



# Paul J. Leibson

## 1952–2007

Hans Schreiber & Vinay Kumar

Paul J. Leibson, professor of immunology at the Mayo Clinic in Rochester, Minnesota, and a pre-eminent researcher of natural killer (NK) cells, died of cancer on 6 August 2007.

Paul grew up in the greater Chicago area in a large, cohesive family with strong intellectual traditions that did not confuse the importance of goodness of heart with the glamour of academic accomplishments. After receiving a BS, magna cum laude, from the honors program at the University of Illinois Urbana-Champaign in 1974, he earned his PhD in immunology from The University of Chicago, where he received his predoctoral training in tumor immunology in the laboratory of Hans Schreiber in 1979 and his MD, with honors, in 1981.

After a pediatric internship and residency at the University of Colorado in Denver, Paul trained for two years as a fellow in allergy immunology with Anthony R. Hayward at the National Jewish Hospital and Research Center, where he began his work on human NK cells. Thereafter, he joined the Mayo Clinic in 1986 for a distinguished career in immunology. During his two decades at Mayo, he poured himself into teaching in both the classroom and the laboratory, serving for five years as dean of the graduate school. His colleagues at Mayo recognized Paul for his service in research and teaching with the Rose M. and Morris Eisenberg Professorship, and he was named Mayo Distinguished Educator for his truly premier mentoring of students, fellows and junior faculty alike.

The name of Paul Leibson is unquestionably linked to NK cell signaling. Together with a small group of other courageous scientists, he pioneered this field well before the characterization of the NK cell receptors that trigger cell-mediated cytotoxicity. It was typical for the signaling section of each NK workshop to begin with a state-of-the-art presentation by Paul. For those outside the field of signaling, Paul's work was essential reading. Pursuing this line of research took a certain amount of faith and courage in that the receptors that mediated one form of NK cell-mediated killing (antibody-dependent cellular cytotoxicity or ADCC) were only partially defined, while the second mechanism of target-cell recognition, which is now leading to the 'natural' killing of tumor cells, was at the time a complete mystery. Paul left the critical work of receptor characterization to other equally skilled NK cell biologists, and concentrated instead on learning how these receptors delivered NK cell-activating signals from the plasma membrane to the cytotoxic effector machinery in NK cells.

His body of work in the 1990s spanned an array of important signaling enzymes, ranging from tyrosine kinases, such as Lck and Syk, to the small, Ras-related GTPases, to the lipid-metabolizing enzymes, namely the phospholipase C  $\gamma$ 1 and  $\gamma$ 2 isoforms and phosphoinositide

3-kinase. Paul's string of publications in the 1990s offered some truly provocative insights into the inner workings of one of the more mysterious cells in the immune system. More recently, he dedicated his efforts to understanding how single NK cell receptors branch out into diverse signaling pathways rather than a single pathway. As a result, he demonstrated that NKG2D could trigger release of phosphoinositide and activation of small GTPases through a single non-ITAM-containing adaptor, DAP10, that can recruit phosphoinositide 3-kinase and the Grb2-Vav complex. Paul's work did not always focus on positive signaling networks regulating NK cell-mediated killing. In fact, his laboratory was among the first to demonstrate that the expression of major histocompatibility molecules on target cells could inhibit cellular cytotoxicity by blocking the most proximal step in the signaling cascade, activation of the Src kinase Lck. He subsequently went on to show, after the identification of killer inhibitory receptors (KIR), that the mechanism of their inhibitory property was due to the recruitment of the tyrosine phosphatase Shp-1 to the KIR cytoplasmic tail. In sharp contrast with other investigators in the field of signaling, he focused on human rather than mouse cells, reaching the same level of experimental sophistication as had been achieved using genetically targeted mice. Indeed, his studies often preceded mouse studies and provided an accurate framework for the interpretation of the results obtained in mouse models. Paul fully recognized and acknowledged the value of studies in mice but, perhaps because of his clinical background, remained devoted to freshly isolated human NK cell lines and cultured NK cell clones as models for the functional characterization of these fascinating cells. There is no doubt that what we know today about NK cell signaling is largely due to Paul Leibson's impressive work and knowledge. His work and ideas in the NK cell field will continue to be influential.

Paul was one of the most positive people we ever met and was truly a man of impeccable integrity. His enormous curiosity in science did not impair his ability to analyze experimental results most stringently and objectively, but rather helped him to ask motivating questions and to propose elegant experiments in the kindest, most considered way possible. Similarly, through the genuine, deep and cordial friendship that he extended to so many of us, he would never ignore a problem, but instead focus on opportunities and solutions, often in a very humorous way.

Paul enthusiastically greeted his friends. He treated every visitor who came to his office with genuine enthusiasm, making each person feel at the center of his universe. Paul loved his family, his friends and his work. Each was properly placed in his priorities, with remarkable balance. He was always happy to come to work, and then to go home to his family. Thus, in addition to research and education, his passions included cooking, learning about wine and gathering for lively discussions and storytelling with family and friends. His love of nature nurtured his enthusiasm for gardening, camping, mushroom hunting and traveling. Paul is survived by his wife Cynthia, daughter Sarah Bryan (Sean), and two brothers, David and Marc. His parents Ruth and Benton preceded him in death.

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