



# BIOGRAPHICAL MEMOIRS

## WILLIAM J. LENNARZ

September 28, 1934–October 27, 2021  
Elected to the NAS, 1989

*A Biographical Memoir by John A. Hanover*

**WILLIAM JOSEPH “BILL”** Lennarz, my graduate adviser and mentor, passed away on October 27, 2021, in Williamsburg, Virginia, at the age of eighty-seven. He had an illustrious career with many distinctions, including serving as president of both the American Society for Biochemistry and Molecular Biology (1989) and the Society for Glycobiology (1994) and receiving the Karl Meyer Lectureship award from the Society for Glycobiology (2004). He was elected to the National Academy of Sciences in 1989. Upon preparing this overview, I have been reminded of the breadth of his scientific accomplishments and enduring legacy. I have also been overwhelmed with the realization of his impact on me and other alumni of the Lennarz lab.

Bill was born on September 28, 1934, in New York City. As he mentioned in his memoir, “How I Became a Biochemist,” Bill’s childhood interests included model railroading and chemistry.<sup>1</sup> He recalls driving his mother from her kitchen by producing H<sub>2</sub>S from a cobbled-together chemistry set in his basement. I must admit that each time I take the train to New York, which passes within sight of our old physiology building at the Johns Hopkins Medical School, I still think of Bill and his childhood interests in railroading and chemistry. Bill’s father worked with engineers but was not himself a part of that profession. Bill began his scientific journey at Pennsylvania State University in chemical engineering but found it too “quantitative” and switched majors to chemistry. In his senior year as an undergraduate, he worked in the laboratory of Philip Skell, a founder of carbene chemistry famous



for the “Skell rule” for predicting the formation of chemical compounds.

After this stint with Skell, Bill chose the University of Illinois for graduate studies in organic chemistry. There, he met Harold Snyder, a heterocycle chemist who became Bill’s dissertation adviser and gave Bill the task of using organic boron compounds in an anticancer context. During this time, Bill convinced the head of the biochemistry division of chemistry, Irwin C. “Gunny” Gunsalus, to allow him to do a sole major in biochemistry. Working in that environment exposed Bill to many young chemists and biochemists and helped shape his interest in both biology and chemistry. Among those notable scientists were William Rutter, Finn



Wold, and Lowell Hager. It was clearly an exciting time to be at the University of Illinois and Bill remembered it fondly.<sup>2</sup> Lennarz then moved to the laboratory of Konrad Bloch at Harvard University. In a 2002 article, Bill described how that postdoctoral position was arranged and said that he imagined he would work on the cholesterol problem.<sup>3</sup> Instead, he worked on fatty acid biosynthesis in yeast and bacteria.<sup>4,5</sup> In a 1993 interview, Konrad Bloch specifically mentioned Bill Lennarz as a highly successful alumnus of his lab, attributing to him the research that led to the concept of enzyme suicide inhibition.<sup>6</sup> Following this successful postdoctoral stint at Harvard, Bill began to seek faculty positions. He was invited by biochemist Albert Lehninger to visit the Johns Hopkins University School of Medicine in Baltimore, and Bill took a job there as assistant professor. After about five years at Hopkins, Bill adopted newly hired associate professor Ed Heath as an informal mentor. Bill shared some research interests with Ed, who clearly influenced Bill's future directions and whom Bill frequently mentioned as an influence.

I joined the Lennarz laboratory at Hopkins in 1976, first doing a research rotation and then staying on for my dissertation research. I was trained in both organic chemistry and biology, and I thought the Lennarz lab would be a good fit for my broad interest in biochemistry, and Bill graciously accepted me. He had already trained several graduate students at that point, including Malka Scher, Claudia Kent, Mary Kennedy, Paul Patterson, Sharon Krag, Eli Schmell, Doug Struck, and Gary Segal. Eli, Doug, and Gary were still in the lab and several postdoctoral fellows were in place at the time I joined the lab.

The lab was split between those doing research on sea urchin biology and fertilization and those doing work on glycoprotein biogenesis.<sup>7,8</sup> I was fortunate to work on both projects. Winston Chen, a long-term postdoc in the Lennarz lab, was tasked with "showing me the ropes." Winston was a wonderful resource, and Lennarz leaned on him heavily for the everyday running of the lab. I remember Winston fondly and was deeply saddened by his untimely passing in 1990 shortly after he began an independent career. Those five years at Johns Hopkins in the Lennarz lab were an exciting period for me. Bill's postdoctoral fellows over the period included Dottie Pless, Aaron Heifitz, Charles Glabe, Dan Carson, Bill Kinsey, Jim Elting, and Jerry Hart, who all later went on to productive careers in academics or industry. The atmosphere of the lab was always competitive but collegial. Lab meetings were highly interactive affairs. There was plenty of discussion and good-natured banter in a small smoke-filled room around a wooden table. A space-filling model of dolichol phosphate was mounted above the chalkboard like the trophy of an ongoing scientific safari. Bill

himself sometimes used his pipe as a gavel calling us to order. Other times he sat and politely listened. Invariably, Bill would succinctly summarize the discussion and place it in perspective for all of us. Bill always encouraged "outside of the box" thinking, and it was clear that he hoped to nurture creative ideas while still subjecting those ideas to rigorous scientific scrutiny.

Lennarz was an avid sailor, and he often used colorful nautical terms and phrases in our discussions. He spent as many days as he could on the water, especially Chesapeake Bay. I vividly remember going on one of his many boat trips on the bay as "crew." Bill also took me on several Saturday lunches at one of the markets in Baltimore to catch up both personally and professionally. In addition, the members of the lab looked forward to July Fourth fireworks at his home and the party leading up to the nighttime display. It was a wonderful environment for a young scientist, and I look back at that period fondly. I did a brief stint as a postdoctoral fellow in the Lennarz lab and with Bill's blessing left for postdoctoral studies with Ira Pastan at the National Institutes of Health in 1981.

In 1983, Bill Lennarz made a major move to become chair of the Department of Biochemistry and Molecular Biology at the University of Texas MD Anderson Cancer Center in Houston. I remained in close correspondence with Bill during this critical period and became aware of the challenges he faced in making this transition. In Houston, the Lennarz lab continued efforts on glycoprotein synthesis and the biochemistry of fertilization and largely transitioned to eukaryotic cell models. As chair, Lennarz successfully recruited several notable scientists as faculty members including Bill Klein, Barry Shur, and Eric Olson. As Bill recounts it, oil prices plummeted, and this decline hurt the University of Texas financially and constrained the growth of the department. In 1989, he made the decision to move to the State University of New York at Stony Brook. That same year, Bill was elected to the National Academy of Sciences, and I fondly remember celebrating that notable achievement with Bill, his lab, and his family. During this period, Bill also became editor-in-chief of the *Biochemical and Biophysical Research Communications* (BBRC) scientific journal. There, Bill initiated a period of leadership that greatly strengthened and expanded the scope of BBRC. His efforts extended its appeal and popularity to countries such as China, which had been largely neglected by the journal.

At Stony Brook, Lennarz's department expanded and thrived. He recruited twelve faculty to the department over the course of the first fifteen years. In 2009, Bill retired as chair at Stony Brook and was succeeded by Robert Haltiwanger, another noted glycobiologist who served as chairman until 2015. Bill's legacy of recruitment at Stony Brook is a

prime example of his ability to build strong teams and sustain a high-quality, productive research program.

No tribute to Bill Lennarz would be complete without a summary of his major research accomplishments over a highly productive independent career. Bill's early work on glycoprotein synthesis was carried out in parallel to similar work done by Luis Leloir, Robert Spiro, and Eduard Heath.<sup>9,10</sup> In these studies, Bill's lab made several noteworthy and unique contributions. Our group found that N-linked oligosaccharides were assembled into a large lipid-linked precursor prior to *en bloc* transfer to an elongating or fully folded glycoprotein.<sup>11</sup> We identified the protein sequence signaling this transfer and defined the structure of the transferred oligosaccharide.<sup>12</sup> The focus of these studies was also directed toward understanding the transmembrane assembly of the oligosaccharide and the sidedness of the transfer steps.<sup>13</sup> The process of N-glycosylation was completed in the lumen of the ER.<sup>14</sup> Oligosaccharide addition was shown to occur shortly after the growing nascent polypeptide chain exited the ribosome.<sup>15</sup> In parallel studies at that time, Lennarz and colleagues used the sea urchin system to decipher the process of fertilization and early development and the potential role of glycans in those processes.<sup>16,17</sup>

After these early studies, the Lennarz lab began to study the peptide N-glycanase NGLY1, an enzyme that cleaves the glycan from glycoproteins derived from the endoplasmic reticulum.<sup>18</sup> The work also focused on the interaction of glycoproteins with proteasomes and how that process was initiated and regulated. Mutations in NGLY1 are now known to give rise to a rare disease in children known as NGLY1 deficiency. The NGLY1 studies were driven by Bill's postdoctoral fellow Tadashi Suzuki, who continued to work on this problem. The Lennarz lab also tackled the question of how the oligosaccharide transferase (OST) interacted with the ribosome. They concluded that OST binds to the ribosome near its exit cleft, consistent with the enzymatic function of the transferase in mediating oligosaccharide transfer.<sup>19</sup> This led to a focus on the structure of the Sec63 translocon complex using cryo-electron microscopy.<sup>20</sup> The complex allows polypeptides to translocate from the cytosol to the lumen of the endoplasmic reticulum. This structural work led to a better understanding of the subunits of the complex and its orientation in the membrane. Thus, in many ways, Bill Lennarz returned to his early interests in the mechanisms by which transmembrane assembly of N-glycans occur.

In 2003, the Willam J. Lennarz Symposium was held in San Diego California. Many of Bill's former trainees and colleagues attended. This event provided a once-in-a-lifetime glimpse of Bill's scientific legacy. I was honored to speak at the symposium, and I both toasted Bill's accomplishments and talked about how he had influenced

my scientific development. Nearly all the speakers did the same. It was an excellent event and served as a kind of reunion for all the generations of scientists who had passed under Bill's tutelage over the many years. In 2007, Bill and I both attended "GLYCO 19," an international symposium on glycoconjugates in Cairns, Australia. We went to the Great Barrier Reef on a chartered boat together and chatted during the trip. Lennarz provided me with a strategy to "get my sea legs" to avoid sea sickness on the choppy ocean. It was a lasting treasured memory for me. Later that week, Bill, his wife Sheila, and I went on a long Aboriginal Australian-led tour in Queensland to view the majestic scenery and learn about the indigenous culture there. We were all struck by the Aboriginal Australian concept of time and the connectedness between humans and the natural world around us. Our discussion was wide ranging on that walkabout, but I distinctly remember thanking Bill for opening my eyes to the scientific world and his constant support during my formative years as a scientist. It was to be the last time we spent a significant amount of time together before his passing. We kept exchanging e-mails, however, and I would often receive a congratulatory note on some important paper or award. I will always be thankful for the support he gave me and my colleagues.

I learned of Bill Lennarz's passing just days before I was to give the Karl Meyer Lectureship Award lecture for the Society of Glycobiology in 2021, an award that Bill had received in 2004. Although saddened by the news, I dedicated my talk to his memory. It is from Bill that we trainees learned to choose important problems and how to tackle them tenaciously. We were encouraged to trust our data, keep a good notebook, and to not "use those weasel words" when presenting our findings. It gave me time to acknowledge the tremendous impact Bill Lennarz had on my career development. His loss was felt throughout the entire biochemistry community, as the many published tributes attest.

William J. Lennarz is survived by his wife Sheila; three sons, Willam, Matthew, and David; stepdaughter Jennifer Lennarz, stepson Simon Dorton (Amanda); eleven grandchildren; two great grandchildren; and his sister, Patricia Ender. He is greatly missed by all of those who had the pleasure and good fortune to spend time with him.

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