Edwin G. Krebs (1918–2009)

The scientific community mourned the passing of a number of brilliant minds in 2009. One of them, Edwin Gerhard Krebs, played particularly important roles at the Journal of Biological Chemistry (JBC), serving as a member of the editorial board and for two decades as an associate editor. Dr. Krebs was also president of the American Society for Biochemistry and Molecular Biology in 1985.

Although Dr. Krebs left a lasting impression upon countless JBC editors, authors, and readers over the years, we asked his longtime collaborator and dear friend, Edmond H. Fischer, to share with us his thoughts about Ed Krebs’ character and accomplishments. Together, Drs. Fischer and Krebs made the key discovery of reversible protein phosphorylation, and they shared the 1992 Nobel Prize in Medicine for their contributions to “the opening up of novel insight into basic protein regulations at all levels and in all cells.”

Edwin Krebs was a man who was known for both his professional achievements and his unique personal qualities; he will be greatly missed.

The JBC Editor and Associate Editors
Memories of Ed Krebs

Ed Krebs died December 21, 2009, after a long illness and an increasingly debilitating disease. For me, it marked the end of an extraordinary era and the end of a lifelong and marvelous friendship.

Born in Lansing, Iowa, on June 6, 1918, Ed undertook his undergraduate studies at the University of Illinois in Urbana and then attended medical school at Washington University in St. Louis. It was during a residency there in 1944 at Barnes Hospital that he met his wife, Deedy, who was then a student nurse. After a stint in the U.S. Navy, where he served as a medical officer, Ed returned to Washington University to join the laboratories of Carl and Gerty Cori as a postdoctoral fellow in 1946. It was there that he started his studies on muscle glycogen phosphorylase, an enzyme that had been shown by Arda Green to exist in two interconvertible forms: phosphorylase $b$, which required 5’-AMP for activity, and phosphorylase $a$, which was fully active in the absence of the nucleotide.

In 1948, Ed was offered a position as an assistant professor of biochemistry at the University of Washington School of Medicine in Seattle. I arrived there as an assistant professor in 1953, and our collaboration began within a few short months.

Because the Coris didn’t know how AMP functioned, nor the way in which the two forms differed, we decided to take a crack at the problem. As it turned out, we never solved the AMP problem either: The nucleotide was recognized to serve as an allosteric activator of the enzyme only eight years later. But, we soon found out that, in reality, the activation of phosphorylase involved a totally different kind of mechanism: a reversible phosphorylation-dephosphorylation reaction that required calcium and ATP and two enzymes that were termed phosphorylase kinase and phosphatase.

We sent our resulting manuscript to the Journal of Biological Chemistry, which, in those days, was the main biochemistry journal published in English. Its editorial board was very small; in fact, there were perhaps only five or six people in the whole country who reviewed all the papers submitted, and we were well aware that Carl Cori was one of them. Although we knew that he would see the article, we had absolute faith that he would not take advantage of his position, and he did not. On the contrary, he was very excited by our results.

Ten years later, Ed would join the editorial board of the JBC. In 1972, he became an associate editor, and he remained one until 1993.

Although the reaction we had found would be viewed today as utterly trivial, it came nevertheless as a great surprise, because, at that time, nobody could imagine that the phosphorylation of an enzyme could be involved in its regulation. In fact, essentially nothing was known then about phosphoproteins themselves. Their only function was thought to be associated with the feeding of the young, and therefore, they were considered to be of no biological relevance. However, it soon became clear that the degradation of glycogen was far more complex—that it involved a cascade of enzymatic reactions, enzymes acting successively on one another.

Note that during the same period of time, Earl Sutherland’s laboratory, working on liver phosphorylase, had arrived at the same conclusion. An epochal finding that resulted from those studies was the discovery by Earl and Ted Rall of cyclic AMP, which served as a second messenger for the action of adrenaline. Together with their description of the adenylate cyclase system, the entire pathway for the phosphorolysis of glycogen was elucidated.

We often have been asked whether we realized, at the beginning, that we were dealing with a ubiquitous and, therefore, very fundamental process. Absolutely not. We stayed with this system because we felt it was an exciting and obviously important one, but we never could have predicted the incredible developments that were to follow. Furthermore, we were blessed by having, over the years, a superb group of students and collaborators, without whom we could not have accomplished all that we did. And then, of course, countless scientists throughout the world contributed greatly to the development of the field. So, although Ed and I were singled out by the Nobel committee for getting the ball rolling, the award we received should be seen as recognition of their collective contributions.

Eraldo Antonini once told me: “Many people can be top scientists, but not that many can also be real gentlemen.” Well, Ed was certainly both: a superb scientist and the absolute epitome of the gentleman.

Eddy Fischer

To find out more about Krebs’ life and seminal work, read the JBC Classic “Reversible Phosphorylation and Kinase Cascades: the Work of Edwin G. Krebs” at http://www.jbc.org/content/280/43/e40.

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