

*A Remembrance of Baruj Benacerraf by
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Baruj Benacerraf, M.D., AAI '57

1920–2011

The AAI and all immunologists mourn the passing of one of the giants in our field—Baruj Benacerraf died on August 2, 2011, at the age of 90. President of the AAI in 1973, recipient of the AAI Excellence in Mentoring Award in 2001, and also past president of the IUIS and FASEB, Baruj is best known for his pioneering work on the genetic control of the immune response and the definition of immune response (Ir) genes, groundbreaking studies that led to his receipt of the 1980 Nobel Prize in Physiology or Medicine. These studies, originally done in guinea pigs with Fred Kantor, Bernie Levine, Ira Green, and Bill Paul, were later extended by Hugh McDevitt in mice to reveal that the relevant genes mapped to the MHC, and then by Emil Unanue and Howard Grey, who determined that MHC class II molecules controlled immunity by allele-restricted binding of peptides from processed antigen.

But Baruj's contributions to immunology were much greater than this prize-winning discovery. Working with Bernard Halpern in France and later with Jeanette Thorbecke at New York University (NYU), he was a leader in developing an understanding of the function of the reticuloendothelial system (now understood to be composed of mononuclear phagocytes in diverse tissues). He described IgG subclasses, discovered Fc receptors, and made the first observations that distinguished the mode of antigen recognition by what were later determined to be B and T cells. With David Katz, Martin Dorf, and others, he elegantly laid out the rules of MHC-restricted co-operation between T and B cells for humoral antibody responses. With the two of us [Ron Germain (RNG); Steven Burakoff (SJB)], he helped uncover the relationship between allorecognition and T cell responses to foreign antigens presented by self-MHC molecules, bringing disparate themes in immunology under a single conceptual framework.

Baruj was born to Sephardic Jewish parents in Caracas, Venezuela, in 1920. He grew up in Paris but moved to the United States in 1940 and attended college at Columbia University. It was at Columbia that he met Annette Dreyfus. She was also a Jewish émigré who had escaped persecution in occupied France through the good graces of her relative, Eugene Meyer, publisher of *The Washington*



Post. When Baruj received the U.S. National Medal of Science, Meyer's daughter, Katharine Graham, was prominent among guests at the award presentation and reception. Baruj and Annette were married in 1943 and were inseparable until her death this June. She traveled with him wherever he went and was a well-known figure at scientific meetings and conferences as well as in his laboratory. She was always at his side, helping him remember to take his medicines, introducing moments of relaxation into his stressful days with his favorite French cookies and tea, and, on more than one occasion, diffusing a tense situation with

colleagues with a simple "Oh, Baruj!"

Baruj received his M.D. from the Medical College of Virginia, served in the U.S. Army in France, and then returned to New York City in 1947 to begin his scientific career at Columbia with the great immunochemist, Elvin Kabat. For family reasons, he returned to France in 1949, where he conducted research at the Hospital Broussais-La Charité in Paris. Lewis Thomas recruited Baruj to NYU in 1956, where he became the intellectual 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.

In 1968, Baruj left NYU to become the chief of the NIAID Laboratory of Immunology (LI). Though he stayed at NIH for only two years, his influence on NIH immunology was enormous, in part because of his prescient decision to recommend the appointment of his former fellow and then colleague, Bill Paul, as his successor as chief of the LI, a position Bill continues to hold 40 years later. During these four decades, the LI became a world-renowned center of immunological research and the training ground for many highly regarded immunologists, a direct legacy of Baruj's time at NIH.

In 1970, Baruj left the NIH to become chair of the Department of Pathology at Harvard Medical School (HMS), a position he held until 1991. There, he built Harvard into a leading center of immunological research. This was not only through the studies conducted in his

Baruj Benacerraf *(continued)*

own laboratory, but also through his use of the Pathology chair's appointment power, which enabled him to recruit a large number of investigators who have gone on to their own stellar careers. His guiding insight was also felt during his 11 years as president of what was initially the Sidney Farber Cancer Institute, now the Dana-Farber Cancer Institute (DFCI); through outstanding scientific taste and administrative acumen, he transformed this institution into one of the premier cancer centers and medical research organizations in the world before stepping down in 1991.

Baruj was justifiably proud of his scientific and organizational accomplishments, but those who knew him well understood that his greatest professional satisfaction came from another source, the successes over decades of his many trainees and the close friendships he maintained with many of them. In his AAI presidential address, in his autobiographies, and in handwritten notes to his closest associates, he repeated again and again the enormous pleasure he took in the accomplishments of those he had helped to develop as scientists and who had shared with him the joys of discovery. Baruj never tired of glimpsing something new about biology for the first time—his eyes glowed, he smiled, he snapped his fingers, and he transmitted to all around him how privileged he felt to participate in unlocking another secret of nature. This ability to remain fascinated with how the immune system did its business, even after years of research and the often-distressing periods of struggle in the lab needed to pry this information loose, was an important part of the valuable lessons all his trainees received from him.

To those who did not know him well, Baruj could be an aloof figure, with an old “European formality” that was not always engaging. But those within his close scientific family knew him to be a generous and caring individual. All of us had enormous respect for his intellect, his accomplishments, and for his insights into immunology and academic administration, but we especially had a deep affection for him as a person. Among his trainees and close colleagues, stories that reveal much about Baruj the scientist and man abound; they are too many to include here. We are grateful to all the many friends who have offered us their heartfelt thoughts about Baruj, which we present here to share with the AAI community.

We start with a tribute from **Bill Paul**, who was a fellow with Baruj at NYU, a colleague during his time at NIH, and a dear friend for 47 years.

I vividly recall my first meeting with Baruj Benacerraf. I had decided I wanted to make a career in immunology and several active immunologists agreed on one name as an ideal mentor, Benacerraf. I came up to NYU Medical School in October 1962 and met with Baruj on a Monday.

I walked into his lab (Room 527 in the NYU Medical Science Building), which by today's standards was dingy, to say the least. Baruj and I had a stimulating talk. After a couple of weeks, I received a letter from him saying I could come to his lab but that I had to be prepared for his being away on sabbatical for a year. Screwing up my courage, I asked if he meant I could work for him, to which he said “yes.” That began a lifetime of scientific excitement and of a relationship that can best be described as close to that of father and son. The years at NYU were continuously exciting. My lab partner (and life-long friend), Ira Green, led the study of immune response genes while my goal was to understand the relative specificity of cellular immune responses and antibodies. Our co-postdoc, Arthur Berken, was defining Fc receptors. In that era, our days were consumed with work and non-stop discussion. Baruj's maxim was everything was fair game; one could disagree (and very vocally) on anything but that those disagreements should be a matter for the lab. Those were simpler days when an idea could be turned to reality in a matter of months rather than years but the force of intellect and of insight was no less central than they are today and it was in the realm of a penetrating understanding of the biology of immunity that Baruj shone and all around him were illuminated!

Other early associates were **Victor Nussenzweig** and **Fred Kantor**. **Victor** writes:

I loved and admired Baruj and Annette, the inseparable and remarkable couple whose hospitality and generosity touched me and Ruth during the happy years we spent at NYU. In the laboratory Baruj treated his fellows as his intellectual comrades in arms. We criticized each other's ideas with gusto and when in agreement went right to the lab to challenge our views. Baruj also worked in the lab, and I admired his dexterity: he was the only one who was capable of precisely cutting the fragile gels used for electrophoresis of antibodies without breaking through them and then comparing patterns of light and heavy chains. Nobody else was capable of finding the veins deep inside the paws of guinea pigs to inject them with antigen. Our weekly journal clubs with Baruj, Bill Paul, Ira Green, Bernard Levine, and Ruben Binagui, among others, were very exciting; at that time the first puzzling observations appeared in press on cell cooperation in the immune response, and Baruj had the initial results of responders and non-responders in guinea pigs that led to his quest for the Ir gene. Those were among the happiest days in my life.

Fred had some insights into Baruj's love for theater and the arts, an aspect of the man not often known among those familiar with him solely through the scientific literature:

My older son was an infant when I was in Baruj's lab, and he met and played with him. Twenty-two years later, I was in Boston when my son visited and I brought him to Baruj's office. Baruj greeted him warmly and asked him what he was doing. Upon hearing that my son was an assistant director of the Hartford Stage Company, Baruj exclaimed that he really envied him and he, Baruj, had wasted his life in the lab and should have stayed in the theater where he had met Annette as she directed a college play in which she had a prominent part.

We suspect the last part was a bit apocryphal, but Baruj and Annette were serious patrons of the arts and they played duets on flute and harpsichord for friends for many years.

This same theme of an artistic side to Baruj (and Annette) is at the core of the following remembrance from **Emil Unanue**, who joined Baruj shortly after he became chair of Pathology at Harvard:

*My major interactions with Baruj took place during the fifteen years I spent at the Department of Pathology at HMS. He recruited me in late 1970 as an assistant professor. The department was a center of activity all during the 1970s and visitors from all over the world were coming by to discuss Ir genes and MHC restriction and to get his opinion on problems that were not yet clear. Of course I was highly influenced by these activities in my own research work on antigen presentation. But I want to focus on another facet of Baruj's personality: his enjoyment (with Annette of course, you could not separate them) of the many beautiful components of life. Both were highly cultured: interested in a good book, listening to and playing music (classical only!), a nice meal, a conversation on politics or religion. Here I saw a different Baruj, one who was relaxed, eager to talk, witty, smiling, devoid of the competitive spirit that showed when immunology was involved. We often spoke in Spanish, a language with which Venezuelan-born Baruj was losing touch. Perhaps it was the use of Spanish that connected us. Shortly after coming to the department, Baruj gave me the first edition in Spanish of *One Hundred Years of Solitude*, the opus magnum of Gabriel Garcia Marquez. He wanted me to read it, had heard great things about it, but was having some trouble digesting it in Spanish. Of course, I did read it, this was my introduction to Garcia Marquez: I have read all his books since. Then came Tolstoy's *War and Peace*. I remember Baruj asking me whether I had read it. When I said no, it shocked Annette and him alike; shortly thereafter the book arrived as a gift. Later, Anna Karenina followed, and then *The Red and The Black* by Stendhal. In a way they were pushing me to add an extra dimension, separate from my laboratory and family commitments. Music was also very high on the list and Bach and Mozart were their favorites—they could not understand my love of Italian opera and Wagner was out*

of the question! After I left Harvard, I saw Baruj on and off and also kept up through e-mails. Science topics slowly disappeared from our agenda, but books, politics, and music were the themes that kept us interacting. Baruj was very special. I appreciate that he made sure that my stay at HMS was a productive and rewarding one through his fostering of immunobiology and by adding a personal and warm touch to our relationship. Both he and Annette will be sorely missed.

Other colleagues at Harvard recalled the mark he left on the institution. **David Nathan** notes:

I have been thinking a lot about Baruj and his enormous contributions to Harvard medicine, to international immunology, and, of course, to Dana-Farber; I've been thinking as well about Annette and her welcoming smile, her cultured grace, and complete commitment to him, and therefore to us. He was a man who demanded total loyalty in return for his support and excellent advice. I admired his brilliance, his organizational skills, his basic understanding of his faculty's strengths and weaknesses, and his willingness to deal with me through thick or thin. Baruj came to Dana-Farber in a time of fractured leadership. We needed Baruj and he came through for us. The results, of course, were a massively strengthened institution, one that was prepared to deal with future buffeting. He left a legacy of strength and excellent recruiting. None of us who were there will forget him. That my portrait hangs next to his is a matter of pride of which I will remind my children and grandchildren.

Harvey Cantor adds:

Baruj became President of the Dana-Farber Cancer Institute (DFCI) and continued to serve as the Fabian Professor Emeritus and as an advisor to DFCI's Board of Trustees. It is remarkable that at about this same point in his career he found the time to found the HMS Graduate Program in Immunology, the oldest degree-conferring graduate program at HMS. It has served as a model for other graduate programs and conferred more than 200 degrees since its inception. His great scientific achievements were possible because he refused to ignore phenomena that most people would overlook or sweep under the rug. He simply would not let go of what he saw as the truth and persevered in the face of substantial obstacles. His genius and dedication were an inspiration to me and to all of his colleagues.

Martin Dorf, with whom Baruj worked on groundbreaking studies of MHC control of T-B collaboration, recalls:

I cannot say enough about Baruj Benacerraf's importance and commitment to the immunology community both

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locally and internationally. In addition to his scholarship, he was a superb mentor who took great pleasure in advancing the careers of his students. In the late '70s Baruj received an invitation from Laurence Rockefeller to discuss an opportunity to head Memorial Sloan Kettering. Shortly thereafter, Harvard and the DFCI countered by offering the DFCI presidency. Months after accepting the DFCI position, Baruj won the Nobel and donated all the proceeds to initiate a fund raising campaign for the DFCI.

Beyond these accolades to his contributions to the larger enterprise of biomedical research in general and immunology in particular, many of us recall the ways Baruj touched our lives more intimately.

Man-Sun Sy provides a telling vignette:

With the passing of Baruj, I don't think we have mentors like him any more. Baruj cared about his fellows' careers as well as their personal lives. When I was a fellow in his lab in the early '80s, with the mortgage interest rate hovering around 15 percent, Baruj gave me a personal loan allowing me to buy my first house. Over the years, Baruj and Annette have given me so much support in and outside the lab that listing all would take an entire page. I saw Baruj for the last time earlier this year, but he and Annette will continue to be part of my life.

Ken Rock reminisced in the same vein:

Many will know of Baruj's brilliance and contributions as a scientist. Fewer have had the privilege of knowing him as a mentor and active partner in plumbing the mysteries of science, and in these aspects he was also a master. Beyond the science, Baruj cared about his trainees like family – I remember the time one of the fellows in the lab had his TV stolen from his apartment and Baruj, unasked, went and bought him a replacement. He will be sorely missed.

Robert Finberg also focused on this personal side of Baruj:

I never thought of Baruj as a "mentor," because for reasons I have never entirely understood and even before I started working for him, he became more like a father to me. Baruj had a strong sense of what he wanted, what should be valued, and who he wanted to work with. Once he selected you, his devotion was life-long and unwavering. A shy person himself, he was able to pursue a full social schedule that was directed by Annette, his lifetime partner and inseparable companion. Over the thirty years that I was his student, he spent time not only with me but with my wife and all my children. He was larger than life to them. When they were young, my children were amazed at how this "old man" was able to relate to them at such an intimate level. When they grew up they were amazed at his intellectual abilities and how he could explain things to them that they had never before understood. Once accepted into Baruj's

"family," one always felt supported. He had a way of both complimenting you on what you did well, as well as always setting a high bar for what he thought you might be able to achieve. He was always available for advice if you wanted to ask him something, but he was always promoting my career without my ever asking. Even after passing 90, he remained interested in what I was doing, and even what my children were doing, and he was always able to find some way to encourage me to do something of value. He was more than a mentor, and he will always be a role model for me in everything that I do.

We (SJB and RNG) both joined Baruj's "family" in the early 1970s and remained extremely close to him until the end. We have many stories to tell, but space permits only a few short recollections.

From **Ron**:

Scientifically, Baruj and I had some sort of 'doppelganger' connection, best illustrated with the following reconstruction of one of many night-time phone calls:

Baruj: "Ron, did you read the latest ..."

Ron: "The Journal of Immunology (or whatever came in the mail that day) — yes."

Baruj: "Did you see the paper by ..."

Ron: "Yes, the one by Zinkernagel (or whoever wrote the most relevant paper in that journal that month!)"

Baruj: "Did you understand that ..."

Ron: "Yes, I realized that the data imply ... (put in whatever new insight one might derive from the paper)."

Baruj: "And did you see that we can ..."

Ron: "The experiment is already set up."

On a personal note, I worked with Baruj for many years as an intermediary between him and a number of French postdocs. He would frequently come into the lab to discuss their work, speaking to them in French, which I do not understand. This began to grate on me and I developed a bit of Francophobia. Baruj learned of this and his response was to insist that I spend time in Paris with him (I had never been there) to learn just how wonderful France and French culture really were. I accepted the invitation on the way to a cytokine meeting in Switzerland. Baruj met me at the Paris airport with his mother's chauffeur, brought me to his apartment along the Bois, introduced me to French cafés, and, together with Annette, personally taught me how to navigate the Paris Metro, leaving me with a carnet in hand for future rides. He took me to my first three-star restaurant for dinner, which was an epiphanal experience, to the Bolshoi ballet, and then, most remarkably, left me the keys to his apartment with the instruction "Enjoy Paris" for the few days before I flew on to Zurich. It was a highly

personal investment in me with no direct relationship to science; Baruj felt this was something “good for my soul” and he was correct. It exemplified the enormous generosity of which he was capable and that I continued to experience for the four decades we knew each other. We shared a common birthday, but I was never permitted to buy him a present; my gifts were always photos I had taken or old pictures Annette provided that I repaired in the days before Photoshop, working in a darkroom and retouching them by hand — I always was proud that the tattered and creased photo I fixed of Baruj at the bench in the Kabat lab hung in his office at Harvard for many years, where I would see it each time we met.

From **Steve**:

Baruj was my mentor and my scientific father and he opened up the world of immunology to me. When I joined him at Harvard in 1973, he had already begun to assemble an extraordinary group of scientists. Baruj was a master psychologist, knowing how to motivate each of his trainees in various ways, and he clearly had my measure. I had been extremely successful during my first year in the lab, and I was convinced that research was going to be a breeze. However, I learned better during my second year when nothing I tried worked. Somewhat despondent, I went to see Baruj expecting that he would give me a pep talk. When I explained to him my frustration, he looked at me and, noting that I was an M.D., said that medicine was an admirable profession and was, perhaps, my real calling. Just in case that was too subtle for me, he then followed by stating that “maybe you do not have what it takes to do science.” Though I did not realize it at the time, he had thrown down the gauntlet. I was furious that he didn’t think I could “hack it” in research. I went back to the lab and worked harder than ever to prove him wrong — only after that would I leave science! Of course, once successful after returning to the bench, I was hooked and continued to do research with abandon for the next 25 years. Baruj’s statement had exactly the impact he wanted it to have. His ability to manipulate people for the better and get the most from them was one of his very special talents, and I am certainly grateful for his application of this skill at a crucial moment in my career.

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 our field 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.

Baruj Benacerraf, M.D., an AAI member since 1957 and Emeritus member since 1996, served as AAI president in 1973 and as a member of the AAI Council from 1968–1975.

He was a member of various AAI committees, including the Committee on Public Affairs (1989–91), ad hoc Steering Committee for International Congress (1968–69), First International Congress of Immunology Committee (1970–71), and ad hoc Committee on Public Relations (1972–73). Benacerraf served from 1968–72 as an associate editor for *The Journal of Immunology (The JI)* and was a member of *The JI* Editorial Board from 1972–79.

In addition to his 2001 AAI Excellence in Mentoring Award, Benacerraf was an AAI Plenary Lecturer at the 1980 AAI Annual Meeting and was one of four featured speakers for the special 75th AAI Anniversary Symposium, “Immunology in Perspective,” at the 1988 AAI Annual Meeting.

Additional Benacerraf tributes and profiles appearing online include:

Boston Globe: http://articles.boston.com/2011-08-03/bostonglobe/29847296_1_immune-response-immune-response-nobel-prize

Dana-Farber: www.dana-farber.org/Newsroom/Publications/Setting-a-New-Standard.aspx

Fox News: www.foxnews.com/us/2011/08/02/nobel-winning-immunologist-benacerraf-dies-at-0

Harvard Gazette: <http://news.harvard.edu/gazette/story/2011/08/baruj-benacerraf-nobel-laureate-90>

Jewish Journal: www.jewishjournal.com/obituaries/article/baruj_benacerraf_90_nobel_prize_winner_20110803

The New York Times: www.nytimes.com/2011/08/03/us/03benacerraf.html

Nobel Media: http://nobelprize.org/nobel_prizes/medicine/laureates/1980/benacerraf-autobio.html

The Washington Post: www.washingtonpost.com/local/obituaries/nobel-prize-winning-immunologist-benacerraf-90-dies/2011/08/02/gIQAnVD0sI_story.html