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In Memorium

Paul Terasaki
September 10, 1929–January 26, 2016

Justice would be poorly served by an attempt to briefly summarize the body of Paul's scientific work that has resulted in more than 1250 publications in peer-reviewed journals. The work itself has been all-pervasive in clinical and basic biology. In 1970, studies had begun at the Institute for Scientific Information (ISI, Philadelphia) of the frequency of attributions to articles published in peer-reviewed journals. Paul Terasaki already was one of the half dozen or so of the most frequently cited scientists in the world. Terasaki's profile has enlarged in subsequent years to the extent that he has been the author of 15 "citation classics," defined as more than 400 attributions.

Paul Terasaki's influence is not hard to explain. In 1963, he described and introduced the microcytotoxicity test that is the practical basis today for tissue typing (2136 citations). Then, "backtracking" from sera which contained unclassified antibodies, he and his associates painstakingly contributed to the identification of the specific antigens at the A, B, and Dr histocompatibility loci. Next, he demonstrated the role of these antibodies in causing hyperacute rejection, and as a result, his so-called crossmatch as means of donor–recipient matching became a worldwide standard. Fifteen years after this remarkable contribution, he and his associates further classified the significance of cytotoxic antibodies and showed which of these were "dangerous" and which could be considered safe.

Paul realized at an early time that advances in tissue matching could not be applied as a practical service within the time limitations of the then current organ preservation techniques. In a remarkable example of translational research, Paul joined with a young Australian surgeon (Jeff Collins) to develop the so-called Terasaki–Collins method for "slush" preservation of kidneys. In the mid-1960s, he showed how kidneys removed in Los Angeles and preserved with his solution could be shipped to Israel, London, or Japan, and made to function after as long as 48 h. These basic principles of the kidney slush preservation have been applied with modifications for the preservation of the liver, heart, lungs, and pancreas.

Courtesy of the Terasaki Foundation Laboratory.

If one examines Paul's publications carefully, it is easy to detect a preoccupation with therapeutic principles. Long before anyone else, Paul was interested in the use of specific antilymphocyte antibodies to treat rejection. This preoccupation premonitored the eventual development of polyclonal ALGs and then monoclonal ALGs after the advent of the hybridoma technologies. Moreover, he and his associates were among the first to develop highly specific monoclonal antibodies with which to potentially intervene at pinpoint levels of the immune response to transplant antigens.

In addition, his observations about the curious enhancement effect of blood transfusions on kid-

ney allograft survival opened up a broad new area for scientific inquiry. At the International Transplantation Society Meeting in Boston in 1980, Hans Balner of the Netherlands was asked to summarize the most influential events in transplantation. The transfusion story from Terasaki as well as the typing events that I have already described were among the three or four most important historical landmarks of the preceding 20 yr.

These and other contributions by Terasaki to science and clinical medicine are readily verifiable. However, there is a feature of Paul's life that is not found in his curriculum vitae, namely uncompromising scientific integrity. In the summer and autumn of 1969, Paul (at UCLA) and I (at the University of Colorado) began a look-back study of all of the typing information accrued on the Denver kidney transplant recipients of the preceding seven yr. What we observed supported in principle the validity of HLA matching inasmuch as a perfect match conferred a strong survival advantage, particularly with family donors and especially if the matched donor was a sibling.

However, the correlation between lesser degrees of matching and clinical outcome with cadaveric or living unrelated donors was poor. Since matching of each of the 6 HLA antigens then available was almost universally expected to provide an incremental advantage, Paul realized that it could be professional and political suicide to reveal the unanticipated findings. He did so anyway, at the histocompatibility session of the International Transplantation Society Meeting at the Hague (Holland) in September 1970. I remember what a somber and lonely figure Paul was as he went to the podium that day, and also his quiet resolve when no one applauded after he finished.

In the months that followed, Paul incurred the wrath of his grant-dependent typing colleagues, and in fact, his own grant support was ruthlessly stripped away after an emergency site visit from NIH officials who seemingly were outraged by the unpredicted results. When he later was proved to have been correct, Terasaki emerged as the doyen of clinical HLA matching and as an enduring symbol of integrity. Extrapolation of his impeccably documented conclusions about HLA matching for organ transplantation breathed life into the still struggling fields of liver, heart, and lung transplantation where most candidates could not wait for a well-matched donor.

These reflections would not be complete without the back story of Paul Terasaki's early life. Seventy-five years ago, the boy Terasaki was peering out through the fence of a desolate concentration camp where he and other loyal citizens of Japanese ancestry were unjustly imprisoned throughout World War II. From this unfriendly soil grew the man. The man became the father of human histocompatibility matching, a genuine American hero, and my good friend. No loss has been felt more deeply.

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