

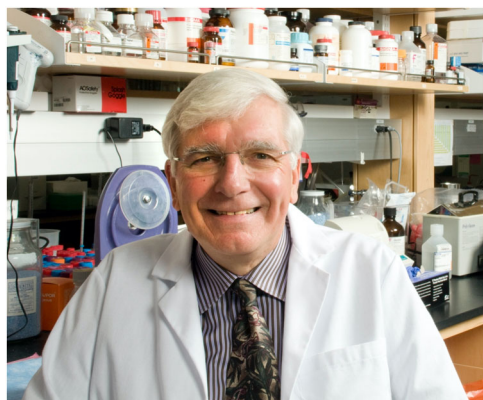


Special issue in honor of Prof. Laurence H. Hurley

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Accepted: 6 May 2022 / Published online: 20 May 2022

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This issue of Medicinal Chemistry Research is dedicated to the many outstanding contributions of Professor Laurence H. Hurley throughout a truly outstanding career in medicinal chemistry research and drug discovery. Professor Hurley's remarkable personal and professional journey is described below.

Laurence Hurley was born in Birmingham, England in 1944. Laurence attended Bordesley Green Technical School, an institution that accepted students who were considered “late developers.” At this school, he flourished, particularly in maths, physics, and chemistry. At the age of 20, he was accepted into the School of Pharmacy at Bath University. As a university student, he found his calling: natural products chemistry.

Laurence's father, Mr. Harold Hurley, played a major role in his decision to further his studies. Despite failing his

Eleven-plus exam, a standardized test administered at the end of primary school that determines educational trajectory, Laurence received tutoring his father arranged for him to help him catch up. Mr. Hurley grew up in a working-class family during an era when academically promising students were not always allowed to pursue their studies, since greater emphasis was placed on going to work at a young age to help support the family. Perhaps because he experienced his own academic disappointment in his family not allowing him to accept an architecture school scholarship, Mr. Hurley actively encouraged his son to advance his education and pursue his studies in America in 1967.

In his last year at Bath University, Laurence selected Pharmacognosy as his major and wrote his honors degree thesis on a microscopical examination of Belladonna root and GLC evaluation of the maturation of fennel oil from fennel plants that he picked from the Bristol Gorge. He was awarded an Upper 2nd Class B Bachelor of Pharmacy degree in 1967. Based on this experience and the suggestion of a college girlfriend, he applied to several Pharmacognosy graduate programs in the United States. One of the programs was at Purdue University, where he was attracted to the research program of Dr. Egil Ramstad, the author of a Pharmacognosy textbook he had used at Bath University. But upon his arrival at Purdue, Laurence learned that Dr. Ramstad accepted students only from more exotic countries. Fortunately, Professor Heinz Floss had just moved from Germany to Purdue, and he accepted Laurence into his research group.

Studying under the German system, it took Laurence less than three years to complete the Ph.D. degree working on the biosynthesis of Indolmycin from *Streptomyces griseus*. It was only later that Professor Floss realized that the American Ph.D. system was typically a four-to-five-year program, rather than the three years Laurence took to complete his doctorate. But by that time Laurence was already doing postdoctoral research in Vancouver, Canada, at the University of British Columbia under James P. Kutney, working on the biodegradation of usnic acid, which was a natural product produced by the lichen usnea in the forests of British Columbia. Immediately prior to moving to

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Vancouver, Laurence married Frances Denham in 1970 with whom he had two daughters, Bridget (1974) and Nicole (1979), who later both became bioengineers and have successful careers in San Francisco.

In September 1971, Laurence accepted the position of Assistant Professor of Pharmacognosy in the School of Pharmacy of the University of Maryland. In accord with those times, he presented a seminar at 11:00 AM and then was offered the position over lunch, which he accepted without negotiating a start-up package. This lack of sufficient funding became a problem, so in 1973 he interviewed at the College of Pharmacy at the University of Kentucky in the hope that he could renegotiate his start-up package at Maryland. Professor George Digenis at Kentucky persuaded him to move to Lexington, which he did in the spring of that year. This was the beginning of his independent career. He received his first NIH grant in 1973 and then a Career Development Award from NIH in 1978. These NIH grants supported research on the biosynthesis of antibiotics including Anthramycin and related natural products. He also served as Program Director for the BRSG grant at the College of Pharmacy, where he first met Jack Cole, the National Program Director of this program and the Dean of the College of Pharmacy at the University of Arizona. Jack tried to recruit Laurence to Arizona in 1979 but the timing was wrong. However, Jim Doluisio, Dean of the College of Pharmacy at The University of Texas at Austin, recruited Laurence the following year as a Professor of Medicinal Chemistry, and later he was named the George Hitchings Regents Chair in Drug Design. At Texas Laurence moved his research program into the mechanism of action of natural products that bound to DNA, a choice made seven years earlier when he selected Anthramycin and related compounds as DNA-reactive compounds to study. Laurence moved his research focus to determining the mechanism by which natural products like Anthramycin and CC-1065 recognized and bound to DNA in a sequence-specific manner.

After about a decade at the University of Texas, Laurence's life changed. In 1995, he married Terry Evers, who was Special Assistant to the President at UT Austin and now is an international award-winning watercolor artist. At about the same time he made a most decisive change in research direction by exploring the idea that secondary DNA structures such as G-Quadruplexes could be targeted by small molecules to more selectively modulate gene expression. He had also joined forces with the world-renowned clinical oncologist Dr. Daniel Von Hoff, who was then located in San Antonio. Dan was recruited to be the Cancer Center Director at the University of Arizona in 1999, and at the same time Laurence was recruited to the College of Pharmacy as the Howard J. Schaeffer Endowed Chair in Pharmaceutical Sciences and the Cancer Center by

Jack Cole and Dean Lyle Bootman. At Texas, Laurence had started Cyternex, later called Cylene, his first biotech company with Tom Farrell (CEO), which they moved from San Antonio, Texas, to Del Mar, California in 2000.

Laurence considers his years at the University of Arizona as perhaps the most rewarding, both personally and professionally. G-quadruplexes became well accepted as biologically relevant structures and as drug targets. Despite multiple rejections from leading science journals, his 2002 publication in the *Proceedings of the National Academy of Sciences*, now cited well over 2000 times, demonstrated for the first time that these structures in promoter elements could be targeted by small molecules to modulate gene expression. He was CSO of Cylene Pharmaceuticals, which later developed Quarfloxin and Pidnarulex (CX-5461). These compounds were derived from the fluoroquinolones developed in his Texas lab for targeting G-quadruplexes. CX-5461 has recently been FDA Fast Tracked Designated for breast and ovarian cancer carrying BRAC1/2 mutations. In 2017 he cofounded a new biotech company with Vijay Gokhale and Richard Austin (CEO) Reglagene, which now has a drug in preclinical development for high-grade gliomas that pass through the blood–brain barrier and is orally active. Laurence believes this is probably the most exciting clinical opportunity of his career, one with special significance because his cousin Susan died of this disease when she was just eight years old in 1952.

Laurence has been recognized over the years with numerous national and international awards. He has authored 278 research papers and has an H-index of 93. Moreover, he has been a recipient of continuous NIH funding since 1973. Among his accomplishments, he served as Senior Editor for the *Journal of Medicinal Chemistry* (1992–2010), Chair of the MEDI Division of the ACS (2010), Chair of the AACR Chemistry in Cancer Research (2009), and Chair of the NCI Board of Scientific Councilors (2010). His awards include the 1988 George Hitchings Award in Innovative Methods in Drug Design and the 1989 Volwiler Research Achievement Award from the American Association of Colleges of Pharmacy. In 1992 he received the APhA Research Achievement Award in Medicinal Chemistry and the 1994 American Chemical Society Medicinal Chemistry Award. Both Bath University (1996) and Purdue University (2013) recognized his career with DSc degrees. In 2005 he received the George & Christine Sosnovsky Award in Cancer Therapy from the Royal Society of Chemistry, and in 2007 he was inducted into the American Chemical Society Medicinal Chemistry Hall of Fame and named Innovator of the Year by the University of Arizona. He was presented with the 2008 AACP Paul Dawson Biotechnology Award and the 2011 Nucleic Acids Award from the Royal Society of Chemistry. In 2017 he was named Arizona Biosciences Researcher of the Year and

in 2018 Innovator of the Year in Arizona Technology Council's Governor's Celebration of Innovation. And most recently, in 2020, he was elected as a Fellow of the National Academy of Inventors. In 2019 Laurence was fêted by his ex-students and past colleagues with a symposium, "Molecular Targeting in Drug Discovery-DNA and Beyond," in honor of his 75th birthday. Currently, he is CSO of Reglagene and Professor Emeritus at the University of Arizona.

Dr. Hurley attributes his scientific accomplishments to an array of people: the many graduate students and post-doctoral associates with whom he has collaborated across the years, a sterling host of faculty colleagues, staff, and mentors, outstanding administrative leadership from James Doluisio, Lyle Bootman, and Jack Cole, and last but not least, a host of family and friends. One notable colleague is Dr. David Bishop, his longtime associate and friend, whose

dedication and contributions to the Hurley research teams' success is immeasurable. Finally, despite the wobbly early years of his studies, Laurence credits his teachers for believing in him and inspiring him, especially Bordesley Green Technical School English teacher Mr. Granger and chemistry teacher Mr. Underhill (affectionately known as "The Mole"). At Bath University, much credit and appreciation are given to Jimmy Mearns (human biology), Terry Jefferies and Margaret Hansen (Pharmacognosy), followed by Heinz Floss at Purdue, who set the standard for creativity and innovation, while Ulf Hornemann mentored Laurence on scientific rigor.

And finally, Dr. Hurley gratefully acknowledges Drs. Elaine and Mike Jacobson for their collegiality during their time together as faculty members in rebuilding the medicinal chemistry program at the University of Arizona, their longtime friendship, and inspiration through their entrepreneurship.