

A tribute to Ralph M. Steinman

Kayo Inaba

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Obituary

Ralph Marvin Steinman, the pioneering immunologist and discoverer of dendritic cells — pivotal cells that initiate and regulate the body's immune response — passed away on September 30, 2011, just three days before it was announced that he was to be awarded the 2011 Nobel Prize in Physiology or Medicine (Figure 1). Ralph was born on January 14, 1943, in Montreal, the second of four siblings. After graduating with a BSc from McGill University, where he studied biology and chemistry, he worked for two years as a predoctoral research fellow at Harvard Medical School before receiving his MD in 1968. He then was an intern and resident at Massachusetts General Hospital. In 1970, he became a postdoctoral fellow at The Rockefeller University in New York, where he worked with Zanvil A. Cohn and James G. Hirsch, leaders in the study of phagocytes. He never left The Rockefeller University, becoming professor and senior physician in the Laboratory of Cellular Physiology and Immunology (1988), Henry G. Kunkel Professor (1995), and director of the Christopher H. Browne Center for Immunology and Immune Diseases (1998). When Ralph joined the lab led by Cohn and Hirsch, each of the researchers — many becoming preeminent scientists in their own right — was working on phagocytes known as macrophages. But in 1973, Ralph and Cohn discovered dendritic [...]

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Ralph was born on January 14, 1943, in Montreal, the second of four siblings. After graduating with a BSc from McGill University, where he studied biology and chemistry, he worked for two years as a predoctoral research fellow at Harvard Medical School before receiving his MD in 1968. He then was an intern and resident at Massachusetts General Hospital. In 1970, he became a postdoctoral fellow at The Rockefeller University in New York, where he worked with Zanvil A. Cohn and James G. Hirsch, leaders in the study of phagocytes. He never left The Rockefeller University, becoming professor and senior physician in the Laboratory of Cellular Physiology and Immunology (1988), Henry G. Kunkel Professor (1995), and director of the Christopher H. Browne Center for Immunology and Immune Diseases (1998).

When Ralph joined the lab led by Cohn and Hirsch, each of the researchers — many becoming preeminent scientists in their own right — was working on phagocytes known as macrophages. But in 1973, Ralph and Cohn discovered dendritic cells — named after the Greek word for tree (*dendreon*) for their long and tree-like arms. For this discovery and subsequent studies exploring the unique capacity of dendritic cells to activate and regulate adaptive immunity, the Nobel Committee bestowed upon Ralph the 2011 Nobel Prize in Physiology or Medicine. The other recipients — Jules Hoffmann of the French National Center of Scientific Research in Strasbourg and Bruce Beutler of the Scripps Research Institute in La Jolla — are being recognized for their discovery of receptor proteins that can recognize microorganisms and activate innate immunity (pattern recognition receptors). Linking these two findings about dendritic cell functions and the role of pattern recognition receptors has helped elucidate how immune self-defense mechanisms work — how activation of the innate immunity leads to adaptive immune responses.

Sadly, Ralph passed away just three days before the Nobel Committee announcement, and after four and a half years battling pan-

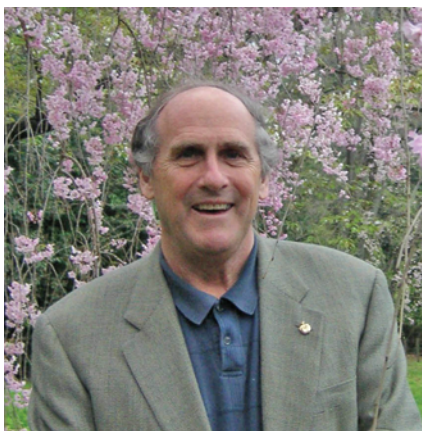


Figure 1
Ralph Steinman in the garden of Nijo Castle, Kyoto, in April 2007 before going to a board meeting at RIKEN, Yokohama.

creatic cancer. He was passionately involved in science until the last days of his life, and it is deeply lamentable that he did not live to hear of his award. The news of Ralph's passing left me with a profound sense of grief, not only because he deeply regretted the loss of the opportunity to continue his scientific work, but also because his passing will be a great loss to the immunology community.

I first met Ralph at the Naito Foundation International Symposium "Self-Defense Mechanisms: Role of Macrophages," which was held in Tokyo November 2–4, 1981. This was Ralph's first visit to Japan. Inspired by Ralph's discovery of dendritic cells, I had started my research into dendritic cells and macrophages at Kyoto University. At that time, few believed that dendritic cells could be a unique cell type that could not only initiate but also regulate immune responses. I joined Ralph's lab in 1982, and stayed for 26 productive months. After I returned to Kyoto, we continued professionally to collaborate in our research while, personally, our respective families kept in close contact. I feel privileged to have had such a rich and rewarding relationship with this great man through these many years.

Ralph was an impressive jogger, hiker, and skier. He always carried jogging shoes with him when traveling to meetings, symposia, and congresses. When he stayed at our house, near the university campus, he would jog on the track every morning. His

shoes, left ready for his next visit, still wait on the top shelf of our shoe closet, watching us as we go about our lives. My hiking shoes, bought for me by Ralph to hike a mountain near Saranac Lake in New York State in 1984, sit comfortably alongside.

Ralph's amazing mind has always commanded my greatest admiration and respect. During his extraordinary career, he trained many excellent graduate students and postdoctoral fellows from around the world; many are now professors in immunology departments worldwide. He was always encouraging, enthusiastic, and excited about the findings of researchers in his lab, and even those from other labs, especially those whose work related to dendritic cells. One of his first questions whenever we met was "What new findings?" I think this was his way of encouraging us in our experiments. His approach actively fostered a worldwide community in which everyone worked together in harmony and in collaboration.

During his career, Ralph published nearly 450 scientific papers, with more slated for publication in the next few months. He was elected to the National Academy of Sciences and won numerous awards, including the Max Planck Research Award, the Robert Koch Prize, the Gairdner Foundation International Award, the Novartis Prize in Basic Immunology, the Debrecen Award for Molecular Medicine, the Albert Lasker Basic Medical Research Award, and, of course, the Nobel Prize. Ralph was the most extraordinarily generous person, whose devotion and unswerving service to the scientific community were unprecedented.

Ralph's family organized an informal gathering on the floor of his new lab on October 10. It allowed me, along with the more than 300 other people from around the world in attendance, to share my appreciation for Ralph's professional and personal guidance over the years and to express just how much he will be missed. It is difficult to believe that Ralph is no longer with us, although in spirit he will be with us forever.

Kayo Inaba

Laboratory of Immunobiology, Department of Animal Development and Physiology, Graduate School of Biostudies, Kyoto University, Kyoto, Japan. Phone: 81.75.753.4088; Fax: 81.75.753.4112; E-mail: Kayo@lif.kyoto-u.ac.jp.