



Norman Letvin

1949–2012

Andrew James McMichael

Norman Letvin lost his long fight with pancreatic cancer on 28 May 2012. The field of HIV-AIDS immunology has lost one of its founding fathers and one of its most clear-sighted and rigorous minds.

Norman (Norm) Letvin grew up in Detroit, Michigan, as a prodigy at playing the clarinet. His achievements in music were extraordinary; for example, he was first chair in the World Youth Symphony Orchestra at Interlochen while still in middle school. He won scholarships to the Juilliard and Curtis music schools but also to Harvard College, where he matriculated at the age of 17. He went on to Harvard Medical School and, after residency training, he married his fellow resident Marion Stein and returned to Harvard. There he joined Baruj Benacerraf's laboratory as a postdoctoral fellow to work on antigen presentation. At that time, this laboratory was a ferment of ideas and discovery, which culminated in the awarding of a Nobel Prize in physiology or medicine to Benacerraf for his part in the discovery of the role of the major histocompatibility complex in the control of immune responses. From there, Norm moved to join the immunology program in the New England Primate Research Center. In 1985, he discovered that simian immunodeficiency virus (SIV) causes AIDS in rhesus monkeys, a finding that opened up this animal model for the development of a vaccine against human immunodeficiency virus (HIV). His discoveries after that were seminal—the first molecular MHC typing of macaques, which led to discovery of the protective MHC types such as Mamu A*01, the first T cell epitope mapped in SIV; the first SIV-HIV hybrid (SHIV), made with Joseph Sodroski; and the first demonstration that induction of CD8⁺ T cell responses via vaccination controls infection with SHIV and then infection with SIV. His finding with Dan Barouch, his postdoctoral fellow, that SIV can escape the vaccine-induced CD8⁺ T cell response, resulting in an increase in the viral load, was the first totally convincing evidence that these T cells control SIV. His study with Joern Schmitz showing that deletion of CD8⁺ T cells, through antibody infusion, abrogates early control of viremia was also of central importance. Later he became increasingly convinced of the additional importance of CD4⁺ T cells, innate immunity and antibodies to vaccine-induced protection against SIV and HIV. He recognized that the whole immune response is critical. He continued to work on the discovery of vaccines against HIV until just a few days before his death.

In the past 10 years he played pivotal roles in major collaborations with the Vaccine Research Center of the US National Institutes of Health, with the Consortium for AIDS Vaccine Discovery (funded by the Bill & Melinda Gates Foundation) and with the Center for HIV-AIDS Vaccine Immunology of the US National Institutes of Health. He was highly influential in these programs and contributed substantially to their success, not only in the publications he authored but also behind the scenes in building up their comprehensive research portfolios.

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Norm had a clarity of vision that was coupled to the highest scientific rigor. He praised outstanding work but would be critical of work that did not meet his high standards. A withering “Oh please.....” would end discussion of some half-baked idea or result. This approach helped his colleagues and students to hone their critical faculties, but it was always linked to his great sense of humor and understanding of the broader issues. He trained many students and postdoctoral fellows, whom he treated with great care and affection. He knew what mentoring meant and set the highest standards. Similarly, he nurtured his scientific collaborations and treated all with respect. Scientific discussions with Norm were always enlightening and could be challenging. He was not afraid to be direct and critical but would also praise enthusiastically when appropriate.

Norm was truly a Renaissance man. In addition to his achievements in science, he continued to develop and express his musical gifts. He was very active in music at Harvard and played the clarinet in chamber groups, forming the Westwood Wind Quintet. From time to time he played with professionals, notably with Yo-Yo Ma, Cynthia Raim and the Ciompi Quartet. He gave first performances for new composers and excelled in classical music. He could identify any piece of music after hearing just two bars, wherever in the piece they were! His love of opera ranged from Gilbert and Sullivan to Wagner—when I last saw him a few weeks before his death, he was off to the Metropolitan Opera House in New York to immerse himself for a final time in Wagner's Ring Cycle. He steeped himself in English literature, from George Eliot to Shakespeare, and spent family vacations at Shakespeare festivals. He could talk at length about the history and architecture of the great European cities as well as their place in art history. But at the same time he was a passionate supporter of his local sports teams, particularly the Boston Red Sox, an American mystery he was happy to explain at length to a British colleague.

Norm was particularly animated when talking about his family. They are closely knit and were at the heart of his life. He and Marion would open their home to friends, and those lucky enough to visit got to know the whole family well. He was immensely proud of them and their successes.

When he developed pancreatic cancer, he fought it with exceptional courage and tenacity. He opted for major surgery that almost took his life, but he pulled through that. He returned to work and re-established his collaborations. We, his colleagues, appreciated his contributions all the more, having lost his participation for several months. He was fully aware of the odds against him but kept going and never complained to us; his courage was astounding. After his surgery he used to say that “every day now is a gift.” Those days were gifts to us as well as to him.

Norm leaves a brilliant legacy. His part in the development of the SIV vaccine model will be central to the ultimate development of a vaccine against HIV. Although he was not the only one working in that field, he was one of the true pioneers and played a huge part in defining its value as well as its limits. We will miss him greatly and would be well advised to remember him and try to live up to his extremely high standards.