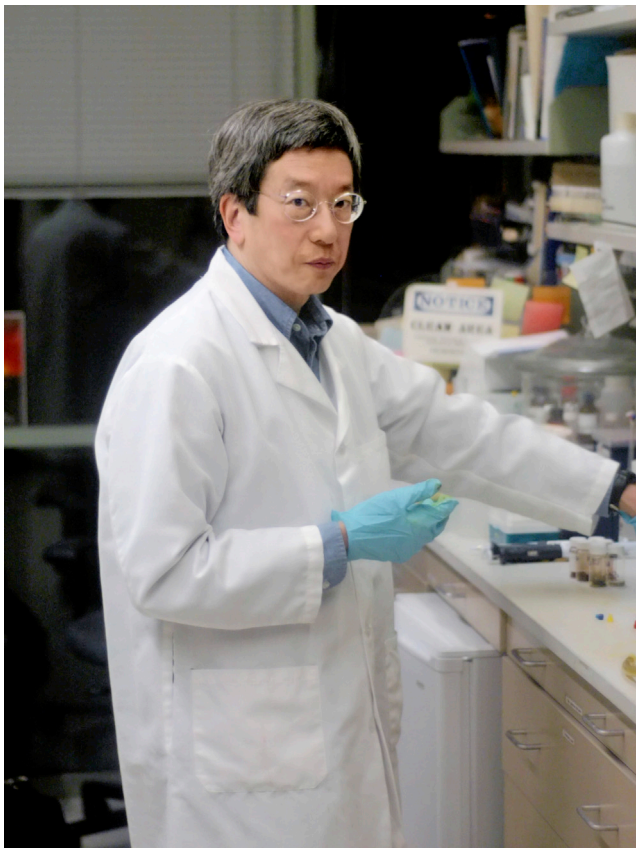
CellPress

Roger Tsien (1952–2016)

I met Roger in 1991, when he and I moved our labs to the new "HHMI floor" at the Center for Molecular Medicine building at UCSD. My first encounter with Roger was quite awkward and memorable: I tried engaging him in conversation, but he was reserved, shy, and very eager to get back to his work. I was outgoing, loud, and totally oblivious to Roger's body language—visibly screaming, "Please leave me alone and let me go." However, after I repeated the same routine over the following several weeks, he realized I was not going away. That was the beginning of a wonderful 25+ year friendship. Soon after, I was exposed to remarkable ingenuity in chemical biology, live-imaging technology, tool-making prowess, how to fix 30-year-old amplifiers, and the extraordinary workings of a brilliant mind, and he—I believe—learned about (quoting his usual line to me) "the power of genetics," to *waste time* being social, and to understand bad words in Spanish.

Roger had the uncanny ability to look at a problem with the innocence of a child and be totally unbound by convention, preconceived ideas, or the concept of impossibility. He would reduce complexity into simple logic and turn the impossible into the possible. In fact, many years before the world knew about GFP, he was already thinking (and searching) for a genetically encoded reporter for calcium, and long before optogenetics become a reality, he was looking for non-invasive ways to manipulate neuronal function. He would regularly come to my office and start the conversation with, "Do you think it would be possible to…," each followed by an extraordinarily unpretentious, and creative, question (for example, could we clone the magnetic sensing system of a given bird, marine organism, or bacterial species and re-purpose it as a non-invasive means for activating neurons with a magnetic field—and this was nearly 25 years ago).

Roger deeply cared about his students and postdocs. He knew he was having them work in very challenging and risky projects, yet he always wanted to make sure they could find jobs. When we were starting the biotech company Aurora Biosciences, he was asked by one of the partners at a prospective venture firm why he wanted to start a biotech company, and he replied immediately, without any hesitation, "I want a place for my people to go." This, of course, was not the answer they were hoping for. Aurora did become a home for many outstanding Tsien students and postdocs, and it is to their credit that the company succeeded in developing a broad range of tools and strategies for drug discovery. In fact, over these past few years Roger would often muse about how proud he was about Vertex Pharmaceuticals' success with Ivacaftor, a drug to treat cystic fibrosis; this entire program originated with a pilot project started by Aurora Biosciences and the Cystic Fibrosis Foundation about 4 years after we started Aurora (Vertex then purchased Aurora in 2001). Over the years, Roger and I got involved in other biotech ventures, together with our dear friend Lubert Stryer, including Senomyx. Roger felt strongly that ultimately, we need to make a difference in helping alleviate human disease, and, perhaps more meaningfully (and personally rewarding), he wanted to directly and tangibly impact human health. This was part of his strong drive later in his career to move into live cancer imaging.



Roger Doing Chemistry, Christmas 2004
Photo by P. Steinbach.

Roger was born in New York City on February 1, 1952. As a young boy, he was already doing absolutely-not-for-children chemistry experiments in his home basement (and when unusually dangerous or stinky, out on his backyard picnic table). In 1968, he won first prize in the National Westinghouse Science competition, and by 1972 he had graduated from Harvard with a bachelor's degree in chemistry and physics. In the fall of 1972, Roger moved to Cambridge, England, to begin his PhD studies; this was the beginning of his life-long love affair with calcium.

Roger's other great love was music. I am not sure when Roger's passion for piano began, but soon after we became friends he told me he had seriously considered moving to Switzerland to study piano full time and become a concert pianist…well, science would have missed out

on one of its giants, but on the other hand, I have no doubt we would have gained a brilliant pianist. Anecdotally, the very first purchase Roger made after Aurora went public was a Bosendorfer grand piano (and he insisted I should learn how to play and buy his old grand piano. I assured him this would never work: "Look," I said, "I had to learn English at 19 when I came to the USA to get my PhD, and I still speak like I just came off the boat; imagine starting piano now." But he insisted, and went out and bought me two books on how to learn to play the piano as an adult—like *Piano for Dummies*, but I do not recall the names of the actual books). One of the great anecdotes of piano playing between Roger and me was at an HHMI meeting where Roger was asked to play the piano. Of course, he needed someone to turn the music pages, and I naturally agreed. After the first few minutes into his concert, he realized I did not read music (I never thought that would be a problem; I assumed I'd figure out on the spot when it was time to turn to the next page). He was incensed; how could I agree to do it? He stopped the concert as soon as he could, asked me to leave the podium, and called on Lily Jan to please be his assistant turning the pages. Afterward, we laughed about it; he could be very funny.

Roger's brilliance helped transform many fields in biology and created entirely new ways to probe and monitor the function of small molecules, proteins, cells, and circuits in vitro and in vivo. His legacy is extraordinary. A simple web search will inform on the breadth and extent of his scientific contributions. Roger had a razor-sharp and laser-focused ability to find the Achilles heel in every argument, but he also had the humility to quickly accept when he was wrong. Those who knew Roger would readily remember (he was unforgettable) how quirky and disarmingly unassuming he could be. Also, he was always willing to share the lab's latest creations with the scientific community, and would eagerly await feedback from users so they could tinker away problems and challenges. Roger always understood that perfect is the enemy of good, so he never let the wait for the perfect solution get in the way of finding a good solution. I always admired that sensible balance between his genius and the need to provide a capable, real-world answer.

Roger always spent time during Christmas holidays at the hood (I mean the chemical hood) extracting, concentrating, purifying, and running chemical reactions; I believe it was his way of staying connected, and perhaps recapturing the intimacy we need to have with our science and experiments. He would often recall that while at Berkeley, he was only given a couple of ancient fume hoods, and that one of the great joys of having moved to UCSD was how nice it was that they gave him so many brand new fume hoods and even dedicated space to do his imaging experiments. Just marvelous, how modest he was.

Roger pushed the boundaries of scientific ingenuity and creativity. He changed the way we could do science. A new generation of scientists can peek into the inner working of cells because of Roger Tsien. For me, he was also a brother, scientific sparring partner, and comrade. We are all better because of him.

Roger is survived by his wife Wendy; stepson Max; brothers Dick and Louis; prodigious life-long chemistry partner Stephen Adams; long-term lab members Larry Gross, Varda Levram-Ellisman, Paul Steinbach, Mike Whitney, and Qing Xiong; many former students and postdocs; and a world full of admirers.

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