

Thomas E. Starzl: Transplantation pioneer

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Thomas E. Starzl, MD, PhD was born on March 11, 1926 in Le Mars, Iowa, the second son of Roman Frederick Starzl and Anna Laura Starzl. His parents were first-generation Americans, the children of Czechoslovakian and Irish immigrants. Roman Starzl was an editor, publisher, and owner of a newspaper. Anna Laura Starzl was first a nurse and then a teacher. As a boy, Tom Starzl worked at every job in his father's paper, and he later credited his experience of sorting type with helping him to develop the manual dexterity required as a surgeon (1).

After serving in the US Navy, Starzl obtained a Bachelor of Arts degree in 1947 from Westminster College in Missouri, and then he earned his medical degree and doctorate (Neurosciences) at Northwestern University in Chicago. Following graduation, he performed surgical residencies at The Johns Hopkins University in Baltimore (1952–1956), the University of Miami (1956–1958), and Northwestern University (1958–1959).

Although his first research as a physician was studying a dog model of complete heart block, Starzl switched research interest to abdominal organ transplantation from 1958 onward. His first published paper in this field was the removal of all intra-abdominal organs, including the liver, and replacement with a multiorgan allograft (2).

Starzl's goal was to establish the use of kidney and liver transplantation for the treatment of kidney and liver diseases. The chief limitation to this program was of course the lack of tolerance for nonrelated donor and recipient tissues, which was appreciated long before the identification of histocompatibility antigens. With the advent of azathioprine as the first antirejection drug, Starzl developed protocols to treat dogs undergoing kidney or liver transplantation and assessed their rejection of

the transplanted organ. These preclinical studies provided the foundation to the launch of a human kidney and liver transplantation program at the University of Colorado (3). The combination of azathioprine and prednisone successfully reversed rejection in human kidney grafts with subsequent development of tolerance.

Using the same type of immunosuppression protocol as was successful with kidneys, several clinical groups attempted human liver transplantation. After failed attempts universally in multiple centers, all liver transplantation was stopped worldwide until the summer of 1967. To improve immunosuppression, Starzl added antilymphocyte globulin to azathioprine and prednisone with improved survival in liver transplant recipients (4). "However, liver transplantation remained feasible but impractical until the advent of cyclosporine" (5). In 1978, Starzl started to use cyclosporine for immunosuppression in liver transplantation, which improved transplant survival.

In December 1980, Starzl moved to the University of Pittsburgh, where he continued his clinical and research advances in liver transplantation. In June 1983, the National Institutes of Health conducted a consensus conference on liver transplantation that concluded that liver transplantation had become a clinical service rather than an experimental procedure. I distinctly remember the excitement at that conference and subsequently throughout the hepatology community, leading to the establishment of many liver transplant centers throughout the United States.

Starzl started preclinical studies on tacrolimus (previously known as FK506) as a new immunosuppressant agent. Tacrolimus greatly improved survival in solid organ transplants and remains a fundamental immunosuppressant (6). Starzl continued his research on transplant biology up until his death. He promoted the concept of microchimerism as a mechanism to explain long-term survival in transplant recipients (7, 8). This is a concept that, in addition to the solid organ, transplanted immune cells from the donor should also become part of the recipient's lymphoid tissues. This results in a balance in the immune system between graft versus host and host versus graft. Starzl also conducted studies to understand the mechanisms of liver



Thomas E. Starzl. Image courtesy of the University of Pittsburgh.

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regeneration with respect to liver translation. Most recently, he analyzed the role of augments of liver generation (ALR, ERV1) in hepatic metabolism, including oxidative stress, mitochondrial transport, and stem cell biology (9).

I remember last visiting Starzl in his office above a storefront in Pittsburgh. He was always energetic,

enthusiastic, and optimistic about the future of medical care in general and liver transplantation in particular. More than anyone else, I believe Dr. Starzl revolutionized solid organ transplantation by his persistence, creativity, and rare combination of clinical and research acumen and accomplishments.

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