



## IN MEMORIAM

Edward Knapp Wagner  
Professor of Virology, Molecular Biology & Biochemistry  
Irvine  
1940–2006

Edward was born in Akron, Ohio, and lived in the Akron or Cleveland area until he was nine. He had one sibling, Gari Lynn, who was two years older. Through his father, Ed had family ties to relatives in Ohio and Bremerton, Washington. Other ties to the West were through his mother, Margaret Garrett Wagner, who was from Boise, Idaho, where her family had lived since the 1800's. Ed used to say that his relations came from almost every profession — from engineers, teachers, and musicians to cowboys, politicians and dirt farmers.

The slow disintegration of his parent's marriage meant that Ed's middle- to- upper class stable life changed to one that involved increasing switches of homes and schools from Ohio to his grandparent's home in Boise. His parents finally divorced in 1949 and his father died in 1950. Two weeks before Christmas in 1949, Ed was sent by himself via plane to Boise. Fortunately, a very fearful nine- year- old Ed was met at the airport by his — then — new Uncle Clyde. From very humble beginnings, Clyde was a Navy- trained master carpenter and cabinet maker in the early 1930s. He then was called up from the Reserves during World War II to fly transport planes from India into China over the Himalayas (called "flying the hump"). He was shot down and managed to walk out of dense jungle despite malaria and wounds. After the war, he became an assistant postmaster in Boise and married Ed's Aunt Faye Marie.

Ed believed his love of baseball and his lifelong support of the Cleveland Indians originated with his father during the Ohio years. The years in Boise and his Uncle Clyde gave Ed a long- term interest in aircraft and World War II history, as well as a love and understanding of woodworking and cabinetry. Years later, after becoming a UCI professor, Ed drew on memories of watching his uncle's projects to teach himself fine woodworking techniques. His many bowls, boxes, and furniture (full- and child- sized) were given to innumerable friends and family members. He designed and built most of his own home's furniture. A toy box and a doll house were planned, and the wood bought, at the time of his death.

Ed also learned from his uncle how to look beyond a person's background and facade to real worth. Clyde repeatedly told Ed that the ability to learn quickly is a gift to be used and urged him to be truthful with himself and others. Ed's political liberality, his distrust and scorn for prejudices, pretense, and intellectual snobbery were legacies from his uncle, as well as the result of his own intellect and keen perceptions. One former graduate student believed Ed lived by these values as a researcher and professor. As stated in a letter recommending Ed for the UC Irvine Mentor Award he received in 2005, "Ed's droll cynicism and resistance to those who would have us accept policies and ideas that emanate from authority rather than from knowledge, analysis and integrity . . . are fundamental traits of a good scientist."

Clyde's final gift to Ed was his traveling from Boise to Irvine to visit Ed's lab and office in Steinhaus Hall just months before his death from cancer. Ed would later share with family and friends that his uncle's obvious esteem and support was as important as any other professional or personal achievements in his life.

The years in Boise were the time in Ed's life that he learned to use knowledge as a way to feel more in control of his world. He read widely and grew to love the West with its multitude of environments and people. In 1962, he took his new bride, Judy, to visit a great-uncle who was a real cowboy, and another hero of Ed's childhood. Some of his fondest memories from later years were camping trips with his wife and children to sites that eventually included most of the West's state and national parks. Environmental causes were always major charitable contributions.

Ed moved with his sister and mother to northern California in the early 50s where he eventually started private high school (Menlo High School) in 1953. A couple of serious illnesses during his freshman year turned Ed from sports to academics. He graduated second in his class, achieved honorable mention for a National Merit Scholarship and was accepted into MIT.

Ed's first sojourn at MIT was not a success. His grades went steadily downhill over three semesters. His youth (17) and being across the nation from an increasingly ill mother (she battled breast cancer and depression) were the main reasons. His attempts to adopt a style of living (in a fraternity) beyond his financial means and social abilities, and recurrence of a systemic infection that hospitalized him were secondary reasons. MIT requested that he consider whether another college might be better for him.

A year living as a pretend-beatnik in San Francisco and working as an insurance underwriter convinced him that he really wanted to finish college and be a scientist. He learned that he could earn admission to U.C. Berkeley if he brought his college average to a C level (because he had been eligible from high school). Ed achieved this by gaining A's in a couple of UC Berkeley summer sessions, and in a semester's worth of courses at Foothill Junior College, a new campus then located in Sunnyvale, California. He chose this campus because it was near his mother, whose cancer had metastasized.

Years later, Ed told his children that although the two years of 1957 to 1959 were very miserable, they taught him, in his words, a hell of a lot about failure. Part of this knowledge was that giving up is never an option, and that there would likely always be personal problems to confront and confound. He learned how important it is to dissociate professional life from personal problems. His discovery in the late 1950s that the California college system was organized to provide — and the teachers within it willing to furnish — second chances to those wishing higher education honed his loyalty to that system, at all levels. During his own 35+ years as a professor and researcher, Ed extended second and even third chances to students he perceived were sincere in their efforts. Teaching, Ed believed, involved more than merely providing students with information.

An added bonus of that semester at Foothill Junior College was he met his future wife, Judy, in a basic biology class there. Ed entered U.C. Berkeley in January 1960 where he began course work for a B.A. degree in Biochemistry. A year later, Judy also became a student at U.C. Berkeley, and a Biology major. Their marriage began in 1961 and lasted until Ed's death, 44+ years later.

In June 1962, Ed graduated with Highest Honors and was elected to Phi Beta Kappa. He chose MIT from among the numerous graduate schools that accepted him because it had an excellent biochemistry graduate program — and, of course, he wanted to succeed where he had once failed. His academic career prospered at MIT. He and Judy began their family (Erica in 1963 and Edward A in 1966). The one sad note was that Ed's mother lost her battle with cancer in February of 1963.

Ed's Ph.D. research project on the sequencing of RNA was in the laboratory of Vernon Ingram. The project was important, but very hard, and Ed remembered that all those then attempting it ultimately failed for what was basically a lack of technical knowledge and techniques. Ed attempted to sequence a nucleic acid macromolecule by making partial enzymatic digests of purified tRNA and doing a kind of overlapping jigsaw puzzle technique for fitting the sequence together. The problem then was that one needed to separate quarter and half tRNA molecules (20-45 bases). This is no problem with today's techniques, but one couldn't obtain the molecules in needed amounts in the early 1960s. A few papers resulted from this tRNA work, a major but somewhat unsatisfying achievement.

Ed then developed a second project by himself. This was a critical analysis of post-transcriptional methylation of ribosomal RNA in cultured HeLa cells-- a collaboration between the laboratories of Vernon Ingram and Sheldon Penman (also at MIT in a different department). The research succeeded but the project was not of sufficient interest to either MIT professor to be further pursued in their labs. Ed completed his Ph.D. dissertation in June 1967 (Structural studies on amino acid transfer RNA from yeast and ribosomal RNA from HeLa cells).

He then decided to work on herpes viruses as a post- doctoral fellow because these pathogens provided a potential model for studying gene expression in animal cells, and because the smaller DNA viruses were already heavily engaged by many other researchers. Another value in working with herpes-- he and many others then believed-- was that there was growing evidence of some association with human cancers and viruses might well be the key to a cancer cure.

Ed went to the University of Chicago and Bernard Roizman's lab to learn about herpes viruses. He was supported during this effort by the very prestigious private Helen Hay Whitney Fellowship. His years at the U. of Chicago were productive. He was elected to the honorary Society of Sigma Xi in 1967. During 1967-70 at the University of Chicago, he learned basic methods for working with herpes virus. Also, he and Bernard Roizman showed that viral RNA was first seen in the nucleus and only later in the cytoplasm associated with ribosomes. Their finding of this was among the first demonstrations of this obvious fact. But Ed and Judy soon realized they were homesick for the West and milder climes. When his friend, Cal McLaughlin (a graduate student with Ed at MIT, and already on the faculty at UC Irvine) told Ed of a possible job at UC Irvine, Ed — and Judy — were seriously interested.

When Ed came to UCI, he was the only faculty member doing herpes virus research. Believing in the importance of virology to students in the School of Biological Sciences, Ed organized the campus program in Animal Virology and served as Director of that Program from 1986 to 1997. He successfully established a NIH- funded training program in Animal Virology to go along with this program as well, and helped organize the first ICN- UCI Symposium in 1986, and participated in subsequent ICN- UCI Symposia when his expertise was relevant. In 1988, Ed and UC Irvine colleague, Roz Sandri- Goldin, hosted the 13th Annual International Herpes virus Workshop attended by some 700 researchers from around the world. During 1989 and 1995, Ed helped another colleague, Krishna Tewari, organize and conduct virology symposia for the UN established International Center for Genetic Engineering and Biotechnology in New Delhi, India.

Ed taught various courses from his arrival at UCI. From 1971 to his death, he taught animal virology (Bio Sci 124), a popular course with an average enrollment of 158 students. He also taught eukaryotic viral gene expression and supervised undergraduate and graduate student research in Bio Sci 199 and 200 respectively. For a number of years, Ed also developed and taught an undergraduate course in molecular biology for non-biology majors. He also helped revise Animal Virology from 4 to 6 units and then back again to 4 units. With colleague D. Senear, he developed a plan for formation and implementation of an undergraduate major in Biochemistry and Molecular Biology. In addition, his internet web site <http://darwin.bio.uci.edu/~faculty/wagner/>, which he initially developed to supplement his UC Irvine teaching, evolved into an award winning and much visited site for information on animal virology.

Over the 35+ years of his career at UC Irvine, Ed's achievements resulted in his obtaining continuous grant support from NIH and other sources, as well as his promotion to full Professor in rapid time. These achievements resulted in invitations to serve on the editorial boards of his field's major journals (Virology, J. Virology, Gene Therapy, Current Topics in Virology, Virus Genes). He also served on the NIH Virology Study Section, Cancer Biology- Immunology Contracts Review Committee, California Cancer Research Coordinating Committee, and grant review committees for the National Cancer Institute and the National Institute for Allergy and Infectious Diseases.

Other honors were election as a Fellow to both the American Academy of Microbiology and the American Association for the Advancement of Science, and as Distinguished Research Lecturer at University of Cincinnati. Another honor highly prized by Ed was his department's nomination and his eventual selection by UC Irvine's Emeritus Association for its 2005 highly esteemed Mentor Award.

Service beyond his own School of Biological Sciences at UC Irvine included the Academic Senate Committee on Teaching in 1998-1999 and the Committee on Academic Personnel from 1995 to 1998. Other UC Irvine service included the Committee on Animal Welfare, Graduate Council and the Council on Planning and Budget. He was also active in UC systemwide service. He recently served as the UCI representative to the systemwide Coordinating Committee on Graduate Affairs (CCGA), and most recently was a premier member of the Academic Personnel Committee for the UC Merced Campus. Ed's interactions during meetings involving administrators as well as professors and UC personnel were sometimes memorable. Stories of his participation show both appreciation and criticism, depending on one's viewpoint. One was never neutral about Ed's interactions.

In 1999, Ed, with coauthor M. Hewlett, published-- through Blackwell Publishing-- a 466- page virology textbook entitled Basic Virology. This book is highly acclaimed and widely used for undergraduate and graduate courses throughout the world. A second edition appeared in 2003. A third edition was begun in 2005. In anticipation of his retirement, Ed asked two younger virology research professors (David Bloom and David Camerini) to join him and M. Hewlett as coauthors. This has unexpectedly assured-- despite Ed's death-- that the third edition will be completed in the timely and excellent manner Ed (and his coauthors) would desire.

The outstanding quality of Ed's research is best demonstrated by his having received two NIH merit grant awards. Despite many difficulties (the Nixon budgets, the Viet Nam war, California's constant political machinations, and even his own wars with others in his field), Ed retained an NIH grant (Control of RNA Synthesis in Herpes Virus Infected Cells) from his arrival at UC Irvine in May 1970, to the closing of his laboratory in 2005, a year prior to what would have been his formal retirement on June 1, 2006. The second grant supported his collaborative work with Dr. J. Stevens on herpes virus pathogenesis (DNA Microarrays for Neurotropic Human Herpes Viruses). This NIH recognition is a significant distinction that is reserved for only a handful of highly meritorious individuals.

Ed constantly adapted his research to take advantage of modern techniques. Use of restriction enzyme and recombinant DNA technology allowed him and his students to isolate herpes virus genes, the mRNA encoded by them, and show how to relatively rapidly characterize it. His lab generated a physical map of the genome at a much higher resolution than was previously available. Throughout his career, Ed focused on the relationship between herpes virus and its host at both the cellular and molecular level. His primary interest, and the areas of his lab's most important discoveries, was gene organization of the virus, regulation of gene expression, and transcriptional control. His lab's identification of the gene expression pattern of herpes virus significantly impacted every current investigator in the field. His work established that, contrary to popular dogma in eucaryotic gene expression at the time, most herpes virus genes do not have introns, a most significant observation. Another significant finding in 1987, published in Science, showed that a portion of the herpes virus genome was, contrary to then common belief, transcribed during the latent period. This finding continues to have broad significance even today.

Another recent adaptation by Ed of cutting- edge technology to herpes virus gene expression is based on oligonucleotide microarrays that permit relatively rapid quantifying of transcript levels as a function of life cycle, host response, or other physiological variables on a whole genome scale. The microarrays permit quantifying and statistical analysis of effects previously addressable only by essentially qualitative approaches. This research also significantly impacted the herpes research community and was recognized by the NIH with an additional research grant. Between 1967 and 2006, Ed published more than 130 peer-reviewed papers, reviews and book chapters. This number excludes his Basic Virology textbook.

A sampling of Ed's peers in the animal virology field consistently ranked him among the top five to ten most accomplished and productive herpes virologists in the world. A recent sampling by a science- field polling firm revealed Ed to be (in his field) among the top 250 researchers cited by others. An example of the esteem in which his peers held him was that, after giving the Keynote address in the Session on Latency at the 2005 Herpes virus International Workshop in Finland, which he believed would be his final scientific talk before retirement, he received a standing ovation. Several of those present told him they had never previously witnessed or given such an acknowledgment.

Ed always felt that the self- confidence, courage, and knowledge that he needed to pursue a career in academic research and teaching came from both the frustrations and successes of his graduate research years. He learned from those experiences that hard work is only part of the story: successful research always requires a good deal of luck. Ed often stated that his own graduate years taught him both the good and bad aspects of working for a research advisor involved with a competitive project in a small lab. Such lessons were important to his own research career because his highly competitive, cutting- edge research projects during his 35+ years as a principal investigator never involved more than a handful of graduate and post-doctoral researchers at any given time.

Ed chose a small laboratory arrangement because he considered teaching as important as research. He believed his laboratory research needed to be high quality and cutting- edge not just for his own competitive satisfaction, but in order to properly train students in quality herpes virus research. He often said that his graduate students and post- doctoral fellows were there to learn how to do excellent research, not merely be extra hands and minds for him to manipulate and direct. He felt strongly that he needed to finely balance a

close intellectual involvement with student projects (to avoid student frustration and wasted effort) with enough separation that students could independently learn how to do productive research. Having fewer persons in his lab meant Ed could act on his belief that the primary purpose of symposia and conferences was to educate. He could afford to more frequently send lab personnel to a variety of symposia and conferences where they could interact with other researchers, while gaining experience from presentation of their laboratory research. Insightfulness, desire for truth, and intense concern for people drove his passion for good science and teaching.

Ed was a large man who expressed his views and emotions with lightening speed, in a loud voice, and sometimes with caustic wit. Many found him somewhat intimidating and overwhelming. But most eventually realized that Ed's views were usually very considered and his emotions were both honest and intensely passionate. As one former graduate student put it, "Wait ten minutes after Ed's initial loud reaction to any type of problem and he'd not only help you find a solution, but give you emotional support over a meal that he paid for." Another former student described Ed as a Pappa bear on the outside and Teddy Bear on the inside.

Whether Ed ever fully realized the complete effect he had on his colleagues and students, he felt humbled by the quality, friendship and loyalty of all with whom he worked and strived to teach. He considered himself fortunate to have had some truly outstanding graduate students and post- doctoral fellows in his laboratory. He expressed satisfaction that he had presented to even his more limited students what quality herpes research was all about. Although he never believed that striving for rewards and awards should be a primary goal of his own career, he always attempted to make sure that he, his laboratory, department, university, and any individual he considered worthy wasn't overlooked or slighted. When discussing his upcoming retirement, he considered he had been well rewarded by getting a good paycheck for doing what he liked to do, and by working every day among people whom he liked and with whom he could do and talk good science. The long- term friendship, loyalty, and quality research support of his laboratory research assistants particularly touched him deeply.

There was much Ed knew he would miss after retiring from UC Irvine and scientific research. But he was satisfied with his contributions to herpes virology and with his years as a professor and researcher. He had confidence in the younger faculty that he and others had helped recruit to UC Irvine. He looked forward to his retirement as an opportunity to spend more time with his adored grandchildren and family, his many friends inside and outside science, and with the innumerable activities and interests that always intrigued him. It is a shame that a too- early and unexpected death robbed him of these desired goals.

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