

## Charles D. Surh, PhD: 1961–2017

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Charles D. Surh, or “Charlie,” a world leader in the field of immune homeostasis and tolerance, passed away on 6 October 2017, after a heroic fight with colon cancer. Charlie died peacefully at his home surrounded by his loving family. It was too soon. Charlie was only 56 years young and at the peak of his amazing scientific career, during which he pioneered the field of T-cell homeostasis.

Charlie’s father moved his whole family from Korea to the United States when Charlie was only 11 years old. Although the road to adjusting to a new language and culture was not easy, nothing could stop Charlie from reaching the highest and achieving the most. In 1978, Charlie enrolled at the University of California, San Diego, where in 1983 he earned his BS degree in chemistry. He went on to obtain his PhD in immunology in 1989 from the University of California, Davis. It was there, in the laboratory of Eric M. Gershwin, that Charlie first became interested in the immune system and the complexity of self-tolerance and autoimmunity. From UC Davis, he went to The Scripps Research Institute (TSRI) in La Jolla, California, and joined the laboratory of Jonathan Sprent as a postdoctoral fellow. His post doc lasted only 3 years (1989–1992), but the friendship and collaboration he established with Jon would be lifelong. As he rapidly defined himself as an independent researcher in the Department of Immunology at TSRI—as an assistant professor in 1993, an associate professor



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in 1998, an associate professor with tenure in 2005, and finally, in 2008, as a full professor—he continued to collaborate with Jon and together they pioneered the field of T-cell tolerance and cytokine-driven homeostasis and immune memory. They coauthored more than 70 milestone papers.

In 2009 Charlie went back to his roots and became a professor in the Division of Integrative Biosciences and Biotechnology at the Pohang University of Science and Technology in Pohang (POSTECH), Korea. Determined to promote research and science in his home country, he started and directed the Academy of Microbiology and Immunology, part of the Institute for

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Basic Science at POSTECH. However, he maintained his presence and influence in the United States, and in 2012 he joined the La Jolla Institute for Allergy and Immunology, in La Jolla, California, as an adjunct professor.

Even from the start of his scientific career, Charlie was determined to understand and elucidate the concept of immune homeostasis and coexistence. His work showed that, in conjunction with sensing self-/major histocompatibility complexes, mature T-cell homeostasis was controlled by the related cytokines, IL-7 and IL-15, and their respective receptors. Just last year Charlie published a brilliant study elucidating the mechanisms that control the IL-7 availability at steady state.<sup>1</sup> He showed that IL-7 is produced mainly by nonhematopoietic cells and that T cells are primarily responsible for limiting IL-7 availability by regulating IL-7R expression. Surprisingly, he also found that innate lymphoid cells have a potent influence on IL-7 homeostasis and that although these non-T cell lymphocytes embody only a minor subset they nevertheless represent major competitors for IL-7 within the T-cell niche. He further elucidated the mechanism and found that, unlike T cells, the innate cells appear to be resistant to IL-7-induced downregulation of the transcription factor FOXO1, which in turn regulates the expression of IL-7R. With this work Charlie showed that competition for survival cytokines is not limited to defined T-cell subsets but that non-T cells are also significant cytokine consumers and compete equally in the struggle for survival and coexistence. As he himself said it so well, “The findings are not only of interest to the esoteric field of immune homeostasis, but also to the broad biological community because they are a stark reminder that life exists as a complex concert and not as a collection of various types of cells that merely just co-exist.”<sup>2</sup>



“A long road ahead.” Young Charlie in Korea. (Photo courtesy of Nicolette Surh Baker.)

Together with Jon Sprent, Charlie also exposed the power of cytokine/monoclonal antibody complexes to expand and activate particular T-cell subsets *in vivo* and explored the therapeutic potential of these findings to boost the immune system for antitumor therapy and to expand regulatory T cells to control autoimmunity, allergy, and other inflammatory diseases.<sup>3</sup>

At POSTECH in Korea, Charlie built a state-of-the-art germ- and antigen-free mouse research facility. He and his team developed a strong interest in mucosal immunology and in uncovering mechanisms and principles that govern the peaceful coexistence of the microbiome, the vast load of harmless dietary and other non-self and self-antigens, the host tissue, and the mucosal immune system in the intestine. Previously, Charlie’s focus had been on understanding self-tolerance, but he quickly realized that at the mucosal interface different rules must apply in order to maintain immune quiescence as well as optimal protection, not only against pathogen-induced damage but also against immune pathology. In 2016, he published an innovative paper explaining how dietary antigens induce regulatory T cells in the lamina propria of the small intestine, thereby preventing aberrant immune responses directed toward harmless luminal antigens.<sup>4</sup> By comparing mucosal T cells isolated from specific pathogen-free mice fed a constant, controlled chow

diet with those isolated from germ-free mice weaned onto and subsequently raised on an elemental liquid diet free of any macromolecules, Charlie and his team were able to demonstrate that in normal laboratory mice the vast majority of small-intestine peripherally induced regulatory T cells are induced by dietary antigens from solid foods. Moreover, he showed that, unlike tissue-resident memory T cells, these intestinal diet-dependent peripherally induced regulatory T cells required constant triggering and were able to repress underlying strong immunity to ingested protein antigens.

Although Charlie was new to the field of mucosal immunology, he quickly understood the uniqueness of the challenges that drive and shape the local immune cells, and he realized that rules and concepts defined for systemic T cells could not simply be translated to explain the protective function and regulation of the mucosal T cells. He also recognized that, although many key mechanisms that regulate the immune system have been deciphered, many more have yet to be discovered, especially in the area of mucosal immunology. Therefore, Charlie's passing is a big loss not only for immunology but particularly for mucosal immunology. He was gearing up for a major effort to explore and promote new research in this area, in part through rigorous control of dietary antigen exposure.

In addition to being a true innovator, always eager to make new discoveries, Charlie had impeccable integrity. He was critical and not easily convinced, but he was equally generous with praise. He was inspiring and sparked enthusiasm in everyone who worked with him. When he was diagnosed with cancer in 2015, Charlie continued his research with the same pace and the same energy and passion as ever.

Charlie had many passions in life in addition to science, the foremost being his wonderful family. He married Helen Roh Oh, the love of his life, whom he met when they were in college. They were blessed with three wonderful children—Nicolette, Christopher, and Natalie—who meant the world to him. As his children grew up and went their own way, they held onto an intimate and unbreakable family circle. That strong bond brought them all together at home those last few weeks, during which they spent quality time with Charlie without focusing on the final moment. Charlie enjoyed togetherness and welcomed friends and family, sharing jokes and laughs and reliving happy moments. He also was an excellent golfer and an avid hiker and fitness enthusiast, and he enjoyed good food and wine, especially from his brother's winery. At the end, wine was no longer on the table, but good memories always accompanied by a good glass of fine wine will certainly be remembered by all who knew Charlie.

Although we have lost a brilliant scientist, an esteemed colleague, and a wonderful friend to many, Charlie's legacy will live on in those who had the good fortune to cross his path and experience his passion for great science and the beauty of life.

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