

RETROSPECTIVE

Thomas Earl Starzl (1926–2017)

Father of modern transplantation

By John J. Fung

Thomas E. Starzl, best known for his contributions to the field of organ transplantation, died on 4 March 2017 in Pittsburgh, Pennsylvania. He was 90 years old. Starzl pioneered many aspects of transplantation, including immunosuppressive drug development, organ preservation, tissue matching, and innovative transplant surgical procedures. He developed the team approach to organ transplantation, thus paving the way for the success and acceptance of heart, lung, pancreas, intestinal, liver, kidney, and composite tissue transplants. Thanks to Starzl's lifetime commitment to transplantation, close to 1 million patients around the world have received a life-saving organ transplant.

Born on 11 March 1926 in Le Mars, Iowa, Starzl spent his childhood helping out at his father's newspaper. In 1947, he earned his B.A. at Westminster College in Missouri after serving a year in the Navy at the end of World War II. In 1952, he graduated with an M.D./Ph.D. from Northwestern University. After postdoctoral work at Johns Hopkins Hospital and the University of Miami, he returned to Northwestern. In 1961, the University of Colorado School of Medicine recruited Starzl as an associate professor in surgery. Over the next 20 years, he was promoted from professor, to chief, to chairman of the Department of Surgery. He then joined the University of Pittsburgh School of Medicine as professor of surgery in 1981. Until his retirement in 1991, he served as chief of transplantation services at Presbyterian University Hospital (now UPMC Presbyterian), Children's Hospital of Pittsburgh, and the Veterans Administration Hospital in Pittsburgh, overseeing what became the largest and busiest transplant program in the world.

Before 1962, the outlook for clinical organ transplantation using an unrelated donor was grim because of the inability to control rejection of the new organ. When I first read about Starzl's pioneering work in

liver transplantation in 1974, surgeons and physicians questioned the future of extrarenal transplantation. But at the University of Colorado and then at the University of Pittsburgh, Starzl found that the immunosuppressant cyclosporine contributed to substantial improvements in transplant success. Based in part on Starzl's work, the U.S. Food and Drug Administration (FDA) approved cyclosporine in 1983, making organ transplantation a viable option for patients with organ failure. The same year, the U.S. National Institutes of Health consensus development conference on liver transplantation recommended broader use of liver transplantation to treat end-stage liver dis-



ease. These two developments paved the way for an expansion of liver transplantation throughout the United States; the number of transplantation centers grew from 3 in 1983 to more than 130 by 2003.

Despite the progress, when I met Starzl and joined him as a clinical research fellow in 1984, clinical transplantation of the liver, kidney, and pancreas remained fraught with failures and complications. As transplantation techniques and medications developed (many initiated by Starzl), transplant outcomes incrementally improved. When tacrolimus, then known as FK506, came into preclinical testing in 1987 and then into clinical testing in 1989, the benefits over cyclosporine quickly became obvious, and patients flocked to the University of Pittsburgh.

To manage this influx of patients, Starzl assembled organ-specific multidisciplinary

teams from the pool of international surgeons and physicians who had come to learn surgical techniques and engage in scientific transplantation inquiries. Investigations into preservation, immunosuppression, infectious disease, oncology, growth factor physiology, and immunology were conducted under Starzl's supervision. During the 7-year period between the introduction of tacrolimus in preclinical studies in 1987 and the FDA approval of tacrolimus in 1994, the transplant program at the University of Pittsburgh produced one peer-reviewed article every 2.7 days, while transplanting an organ every 14.2 hours. Starzl's work ethic and inspirational leadership allowed him to mold a diverse group of scientists into an effective, motivated team.

Starzl analyzed each failure and took it into account for the next procedure, and he deemed each success a reaffirmation of modifications. Only by this critical analysis could a single visionary have developed the field so quickly and completely. Meanwhile, Starzl never lost sight of the people his work affected. To him, each patient was a human being, with a name, a face, and a unique history. In his autobiography *The Puzzle People: Memoirs of a Transplant Surgeon*, he vividly recalled each patient account from memory, rather than from a patient medical record.

Through Starzl's work, the risk of losing a transplant from acute rejection has been reduced to less than 5%. On the way to demonstrating the feasibility of organ transplantation, Starzl made seminal discoveries in the fields of physiology and immunology. For example, Starzl was instrumental in unraveling the liver-based metabolic defect underlying familial hypercholesterolemia, a genetic disorder. Geneticists Joseph L. Goldstein and Michael S. Brown confirmed his hypothesis, winning the 1985 Nobel Prize in Physiology or Medicine for their work.

I had the privilege of studying under and then working with Starzl for more than 30 years. He was an iconic surgeon, mentor, friend, and role model. He created a surgical discipline that has saved countless lives around the world. He led transplant development, and he trained and inspired a generation of transplant professionals. His legacy lives on as thousands of health-care providers continue his work across the globe. He is survived by his wife of 36 years, Joy Starzl; a son, Timothy Starzl; and a grandchild, Ravi Starzl. ■

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