

A tribute to Lloyd Hollingsworth “Holly” Smith Jr. (1924–2018)

Dr. Lloyd Hollingsworth (Holly) Smith Jr. passed away in his sleep on June 18, 2018, in his home in Marin County, California. He was 94. It is difficult to imagine a fuller life than Holly Smith's, or one whose impact on an institution — in this case, the University of California, San Francisco (UCSF) — and its people, was more profound.

Holly Smith (Figure 1) was born in Easley, South Carolina, a town with a population of about 3,000 in the northwest corner of the state. While his father, Lloyd H. Smith, was an attorney and cotton farmer, there was plenty of medicine and science in his family tree. His grandfather had been the town's physician, and his uncle, Hugh Hollingsworth Smith, MD, helped to develop the yellow fever vaccine while working at the Rockefeller Foundation in the 1930s (1).

After attending Washington and Lee College, in 1943, at the age of 19, Holly was accepted (without an interview) into Harvard Medical School (2). Following his superb performance at Harvard, he completed his residency in medicine at Massachusetts General Hospital, after which he entered the Army, where his work during the Korean War included some of the early experiments with the artificial kidney. After returning to the US, he conducted seminal studies on pyrimidine and oxalate metabolism, some of the latter while on sabbatical in the laboratory of Sir Hans Krebs at Oxford University. Dr. Smith's skills as a researcher and leader were quickly recognized at Mass General, where the legendary chair of medicine, Dr. Walter Bauer, named him assistant chief of medicine and chief of endocrinology — the latter despite the fact that he wasn't an endocrinologist!

The pivotal moment for UCSF came in 1964, when Holly was 40 years old. The

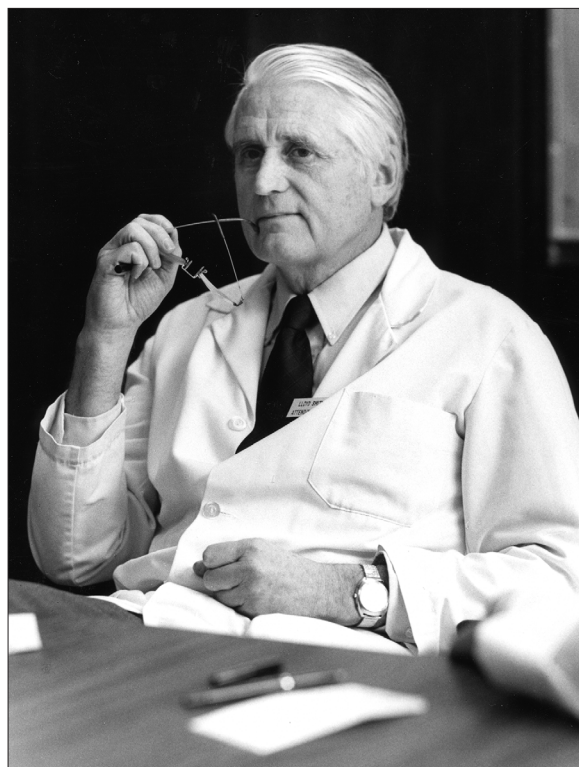


Figure 1. Lloyd Hollingsworth “Holly” Smith Jr. Image courtesy of the UCSF Archives.

medical school, a fairly undistinguished institution at the time, was searching for a new chair of medicine. “It was celebrating its first century,” Dr. Smith said in a 2017 interview, “and there wasn't much to celebrate” (3). Holly came out from Boston to visit and immediately recognized the vast potential, owing to the preeminence of the Berkeley campus and the University of California system more generally, the recent decision by Stanford's medical school to leave San Francisco and consolidate its operations in Palo Alto, the splendor of the Bay Area, and the emergence of jet travel, which halved the commute to the East Coast (and particularly to the NIH). After taking all of this in on his visit to UCSF, he sent a one-word telegram to his wife Margaret. It said, “Pack” (3).

In the 2017 interview, Dr. Smith was asked what led him to leave Harvard and place his bet on UCSF (3). Today, of course, with UCSF among the leading medical institutions in the world, this seems like a quaint question, like asking how anyone got anywhere before GPS. But times were very different back then, and the move was not without risk. “It was worth a shot,” he said. “If you're going to make a change and take a chance, that is the time to do it — when you are young and feisty.”

On his arrival in San Francisco, Holly immediately set out to change UCSF's culture, one he characterized as “malignant complacency.” He and the other chairs quickly ousted what they considered to be an ineffective Chancellor, built a tighter integration with the San Francisco VA Hospital and San Francisco General Hospital (when he arrived, each ran separate residency programs; today, UCSF's three-hospital system is one of its defining characteristics), and markedly elevated the school's

academic standards. The full-time faculty in the department, which numbered 50 when he arrived, grew tremendously under his tenure (now at nearly 800), as did the stature of the department and institution. Many of Holly's faculty and trainees would go on to become important leaders in their own right, including several Nobel prize winners, chairs and deans, and heads of major organizations including the Centers for Disease Control and Prevention (Julie Gerberding), the NIH (Harold Varmus), the Food and Drug Administration (Rob Califf), and both the Robert Wood Johnson (Steve Schroeder) and Gates Foundations (Sue Desmond-Hellmann). Moreover, one can trace the origins of the biotech revolution to Holly Smith and the faculty whose careers he launched and nurtured, including Bill Rutter, founder of Chiron, and Herbert Boyer, cofounder of Genentech (4).

In addition to his accomplishments at UCSF, Holly had a substantial impact nationally and internationally. A partial list of his activities and honors includes the following: (a) he served as coeditor for several editions of one of the major textbooks of medicine, *Cecil Textbook of Medicine*; (b) he received three honorary degrees and the highest awards bestowed by the American College of Physicians, the Association of American Physicians, the Association of American Medical Colleges (and, of course, by UCSF); (c) he served as a member of the President's Commission on Science in the Nixon administration; (d) he served as a senior advisor to the Shah of Iran; and (e) he served as chair of the Howard Hughes Medical Institute's advisory board.

In recognition of Holly's many accomplishments, the UCSF School of Medicine's top service award is named in his honor. So too is the UCSF Department of Medicine's annual visiting professorship. Finally, the Seldin-Smith Award, given annually by the American Society for Clinical Investigation, honors an early-career physician-scientist who has demonstrated exceptional creativity and accomplishment. It is named for Dr. Smith and his colleague, Dr. Donald Seldin, long-time chair of the Department of Medicine at the University of Texas-Southwestern, who passed away two months before Dr. Smith, at the age of 97.

For those of us who had the joy of knowing Holly Smith, he was unforgettable — larger than life, with a rare combination of southern charm, blinding brilliance, and disarming humility. One of his most memorable traits was his sense of humor — most tangibly illustrated by his celebrated aphorisms. There are many favorites that we recall: “Never attribute to malice what you

can attribute to incompetence”; “Experiment. Take some chances. Remember the Peter Pan principle: ‘Most things peter out but some will pan out’”; “The tyranny of trivia: A thing not worth doing is not worth doing well”; (About a clueless leader) “He has mural dyslexia — he can't read the handwriting on the wall”; and (his famous line about a prominent national medical organization) “It's the only organization that chews more than it bites off.”

And two bon mots that he began using as he grew older: “Every time I reach down to tie my shoes, I ask myself, ‘Is there anything else I need to do as long as I'm down here?’”; and “People ask me how I feel. I say ‘fine.’ But if I was 21, I'd be calling 9-1-1.”

Holly Smith cared about people deeply and managed to inspire professional excellence while also emphasizing the importance of a balanced life. “Carefully guard the frontier between commitment and obsession,” he said in a 2012 interview with the *JCI*. “It is important to be a participant in the pageantry of one's times. There are no recorded deathbed statements, ‘I wish I had devoted more time to my profession’” (5). And, remarkably given his enormous productivity, Holly managed to do just that. He was an avid tennis player, boater, and skier, and he loved nothing more than spending time with his large family (which he affectionally called his “biomass”), beginning with his wife of 64 years, Margaret, along with his six children, 17 grandchildren, and five great-grandchildren.

In 2017, he was asked about what worried him the most about today's world of academic medicine, and what excited him. “What worries me in academic centers is that we're getting so big...the communication between those in the forefront of patient care and those in the forefront

of medical advances is not as intimate... we knew each other, we supported each other...we were unified as an academic community” (3). What excited him was, “The new science. The way we're skipping up and down the DNA...what can be done now in an afternoon by a post-doc would have won the Nobel prize many times over [when I was a young scientist]” (3).

At UCSF's Parnassus Heights campus, the entryway to the Medical Sciences Building connects UCSF's medical center to the campus's scientific enterprise. Fittingly, last year it was renamed the Holly Smith Gateway, since nurturing this connection is precisely what Holly did, at UCSF and throughout American medicine, during his long and uniquely distinguished career.

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