In Memoriam: Denise A. Chan (April 4, 1977 - October 24, 2014)

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Dr. Denise Chan, principal investigator and assistant professor in the Department of Radiation Oncology at the University of California, San Francisco, died Oct. 24, 2014, from metastatic breast cancer. Denise was diagnosed with breast cancer at the age of 23 and courageously fought the disease for 15 years. A memorial service was held at the Stanford University Alumni Center, Nov. 22, which was attended by an extraordinary array of researchers from the fields of radiation oncology and cancer biology. In memory of her remarkable accomplishments in the face of adversity, an award has been established by the Cancer Biology Program at Stanford entitled “The Denise Chan Award for Best Thesis in Cancer Biology at the Stanford University School of Medicine.”

Denise was born in Los Angeles, where she also completed a bachelor’s degree in microbiology and molecular genetics in 1999. Despite her love for the southern Californian sports teams, especially her beloved UCLA Bruins, she then made the move north to undertake a doctorate at Stanford University. She joined the Giaccia lab in 1999 as a rotation student, and it was during this time she was diagnosed with breast cancer. Although it was immediately obvious that Denise was one of the brightest students, it was not until her diagnosis that those of us in the lab at the time truly appreciated the forceful determination that we will now forever associate with her. Denise successfully completed her doctorate without delay in 2004 despite enduring surgery, chemotherapy, and radiotherapy.
The focus of Denise’s doctorate was the role of prolyl hydroxylation in the coordinated regulation of the oxygen-dependent degradation domains of hypoxia-inducible factor (HIF-1α) (Mol Cell Biol, 2005; 25:6415-6426). This work was highly innovative, as Denise used domain swamping of the degradation domains within the full-length HIF-1α protein to demonstrate that hydroxylation of proline 402 was the key residue in HIF-1α that was highly responsive to physiologic changes in oxygen tension. As part of these studies, Denise generated and characterized a valuable resource, an antibody, which could be used to determine the hydroxylation status of HIF-1α. This was significant as it allowed Denise to collaborate and assist numerous other researchers in the field, firmly establishing her as a rising star. In the 10 years between publishing this article and her death, it was cited 174 times. For her novel approach to understanding the structural basis of oxygen sensing in mammalian cells, Denise was awarded the Malcolm A. Bagshaw Award by Stanford University School of Medicine in 2004.

As a result of the success of her doctoral studies, Denise extended her stay in the Giaccia lab, branching into new directions upon being awarded an individual Ruth L. Kirschstein National Service Postdoctoral Fellowship from the National Cancer Institute (2004-2009). This was an extraordinarily productive time in Denise’s research career in which she published 17 papers. Among these papers, a seminal piece of work stands out, which was published in Cancer Cell about the recruitment of tumor vasculature to solid tumors (Cancer Cell, 2009; 15:527-538). While it had been appreciated that bone marrow-derived cells are important in the maintenance and development of the tumor vasculature, mechanisms that governed their recruitment to tumors were poorly understood. Denise’s elegant studies showed that PHD2, a member of the prolyl hydroxylase family that hydroxylates HIF-1α and HIF-2α, acts to suppress tumor angiogenesis not only by regulating HIF protein levels, but also by limiting the expression of IL-8 and Angiogenin independent of HIF.

By this time, Denise had developed into a confident and independent researcher, well able to present her work in an engaging and entertaining manner. She was
also in large part responsible for the fun and lively atmosphere in the laboratory at that time. We are sure that few laboratory members of that era will ever forget the year we dressed up as Super Mario characters or, of course, her night out as a Spice Girl (she was Sporty Spice). Denise embraced every opportunity to further develop an enjoyable community, going so far as to turn the shaving of her head prior to chemotherapy into a lab event. It is clear that this strong sense of enjoyment for research and life, and the drive to lead a close team, was something she valued immensely as she started her own laboratory.

In 2009, Denise joined the Department of Radiation Oncology at University of California, San Francisco as an assistant professor. She was mentored at UCSF by Dr. John Murnane and embraced her new position with her characteristic joy and passion. She soon put together a strong research team, with two postdoctoral fellows and a large number of student volunteers. Denise was the ideal adviser, and showed great interest in the lives and aspirations of everyone who worked for her. Her door was always open, both to discuss science projects as well as day-to-day matters, and all of her employees adored her and considered her a friend. Denise and her group made impressive progress in several projects, including the effects of hypoxia on estrogen receptors in breast cancer. She also continued to pursue her interests in synthetic lethality screening for new therapeutics, which she nicely reviewed (Nat Rev Drug Discov, 2011; 10:351-364). All of this was accomplished despite the fact that her breast cancer had reappeared in a metastatic form soon after her recruitment to UCSF. Unfortunately, although she fought very bravely for five years, she ultimately succumbed to the disease. However, until the day she died, her passion for science and research were always evident. Even while undergoing treatment, she continued to work in the laboratory, somehow balancing those efforts with a variety of treatment schedules and an unyielding devotion to family and friends. She refused to let her disease define her, and few besides those closest to her at UCSF knew what she was enduring. She was an inspiration to everyone who knew her on how to face adversity and live life to its fullest.
Denise Chan serves as a role model for all of us and should also make us all work harder to better understand the complexity of cancer evolution and expansion so that we can develop more effective therapeutics.