Ralph Steinman

(1943–2011)

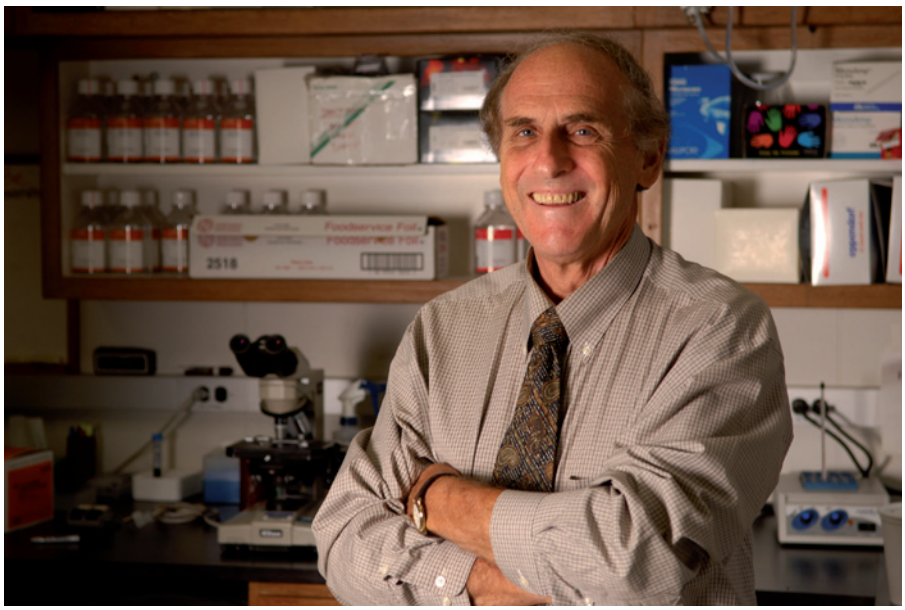
Immunologist and cheerleader for dendritic-cell biology.

Ralph Steinman changed the world of immunology when he discovered dendritic cells, but it took the field a long time to recognize the importance of his discovery. The idea that a new type of immune cell could be found in 1973 — in the era of molecular cell biology — simply by looking down a microscope seemed far-fetched. The early criticism was relentless. Steinman's road to the Nobel Prize in Physiology or Medicine — awarded (unusually) just days after his death — was full of obstacles. That the journey was even possible was down to his forceful personality, energy and focus.

Steinman was born in 1943 in Sherbrook, Quebec, Canada, as the second son in a family of Jewish immigrants originating in Moldavia and Poland. The Steinmans owned Mozart's, a general store selling everything from appliances to clothing. His parents wanted him to study religion and take over the family business, but summers working in the store reinforced Steinman's desire to do something else. His love of science led him to McGill University in Montreal, Canada, then to Harvard Medical School in Boston, Massachusetts, where in the late 1960s he heard lectures by Kurt Bloch on the initiation of immunity and studied Peter Medawar's work on tolerance and Frank Mcfarlane Burnet's ideas on clonal selection.

Although Steinman did a residency in internal medicine at Massachusetts General Hospital in Boston, he was drawn to basic research. In 1970, he joined Zanvil Cohn and James Hirsch's laboratory at Rockefeller University in New York to work on the initiation of immune responses. Cohn and Hirsch were focusing on macrophages, but Steinman was also influenced by his campus neighbours: Christian de Duve, George Palade, Philip Siekevitz, David Sabatini and Günter Blobel were inventing modern cell biology a few floors above. Steinman soon characterized pathways for the engulfing of molecules by cells (endocytosis) and, with Cohn, proposed the involvement of membrane recycling in this process.

"As a basic scientist he recognized the enormous challenge of taking a discovery from the laboratory to the patient."



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At that time, in the early 1970s, immunologists were developing culture systems to help study the cellular basis of immunity. An early finding was that, in addition to B and T lymphocytes, antibody responses required another type of cell, dubbed an 'accessory cell'. The mysterious accessory cells stuck to glass, so Steinman — inspired by his cell-biology colleagues' emphasis on microscopy — decided to examine glass-adherent spleen cells using phase contrast, live imaging and electron-microscopy techniques.

What he saw under the lens was a new type of immune cell that had branching, rapidly changing projections. Three experiments (on two of which, one of us, MCN, was involved) then convinced Steinman that these 'dendritic' cells were the missing accessory cells: they could induce T-cell division and initiate killer-T-cell responses to antigens, and were biochemically distinct from macrophages.

For decades, Steinman was the consensus leader of, and the most enthusiastic cheerleader for, the field of dendritic-cell biology. He brought in numerous scientists from other fields, and loved to collaborate. With Wesley van Voorhis, he showed that dendritic cells exist in the blood of humans. With Kayo Inaba, he established, among other things, that when loaded with antigen, dendritic cells could induce anti-tumour immunity in mice. With Gerald Schuler, he saw that dendritic cells could be activated by pathogens to initiate immunity.

Steinman was generous and much loved by his colleagues. Even when he was terribly ill, he spent the little time he had left ensuring that his students and fellows would land on their feet after he passed.

He was passionate about his work as editor of the *Journal of Experimental Medicine*, a responsibility that he enjoyed for more than 40 years. His focus on publishing outstanding science had a profound influence on his field.

And he was equally passionate about making the leap from the bench to the bedside. In recent years, he tried to use dendritic cells to develop vaccines. As a basic scientist he recognized the enormous challenge of taking a discovery from the laboratory to the patient. But he relished the task because of its importance in treating infectious diseases and cancer. Steinman's passion continued even when it was him in the bed, receiving dendritic-cell therapy of his own design. ■

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