RADIATION RESEARCH **175,** 101–103 (2012)
0033-7587/12 $15.00

DOI: 10.1667/RR3073.1

IN MEMORIAM

William A. Bernhard (1942–2012)

Dr. William A. Bernhard, Professor of Biochemistry and Biophysics at the University of Rochester, and past president of the Radiation Research Society, died peacefully May 9 at his home in Mendon, NY. Dr. Bernhard was an internationally known expert on the effects of ionizing radiation on the chemical structure of DNA.

Dr. Bernhard earned his B.S. degree in Physics at Union College in 1964, and his master's and doctoral degrees in Biophysics at Penn State University in 1966 and 1968. Dr. Bernhard then received postdoctoral training at the Argonne National Laboratory from 1968–1970. He joined the faculty of Biophysics at the University of Rochester as an assistant professor in 1970 with an NIH Career Development Award. He was appointed professor of Biophysics in 1985. He served as associate chair or co-chair of the Department of Biochemistry and Biophysics from 1996 to 1998.

Dr. Bernhard was a biophysicist of the highest order, working at the forefront of understanding how radiation damages our genetic material. His unique command of both the biological and physical aspects of radiation damage earned him the respect and recognition of colleagues worldwide. The longevity of his research program, funded by the National Cancer Institute for 37 consecutive years, and the successful careers of his many trainees are testaments to the consistent high quality of his work, the high regard his peers, and his commitment to training future scientists. Bill also was a wonderful person and colleague. His kindness to his colleagues and passion for his work made him a trusted friend and ideal colleague.

His renowned research program has focused on understanding the physical and chemical processes by which radiation affects biomolecules, especially DNA. His results have helped guide industrial and government policies regarding radiation risk assessment and have provided critical details to predict the biological consequences of radiation and understand DNA damage mitigation and repair processes.

Throughout his career, Bill was committed to mentoring and developing young scientists, and he felt strongly about investing in people and their careers. Bill was the Ph.D. thesis supervisor for 14 students. He had 9 post-doctoral students, and worked with 2 research assistant professors. Many of these former co-workers have moved on to academic positions and are doing research in radiation damage studies in DNA.

Bill's important influence on the field of radiation chemistry has been long and continuous with over 100 publications. His contributions can best be illustrated by looking at some of his important papers.

1. *Solid State Radiation Chemistry of DNA. Part I. The Bases*, which was a book chapter in the famous series edited by John T. Lett and Warren K. Sinclair, *Advances in Radiation Biology* (*1*). This article reviews the previous work on the radiation chemistry of the DNA bases. This is a critical review, in that previous free radical assignments are reviewed and rated on whether or not they are plausible. It is important here to describe how this can be done.

Bill had worked on characterizing the primary radiation induced free radicals in DNA constituents. He used the single most sensitive technique available for detecting free radicals, Electron Paramagnetic Resonance (EPR), with the simultaneous application of Nuclear Magnetic Resonance (NMR). With this combination called ENDOR (Electron Nuclear Double Resonance), it was possible to positively identify the free radicals detected. Therefore he was able to review the literature and tabulate the free radical assignments. From the tables in this article it is easy to see the trends and one can easily see which free radical assignments are reasonable. There are extensive diagrams that map the free radicals present at low temperatures (the primary radiation induced products), and the more stable products observed upon warming observed. This article then formed the basis of what we know about the radiation damage to DNA constituents at the molecular level.

2. In the 1970s Bill's group described a low temperature radical in several cytosine derivatives that had the features of a radical seen in thymine called the ''3alphaH radical'' (*2*). In thymine this is a well-known oxidation product formed by deprotonation at the C5-methyl group. The problem is that cytosine doesn't have C5-methyl group. Later it was discovered that commercial cytosine derivatives have about 1% 5-methylcytosine impurities. The amazing thing here is that in a single crystal of 5dCMP, one of the dominant radiation induced products is this 3alphaH radical. This means that electron loss products formed at random in this crystal are free to move about and eventually encounter the 5-methylcytosine impurities where they are stably trapped as one of the dominant radiation induced products in 5dCMP.
3. One of Bill's most important papers is the one entitled ''*Sites of Electron Trapping in DNA as Determined by ESR and One-Electron-Reduced Oligonucleotides''* (*3*) which represents an enormous effort to determine the percentage of electron trapping by each of the four DNA bases. Many thought that only thymine was important in trapping electrons in DNA. This paper clearly showed us that cytosine is actually the dominant site of electron trapping in DNA.
4. Another important paper by Bill and two of his Ph.D. students, is entitled ''*The Influence of Packing on Free Radical Yields in Crystalline Nucleic Acids: The Pyrimidine Bases*'' (*4*). This paper addresses a fundamental question. If the effect of radiation is to ionize molecules at random, why are only certain free radicals observed in DNA? The answer is that radicals have to be trapped in an environment where they are not susceptible to destruction by recombination. There are wonderful examples in this paper of the intricate hydrogen bonding networks that promote reversible proton transfer that allow free radicals to become stably trapped.
5. Bill was not afraid to stir up controversy by publishing an article entitled ''*DNA Responds to Ionizing Radiation as an Insulator, Not as a Molecular Wire*'' (*5*) that called into question the work of Barton *et al*. which asserts that DNA is a molecular wire. The basic question here is why irradiated DNA has such a high radical yield? If the products of radiation (electrons, and holes) are free to move about, why don't they recombine (annihilate) producing a very low radical yield. Bill's approach to the problem lies in his deep understanding of the fundamentals of radiation chemistry. This work nicely shows that in oligodeoxynucleotides at 4 K electron and hole migration distances are short. It follows that DNA is therefore is not a conductor.
6. Recently the current emphasis of Bill's research can be seen in ''*2-Deoxyribono-lactone Lesions in X-ray Irradiated DNA: Quantitative Determination by Catalytic 5-Methylene-2-furone Release''* (*6*) which covers the detection of a nonradical end product in irradiated DNA. This important paper in collaboration with his long time research colleague Yuriy Razskazovskiy shows that ribonolactone lesions are formed in high yields in irradiated DNA, and involve a doubly oxidized site. The important involvement of C1 chemistry in DNA radiation damage is explained in this article. This paper is an important departure for Bill. His previous work has mainly involved the free radicals associated with radiation damage to DNA. Bill's research represents groundbreaking efforts to apply his extensive knowledge of free radical chemistry to identifying the final end products observed in irradiated DNA.

Bill's contributions to radiation chemistry went beyond his published works. His presentations at meetings and conferences were always models of clarity and insight. It was impossible to attend one of his talks without learning something new. This, in a way, was also a show of respect and affection for both his colleagues and for his field of research.

This February Bill submitted a grant renewal request to NIH/NCI that proposed to continue his research into new areas that showed his continuing strong interest in DNA damage processes. It is truly a loss that Bill cannot lead this research. His long time research colleagues will no doubt carry the work on DNA forth in their future efforts and bring to fruition Bill's goal of a better understanding of the fundamental processes of radiation damage to DNA.

Bill gave his time, energy and heart to numerous duties for the Radiation Research Society. He was on six Program Committees for annual meetings of the Radiation Research Society. He served two 4-year terms as Associate Editor of Radiation Research Journal. Bill was elected Vice-President elect of the Radiation Research Society, and served as Vice President in 1997 and President in 1998 of the Radiation Research Society. He served on the Program Committee of the 13th ICRR in San Francisco in 2007, and was the Treasurer and member of the Executive Committee for this meeting. Bill had an understanding of the benefits of the multi-dimensional nature of RRS and upheld the importance of the smaller scientific groups being represented in leadership and on the meeting program. His vision, enthusiasm and vocal support for this broad approach to radiation sciences are being proven correct as science among the disciplines merge. In his final days, Bill talked

at length about how important it is for scientists to lack a fear of mistakes. He felt strongly that mistakes could open important new avenues of thought and that strong scientists take risks into areas where the answers are not obvious or certain.

Bill was chair of the Gordon Research Conference on Radiation Chemistry, which is scheduled in July of this year. The program as was typical of Bill is well planned and balanced in disciplines. He raised enough money to ensure the success of this meeting.

Bill was a talented craftsman and his great technical skill shows in his home and hobbies. He was an amazingly fit tri-athlete and would discuss ''aero-bars and error-bars'' with equal facility. In the last year of his life before his illness, Bill finished the Alpe d'Huez Triathlon in France, earning the title of the oldest finisher of the SavageMan Half-Ironman in Maryland, and took a three-week Himalayan trek in Bhutan, numerous trips with his wife and skiing days with his children and grandsons. Bill told his daughter, Mandy Kittelberger, ''a number of times that if a person could script his last year of life, his was perfect.'' He had great dedication to his family and to truly living life fully with principle, curiosity and great joy.

Bill is survived by his wife of 46 years, Patricia Bernhard, his son Casey Bernhard, his daughter Mandy Kittelberger and five grandchildren.

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