AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Bacteriology®

EDITORIAL

Olaf Schneewind, 1961–2019: Scientist, Mentor, Friend

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On 26 May 2019 the scientific community lost Olaf Schneewind of the University of Chicago, who passed away following a 3-year battle with cancer. He was just 57 years old. Olaf taught us much about bacterial cell biology. In particular, he discovered and characterized a novel mechanism for anchoring proteins to the cell surface that is unique to all Gram-positive bacteria. Following four terms on the *Journal of Bacteriology* (JB) editorial board, he served as an extremely effective and very efficient editor of JB from 2010 to 2018. He was also a gifted mentor, evidenced in part by the tribute below, which was contributed by 18 former trainees, listed at the end, who are now principal investigators.

IN MEMORIAM

Olaf was a pioneering figure whose career impacted various disciplines within microbiology. He was a leading authority on Gram-positive and Gram-negative pathogens, was unabashedly a basic scientist who also spearheaded vaccine development, and was able to switch from genetics to molecular biology to biochemistry to immunology effortlessly as a project demanded.

Olaf was born in Germany and completed his M.D. and Ph.D. at the University of Cologne. He then moved to the United States and conducted research as a postdoctoral fellow at The Rockefeller University in the laboratory of Vincent Fischetti. While at Rockefeller, Olaf met the bacterial and phage geneticists Peter Model and Marjorie Russell, who became his lifelong mentors. In hindsight, one could trace the explosion of Olaf's career to a tiny note published in *Molecular Microbiology* (V. A. Fischetti, V. Pancholi, and O. Schneewind, Mol Microbiol 4:1603–1605, 1990, https://doi.org/10.1111/j.1365-2958.1990.tb02072.x) which simply reported an observation that all known (11 at the time) surface proteins in Gram-positive cocci harbored a simple conserved

Citation Silhavy TJ. 2019. Olaf Schneewind, 1961–2019: scientist, mentor, friend. J Bacteriol 201:e00422-19. https://doi.org/10.1128/JB.00422-19.

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Accepted manuscript posted online 29 July 2019
Published 6 September 2019

C-terminal sequence: the now famous LPXTG motif. Olaf concluded in that paper that this motif may contribute to anchoring proteins to the bacterial cell surface. Following that report, Olaf defied conventional thinking, which suggested that these proteins are likely simply anchored to the membrane just like surface proteins in other organisms, and made the seminal discovery that the LPXTG motif mediates the covalent attachment of proteins to the peptidoglycan of Gram-positive bacteria—a previously undescribed pathway for protein localization.

In 1992, Olaf started his lab at the University of California, Los Angeles (UCLA), as an assistant professor. Olaf predicted that the anchoring of proteins to the cell wall would be catalyzed by an entity that he preemptively named "sortase" and began his hunt for this elusive enzyme (O. Schneewind, A. Fowler, and K. F. Faull, Science 268:103–106, 1995, https://doi.org/10.1126/science.7701329). After several years and multiple (elegantly designed) genetic and biochemical strategies failed to isolate the sortase protein or identify the sortase gene, Olaf's group, in a biochemical/genetic tour de force, performed ~1,000 radiolabeling/immunoprecipitation experiments on chemically mutagenized *Staphylococcus aureus* to first isolate a mutant that was defective in anchoring a model protein substrate to the cell wall. Through genetic complementation, an additional ~3,000 similar experiments were performed to isolate the gene responsible for this phenotype (S. K. Mazmanian, G. Liu, H. Ton-That, and O. Schneewind, Science 285:760–763, 1999, https://doi.org/10.1126/science.285.5428.760).

Those of us in the laboratory at the time learned a valuable lesson from watching this project unfold: it is great to design clever experiments (and Olaf certainly designed many of those), but for some scientific problems, old-fashioned hard work can trump elegance. Since the initial discovery of sortase in *S. aureus*, other sortase homologs with slightly different substrate preferences have been uncovered and have been implicated in multiple cellular functions, including metal transport across the bacterial cell envelope and Gram-positive pilus assembly. In an unexpected twist, recombinant sortase is now widely used as a bioengineering tool to site specifically ligate molecules onto targets of interest bearing a C-terminal LPXTG motif (N. Pishesha. J. R. Ingram, and H. L. Ploegh, Annu Rev Cell Dev Biol 34:163–188, 2018, https://doi.org/10.1146/annurev-cellbio-100617-062527).

While at UCLA and before receiving tenure, Olaf broadened the scope of his research on protein localization and began to work on type III protein secretion in Gram-negative bacteria (initially *Yersinia enterocolitica*, later expanding into the causative agent of plague, *Yersinia pestis*). Olaf's lab provided insights into how type III-secreted proteins are recognized as secretion substrates, how their synthesis can be regulated, and how these protein toxins are injected into host cells.

In 1997, Olaf married Dominique Missiakas, a biochemist by training with whom he began collaborating on microbial pathogenesis and vaccine development and continued to do so for the rest of his career. In 2001, Olaf and Dominique moved their laboratories to the University of Chicago, where Olaf was hired as the chair of the Committee on Microbiology. Shortly afterwards, Olaf established the Department of Microbiology at the University of Chicago. In Chicago, he expanded his research program to include biodefense, and from 2003 to 2014 he was the principal investigator of the NIH/NIAID Great Lakes Regional Center of Excellence for Biodefense and Emerging Infectious Disease Research, which formed a consortium of top academic institutions in the upper Midwest to study the pathogenesis of microbial agents with bioterrorism potential to develop new methods for prevention and treatment. To complement this effort, Olaf also established the Howard Taylor Ricketts Laboratory at the Argonne National Laboratory in 2010. Olaf's growing interest in vaccine development became a focus of his biodefense research and led to several U.S. patents for vaccine platforms for plague, anthrax, and *S. aureus*.

Olaf received many awards during his career, including the Shipley Award from Harvard Medical School, election to the American Academy of Microbiology, and selection as a fellow of the American Association for the Advancement of Science. In 2018, he was elected to the National Academy of Sciences. Most recently, he served as an editor for the *Annual Review of Microbiology* and JB, a society journal of which he was very fond.

Olaf's principal legacy, though, may be the exceptional training that he provided to young scientists in his laboratory. Many of his former students and fellows now serve as leaders in industry and science policy, and a remarkable proportion of his trainees are now principal investigators of their own laboratories, studying a diverse array of topics in microbiology and beyond. Considering the current scientific landscape of reduced funding and the unprecedented scarcity of academic positions, combined with the fact that Olaf only started his independent career in 1992, the fostering of so many independent scientists from a single training environment is extraordinary. The breadth of topics studied by his scientific progeny is so large undoubtedly because Olaf stressed to his mentees the importance of first identifying an important scientific problem—even if one may be considered unqualified initially to study that problem—and then breaking the problem down into distinct parts that could be systematically solved through experimentation.

According to this philosophy, any specific techniques required to solve that problem could be learned and were therefore a secondary consideration. Projects were driven by biological questions and unfettered by the technologies required to answer them, resulting in boundless opportunities for discovery. For example, when he uncovered that proteins are covalently anchored to the Gram-positive cell wall, he became an expert on mass spectrometry, which allowed him to understand the chemical linkage by which this is achieved. When he became interested in type III secretion systems, his laboratory set up tissue culture infection models and developed biochemical fractionation techniques to identify where different secreted proteins ended up. When he sought to design vaccines, he developed new experimental models and immersed himself in the language of immunology. Even while battling his illness, Olaf's enthusiasm for and devotion to microbiology research remained, with his last manuscript accepted for publication in *Nature* just days before his death.

Olaf's unwavering devotion to science and scientific training, his timely words of wisdom, his staunch integrity, and his enduring mentorship and friendship, as well as his oversized personality, will be missed. Olaf inspired those around him with his remarkable approach to science and life. He was an outstanding father, husband, friend, mentor, and scientist who made a tremendous impact in only a short time. Olaf is survived by his wife, Dominique Missiakas, who is a professor of microbiology at the University of Chicago, and his three daughters, Daphne, Chloe, and Penelope, as well as his mother and brother, over fifty former graduate students and postdoctoral fellows in microbiology, and many friends and colleagues.

This tribute was written by the following:

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