

Eli E. Sercarz (1934–2009)

We are sad to inform the scientific community of the death of Eli Sercarz in Topanga Canyon, California, on November 3rd, 2009. After receiving a Ph.D. from Harvard in 1960 and doing postdoctoral work at Harvard and MIT, Eli had a career of more than 45 years as an independent investigator, including 37 years on the faculty of UCLA, followed by stints at the La Jolla Institute for Allergy and Immunology (1997–2002) and at the Torrey Pines Institute for Molecular Studies (TPIMS). Although Eli had been suffering from renal cancer for several years, he remained active at TPIMS until his death, with ongoing NIH-funded projects and manuscripts in preparation, as well as lectures at international meetings, as recently as last October. Eli and his colleagues made major contributions to our understanding of antigen presentation, immune regulation, tolerance, and autoimmunity. Research in each area was anchored by a focus on the generation of peptidic epitopes for presentation to T cells, and they imprinted these fields with a unique vocabulary, reflecting a research program that was both idiosyncratic and innovative.

Eli's research career featured a number of seminal contributions that helped shape immunology, which was just developing when he entered the field. Starting in the 1960s, his lab was among the first to study the T and B cell response to protein antigens. Using the tools available at that time (i.e., before recombinant DNA and synthetic peptide technologies), he published a landmark series of studies on the antigenic structure of the protease lysozyme that helped define the specific regions of this protein that were the focus of the T cell response in different mouse strains. These early observations formed the basis for the major questions that would occupy the rest of his career, which centered on understanding which antigenic determinants within a protein were selected by the immune system as the targets of the T cell response and on characterizing the pathways and mechanisms that controlled this process. During the course of these studies, Eli showed that a hierarchy of responsiveness could be demonstrated for different antigenic

determinants within a single protein, with some peptides eliciting the greatest response magnitude ("immunodominant"). Others still capable of major histocompatibility complex (MHC) binding either were the targets of a quantitatively smaller response ("subdominant") or were ignored in the context of the intact antigen, despite the presence of a T cell repertoire capable of recognizing them ("cryptic"). He further demonstrated that these concepts, developed from immunization studies, could also be applied to the response to self-antigens, with immunodominant antigens likely to induce deletional tolerance, leaving the subdominant and cryptic epitopes as the targets of self-reactive T cells. These ideas have had a guiding influence on understanding T cell responses in infectious disease, cancer, and autoimmunity.

The role of determinant hierarchy in self-reactivity became a major theme in Eli's research, and he began working to elucidate how epitope selection could guide the course of autoimmune disease. Working in animal models of multiple sclerosis (experimental autoimmune encephalomyelitis) and arthritis (collagen-induced arthritis), his lab showed that



Photograph of Eli E. Sercarz.

an autoimmune response initiated to a specific immunodominant epitope could develop over time to include other determinants within the same antigen ("intramolecular determinant spreading") or to other proteins expressed within the same target cell or tissue ("intermolecular determinant spreading"). He later showed that this determinant spreading can be promulgated by a specific T cell clone against an immunodominant peptide (called the "driver clone") and that disease resolution can involve a regulatory response against idiotypic determinants of the TCR expressed by the driver clone. These findings have had a far-reaching impact on our understanding of autoimmunity, and evidence for determinant spreading has been found in the immune response to human cancer. Additionally, Eli maintained an avid interest in understanding the molecular regulation of immunodominance and crypticity, making key contributions to understanding how MHC molecules guide the processing of proteins to peptides, how different antigen-presenting cells produce and present distinct determinants from the same source antigen, and how neonatal tolerance is caused by clonal deletion. These achievements reflect the breadth and depth of Eli's insouciant curiosity and formidable intellect.

Although born in the Bronx, much of Eli's life was rooted in Southern California. As a youth, in order to help him recover from rheumatic fever, his mother took him to live in a health spa in Tecate, Mexico. While there, Eli would ride his bike across the border to attend high school in San Diego County, and he later attended San Diego State College. As an adult, he and his wife, Rabyn, enjoyed the bucolic ambience of Topanga Canyon, known to inspire artistic creativity from the likes of Woody Guthrie, Joni Mitchell, and many others.

For Eli Sercarz, the aspects of playfulness and enjoyment were never far removed from the intensity and effort of research. You could count on the fact that detailed discussions in his group meeting, "data circus" in the lab lexicon, and journal club would be accompanied by good food, particularly flavorful

cheeses, fresh bagels or pastries, and sometimes wine (in the afternoon). Eli's love of dancing and travel to scientific meetings were legendary, and he maintained close contacts with colleagues around the world. Although the competition and stress of modern biomedical research were unpleasant facts to be acknowledged, in Eli's view success is not zero sum game, and an individual's accomplishments should not come at the expense of another. With his highly

sympathetic character, Eli rarely had a negative word to say about colleagues or competitors.

The stimulating and nurturing atmosphere in the Sercarz group was fueled by Eli's concern for his trainees as people and as scientists, and his utter respect for the ideas of everyone in the group, neophytes as well as seasoned veterans. It is therefore appropriate that in addition to his other awards, Eli Sercarz received the Excellence in Mentoring Award from

the American Association of Immunologists in 2007. In addition to his many former trainees, his many good colleagues, who can be found on nearly every continent, will also deeply miss Eli.

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