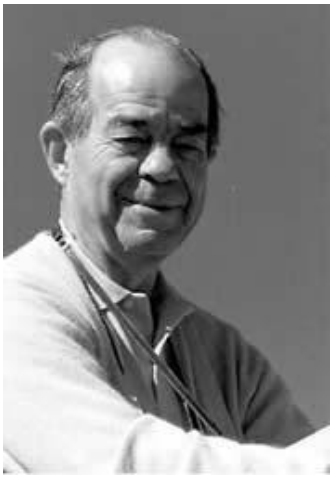

IN MEMORIAM

Morgan Harris
Professor of Molecular and Cell Biology, Emeritus
UC Berkeley
1916– 2005

Morgan Harris's association with the University of California, Berkeley spanned almost 70 years with only a four- year hiatus early in his career. He was born 25 May, 1916 in St. Anthony, Idaho, and began his UC career in the mid-1930s with enrollment as an undergraduate leading to an A.B. in zoology in 1938. A tribute to his skill, energy and concentration is the completion of his graduate work toward a Ph.D. in embryology in the record time of three years. He left Berkeley in 1941 for post- doctoral research at the University of Pennsylvania, followed by two years of war- related research in aviation physiology and one year on the faculty of the University of Washington. Morgan returned to Berkeley in 1945 as a member of the faculty in the Department of Zoology and became professor emeritus in 1982. With the reorganization of biology on the campus he became associated in 1991 with the new Department of Molecular and Cell Biology, where he continued his research until the late 1990s.

Harris's Ph.D. research concerned differentiation and growth of gastrular anlagen implanted into tadpoles. Shortly thereafter he began studies of animal cells in culture. In the 1950s he concentrated on nutritional studies of cells, which included utilization of sugars, the role of bicarbonate, and the synergistic effects on growth of dialyzable and non- dialyzable factors in the medium. In the late 1950s and early 1960s he developed differential toxicity tests in studying the effects of drugs on growth and analyzed the chromosome constitution of cells. This work led him into the cellular origin of resistance to purine analogs and its relation to genetic and epigenetic changes in the cells. The mechanism of drug resistance had been most decisively worked out in bacteria, where it was clear that resistance almost invariably arises through direct genetic change. Morgan's early studies of drug resistance in cultures of somatic animal cells indicated that the picture there was more complicated, and in certain conditions might involve physiological adaptation of the cells to the drugs in addition to genetic changes. Such questions about the nature of heritable change in somatic animal cells probably motivated his 1964 book, Cell Culture and Somatic Variation. This book marked a watershed in the study of variation of animal cells. It is the classic volume on cell variation, and is still a fountainhead of basic information about the subject. It provides a thorough grounding in the embryological development of different tissue types of cells; exhibits a full understanding of the then rapidly advancing field of microbial genetics; and covers the art of cell culture, including cell types and their changes, chromosome variations and nutrition, as well as tumor production and viral transformation. The book not only displays Harris's encyclopedic knowledge in all these areas but does so with critical analysis that sets the direction for the research that defined the rest of his career.

A stream of publications on somatic cell variation flowed from Harris's laboratory beginning in 1971 and continuing into the early 1990s. In particular, he noted adaptive shifts to purine analog resistance in Chinese hamster cell hybrids heterozygous for resistance that suggested a true population shift in response to the drug,

not just the accumulation of genetically resistant segregants. The suggestion of adaptive change was supported by the instability of the resistant phenotype and by findings of other laboratories that the associated enzyme activity thought to be lost in resistant cells could be recovered by fusing them with cells of another species.

A second source of evidence that mechanisms other than mutation could account for heritable changes in expression of a recessive mutant- like phenotype came from Harris's comparison of the frequency of such phenotypes in near- diploid and near- tetraploid cells. If mutation is the only event taking place, the frequency of the mutant phenotype should be much lower in the near- tetraploid than in the near- diploid cell, since there are twice as many dominant alleles to be inactivated in the former. Morgan found in the cell system he was studying that the frequency of the mutant phenotype was the same in both cell types, supporting a non-mutational origin of the resistant phenotype.

A third study that indicated a non- mutational origin of drug resistance arose in a Chinese hamster cell line during long term exposure to low doses of bromodeoxyuridine (BUdR). Clonal variants with widely different degrees of resistance to BUdR arose in high frequency and were initially unstable, consistent with gene inactivation by an epigenetic mechanism that did not involve a change in DNA sequence. The average degree of resistance in a cell population increased gradually with time of exposure to BUdR, as would be expected with adaptive change rather than a structural change in the gene encoding thymidine kinase, the enzyme responsible for sensitivity to BUdR. Morgan then found that these variants massively reverted to near their original state when they were exposed to the demethylating agent 5- azacytidine. Such high frequency reversion indicated that gene inactivation played a central role in producing the resistance to BUdR and probably involved silencing by methylation of the gene for thymidine kinase. Related types of experiments indicated that the inability of cells to synthesize certain amino acids was often a result of epigenetic silencing of a normal gene in the biosynthetic pathway of the amino acid. Molecular experiments in Harris's laboratory in the late 1980s showed directly that hypermethylation of the gene for thymidine kinase would account for the development of resistance to BUdR. Thus Morgan pioneered the field of the epigenetic origin of heritable change in cells. He was so far ahead of his time in that respect that his contribution is rarely acknowledged in the current flush of interest in the role of epigenetic change in the origin of cancer.

Harris was one of those rare cell biologists who had a systems perspective on life processes; probably as a correlate of this, he understood what was going on across biology in general. He was an avid reader of the biological literature, and could frequently be found in the biology library. As a result, he was an excellent source of authoritative information when questions arose in cell biology. He was also a willing and perceptive reviewer of the scientific manuscripts of colleagues. His comments were made in a detailed and constructive manner, and invariably improved the manuscript.

Although Harris was hired as a cell biologist in 1945, initially his major teaching assignments until 1956 were general zoology and comparative vertebrate anatomy. His signature course for many years was called Growth and Form. For the very large introductory zoology course Morgan's habit was to prepare his lecture notes and a tray of 20 or so slides for the lecture; however, the notes stayed in his office while he lectured. He always made a short outline on the blackboard so students could organize their notes. Each day after lecture he went back to his notes to write notes- on- notes regarding what needed more emphasis, or what to delete, or what had inadvertently been left out while lecturing.

Harris regularly attended a weekly research seminar on animal cells and viruses, in which the participants took turns speaking. His own talks were beautifully organized and clearly presented. Slides were not permitted in this seminar, so he illustrated his talk with easily understood tables and graphs on the blackboard. It was a true learning experience for his listeners, most of whom were hearing about epigenetic inheritance for the first time. He also supervised the research of a series of graduate students, some of whom became leading cell biologists.

Harris served as vice chair of the Department of Zoology from 1952 to 1957 and as chair from 1957 to 1963. He was a low- key but extremely competent administrator. During this period he regularly attended the weekly meetings of the Museum of Vertebrate Zoology. Not only was he interested in the museum's program, but this gesture served to maintain good relations between the museum and the rest of the department. Following years of intra- and interdepartmental strife, Richard Eakin started the healing process when he was departmental chair, and Morgan had the wisdom to continue it. He was also a contributing member of the Cancer Research Laboratory, a source of wise counsel to its director and his other colleagues, who benefited from his acumen and his prestige.

Harris was an active participant in professional societies, and was one of the founders of the American Society of Cell Biology, serving on its executive council from 1964 to 1968. He was also on the executive committee of the Federation of Cell Biologists and served as president of the Tissue Culture Association. He was treasurer and executive committee member of the International Society of Cell Biologists. Professional honors included a Merck Senior Postdoctoral Fellowship at the University of Paris and a Guggenheim Fellowship at Cambridge University. In the 1960s he held a prestigious Miller Institute Research Professorship at Berkeley.

In his earlier life Harris was a pioneering rock climber in Yosemite. Together with frequent climbing partner David Brower, the environmentalist leader of the Sierra Club, he established 11 climbing routes in the 1930s. Famed nature photographer Ansel Adams captured the two of them reaching a summit in a photograph that later appeared on the cover of an early climbing guide. In 1936, Morgan and his fellow climbers pioneered the pendulum traverse, the use of a rope to swing from point to point during the first ascent of the "Rotten Log" route on Royal Arches. In all, he is credited with 14 first ascents in the Yosemite Valley and with establishing the "Shaky Leg Crack" route on the east face of Mount Whitney.

Harris was also an avid bird- watcher, an activity that began in high school, where he formed a club of classmates. This interest continued throughout the rest of his life. After his retirement he traveled the world, mostly on trips focused on birds. He compiled a world list of almost 2,500 bird species. He and his first wife were devoted folk dancers. They were members of the local club starting in 1958. Morgan served as secretary and president of the club. He did not drop out of dancing until 2000, but even then kept in contact with the group socially. He died 14 February, 2005.

Harris was married for 45 years to Marjorie Ruth Mason who died in 1985. In 1989 he married Lola Houston, who survives him. He is also survived by his sons Roger of the University of Washington and Ronald of Cornell University, both of whom are neurobiologists, and four grandchildren.

In sum, Harris lived an active and varied life. He usually maintained a serious demeanor which was combined with solid integrity and an essential warmth and kindness. Sincerity, in science and in personality, is a keyword in describing his makeup. His intellectual rigor and his genuine collegiality will long be remembered by his friends and associates. He will be deeply missed.

Harry Rubin
Howard Bern
William Lidicker