Christian R. H. Raetz

1947–2011

Teresa A Garrett

The research community lost one of its finest members when Chris Raetz succumbed to cancer in August. Through his research and training of more than 30 students and 40 postdoctoral fellows, Chris made an indelible and lasting mark on many in the lipid biochemistry community both personally and professionally.

After immigrating to the United States from Germany, Chris began his scientific training with a chemistry degree from Yale University. He moved on to medical school at Harvard but became sidetracked from a medical career when he began lab research with Eugene Kennedy. In the Kennedy lab, Chris began his life-long study of the enzymes of lipid metabolism. With Kennedy, he investigated the metabolism of cytidine diphosphate diacylglycerol (CDP-DAG), first by identifying CDP-DAG as a minor metabolite in *Escherichia coli* and then by characterizing enzymes involved in its metabolism, particularly phosphatidylsynthetase and CDP-DAG hydrolase. Chris attributed much of his approach to science and the way he mentored to the training he received from his own mentor and friend Eugene Kennedy, who also passed away recently.

With MD and PhD degrees in hand, Chris became a house officer at Brigham Hospital in Boston and then a postdoctoral fellow with Herbert Tabor at the National Institutes of Health in Bethesda, Maryland. In 1976, Chris took a faculty position at the University of Wisconsin at Madison and rapidly rose to the rank of professor. At Madison, he developed techniques for the identification of mutations in phospholipid biosynthesis and began his seminal work on the biosynthesis of lipid A, the lipid anchor of lipopolysaccharide, which is the major outer-membrane glycolipid of Gram-negative bacteria.

While investigating the interactions between mutations in the *E. coli* *pgsA* and *pgsB* genes, Chris observed the accumulation of a new lipid he called lipid X. Prior to the discovery of lipid X, the proposed structure of lipid A had been incorrect. With the demonstration of the structure of lipid X as diacylglucosamine-1-phosphate, the correct structure of lipid A was proposed. On the basis of this

foundational work, Chris elucidated the biosynthetic pathway of lipid A biosynthesis in *E. coli*.

His unique training in both medicine and lipid biochemistry led him for a time to Merck, where he served as executive director of biochemistry and then as vice president for research in biochemistry and microbiology. While at Merck he oversaw the development of the cholesterol-lowering drug simvastatin (Zocor) and began to pursue his interest in developing lipid A biosynthesis inhibitors as new antibacterials. The first committed step in the lipid A biosynthetic pathway, catalyzed by LpxC, became a prime target and may yet yield new drugs to combat multidrug-resistant Gram-negative bacteria.

When Chris became the George Barth Geller Professor and chair of biochemistry at the Duke University Medical Center in 1993, he returned to training students and postdoctoral fellows through a research program that involved identifying the enzymes involved in lipid A biosynthesis in *E. coli*. He and his colleagues identified the gene encoding each of the enzymes responsible for the nine steps of lipid A biosynthesis in *E. coli*. In addition to studying the enzymes directly involved in lipid A biosynthesis, he also investigated the proteins involved in lipid A transport and assembly, discovered enzymes involved in the inner and outer core glycosylations of lipid A and eventually branched out to investigate the pathways of lipid A modification in other Gram-negative bacteria.

In the past decade, Chris' involvement in the LipidMAPS consortium stimulated his interest in determining new lipid structures. His core facility developed MS techniques to identify unique lipids in a variety of systems, including *E. coli* and *Clostridium tetani*, as well as to quantify cardiolipin and prenol lipids in macrophages. This work, with a strong focus on determining

new lipid structures, drew directly on his successful approach to determining the lipid A biosynthetic pathway as well as his training with Gene Kennedy.

In all his work, Chris linked structure to biosynthesis. Though a molecular genetic- and enzymology-based approach was often his mainstay, he embraced NMR, MS and, most recently, X-ray crystallography. Before his passing, he was involved in determining the crystal structure of five of the nine lipid A biosynthetic enzymes.

In the past two years, Chris was particularly excited to return to studying glycerophospholipid biosynthesis in *E. coli*. He identified the final phosphatidylglycerolphosphate phosphatase in *E. coli* and would have loved to have finally understood why mutations in *pgsA* are compensated for by modulation of lipid A biosynthesis. There is no doubt that, given the time, he would have accomplished just that, coming full circle at the intersection of glycerophospholipid and lipid A biosynthesis.

Throughout his career Chris was bestowed many honors, including the 1979 Camille and Henry Dreyfus Teacher-Scholar Award, the 2002 American Society for Biochemistry and Molecular Biology Avanti Award in Lipids, the 2006 L.L.M. van Deenen Medal from the University of Utrecht and the 2006 Frederik B. Bang Award from the International Endotoxin and Innate Immunity Society. One of his proudest moments was his election to the National Academy of Sciences in 2006. He published more than 270 peer-reviewed papers and nearly 30 reviews. His scientific legacy will be carried on by those that he trained. Everyone who worked with him or knew him, especially his wife Madeline, his daughters Jackie and Lizzie, and his grandson Leo, will miss him.

Teresa A. Garrett is in the Department of Chemistry, Vassar College, Poughkeepsie, New York, USA.
e-mail: tegarrett@vassar.edu