

## IN MEMORIAM

# Tom Force (1951–2020)

## Our Dearest Friend, Our Mentor, and a Brilliant Cardiovascular Scientist



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**O**n November 30, 2020, our friend, colleague, and mentor, Tom Force, passed away, leaving a void in our community. Tom was our mentor, advisor, and friend—a pioneer in the field of cardio-oncology, making many lasting contributions as a clinician and investigator. He brought basic research to the nascent field of cardio-oncology and inspired many of us to pursue science. He served as a mentor for many in the field, inspiring and motivating us in his extraordinarily affable and humble way.

### THE EARLY YEARS

Thomas Lee Force was born on March 25, 1951, in Vandalia, Illinois. He graduated Phi Beta Kappa from Harvard College in 1973, majoring in psychology, although Tom would often admit that his passion in college was music. After taking a year off, he matriculated at Harvard Medical School. He stayed in New England for much of his subsequent training, at the University of Vermont, where he was a resident, and at the West Roxbury Veteran's Hospital and Brigham and Women's Hospital, where he completed clinical and research training in cardiology. In 1984, he joined the faculty at Massachusetts General Hospital and Harvard Medical School as an instructor.

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Although he did not have much prior experience in research, he was quickly drawn to medical investigation. Working with the late Alfred Parisi at the West Roxbury Veterans Administration, he was initially drawn to clinical imaging research. In the 1980s, along with Dr. Parisi, he made early contributions using then-novel techniques of 2-dimensional and contrast echocardiography in defining various cardiac pathologies, including myocardial infarction and valvular disease. These became seminal observations in the field of echocardiography, resulting in important manuscripts, many published in *Circulation*.

At Massachusetts General Hospital, when he became an Assistant Professor of Medicine, he became an active clinician and an attending in the coronary care unit, where he was affectionately called "T. Force." At this point, he also found himself on a new research path of basic science investigation. Working with Joe Bonventre, a physician-scientist and nephrologist, he became interested in cell signaling. Many of Tom's early grants, especially career development grants in the 1990s, focused on renal mesangial cells and were funded through the National Institute of Diabetes and Digestive and Kidney Diseases. With these basic laboratory skills, he embarked in a new direction in cardiac signaling, focusing specifically on stress-activated pathways, particularly kinases. Using preclinical models, he made seminal contributions to the divergent roles that kinases play in the myocardium. At the same time, he quickly rose through the ranks, becoming an Associate Professor at Harvard Medical School.

### SEMINAL CONTRIBUTIONS IN THE MECHANISMS OF TYROSINE KINASE INHIBITOR CARDIOTOXICITY

In 2000, he moved his laboratory to Tufts University Medical Center, where he treated patients at the New

England Medical Center and became an investigator in the newly formed Molecular Cardiology Research Institute. In continuing his research in kinase signaling in the heart, his pioneering work provided unique insights directly relevant to the cardiotoxic effects of targeted therapies. Aberrant kinase signaling had been earlier recognized as an important contributor to tumorigenesis, motivating efforts to introduce tyrosine kinase inhibitors (TKIs) for the treatment of cancer. In the early 2000s, targeted therapies such as trastuzumab and imatinib became important in the new armamentarium for cancer treatment. These drugs also introduced the paradigm of precision or personalized treatment in oncology. The hope was that because of the targeted nature of these therapies, fewer toxicities, especially cardiovascular toxicities, would be observed. However, Tom's research demonstrated a critical role for kinase signaling in the cardiovascular system, especially at times of stress. As he subsequently demonstrated in a variety of elegant scientific observations, TKIs were associated with the inhibition of many tyrosine kinases, with the potential for clinically relevant cardiovascular toxicities.

In 2006, Tom's laboratory published a seminal manuscript in *Nature Medicine*, where he used cell-based and mouse models to demonstrate a cardiotoxic signal for imatinib and a genetic approach to show that imatinib's effects on the myocardium were "on target" because of inhibition of the intended target of imatinib, *Abl1* kinase. Although the clinical translation was unclear at the time, it opened the door for using cardio-oncology as a novel platform for basic cardiac investigation. The later-generation *Abl1* kinase inhibitors, presumably due to off-target effects, showed various cardiovascular complications. The combination of preclinical models with careful clinical adjudication served as a platform for investigating the cardiovascular sequelae of other kinase inhibitors. Beyond focusing on other TKIs such as sunitinib, Tom additionally introduced new platforms, such as zebrafish models, for investigating the toxicities of new drug therapies.

#### LEADERSHIP IN INTERNATIONAL CARDIOVASCULAR SOCIETIES

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In 2005, Tom moved his laboratory to Thomas Jefferson Medical College in Philadelphia, then to Temple University in 2012, and finally to Vanderbilt in 2014. We are all fortunate to have had the opportunity to know Tom and work with him closely during these years. As one of his contemporaries would say, "Tom is the one myocyte biologist who has no bad

bones in his body and does everything he can to help you. He was a joy to be around." By 2010, Tom had become an active leader in cardiovascular research across the county, serving in multiple National Institutes of Health (NIH) study sections, chairing the American Heart Association Basic Cardiovascular Sciences meeting, and ultimately becoming president of the Heart Failure Society of America (HFSA). He chaired or co-chaired multiple meetings with the NIH, which ultimately led to cardio-oncology-specific NIH funding initiatives. He used each of these forums to advance the burgeoning field of cardio-oncology and to create opportunities for many in the field, particularly young investigators.

#### AMONG HIS GREATEST CONTRIBUTIONS: HIS ROLE AS OUR MENTOR

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Tom was the ultimate mentor—he was kind and approachable, and he had incredible humility; he was smart and incisive. He made us laugh: to one of us (B.K.), he often stated, "I'd nickname you 'Shorty,' but that's reserved for my friend R.L." He created opportunities for his mentees and colleagues and was extremely generous. He often worked in the background, without recognition, to advance careers, and he played a particularly important role, for many of us, as we were developing our careers. As just one example of many, he invited 2 of us (J.M. and B.K.) to coauthor an authoritative review in cardio-oncology for *Circulation Research*. Even though it was Tom who had been asked to write the review and be the lead author, he wanted to give credit to others, ultimately being a middle author on the manuscript.

Another one of us (H.L.) started in Tom's lab as a junior post-doc and transitioned to full faculty, all under his guidance. This included securing a post-doc fellowship, career development award, and first NIH RO1 under Tom's mentorship. This is a strong testament to Tom's exceptional support to his trainees. In H.L.'s words, "Even now, I refer to him almost every day while explaining something to my lab trainees. The usual phrase is, 'In this scenario, Tom would say this.'"

Tom had extraordinary intelligence and an ability to connect seemingly disparate concepts into meaningful interpretation. He was always willing to help, offer scientific advice on grants, and collaborate on initiatives within cardio-oncology. He was brilliant, but humble and incredibly modest. He loved to laugh and joke, and his smile was infectious. For all of us who were blessed to know and work with him, he brought joy into our lives. It is perhaps no surprise that by the time he retired in 2016, multiple

**FIGURE 1** Dr. Thomas Force (left) Receiving the International Cardio-Oncology Society Thomas Force Pioneer Award



international organizations—the International Cardio-Oncology Society and HFSA—named leading talks at each annual meeting in his honor, including the International Cardio-Oncology Society Thomas Force Pioneer Award (Figure 1).

### IN CLOSING

Besides being a phenomenal cardiologist, scientist, and mentor, Tom made sure we all laughed and had fun, in work and in life. He was a strong advocate of

following one's passions. In his own career, he had transitioned from a clinical researcher and leading echocardiographer to a basic scientist, teaching himself essentially a whole new way of doing science. As stated, even though Tom's major at Harvard was psychology, his real passion was music. He was specifically interested in the technology of music. Therefore, he delayed medical school matriculation in 1973 to pursue this passion. He became a roadie, and not for just any band, but for the Rolling Stones. The thought of Tom jamming with Mick Jagger and Keith Richards in 1973/1974 can only bring a "Tom Force" smile to our collective faces now. Tom is survived by his loving wife, Wendy Buck, and his children, Meghan Force (m. Alex Rein, grandsons Matthew and Henry), Emily Force, and step-children Alison and Morgan Buck. We miss our dear friend, colleague, visionary, leader, and mentor.

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