

Martin A. “Mac” Cheever, MD: In Memoriam (1944–2021)

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The field of cancer immunotherapy deeply mourns the loss of one of its founding giants. Dr. Martin A. “Mac” Cheever, an immunotherapy pioneer whose scientific accomplishments initiated and informed the development of cancer T-cell therapy, passed away on September 23, 2021. In addition to his clinical and scientific contributions, Mac led critical initiatives advocating for and garnering resources for cancer immunotherapy at a time when its astounding potential had not yet been fully recognized. He was a visionary. Most importantly, he provided expert, tireless leadership and had a unique gift of bringing out the best in everyone with whom he worked. In his calm, unassuming wisdom, he made all those around him feel important, driving their aptitude to advance health care in cancer.

At his passing, Mac was director of the NCI-funded Cancer Immunotherapy Trials Network (CITN); member of the Fred Hutchinson Cancer Research Center; professor of Medicine/Oncology; and past director of the Solid Tumor Program at the University of Washington. He was an early member of the Seattle Bone Marrow Transplant Team, which provided data central to the concept that bone marrow transplantation cures could be attributed to the transferred immune system, a striking demonstration of T cell–mediated cancer immunotherapy. For more definitive proof, and the direct forerunner of T-cell and CAR T-cell therapies, he pioneered mouse models to cure leukemia with leukemia-specific autologous T cells expanded to overwhelming numbers *in vitro*. A subsequent highly productive, 15-year collaboration with his colleague, Phil Greenberg, established important principles of T-cell therapy that are now widely applied and have been translated into the clinic leading to cures.

In the early 1990s, cancer T-cell therapy was ripe for testing in humans, but the field had not yet identified appropriate cancer targets. With T-cell therapy as his ultimate goal, Mac then sought to identify T cell–targeted cancer antigens. He was the first in the field to focus on oncogenic proteins such as mutated ras, bcr-abl, HER-2/neu, and WT1. For these studies, he was awarded two NIH MERIT Awards and held 25 patents. In 1994, he cofounded Corixa Corporation to develop cancer vaccines as therapeutic products, which was a concept before its time. Two vaccines he invented at the University of Washington (HER-2/neu

and WT1) were taken into collaborative clinical trials with GlaxoSmithKline.

In 2005, Mac was recruited to form and lead the American Association of Immunologists/American Association for Cancer Research Extramural Immunology Expert Steering Committee, serving as extramural cancer immunotherapy community liaison to the NCI to ask, “Why is it that scientists have invented so many immunotherapy agents that could benefit patients and so few are being tested in patients?” Accordingly and presciently, Mac instigated the NCI Immunotherapy Agent Workshop in 2007 that developed a list of 20 “high-priority” immunotherapy agents that could potentially benefit cancer patients. Correspondingly, he instigated the Cancer Antigen Pilot Prioritization Project in 2008 and mobilized leading cancer immunologists to develop predefined and preweighted objective criteria for optimal cancer vaccines to rank the top 75 known cancer antigens. These criteria continue to be used by academics and industry to assess the relative worth of cancer antigens.

With the Steering Committee, Mac successfully lobbied the NCI to fund the CITN at a time when the full potential of cancer immunotherapy was not yet appreciated. The CITN now has more than 18 trials with high-priority immuno-oncology agents, either open, soon to open, or successfully completed. These trials have led to new approved therapies and generated new paradigms in immuno-oncology. With his selfless leadership, the CITN has become a model of collaboration and research to accelerate cancer immunotherapy treatment.

CITN’s success can be attributed to Mac’s gentle, inclusive, collaborative, and selfless personality, as much as his generous and tireless efforts to include the field broadly and his laser-like focus on agents useful in many different regimens and clinical situations for patient benefit. He always thought first of patients. For his outstanding science, leadership, and selfless service he received several awards, the latest being the Society for Immunotherapy of Cancer Inaugural Distinguished Service Award in 2019.

Mac opened and expanded the field of cellular immunotherapy, led important initiatives that supported all cancer immunotherapy efforts, and drove innovative trials with agents for patient benefit. We are indebted to his vision. He published over 150 research papers and over 60 reviews. He served on over 20 different advisory boards and review panels. These numbers cannot fully represent the scientist, leader, and man he was. He was a consummate mentor not only to his fellows but also to innumerable colleagues benefiting from his profound wisdom. He was a proud husband of his highly accomplished wife, Linda, of whom he always spoke with great admiration. He will be remembered, not only as a highly devoted father to Alex and Paul—doing all his work while listening to the music they were creating—but also as a father to patients and work colleagues. He will be remembered and missed deeply.

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Authors’ Disclosures

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