Princeton University

Honors Faculty Members Receiving Emeritus Status

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for Receiving Emeritus Status

Lynn William Enquist

Lynn William Enquist, the Henry L. Hillman Professor of Molecular Biology, Emeritus, came to Princeton after nine years as a staff fellow in the Public Health Service at the National Institutes of Health (NIH) and twelve years in the biotech industry. He retired on December 31, 2020, after twenty-seven years on the Princeton faculty, having also served as chair of the Department of Molecular Biology for nearly a decade.

Lynn grew up in his parents' hometown of Milbank, South Dakota, and graduated from South Dakota State University in 1967 with a bachelor's of science in bacteriology. At a meeting of the local branch of the American Society for Microbiology (ASM), he met S. Galen Bradley, who convinced Lynn to join his lab at the University of Minnesota for his graduate studies. Two years later, Bradley left Minnesota to become chair of the Department of Microbiology at the Medical College of Virginia; Lynn received his Ph.D. there in 1971. During his graduate studies, Lynn began working with DNA, using techniques like DNA-DNA hybridization to determine the relatedness of Streptomyces species.

For his postdoctoral work, Lynn joined the lab of Ann Skalka at the Roche Institute of Molecular Biology to study bacteriophage λ. At this time, research with λ was at the forefront of molecular biology; it was fast-moving and competitive. Lynn's work with Skalka focused on understanding the relationship between DNA replication and recombination providing evidence that λ's recombination proteins are required for late-stage DNA replication. We now know that this is true for eukaryotic viruses as well.

Following his postdoctoral work, Lynn joined the Public Health Service as a staff fellow at NIH in Phil Leder's lab, where he continued work on λ with Bob Weisberg. Lynn developed a simple color-based assay that allowed detailed genetic analysis of the site-specific recombination system λ uses to integrate into the host chromosome. These were the early days of recombinant DNA and Lynn contributed to this powerful technology by using his knowledge of λ to construct cloning vectors that could not replicate outside of the laboratory; he also developed procedures for packing these vectors back into the phage head, allowing efficient transfer of recombinant DNA into cells. Indeed, Princeton University President Emerita Shirley M. Tilghman, who was also in Leder's lab at this time, used one of these vectors to clone the first mammalian gene.

Lynn's interests broadened from λ to eukaryotic viruses and in 1977, he accepted a staff scientist position in the NIH lab of George Vande Woude to work on herpesviruses and retroviruses. In these early days of recombinant DNA, work with these viruses required the highest level of containment, biosafety level 4 (BSL4), and Vande Woude had the required facilities in Building 41. This mausoleum-like building had suites of isolated labs that required one to enter through a shower! There Lynn constructed the world's first reported viral genome clones, providing a means to study the complex genome arrangements of herpesviruses.

The advent of recombinant DNA technology spurred the growth and development of the biotech industry and Lynn decided to join the new company Molecular Genetics, Inc., in Minnesota. There Lynn and colleagues cloned the herpesvirus gene for the major surface-exposed glycoprotein and expressed this gene in *Escherichia coli*, demonstrating the potential of this technology for the development of safe and effective vaccines against herpesviruses and other viruses. Despite these successes, he found that the business of science was not as fulfilling as basic research, so in 1984 he joined the new life sciences initiative at DuPont Corporate Research and Development. Here he developed a significant interest in how neuroinvasive herpesviruses infect and travel in the mammalian nervous system. However, after six years, the company's strategic plans changed, and a new company, DuPont Merck Pharmaceuticals, was formed. This new company was more interested in applied research than fundamental research, and Lynn's administrative duties increased.

Despite the fact that Lynn had not been at a teaching institution since he was a graduate student, he is a gifted teacher. This talent, and his passion for it, was revealed when he taught the "Cold Spring Harbor Advanced Bacterial Genetics" course with Tom Silhavy, which met for three weeks each summer from 1981 to 1985. Together with Mike Berman, Lynn and Silhavy wrote a very popular methods book called "Experiments with Gene Fusions." Lynn watched his friends, virologists Arnie Levine and Tom Shenk, recruit Silhavy to Princeton as the new Department of Molecular Biology was created, just as Lynn was moving to DuPont. Since Wilmington was only about seventy-five miles from Princeton, a relationship began. Lynn taught in several classes, attended the annual retreat, and participated in other departmental functions. This interaction flourished and he joined the faculty as a professor in 1993.

Lynn's assignment when he arrived at Princeton was to design and teach a virology course for upper-level undergraduates and first-year

graduate students. The course, "Viruses: Strategy and Tactics," was very successful. Together with his Princeton colleague Jane Flint, his former mentor, Ann Skalka, and Vincent Racaniello, he wrote a popular textbook that was published by ASM. He also received the Princeton President's Award for Distinguished Teaching in 2001. During his career, Lynn mentored over one hundred trainees. They included undergraduate students, graduate students, and postdoctoral fellows.

Lynn's research, which became focused on a model herpesvirus that infects a number of different animals, but not humans, flourished at Princeton. Viral infection leads to entry into the peripheral nervous system followed by retrograde transport up the axon to the nuclei where latency is established, and this movement can cover considerable distances; indeed, it can follow neural circuits to the brain. Reactivation can happen throughout the life of the host and anterograde transport to the dermis causes cold sores or more severe consequences, such as shingles. Lynn's lab worked out the molecular details of the virus's movement up and down the axon. They also harnessed the virus for studies of neuroanatomy because movement of the virus can reveal how neurons are connected, and these viral tools are extensively used throughout the neuroscience community to trace neural circuitry. His lab also developed a clever tri-chamber culture system that physically separates axons from cell bodies, allowing demonstration of gene-expression independent of immune defenses in infected axons.

As chair of the Department of Molecular Biology, Lynn hired several new faculty who have since prospered. He upgraded the department's facilities, revamped both the graduate and undergraduate curricula, and shepherded the department through the recession of 2008. In addition, he did much to facilitate the growth of the Lewis-Sigler Institute for Integrative Genomics and the establishment of a neuroscience curriculum and the Princeton Neuroscience Institute.

As a member of the scientific community, Lynn's service is exemplary. He served on and chaired the major virology study section at the NIH, served as the editor in chief of the *Journal of Virology* for a decade, and was the founding editor in chief of the *Annual Reviews of Virology*. Remarkably, he served as the president of both the American Society for Virology and ASM; he also served as a member of the board of directors for the American Association for the Advancement of Science (AAAS). He is a fellow of the American Academy of Microbiology and AAAS. He also was elected to the American Academy of Arts and Sciences.

Lynn will be sorely missed by the department and the international virus community. We wish him well in his retirement and we thank him for his many contributions.