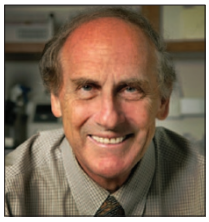

Ralph Steinman 1943–2011

Carl Nathan

On 3 October 2011, immunologists in many parts of the world heard that Ralph Steinman shared the 2011 Nobel Prize in physiology or medicine and fired off congratulatory emails. Hours later, they were shocked to learn of his death three days earlier from pancreatic cancer. Following an unprecedented second meeting on the day of its decision, the Nobel Prize Committee for Physiology or Medicine judiciously tempered the application of its rule against posthumous awards. Below are brief reflections of a scientist who is grateful to the committee for its dual display of wisdom and to Ralph Steinman for 34 years of friendship.

It is only with the benefit of hindsight that immunologists now understand that Ralph Steinman put dendritic cells (DCs) on the scientific map in 1973. For years thereafter, DCs were ignored, doubted and disbelieved, as their origins were first obscure, then said to be from macrophages and their precursors and then from lymphocytes as well. Having once discounted antigen presentation, Ralph then hailed the concept and ascribed the process to DCs and then to many other cells, but none as potent as DCs. DCs could ingest but refrain from digesting. They could hug epidermal cells but then let go and swim through lymph to nodes. DCs were assigned to subsets faster than their mechanisms of T cell activation could be identified. All this engendered conflict of the sort that most scientists shun, but not Ralph. He recognized that a battle of ideas is a productive way to advance a field. Decades passed; Ralph soldiered on. Gradually, he went from embattled to embraced.

Ralph was widely known for his passionate conviction that DCs have the potential to rationalize and thereby revolutionize immunization. However, his passions extended to four more spheres as well: education, the *Journal of Experimental Medicine* (JEM), human studies and family. Ralph was committed to promoting young scientists' education and careers. Bylines of Steinman obituaries appearing in scientific journals around the world will give the names of some he helped. My own involvement in Ralph's educational endeavors had to do with his interest in physician-scientists. In the 1980s, Cornell University Medical College maintained three different MD-PhD programs: Cornell-Cornell, Rockefeller-Cornell and Sloan Kettering–Cornell. Eventually site visitors from the US National Institutes of Health decided this had gone far enough. They recommended that funding be continued only in the 'unlikely event' (in their words) that the separate programs be merged. The prospect was daunting because the three contiguous institutions shared no activities. In fact, it was commonplace for scientists at Rockefeller at the time to refer to Cornell and Sloan Kettering as "across the street," without bothering to distinguish one from the other. Having moved from Rockefeller to Cornell in 1986, I was tapped to meet the challenge. The boulder only began to roll when Ralph put his own shoulder to it. The Tri-Institutional MD-PhD Program launched in 1991 with Ralph as founding codirector and has thrived ever since.

Ralph's allegiance to the JEM was based on his belief in the value of face-to-face meetings by active investigators to discuss both the merits of manuscripts and the soundness of their critiques. The advent of tele- and video-conferencing allowed this philosophy to continue even as the board grew to include people who were not just from "across the street" but from blocks away and from other cities and continents. When I visited Ralph in the hospital about four-and-a-half years ago, two days after his cancer surgery, he was editing JEM manuscripts in bed. It was not until 23 September 2011, one week before his death, that I received a manuscript from the JEM office marked "reassigned from Ralph." That was the measure of his passion for the JEM.

For the 30 years we shared on the JEM editorial board, I watched Ralph in battle nearly once a week at the board meetings. At first he was fighting for the application of scientific rigor. About 10 years ago it became clear that he was swept up in an additional campaign—to move immunology beyond *in vitro* studies and animal models to human investigations. A commentary he coauthored for *Science* conveyed his passion for this issue (http://www.sciencemag.org/content/305/5681/197.abstract?sid=111f40f7-1528-4496-8518-8a082e7e305c). He conveyed this even more vividly by mobilizing his associates to experiment on him with DC-based immunotherapy. Whether the experiment 'worked' is unanswerable, but the fact that Ralph was energized by it was unarguable, and that he was productive for four more years was a gift.

Ralph was devoted to family—in fact, to two of them. One centered on his beloved Claudia and their three children. His relationship with Claudia was magical: Ralph aged, but she did not, and the decades did not dim their delight with each other or their love of dancing. Ralph was also devoted to a family of colleagues, coworkers and trainees. For them, the scientist-soldier was sentry, guardian and guide.

In his last weeks, Ralph arranged transitions for his laboratory colleagues, bade his family keep their mourning to a minimum and gave instructions about his memorial service: no classical music—a dance band instead. Thus, Ralph left us a lesson in how he left us. Few can aspire to have such an impact on the world; we can only hope to depart it with such grace.

Just as DCs generate an immune response by educating cells in their family, Ralph generated knowledge by educating a family of scientists. He lived what he studied.

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