PublisherInfo				
PublisherName		BioMed Central		
PublisherLocation		London		
PublisherImprintName		BioMed Central		

Charles A. Janeway, Jr

ArticleInfo		
ArticleID		4756
ArticleDOI		10.1186/gb-spotlight-20030422-02
ArticleCitationID		spotlight-20030122-02
ArticleSequenceNumber	$\begin{bmatrix} \vdots \end{bmatrix}$	108
ArticleCategory	\Box	Research news
ArticleFirstPage	\Box	1
ArticleLastPage	$\begin{bmatrix} \vdots \end{bmatrix}$	3
ArticleHistory	:	RegistrationDate : 2003–4–22 OnlineDate : 2003–4–22
ArticleCopyright		BioMed Central Ltd2003
ArticleGrants	\Box	
ArticleContext		130594411

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Charles A. Janeway, Jr, an immunologist known for his work on innate immunity and as the principal author of the acclaimed textbook, *Immunobiology: The Immune System in Health and Disease*, died in New Haven on April 12 after a long struggle with B-cell lymphoma. He was 60 years old.

During his 34-year career, Janeway tackled many of immunology's big questions, and he formulated many of the concepts that are the basis of the field today. He made major contributions to the understanding of T-lymphocyte biology and is regarded as the father of innate immunity, the body's first line of defense against infection.

"He was known for generating ideas, often controversial, provocative, and ahead of their time, but often proving to be right - a truly intuitive scientist," said Peter Newmark, copublisher of the first four editions of the *Immunobiology* textbook. Newmark is now editorial director at BioMed Central.

Janeway was born in Boston on February 5, 1943 and received his bachelor's degree in chemistry from Harvard University in Cambridge in 1963. After earning his medical degree from Harvard Medical School in 1969, Janeway joined a long family line of prominent physicians, which included his great great-grandfather, Edward Janeway, who was a New York City health commissioner.

After completing a medical internship at the Peter Bent Brigham Hospital in Boston, Janeway spent five years doing immunology research at the National Institutes of Health in Bethesda, followed by two years at Uppsala University in Sweden. In 1977, he joined Yale University, where he was named a Howard Hughes Medical Institute investigator. In 1983, he was promoted to Professor of pathology, and in 1988, he became one of the founding members of the newly created section of immunobiology at Yale University School of Medicine.

Janeway's work at Yale refocused research on how the cells of the innate immune system activate the lymphocytes - the T and B cells - of adaptive immunity. In the early 1980s, while most immunologists were studying interactions between lymphocytes *in vitro*, Janeway turned the spotlight on what he called "the immunologists' dirty little secret" - according to Miranda Robertson, copublisher and editor of the first three editions of the *Immunobiology* textbook. By this, Janeway meant the requirement for adjuvants, notably those containing bacteria or bacterial extracts, in order to generate immune responses. The adjuvants stimulate phagocytes, which are the cells of the innate immune system that recognize conserved and distinctive features of pathogens. Unless phagocytes are stimulated, there is no adaptive immune response.

This formed the basis of his thinking about the role of costimulatory signals in inducing immune responses. By 1989, Janeway correctly predicted that pattern recognition receptors are what allow cells of the innate immune system to recognize pathogens directly. From his insights, said Paul Travers, deputy director of the Anthony Nolan Research Institute in London and co-author of the *Immunobiology* textbook, immunologists ultimately came to the role of dendritic cells (a type of phagocyte that can present antigens to T cells) and the nature of the dialogue between T cells and dendritic cells that shapes the immune response. "This, as we understand it now (which is not fully), is a more dynamic and interactive process than the somewhat passive model of antigen presentation that prevailed previously."

In his lifetime, Janeway published more than 300 scientific articles, became a member of the National Academy of Sciences, and received numerous scientific awards, including the American Association of Immunologists Lifetime Achievement Award. One of his proudest achievements was his textbook, which is now in its fifth edition and the leading textbook in immunology. The first edition took seven years to write.

Friends, family, and colleagues called him Charlie and knew him as a man who took great pride in training his students, many of whom are now professors in immunology departments around the world. His trademark look was a red pixie hat, which he wore everywhere. "I don't know the origin of the hat but, with his beard, it tended to make him look a bit like a garden gnome," said Travers.

Despite this wayward look, Janeway was hugely intelligent and fearlessly outspoken. "Charlie was quite an iconoclast but, because what he suggested was so often correct, all those iconoclastic ideas turned into accepted facts," said long-time friend and colleague Philippa Marrack of the National Jewish Medical and Research Center in Denver who first met Janeway at the National Institute for Medical Research in London and at Cambridge University, where they both worked in the late 1960s. "Like many people with lots of good ideas, he favored his own thoughts in discussions over those of others, and this ruffled feathers," she said.

Those who knew him agree that Janeway was most brave about his illness. Diagnosed in 1995 with the cancer that eventually took his life, he had huge energy and vitality, which even a long and debilitating illness could not subdue for many years. "When he couldn't travel unaided, he would call on his old friends and take them on trips to Europe," recalled Travers. "When his short-term memory began to lapse, he carried around a little notebook full of jottings as an aide-memoire. Charlie never gave up."

Janeway is survived by his wife and colleague of 25 years, Kim Bottomly, also a professor of immunobiology at Yale University School of Medicine, and their three daughters.

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