RETROSPECTIVE

Todd R. Klaenhammer, an inspirational food microbiologist who leaves a lasting legacy

Rodolphe Barrangou[a,1] and Colin Hill[b]

Todd R. Klaenhammer (1951–2021) dedicated his professional life to the study of bacteria of importance to food. He conducted his doctorate under the guidance of Larry McKay at the University of Minnesota, who inspired him to apply the newest advances in bacterial genetics to the lactic acid bacteria, responsible for many food fermentations. Todd stood out from his peers at an early age. He was offered a position and started his 40-year academic career in the prestigious Food Science Department at North Carolina State University before he had even defended his doctorate. Todd always had a singular focus. While most food scientists followed the lead of the funding agencies and "better" journals by working on foodborne pathogens responsible for infectious diseases, he preferred to study the beneficial bacteria associated with food. Todd forged his illustrious career by working on commercially important bacteria, such as the dairy starter cultures responsible for cheese fermentations and probiotics that were associated with diverse health benefits. Over his long career, Todd managed to combine fundamental science with commercially relevant research. It is a measure of his accomplishments that you could spend a long time in your university library reading the many influential scientific articles Todd wrote, but if you took a lunch break and went to the dairy section of the canteen you could also choose from a variety of cheeses that were made with phage-resistant starter cultures that he generated, or perhaps enjoy a yogurt formulated with some of the health-promoting probiotics he pioneered.

Throughout his career, Todd navigated the food microbiology research landscape with flair and intuition. He was always true to his favored lactic acid bacteria, but he repeatedly and skillfully adjusted the focus of his laboratory group, often leading the field into new areas. Todd was particularly attracted to using the emerging science of molecular biology to unravel the mechanisms by which these diverse bacteria play important roles in food. One of his most noteworthy pursuits included his early studies on bacteriocins that remains his most highly cited work (1). He also developed genetic engineering tools to provide the means of genetically dissecting the previously inaccessible streptococci, lactococci, and lactobacilli. These tools are still widely used in both academia and industry. Bacterial viruses (phage) were a constant source of disruption to the cheese industry, and Todd did some of his most elegant work on defining phage-resistance mechanisms and impressively managed to deploy abortive infection and restriction modification defense systems in commercial starter cultures. In this research, he even conducted some of the earliest bacterial work on RNA interference and CRISPR. He also worked extensively on the genetic basis of health-promoting lactobacilli, widely used as commercial probiotics. Much of this latter work built a foundation for the development of next-generation probiotics and Todd provided the tools used in the first series of experiments that laid the basis for the characterization of CRISPR-Cas as the bacterial adaptive immune system, fittingly in dairy cultures.

Todd R. Klaenhammer. Image credit: North Carolina State University/Marc Hall.

Todd remained fascinated by the molecular mechanisms underpinning the interplay between bacteria and their environment, whether as hosts in need of evading predatory phages, as fermenting cultures responsible for the organoleptic properties of dairy products, or as health-promoting agents for consumers.

[a]Department of Food, Bioprocessing, and Nutrition Sciences, North Carolina State University, Raleigh, NC 27606; and [b]APC Microbiome Ireland and School of Microbiology, University College Cork, T12 YT20 Cork, Ireland

Author contributions: R.B. and C.H. wrote the paper.

The authors declare no competing interest.

Published under the PNAS license.

[1]To whom correspondence may be addressed. Email: rbarran@ncsu.edu.

Published May 19, 2021.

Downloaded at Palestinian Territory, occupied on November 30, 2021

www.manaraa.com

He was always ready to take advantage of new technologies and advances in sequencing and bioinformatics, but he was never bewitched by them and remained a dedicated experimental scientist to the end of his career. For example, Todd raised millions in funding in the 1990s to sequence the complete 1.9-Mbp genome of the probiotic strain *Lactobacillus acidophilus* NCFM. Only a short time earlier this would have seemed an impossible task, but Todd believed that this was the path forward, and with typical determination and passion he made it happen. Todd was thrilled that a project so close to his heart made the cover of PNAS for his inaugural article (2). He was also ahead of his time in the early 2000s in building costly custom cDNA spotted microarrays in an attempt to gain mechanistic insights into probiotic mode-of-action studies. But despite leading the charge in the application of these technologies, Todd chose not to continue sequencing more and more bacteria, but rather went on to conduct his favorite and most impactful work in a series of PNAS papers documenting carefully designed experiments to establish the genetic basis of how probiotics can colonize the human gastrointestinal tract and how they can improve digestion and relieve the symptoms of lactose intolerance (3). Todd also engineered lactobacilli to control gut inflammation and manipulate the host immune response (notably dendritic cells) (4). He even expressed antigenic motifs on the outer surface of probiotics as a means of immunizing the host against pathogens (5).

As a result of the opportunities and the mentorship he received himself as a young scientist (notably from Larry McKay, who piqued his interest in food microbiology), Todd was always determined to "pay it forward" and play a role in developing the next generation of talent. Indeed, he always had a strong sense of the scientific continuum within the food microbiology community (often referencing the foundational work of Louis Pasteur, Elie Metchnikoff, and even occasionally quoting Antonie van Leeuwenhoek). He was incredibly generous to his colleagues, both in terms of sharing reagents and giving credit to scientific excellence wherever he saw it. One of Todd's most valuable and impactful skills was his ability to humorously share his passion with others and to inspire the next generation of food microbiologists. His caring mentoring was appreciated by all who worked with him and he put huge efforts into recognizing and nurturing emerging talent. Todd made himself accessible to all and was an advocate of inclusivity throughout his career. We suggest that his biggest impact was as a remarkable scientist who inspired countless food microbiologists. This is true for those who worked under his supervision and many others who had contact with Todd over the years. Many of his alumni have been successful in industry and academia as a direct result of the experience of working for such a generous and yet rigorous scientist.

We remember the day Todd received the news of his election into the National Academy of Sciences (NAS). He had a hard time believing the unexpected call and was honored by the fact that he was the first food scientist to join the ranks of the Academy. He religiously attended the NAS annual meeting with his wife Amy, always happy to share his own excitement about the first visit to the Kavli auditorium, to serve and connect with his peers in Section 62—Plant, Soil, and Microbial Sciences—and ensure he dutifully nominated, supported, and voted for worthy individuals. Todd took advantage of his membership to encourage his colleagues and competitors in food microbiology research to publish their best work in PNAS, but as was typical of Todd, he also acted as a rigorous and critical editor. He was determined that any work published in the journal should stand comparison with the best work in any other scientific field. Fittingly, he cohosted a NAS colloquium with Jeffrey Gordon in 2009, entitled "A rendezvous with our microbes," identifying the "pressing need" for the newly developing microbiome field "to define the challenges, gaps in knowledge, and opportunities that this exciting field of study offers" (6). His appetite for service to the wider scientific community also extended to editorial duties (together with Mike Doyle, he established the *Annual Reviews in Food Science and Technology*), his reviewing responsibilities (for many journals and funding agencies), and his role in establishing the International Scientific Association for Prebiotics and Probiotics and serving on its board and many other advisory boards and scientific committees.

While Todd received many national and international accolades, perhaps his greatest source of fulfillment was the respect he earned from his colleagues. It is remarkable that he achieved such international prominence despite maintaining a relatively small laboratory group throughout his career. Todd openly admired the work of international colleagues and he gained and maintained their respect and admiration in return. For those of us who worked in Europe, a historical powerhouse in food microbiology, Todd was always regarded as a friend and colleague, while we also respected his many contributions to the field. He was also a superb communicator. While his science spoke for itself, Todd had an eloquent and engaging style and he captivated audiences in hundreds of seminars, lectures, and keynotes delivered across the globe. If you were fortunate enough to encounter Todd at the social fringes of a scientific conference, you soon learned that he was a born raconteur who loved sharing entertaining stories about his experiences and telling compelling jokes about prominent scientists and their adventures, most often with the joke being at his own expense. He was a driven competitor outside of the laboratory, whether on the golf course, the squash court, or the hunting grounds, where his highly trained dogs were a source of pride and relaxation. Todd was a trusted friend to many and was devoted to his family, always speaking so proudly of his wife Amy and his daughter Ellen.

It now falls to those of us who knew Todd to extend his legacy and share his passion, and prompt the next generation of food microbiologists to "get cultured and eat bacteria."

Downloaded at Palestinian Territory, occupied on November 30, 2021

www.manaraa.com

1 T. R. Klaenhammer, Genetics of bacteriocins produced by lactic acid bacteria. *FEMS Microbiol. Rev.* **12**, 39–85 (1993).
2 E. Altermann *et al.*, Complete genome sequence of the probiotic lactic acid bacterium *Lactobacillus acidophilus* NCFM. *Proc. Natl. Acad. Sci. U.S.A.* **102**, 3906–3912 (2005).
3 M. A. Azcarate-Peril *et al.*, Impact of short-chain galactooligosaccharides on the gut microbiome of lactose-intolerant individuals. *Proc. Natl. Acad. Sci. U.S.A.* **114**, E367–E375 (2017).
4 M. Mohamadzadeh *et al.*, Lactobacilli activate human dendritic cells that skew T cells toward T helper 1 polarization. *Proc. Natl. Acad. Sci. U.S.A.* **102**, 2880–2885 (2005).
5 M. Mohamadzadeh, T. Duong, S. J. Sandwick, T. Hoover, T. R. Klaenhammer, Dendritic cell targeting of Bacillus anthracis protective antigen expressed by *Lactobacillus acidophilus* protects mice from lethal challenge. *Proc. Natl. Acad. Sci. U.S.A.* **106**, 4331–4336 (2009).
6 J. I. Gordon, T. R. Klaenhammer, A rendezvous with our microbes. *Proc. Natl. Acad. Sci. U.S.A.* **108** (suppl. 1), 4513–4515 (2011).

Downloaded at Palestinian Territory, occupied on November 30, 2021

https://doi.org/10.1073/pnas.2107754118
www.manaraa.com