



Baruj Benacerraf



Baruj Benacerraf, former George Fabyan Professor of Comparative Pathology, Chair of the Harvard Medical School (HMS) Department of Pathology (1970-1991), President of the Dana-Farber Cancer Institute (1980-1991), served as Professor and President emeritus (1991–) until his death on August 2, 2011 at the age of 90. Baruj is best known for his pioneering work on the genetic control of the immune response and definition of immune response (IR) genes. His seminal work in this area resulted in his receipt of the Nobel Prize in Physiology or Medicine in 1980. In addition, he helped develop an early understanding of the

organization and function of mononuclear phagocytes, characterized IgG subclasses, discovered Fc receptors, and made the first observations that distinguished the modes of lymphocyte antigen recognition by cells later shown to be B and T cells. At HMS, he and his trainees conducted seminal studies that demonstrated MHC-restricted cooperation between T and B cells for humoral antibody responses. He also helped uncover the relationship between allo-recognition and T cell responses to foreign antigens presented by self-MHC molecules, creating a single conceptual framework with respect to MHC molecule function in immunity.

Born in 1920 in Caracas, Venezuela to Sephardic Jewish parents of Spanish Moroccan and Algerian descent, Baruj spent his formative years in Paris. Escaping in 1939 from the imminent German invasion, he arrived in New York City and matriculated at Columbia University where he met the love of his life, Annette Dreyfus, who had also fled Europe. Baruj and Annette were married in 1943, and were inseparable until her death in June 2011. They always traveled together and she was a well-known figure both in the laboratory and at scientific meetings.

After receiving his M.D. from the Medical College of Virginia, Baruj served in the U.S. Army, returning in 1947 to New York City to train at Columbia with the eminent immunochemist, Elvin Kabat, a highly effective but rigorous master. Benacerraf stands as his greatest student. Armed with his introduction to

immunochemistry, Benacerraf returned to Paris in 1949 and joined Bernard Halpern's lab at the Hôpital Broussais where he studied the phagocytes of the reticuloendothelial system (RES). For this elegant work, he was awarded the gold medal of the Reticuloendothelial Society.

His luster did not go unnoticed. Lewis Thomas, a preeminent biomedical scientist of the era, was shopping for talent in his efforts to make the NYU medical school an immunological powerhouse. In persuading Baruj to return to New York in 1956, Thomas gained an outstanding faculty member and a scientist who would prove to be the intellectual guru of world-leading research in immunology. At NYU, Baruj became the center of a distinguished group of scientists that included Michael Heidelberger, Zoltan Ovary, Edward Franklin, Jonathan Uhr, Ellen Vitetta, Bernard Levine, Jeanette Thorbecke, Gregory Siskind, Robert McCluskey, and Victor and Ruth Nussenzweig. This period (1956-1968) at NYU would prove to be the Benacerraf wunderjahrs. He made seminal contributions to several fields of immunology, essentially creating some of them. Among his great accomplishments were the discovery of the Fc receptors through which antibodies mediate their biologic functions, his subdivision of IgG antibodies into subclasses with distinctive functions, and characterization of the carrier specificity of cellular immune responses and of immunologic memory, fundamentally leading to the concept that T cells and B cells display distinct patterns of specificity, foretelling T and B cell cooperation.

The NYU era marked his training, in a very small lab, of a series of outstanding scientists, including Jeanette Thorbecke, Stuart Schlossman, Lloyd Old, Ruth and Victor Nussenzweig, Bernard Levine, Fred Kantor, Kurt Bloch, François Kourilsky, Arthur Berken, Ira Green and Bill Paul. This period initiated a tradition of training that Baruj regarded as among his greatest achievements*, but, of course, the greatest work of this period (and of his life) was the discovery with Levine that the capacity to mount immune responses to very simple antigens was often determined by which allele an individual possessed at a key genetic locus, termed the immune response (IR) locus. He established that IR genes determined whether a given structure was capable of being immunogenic in a particular animal. With Green, he showed that the gene that controlled the capacity to respond to a given antigen also determined the ability of an animal to be the successful recipient of lymph node cells capable of responding to that antigen, implying that IR gene function was expressed in "innate" cells and foretelling McDevitt's subsequent discovery that IR genes were major histocompatibility (MHC) genes.

In 1968 Benacerraf accepted the post of chief of the NIAID Laboratory of Immunology in Bethesda, MD. At the NIH, with Ira Green and Bill Paul, he completed the IR gene work that would merit receipt of the Nobel Prize in Physiology or Medicine a decade later. It was here that he initiated the T cell-B cell cooperation studies that became so important later in his career. Although his stay in Bethesda was brief, Baruj's efforts set the stage for the remarkable flowering of immunology in Bethesda that was to come.

*Benacerraf, B. 1974, Presidential Address to the American Association of Immunologists: The Training Experience. *Journal of Immunology* 113:431-437.

The Harvard Medical School years

In July of 1970, Baruj entered a new era as he moved his laboratory to Boston to become chair of the Department of Pathology at HMS and George Fabyan Professor of Comparative Pathology. Baruj played a crucial and central role in the emergence of Harvard as a leading center of immunological research. This resulted from the enormously influential studies conducted in his own laboratory, as well as his remarkably effective and perceptive use of the Pathology chair's appointment power, which permitted him to recruit a cadre of outstanding faculty members who have gone on to their own stellar careers. He also trained a generation of immunologists who have become leaders in their own right, including Steven Burakoff, Ron Germain, Ken Rock, the late Norman Letvin, Marc Greene, Robert Finberg, and others. Not long after his arrival, he founded a graduate program in Immunology, the oldest degree-conferring graduate program at HMS, which has served as a model for other HMS graduate programs. The Benacerraf legacy now includes more than 200 Program in Immunology students who have obtained degrees since 1971. Baruj also initiated the first course in Immunology at Harvard University – the HMS course in Immunology for first-year medical students (taught with Emil Unanue) – and provided the bulk of the lectures. This course presented immunology in the framework of landmark experiments, giving students not only knowledge of the dynamically evolving field of immunology, but also life-long insights into the scientific method.

One of Baruj's great gifts was his ability to bring people into his family. There are numerous stories of his generosity when members of his laboratory suffered misfortunes. His personal support for those who worked with him was legendary. In addition he created an atmosphere of free thought and promoted an advanced level of intellectual discourse on all subjects. He and Annette lunched every day in the small cafeteria that the Department subsidized and anyone could join them to talk about the important issues of the day. The conversation was as likely to turn to music and literature as it was to science, but all topics were accepted and encouraged.

The Dana-Farber years

At the time of his receipt of the 1980 Nobel Prize for Physiology or Medicine, Baruj had recently accepted the position of President of the Sidney Farber Cancer Institute, now the Dana-Farber Cancer Institute (DFCI). Beyond his talents as a scientist, Baruj proved to be a brilliant administrator through the application of outstanding scientific discernment in hiring and highly effective fiscal management, he transformed DFCI into one of the premier cancer centers and medical research organizations in the world before stepping down in 1991. He continued to serve DFCI as a member of the Board of Trustees until his death.

Baruj brought stability and grace to DFCI. His European formality was not always engaging, yet those within his 'scientific family' knew him as a generous and caring individual. Although never pretending to be democratic in his decisions, he was regarded by everyone as an innovative and just leader who

gave everyone a chance, but retained only those who excelled. His contributions included establishment of a large endowment, construction of new research facilities and recruitment of many outstanding clinicians and scientists while at the same time reassuring everyone from the housekeepers to the trustees that the institution had a mission and a clear direction. As he had at HMS, he brought an aura of culture to DFCI from the chamber music he enjoyed to the well appointed dinners he and Annette hosted at their home for faculty and administration.

Summary

Baruj was quite proud of his many scientific and administrative accomplishments, but it was clear to his close associates and friends that he took the greatest pride in the successes of his trainees and in the close friendships he maintained with many of them. Baruj served as the President of the American Association of Immunologists and in his Presidential address, he focused on the theme of training, making clear just how important this aspect of the scientific life was to him. He was also immensely proud to receive the AAI Mentoring Award in 2001. In his autobiography and in handwritten notes to his closest associates, he reiterated the enormous pleasure he took in the accomplishments of those he had helped to develop as scientists and with whom he had shared the thrill of discovery.

While Baruj befriended, supported, and mentored a generation of immunologists, he always reserved time and energy for his closely knit immediate family. In addition to his constant companion and confidant Annette, he was extremely close and enormously proud of the accomplishments of his daughter, Beryl Benacerraf, Clinical Professor of Obstetrics, Gynecology and Reproductive Biology at BWH/HMS and internationally renowned expert and pioneer in the field of prenatal diagnostic sonography, and his son-in-law, Peter Libby, a clinician-scientist and Chief of Cardiovascular Medicine at Brigham and Women's and Mallinckrodt Professor of Medicine at HMS. Perhaps his greatest joy, however, came from the time he spent with his grandchildren, Oliver Libby and Brigitte Libby. He took pride in all their accomplishments and never tired of spending time with them.

Baruj also never tired of learning something new about biology – at such moments, he had a twinkle in his eyes, a smile on his face, and he often snapped his fingers as if to say “We did it!”. Through these simple gestures he transmitted to all around him how privileged he felt to participate in unlocking another secret of nature. His ability to remain fascinated with uncovering insights into the immune system, despite the day-to-day problems and concerns of running a large laboratory and administering a large institution, had a major impact on his trainees.

There are many excellent scientists who contribute greatly to the advancement of knowledge, others who are especially adept as administrators, and yet others who are wonderful mentors. It is exceedingly rare for all these qualities to be combined in one individual along with a lifelong devotion to the personal growth and professional success of such a large number of colleagues and trainees. Baruj Benacerraf was all of these and more – he has left an indelible mark on the field of immunology through his

research, his impact as a leader at multiple institutions, and through the generations of immunologists he has guided as a mentor and friend. Those who knew him well will miss Baruj greatly at a personal level. Immunology as a discipline has lost one of its greatest contributors.

Respectfully submitted,

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