely related plant. To address this question, Noel chose the most tractable experimental system at the time. He was not shy about applying new technologies to solve this age-old question. Throughout his career Noel was open and generous, always willing to share his ideas and expertise with both colleagues and competitors. Noel not only excelled in scientific contributions but also served as Department Chair from 1983 to 1989 and as the President of the American Phytopathological Society until his untimely death in 2002.

Early life

Noel was born in Marshalltown, Iowa on August 13, 1940. He was raised on a farm there and attended a small rural school. Many of Noel's traits can be traced back to his Midwestern farm youth, including his deep interest in nature and agriculture, his legendary work habits, and his egalitarian manner.

After attending Iowa State University in Ames, Noel obtained a BS in botany in 1963 and an MS in plant pathology in 1965. His MS thesis research, guided by James C. Horton, addressed the regulation of plant cell wall-degrading enzymes in *Phoma* (*Pyrenochaeta*) *terrestris*, the causal agent of pink root of onion. Noel then moved to the Department of Plant Pathology at the University of Wisconsin, Madison, where he

Seiji Ouchi of Kinki University recalls that a highlight of that meeting was Noel leading a "hot discussion on molecular models of gene-for-gene interactions during an unofficial evening beer party." This was both a characteristic activity of Noel and a harbinger of breakthroughs to come.

pursued his PhD under the guidance of Paul Williams. He studied proteolytic activity and histology of *Pseudomonas syringae* pv. *lachrymans* in angular leaf spot of cucumber and the physiology of clubroot of cabbage disease caused by *Plasmodiophora brassicae*.

Noel's graduate research set the tone for his subsequent career. His work used a variety of biochemical techniques and experimental systems to address interaction mechanisms involving both the pathogen and the host, and it yielded insights potentially useful in disease control. Also, several of Noel's legendary personal traits became evident during this time, including his remarkable generosity with colleagues, his ferocity in scientific debates, and his spell-binding speaking ability, which combined a colorful, rural vernacular with flawless scientific clarity. Noel, with his tall, lanky frame, his deep Midwestern drawl, and his encyclopedic and visionary view of the field, was a major presence at any scientific gathering.

Not surprisingly, as Noel's career developed, he became a prominent speaker at international conferences, and through these conferences and research collaborations forged many friendships. Noel's long relationship with many Japanese scientists was notable in this regard. These relationships began with his participation in the U.S.-Japan Scientific Seminars, which were held every four years, and were supported by the National Science Foundation and the Japan Society for the Promotion of Science. The seminars focused on plant host-parasite interactions and alternated between the U.S. and Japan. Noel first participated in the 3rd seminar, in Lincoln, Nebraska, in 1977. The seminar focused on "Recognition and Specificity in Plant Host-Parasite Interactions." The 4th seminar, held in 1981 in Brainerd, Minnesota, addressed the topic "Plant Infection — The Physiological and Biochemical Basis." Seiji Ouchi of Kinki University recalls that a highlight of that meeting was Noel leading a "hot discussion on molecular models of gene-for-gene interactions during an unofficial evening beer party." This was both a characteristic activity of Noel and a harbinger of breakthroughs to come. The 8th seminar, titled

"Delivery and Perception of Pathogen Signals in Plants," was co-organized by Noel and Shigeyuki Mayama of Kobe University in Marina del Rey, California, in 1999.

Noel developed collaborations with both younger and established Japanese scientists, such as Ouchi, Mayama, Masaaki Yoshikawa of Kyoto Prefectural University, and Shinji Tsuyumu of Shizuoka University. He visited Japan many times to give lectures in various institutes and universities, and collaborators like Ouchi, Mayama, and Tsuyumu have warm memories of being guests of Noel and his wife Diane in their home in Riverside, driving around in Noel's favorite sports car and looking over Riverside at night from the perspective of the hot tub in Noel's yard. Noel maintained his farm-youth work habits throughout his life, but fortunately for his many friends around the world, he also knew how to enjoy life.

Noel Keen in 1969 mentoring a very young Rob Horsch–then a Riverside high school student supported by an NSF internship grant, now leading the agricultural research and development team for the Bill & Melinda Gates Foundation.

Developing Research Techniques

Noel was an extremely prolific graduate student at Madison, and produced at least twelve publications from his thesis work, which ultimately resulted in a job offer from the University of California, Riverside even without postdoctoral experience. Noel's initial research focus after he arrived in Riverside was the role of toxins and extracellular enzymes produced by *Verticillium albo-atrum* that were responsible for *Verticillium* wilt of cotton. However, Noel's major interest was to elucidate the biochemical basis of how a plant pathogen elicited a race-specific defense response on one cultivar of a plant but not on a closely related cultivar of the same species. To address this question he developed the *Phytophthora sojae* system on soybean, and isolated the first race-specific chemical elicitors that induced phytoalexin production in resistant cultivars of soybean. This seminal work was published in *Science* in 1975 and initiated a life-long career in understanding the

biochemical and genetic basis of plant-pathogen specificity.

My (B. S.) first encounter with Noel took place when I was a graduate student at the University of California, Berkeley in the late 1970's. At that time I was also developing an interest in trying to elucidate the molecular basis of plant-pathogen specificity, mainly in phytopathogenic bacteria in different pathovars of *Pseudomonas syringae*. My thesis research involved working with *Pseudomonas syringae* pv. *phaseolicola* and the mode of action of phaseolotoxin on susceptible bean plants. However, while I was attending the third International Congress of Plant Pathology in Munich in 1978, I saw a presentation on the role of specific elicitors in the *Pseudomonas glycinea*-soybean host-parasite system that was published later that year. This presentation laid the foundation for the system that we would eventually clone to characterize the first avirulence gene (effector) from a plant pathogen.

Two years later, I had joined the first plant biotechnology company, called International Plant Research Institute (IPRI), located in San Carlos, California. I started to employ molecular cloning to replicate genes from phytopathogenic bacteria, and consulted with Noel several times on the phone. We agreed that this approach would allow us to get at the molecular basis of plant pathogen specificity, and Noel came to do a sabbatical with me in 1980 and 1981 to learn DNA library construction and gene cloning techniques. Fortuitously, we had just heard a seminar from Fred Ausubel, who described the cloning of the *Rhizobium nod* genes by constructing a cosmid library in a wide host range cloning vector and screening nod- exconjugants for complementation for nodule formation. During that seminar it became obvious to me that cosmid cloning was the solution for cloning many genes involved in plant-pathogen interactions. However, as a proof of principle, Noel and I decided to construct a cosmid library of DNA from a strain of *Erwinia chrysanthemi* that produce extracellular pectate lyase enzymes in *Escherichia coli*.

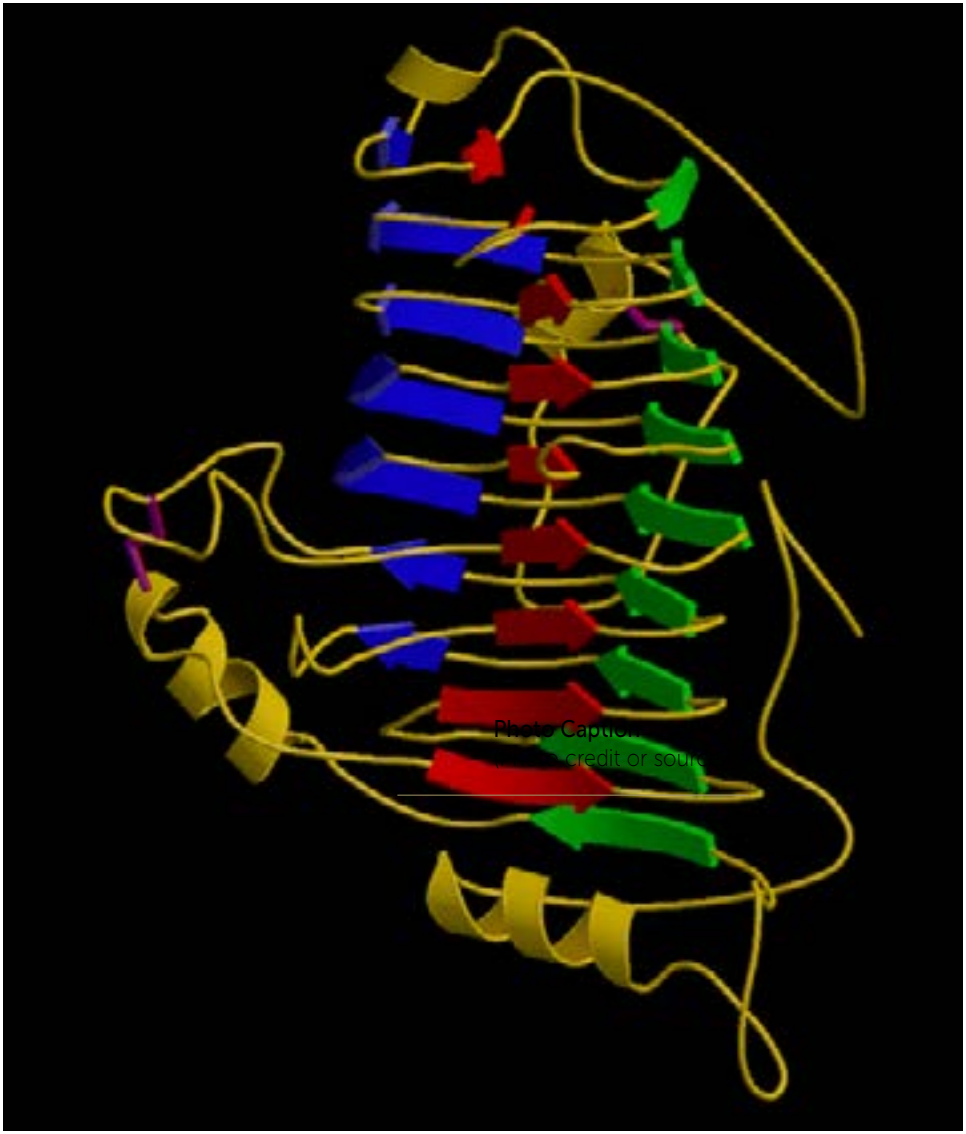
Our rationale was simple, as we just patched the cosmid clones on an agar medium that contained pectate and looked for cleared zones around the bacterial colonies. To our amazement, we isolated several clones that produced pectate lyase enzyme activity while expressed in *E. coli*. Furthermore, the *E. coli* strains expressing the *Erwinia chrysanthemi* genes were able to macerate potato tissue, proving for the first time that these enzymes could recapitulate disease symptoms. We both realized at the time that this would be a very powerful technology to isolate any gene that we had a screen for.

We next turned our attention to our long held interest in plant pathogen specificity. Noel had already established an excellent bacterial system to study different races of *P. glycinea*

on differential cultivars of soybean and thus we employed this system to clone a "hypothetical bacterial avirulence" gene since up to this time there was no way to perform genetic analyses between two different races of *P. glycinea*. However, based on the work previously carried out by Harold Flor, we hypothesized that if we constructed a DNA library from one strain of *Pseudomonas glycinea* that elicited a hypersensitive cell death defense response on a specific cultivar of soybean and conjugated those clones into a strain that did not elicit a hypersensitive cell death response, we should find a DNA clone that would convert a virulent strain into an avirulent strain. Once again, we hypothesized correctly and found a DNA fragment that encoded a gene that we termed *avrA* that determined race-cultivar specificity on differential soybean cultivars. This was obviously a very exciting time in the history of molecular plant pathology as it set the stage for the discovery of pathogen effectors in various classes of phytopathogenic microbes.

On the personal side, Noel also was a fabulous colleague who not only worked hard but also played hard. Noel was an avid tennis player and could often be found playing tennis at noon or after work. He also often led the research scientists at IPRI to the local pub after work or Friday lunches where we often discussed (argued about) scientific strategies, exchanged stories and told jokes. The time that Noel spent on sabbatical at IPRI had a major influence on how I thought about science, and taught me how to be open about ideas and results with my colleagues. After his return to U.C. Riverside, Noel continued to clone and characterize new avirulence genes that revealed that effectors were also important for determining host range on unrelated species of plants. These projects also led to the discovery of the syringolides that were controlled by the *avrD* gene of *Pseudomonas syringae* pv. *glycinea*.

Noel also had a major interest in the role of pectic enzymes in pathogen virulence. Having cloned and expressed the *Erwinia chrysanthemi* (*Dickeya dadantii*) pectate lyase C gene in *E. coli*, Noel next turned his attention to collaborating with Fran Jurnak on solving the 3-D crystal structure of this protein. This work revealed a new domain motif termed the parallel β-helix, which is formed by the parallel association of the β-strands. Subsequent work revealed that the parallel β-helix structure motif was found in other diverse proteins. This discovery once again highlighted Noel's ability to pursue new research frontiers that had a major impact in molecular and structural plant pathology.

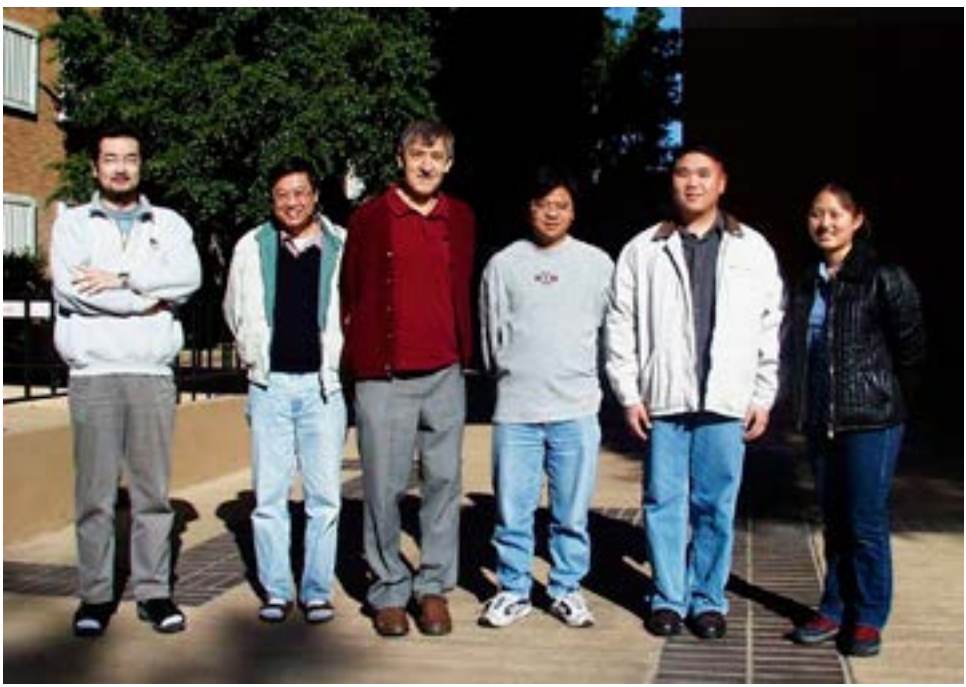


The crystal structure of pectate lyase C. revealing a new domain motif termed the parallel β-helix.

During the later part of his career Noel pioneered the sequencing of bacterial genomes and understood that this would open up new areas of research on the evolution of bacterial virulence and functional genomics. Noel was a real visionary in this area, as it was only just being appreciated how genome sequencing of plant pathogens could impact the field of molecular plant pathology.

Department of Plant Pathology, U.C. Riverside

Noel arrived at U.C. Riverside (UCR) in 1968, after completing his PhD in plant pathology from the University of Wisconsin. He hit the ground running, not only in research, but in his life-long commitment to graduate education. He reorganized the department's graduate course in physiology of plant disease, which he taught throughout his career, while also contributing to other plant pathology, genetics, and biochemistry curricula. He served as major professor to numerous PhD students in plant pathology,



Noel Keen's final laboratory group in 2002.

as well as the interdepartmental Graduate Program in Genetics, which he chaired during the 1990s.

A portrayal of Noel Keen with a model of his pectate lyase C Structure. Part of the Gluck Gateway Mural between the City of Riverside, California and the University of California, Riverside. The mural was painted in 2000 and included key moments in the history of Riverside and UCR.

His mentorship of graduate students, postdoctoral researchers, undergraduates, and many high school students was enhanced by his active presence in the lab. He spent time at the lab bench nearly every day of his career, including weekends and evenings, unless he was traveling to conferences or to give frequent invited talks. He viewed common illnesses as insignificant distractions and worked through them. It was not until his car was hit by a truck that ran a red light at the entrance to campus one Saturday morning that there was a prolonged absence from the lab. He did return to the bench eventually, but only for a few months before the effects of leukemia ended his work.

Noel was a leader among faculty at UCR. He chaired the Department of Plant Pathology for six years and was Director of the UCR Biotechnology Center. In the early 1980s, he led a regular Monday lunch meeting with campus researchers trying to learn molecular biology techniques. He was always a patient listener and a tremendous resource for colleagues to consult with on scientific approaches. He was elected the UCR Faculty Research Lecturer for 1996 and held the William and Sue Johnson Endowed Chair in Molecular Plant Pathology since 1997.

Noel was also a leader in social events, which he took as seriously as his science. Departmental coffee hour, Friday evenings at "The Barn" on campus, oyster parties, cribbage games, softball, volleyball, badminton, and tennis were among the activities that he often organized, contributing to a strong camaraderie among scientists and students from many disciplines. In his later years, he developed an appreciation for fine wine and hosted many tasting events. He also became a serious audiophile, putting together a home system that sounded like a live concert hall. He even authored a number of written reviews of fine audio equipment. He enjoyed owning a series of fast sports cars, which were always red and referred to simply as "the red car," to distinguish them from his every day commuting car.

Noel displayed a favorite Mark Twain quote on the wall of his office: "I have never let my schooling interfere with my education." His work at the bench at UCR and his science-driven camaraderie among colleagues of all ranks brought that quote to life. Through his adventuresome curiosity and egalitarian generosity, Noel opened new research territories and brought together workers from many disciplines to further his quest to understand how plants and microbes interact with such remarkable specificity. Noel's leadership is missed, but his spirit endures through the many younger investigators he inspired.

PROFESSIONAL HONORS AND SERVICE

Noel was elected a fellow of the American Phytopathological Society in 1991. This was followed by numerous honors and lectureships, among which were: the President's Endowed Chair of the University of California, 1990-1992; the Ruth Allen Award of the American Phytopathological Society, 1995; U.C. Riverside Faculty Research Lecturer, 1996; USDA Secretary's Honor Award for Personal and Professional Excellence, 1996; Award of Merit, CSREES, USDA, 1996; William and Sue Johnson Endowed Chair in Molecular Plant Pathology, 1997; Fellow, American Academy of Microbiology, 1997; Elected Member, National Academy of Sciences, USA, 1997; Distinguished Lecturer, Japan Society for the Promotion of Science, 1998.

Noel served as chair of the Department of Plant Pathology at U.C. Riverside from 1983 to 1989, and as chair of the Genetics Graduate Program there from 1994-1997; acting director, UCR Biotechnology Center, 1997-2001; member Board of Directors, CORE21, UCR, 1998-2002. He served as vice president (1999-2000), president-elect (2000-2001) and president of the American Phytopathological Society (2001-2002). He was still serving as president at the time of his death. During his time as president of the American Phytopathological Society, Noel was dedicated to increasing the funding for the field of Agricultural Biotechnology.

Noel served on numerous journal editorial boards including *Phytopathology, Molecular Plant-Microbe Interactions, Journal of Bacteriology, Journal of Phytopathology, Annual Review of Phytopathology, Plant Physiology,* and *Applied and Environmental Microbiology.* In addition, he served on many scientific advisory boards: the external advisory board of the NSF Center for Engineering Plants for Resistance Against Pathogens at U.C. Davis; the Life Sciences Review Panel of the National Research Council's Associate Program; the Noble Foundation, Ardmore, OK; the grants program of the National Research Council Committee on the USDA/NRI; and the technical committee of the U.S.-Israel Binational Agricultural Research and Development Fund.

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