



# Paul Ichiro Terasaki September 10, 1929 to January 25, 2016: Transplant Pioneer

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**M**y laboratory career started with chickens, then mice, then rabbits. In every instance I became allergic to the animals that I was working with. Finally, I had to turn to humans, my real interest.

It is difficult or impossible for anyone involved in experimental or clinical transplantation to imagine a world without Paul Terasaki. Much of what we take for granted in our everyday activities, such as donor-matching, lymphocytotoxin panels, cross-matching, transporting kidneys, transplant recipient registries, and more derives from studies by Paul and his colleagues over 50 years. Paul was born in Los Angeles. He was a *nisei*, a first-generation Japanese-American whose parents immigrated to California. Incredibly, embarrassingly, and despite his American citizenship, he spent his high school years in a Japanese internment camp with the innocuous name Gila River War Relocation Centre near Phoenix, AZ. However, Paul was a big person; he rarely spoke of this experience and never with resentment. But it greatly influenced him as we shall see.

Prof. Terasaki finished high school in Chicago and began university there as a premedical student. His parents could

not bear the dreadful winters in Chicago, so he transferred to University of California, Los Angeles (UCLA) where he switched to zoology receiving bachelor, master, and doctoral degrees in zoology from UCLA. Soon he joined the UCLA Department of Surgery chaired by Prof. William Longmire. His work focused on skin grafts in chickens. This led to his interest in transplant tolerance and eventually to a postdoctoral position with Sir Peter Medawar at University College London followed by a fellowship in Paris with Prof. Jean Dausset. Dausset, quickly discovered Paul's expert correspondence in French (aided by a teacher) was, unfortunately, accompanied by an inability to speak French. Dausset promptly dispatched him to the Pasteur Institute. Discouraged, he returned to Los Angeles after a few months.

Paul's interest was predominately in antibody-mediated immunity and its role in transplantation in humans. He had little patience for T cells, NK cells, T regulatory cells, and the like. He could never explain why. Perhaps, it was rebelliousness (his suggestion) or perhaps the allure of French cooking from his brief Paris sojourn. In 1964, Terasaki introduced the microcytotoxicity test at a conference at Duke University. It was revolutionary and was quickly adopted as the international standard for matching transplant donors and recipients. Thomas Starzl, Jon van Rood and Sir Walter Bodmer were early supporters. Terasaki's invention was prompted by his inability to do a venipuncture on his technician John McClelland and vice versa. They had to resort to finger sticks and could get only a few lymphocytes. Also, they had access to only small serum samples left over from Rh-testing of pregnant women proving necessity is the mother of invention (for intelligent people). Paul was remarkable in always trying to improve on anything he invented. In a precomputer era, he and McClelland hooked up their microscope to an electric typewriter. Terasaki also invented (with Jeffrey Collins) a simple cold storage solution for transporting kidneys from deceased donors so that they could be used with the most HLA-compatible recipient and set up a kidney transplant recipient registry before the US Government became involved through UNOS. It is safe to say Paul was a Silicon Valley genius entrepreneur before there was a Silicon Valley (intellectually, not physically) and before the term high-throughput screening was coined.

In 1969, Professor Terasaki established the UCLA Tissue Typing Laboratory, directing it for 30 years. For nearly 50 years, he focused on the study of the humoral theory of transplant rejection. After his retirement from UCLA, he founded the Terasaki Foundation, a research center dedicated to cancer immune therapy and the study of humoral immunity and transplantation.

Received 5 February 2016.

Accepted 10 February 2016.

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The authors declare no funding or conflicts of interest.

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ISSN: 0041-1337/16/10005-968

DOI: 10.1097/TP.0000000000001178

In 1984, Paul founded One Lambda, Inc (the amount of anti-HLA-anti-sera needed for the microcytotoxicity assay) to develop and provide transplant centers worldwide with the tools needed to better match transplant donors and recipients. It was later bought by Thermo-Fisher for US \$920 million dollars making Paul a reluctant multimillionaire. However, this vast fortune did not change him, and he invested most of his money in research and gave generously to charities including about US \$60 million to UCLA.

Both of us worked with Paul for many years. Gerhard Opelz who spent 10 years in the Terasaki laboratory and published more than 100 typescripts with Paul relates the laboratory was incredibly crowded with more than 100 people. Whenever someone went on holiday, however brief, a huge Revco freezer was wheeled into their office. On your return, you had to find an empty office to move the Revco to or face the prospect of working standing.

Robert Peter Gale owes his bone marrow transplant career to Paul. When I was working with Prof. E. Donnall Thomas at Seattle, I asked to see the HLA-typing laboratory. Don replied: "We don't do it here. Terasaki at UCLA does for everyone, everywhere". It dawned on me that if we were doing Don's HLA-typing at UCLA, we could also do the transplants. Paul supported the idea and, with his help and support, off we went. Years later, we discussed the cognate mirror images of graft-rejection and graft-versus-host disease in transplant recipients. Paul's approach was an engineer's. He asked why we did not simply monitor levels of donor and host lymphocytes with HLA-specific antibodies and give cytotoxic antidonor or antihost antibodies if one side or the other got the upper hand. A sensible idea; I'm still uncertain why we don't do it?

An inspirational role model, Dr. Terasaki published many books and scientific reports and served on several editorial boards. A quick PubMed search indicates 830 publications, surely an underestimate considering the 20 annual editions of *Clinical Transplant* (with Michael Cecka) published since 1985, an encyclopedia of global transplant activity. Paul received many awards including the Medawar Prize from the International Transplantation Society. In 2003, the American Society for Histocompatibility and Immunogenetics (ASHI) established the Paul I. Terasaki Clinical Science Award recognizing a transplant physician whose scientific contributions have a major impact in the field of transplantation.

Paul was a true scientist. His uncompromising devotion to honesty in research was legendary. Gerhard Opelz first met Professor Terasaki at the 1970 Congress of The Transplantation Society at Den Hague when Paul delivered his stunning report that HLA-matching using the then-available technology did not correlate with kidney-graft survival. As a

consequence, Paul lost his NIH grant and his laboratory went through a period of financial hardship. However, he believed in the power of large numbers and statistics and thought the computer a great tool for transplant outcome research "because it keeps you honest". The facts are what mattered and if something has to be adjusted or modified it is our hypotheses, not the facts.

Many readers of *Transplantation* may not know of several other of Professor Terasaki and his wife Hisako activities. For example, they were committed to preserving the history of Japanese Americans in the United States. Paul served on many committees including the Japanese American National Museum in Los Angeles, the Memorial to Japanese-American Patriotism in World War II in Washington, DC, and the Paul I. and Hisako Terasaki Center for Japanese Studies at the UCLA International Institute. Paul and his wife were also major contributors to UCLA leading to the creation of the Terasaki Life Science Building and the Paul I. Terasaki Chair in Surgery. In 1998, Paul established the Nibe Foundation offering postdoctoral Japanese physicians opportunity to meet and participate in research projects with Los Angeles-based Japanese/American physicians.

In 2014 we had a *Festschrift* for Prof. Terasaki in Los Angeles attended by more than 300 colleagues, collaborators, students and friends including a star-studded list of Who's Who in transplantation. It was a marvelous tribute to Paul's global impact with talks covering every sphere of transplants: faces, hands, hearts, livers, kidneys, pancreases, bone marrow, and more; name your favorite tissue or organ. However, kidney transplants were always his favorite. It is hard to calculate how many people are alive today because they had a successful kidney transplant facilitated by technology developed by Paul Terasaki. Paul and Hisako loved Mexican mariachi music. The *Festschrift* coincided with their 50th wedding anniversary and they danced to a mariachi band. Paul also had a deep, abiding love of ice cream and red bean cakes, the latter perhaps hereditary. He was often seen at the Sizzler in Santa Monica, usually at an early hour, he said because of a senior early-bird discount.

Paul Terasaki, despite great fame and fortune, was always modest and approachable. He had a wry sense of humour, an infectious laugh and genuine affection for colleagues and coworkers. Also, he loved debating colleagues and his lectures always had an element of humour.

Professor Terasaki is survived by his wife Hisako, an accomplished artist, his 4 children, Mark, Keith, Taiji, Emiko, 6 grandchildren and his brother Richard. He will be greatly missed but long remembered. What current or future scientist has not or will not encounter a Terasaki microwell plate? Think of him when you do your next experiment.