



Richard A. Lerner (1938–2021)—a structural biochemist and president of Scripps Institute

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Abstract

Richard A. Lerner (1938–2021) was both a chemist and an MD. He investigated the structure of peptides and proteins, identified a sleep-inducing lipid, and is best known for his pioneering work on catalytic antibodies. He is credited with making the Scripps Research Institute in La Jolla into a world-class center of chemistry, biochemistry, and biology.

Keywords Richard Lerner · Catalytic antibodies · Scripps Institute · Linus Pauling

For Richard Lerner (1938–2021, Figs. 1 and 2) [1], Linus Pauling's legacy was a determining factor in his scientific aspirations. He liked to refer to Pauling's 1948 Silliman lecture as the beginning of antibody catalysis. Pauling's broad-based presentation took stock of what was known in chemistry and what was left to learn. He discussed antibodies and enzymes and formulated their principal difference in the following: enzymes bind to transition states and antibodies bind to ground states. The task of the enzymes is to facilitate transformations. As antibodies bind to targets, they alert other systems to eliminate the molecules to which the antibodies are bound. Enzymes make and break bonds, rearrange them, and isomerize them. Antibodies bind. Lerner decided to continue Pauling's relevant program and became very successful in it.

Lerner was born and grew up in an East-European immigrant family on the South Side of Chicago. In school, he excelled in chemistry and in wrestling. Between 1956 and 1959, he attended Northwestern University and continued his studies at Stanford University School of Medicine, where he earned a BS degree in 1959 and his MD in 1964. He worked at the Scripps Research Institute, then at the Wistar Institute in Philadelphia, and rejoined Scripps in 1970 to stay with it for the rest of his career in various positions. He was its director, 1986–1991, and president and CEO, 1991–2009.

He was active in a number of other institutions and organizations, science academies, and editorial boards. A sampler of his distinctions is as follows: the Arthur C. Cope Award of the American Chemical Society, 1991; Member, National Academy of Sciences, 1991; Wolf Prize in Chemistry, 1994; Foreign Member, Royal Swedish Academy of Science, 1995; Member, American Academy of Arts and Sciences, 2000. He co-authored a book in 1984, *Molecular and chemical basis of virus virulence and immunogenicity* [2], and, over the years, as editor and author, contributed to the book series, titled *Vaccines*.

Lerner's approach to his chemical research was quite philosophical. Consider his work in antibody catalysis, which began in 1986. We talked about this when I recorded a conversation with him in 1997 in his office in La Jolla [1]. At the time, this project carried a lot of uncertainty and it was impossible to predict whether it would lead to success or to a spectacular failure. The risk was not existential, because he was already a tenured professor. Nonetheless, I asked him whether being in charge of a large research institute—at the time he was the President and CEO of Scripps—if he would be willing to hire somebody like his old self. He did not respond at once; obviously, he found the question intriguing. His response, finally, was that he would probably not hire such a person. When he started, back in 1986, antibody catalysis was not a fashionable area of research and it was a formidable task to secure grants for support. The skeptics had an easy task to show that his goals were unattainable, so he had to take considerable risk pursuing it.

Lerner and his colleagues synthesized a series of peptides that they knew exactly at which specific sites the antibodies

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Fig. 1 Richard Lerner in his office at the Scripps Institute, 1997 (photograph by I. Hargittai)

attacked. Their work enhanced knowledge about the mechanism of antibody action. Above I mentioned Pauling's view about the difference between enzymes and antibodies. However, opinions are divided whether enzymes and antibodies are truly so different. They are both proteins and possess the ability of binding. Both have the capability of using so-called co-factors when the required chemistry is not inherent in all the amino acids available to them. Such co-factors may be transition metals, redox systems, vitamins, and others. Lerner did not see fundamental difference between the enzymes and antibodies, at least not in their structural characteristics. However, there is a huge difference between the timescales of their production. The enzymes have evolved during millions and millions of years, and in evolution, there are no instructions. He mentioned Richard Dawkins's book *The Blind Watchmaker* to illustrate how it happens.

Lerner saw the main purpose of making antibody catalysts in the quest to understand how enzymes work. He quoted Richard Feynman: "What I cannot create, I do not understand." Lerner likened the approach to the natural products chemist synthesizing natural products to learn their chemistry. But he stressed that it was difficult to produce perfect enzymes, mimicking those operating in our organism. They function to perfection under the circumstances in the organism, including mild conditions, narrow pH range,

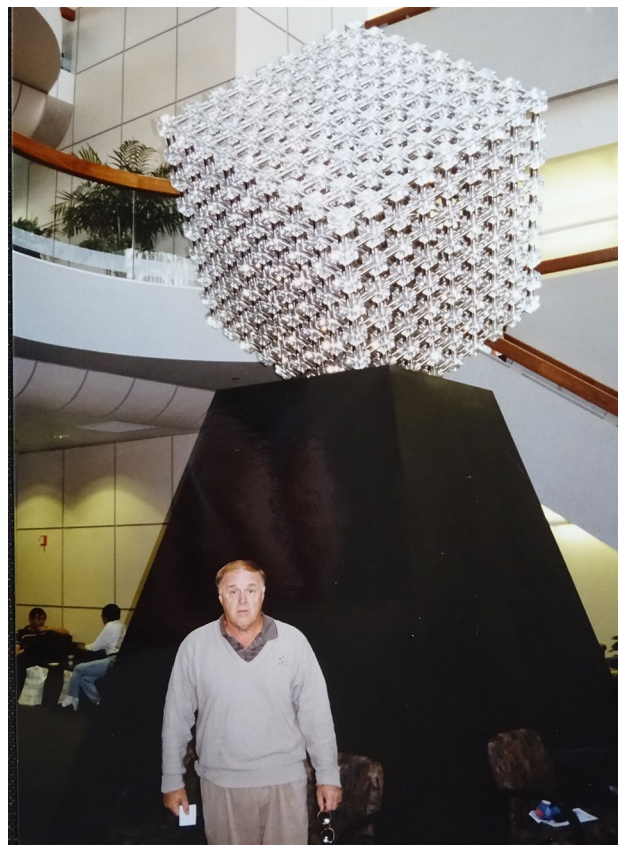


Fig. 2 Richard Lerner in the lobby of the Scripps Institute, 1997 (photograph by I. Hargittai)

and aqueous solutions. Many such enzymes must operate in a coordinated unison.

Being in charge of Scripps, he considered his principal task to ensure the possibility of unhindered research for its associates. He compared its mode of operation to the 47th Street jewelry district in Manhattan. The scientists have their own booths and the administration of Scripps makes sure that they can do whatever science they want to. As President and CEO, he decided only the general direction in which Scripps headed. Although most of the scientists had NIH grants, philanthropy was the most important source of support. He saw great advantage for research in Scripps in comparison with the usual university setup: Whereas research was the only consideration at Scripps, at a university, it was only one of several, such as teaching, the football team, and all kinds of university politics. Yet, Scripps was also a graduate school and the Rockefeller University and the research institutes of the German Max Planck Society might be the closest for comparison. Lerner likened biological experiments to archeology. The archeologists research the ruins of ancient civilizations and the biologists the ruins of evolution. He was in charge of a leading research institution on an international scale yet his greatest

pleasure came from his own “archaeological” exercises. He left his footprints in both.

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