Shu Chien, a 2010 National Medal of Science Awardee

Shu Chien in Singapore (2008).

On his 70th birthday, Shu Chien's colleagues put together a 600-page book of letters, essays, and photographs as a tribute not only to his contributions to the field of bioengineering but also in honor of his character as a valued friend, research collaborator, and family member. Perhaps they thought that the book would commemorate the moment when Chien began to consider retirement. But in the last decade, he has added more than 140 publications to an already impressive list of 379. And he shows no sign of slowing down.

During his career that has spanned more than 50 years and two continents, Chien was one of the first physiologists of his time to apply engineering principles to understanding biological systems. He has explained the

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physics behind how red blood cells travel through vessels, detailed how the stress of blood flow against the endothelial cells lining vessel walls can cause cardiovascular disease, and investigated the optimal growth conditions for stem cells used in regenerative medicine. He started out as a physician, obtaining his M.D. degree from National Taiwan University, but later pursued his Ph.D. degree in physiology at Columbia University. Chien felt that switching to a research career would offer more opportunities to be creative and to test innovative ideas. He spent nearly 30 years, first as a student and then a professor of physiology and biophysics, at Columbia before he was recruited, at the age of 57, to the bioengineering program at the University of California at San Diego (UCSD). Within six years, he transformed the program into its own department, serving as a founding chair and amassing US$18 million in funding from the Whitaker Foundation and matching funding from other sources to construct the first UCSD building with the name *bioengineering* on its edifice. The department now ranks first in the nation, according to the National Research Council.

The length of Chien's list of awards and honorary memberships rivals that of his publications. In addition to being an honorary member of the IEEE Engineering in Medicine and Biology Society (EMBS), he has the distinction of being

A Humble Man in Tireless Pursuit

By Jessica P. Johnson

one of only 11 living people elected to all three national academies: the National Academy of Engineering, Institute of Medicine, and National Academy of Sciences. He is also a member of the American Academy of Arts and Sciences, the oldest scientific academy in the United States. To top the list, President Obama awarded him the 2010 National Medal of Science, the nation's top award to scientists and engineers. By most accounts, Chien is one of the most eminent bioengineers in the country, but his life nearly took a completely different path.

In 1949, the Communist army laid siege to Peking (now Beijing), and Chien's father was forced to make a sudden decision that would ultimately determine the fate of his son's career. Chien was a premed student at Peking University, where his father was a professor of chemistry. "The Nationalist Government sent two small military airplanes to evacuate some of the professors, and our family decided to leave," Chien says, "It was not because my father was anti-Communist or pro Nationalist Government, but he just sensed it was not going to be too good in the future." Chien's family left their home on the same day they were notified. Two days later, Peking fell to the Communists. "And after that, it was not possible to leave," he says.

The family eventually made their way to Taiwan, where Chien was able to continue his medical education. "If my parents did not decide to leave, we would have had a totally different life," Chien says. "During the Cultural Revolution in China, the whole country was anti-intellectual. My father, being a professor, would have had a difficult time. Some of his colleagues who were left behind went through hard times. I probably wouldn't have been able to continue in college or do anything intellectually inclined. We lost a whole generation in China—about ten years of people not pursuing anything intellectual; not only science, but other aspects as well. In recent years, it came back so strongly, but if not for those ten years, China would have been even more progressive today."

Chien's sensitivity to the consequences of such lost time manifests in his daily life. "Time is the most important element," he says. "I try to tell my students to manage their time better than they manage their money. Because money you can earn, but time you cannot. Everybody has the same amount of time. The key is how we use it," he says. At Columbia, Chien wasted no time, publishing an average of nine papers per year. In 1967, three of these appeared in the same issue of *Science* magazine. His studies revealed how the deformability of red blood cells allows them to squeeze through tiny capillaries, and Chien was the first to identify the mechanical and biochemical factors that control this unique cellular characteristic. Chien later applied these basic biological concepts to understand diseases such as sickle-cell anemia, in which red blood cells lose their flexibility, become rigid, and disrupt normal blood flow.

By 1985, the founder of UCSD's bioengineering program, Yuan-Cheng Fung, was well aware of Chien's pioneering work and he began courting Chien as his eventual replacement to lead the program. Chien and his wife Kuang-Chung, a pediatrician working in East Harlem at the time, were reluctant to move because of the many friendships and

Chien with his family at the 2010 National Medal of Science Award ceremony on 21 October 2011.

research collaborations they had formed in New York. While considering the offer, Chien took a sabbatical to set up Taiwan's Institute of Biomedical Sciences in Academia Sinica. After returning to the United States in 1988, he agreed to give UCSD a try, but not before he convinced Fung to recruit one of his close friends and long-term collaborators, Richard Skalak, a professor of engineering mechanics at Columbia. Ultimately, it was the promise of continued collaboration with Skalak and the attractiveness of a young university that swayed Chien. "UCSD was on a very different trajectory than Columbia," he says. "It had tremendous potential for growth. There was more opportunity to do things that are innovative and creative." Chien and Skalak continued to investigate the mechanical properties of red blood cells and blood flow until Skalak's death in 1997. "We collaborated well because of our personalities—we're very easygoing and cooperative," Chien says. "but also because of our complementary strengths. I was trained in medicine and physiology and he was trained in engineering, but we both liked the other side. We both needed someone to collaborate with and learn from."

Chien's friends and colleagues use superlatives not only when speaking about his contributions to bioengineering but also about his character.

With red blood cell mechanics largely elucidated, Chien expanded his scope to diseases of the vascular system linked to blood flow, including atherosclerosis and hypertension. He first focused on endothelial cells that line the inner surface of blood vessels and respond to shear stresses caused by blood flow. He identified how mechanical forces, such as pressure and flow, impact molecular signaling inside the cells and, ultimately, gene expression, that determines whether a cell will grow, migrate, or die. He discovered that diseases such as atherosclerosis—in which vessel walls thicken in response to accumulations of white blood cells, smooth muscle cells, and fatty deposits such as cholesterol—occur most frequently at points where vessels branch. He translated this work into recommendations for treatments and the prevention of stroke and heart disease and also how blood vessels should be connected during surgery to minimize atherosclerotic plaque buildup.

"Chien didn't just contribute to the understanding of how blood vessels respond to fluid flow stresses, he defined every step in the process, and the rest of the field springs from that research," says Jeffrey Jacot, an assistant professor of bioengineering at Rice University and Texas Children's Hospital. "He not only had to understand the engineering analysis of it but also the biophysics of that interaction and the basic biology, and then he applied it to clinical biology to explain how this affects hypertension and atherosclerosis—really huge problems in the United States."

In all of his work, Chien takes a multidisciplinary approach, combining engineering and physiology principles, and never hesitates to incorporate the most advanced technologies as they evolve in molecular biology, nanotechnology, and biomechanics. His research begins at the cellular level and progresses to the tissue, organ, and systems levels. Most recently, he has devised a high-throughput approach to investigating a proper combination of proteins such as fibronectin and collagen in the extracellular matrix surrounding stem cells that cause them to either grow or differentiate into bone, brain, liver, heart, pancreas, or blood vessel cells.

In addition to the chemical properties of a stem cell's microenvironment, Chien recognized that physical factors also play a

role in their fate. For example, stem cells that are surrounded by a soft matrix are more likely to become brain cells, while those in a stiff matrix tend to become bone. And mechanical forces such as shear stress from flowing blood turn stem cells into blood vessel endothelial cells, but stem cells subjected to stretching tend to form bone. Chien sees clinical applications for these techniques in regenerative medicine. "This will allow us to select the conditions that will generate the kind of stem cells—and hence adult cells—we want, sort of a factory, so that clinicians can put them into a patient to treat disease," Chien says.

In addition to his research, Chien tirelessly pursues opportunities to improve UCSD's bioengineering department, which he created in 1994. In 2008, he founded the Institute of Engineering in Medicine to facilitate collaborations among the university's engineering, medicine, and pharmacy school faculty. "I think he's been able to bring together a group of people from disparate organizations, departments, and schools in a way that I've seldom seen before from an administrator," says Kirk Knowlton, chief of cardiology at UCSD and codirector of the institute's Cardiac Biological Science and Engineering Center.

Kuang-Chung and Shu during their wedding on 7 April 1957.

Chien's contributions to the university and in the field of bioengineering have not gone unnoticed. In 2002, he was promoted to university professor, one of only 20 such positions within the ten campuses in the University of California system. In 2009, the President of Taiwan awarded Chien the Presidential Science Prize for the Life Sciences, making him the first scientist living outside of the country to be so acknowledged. But his most hard-won award was his election to the Academia Sinica, Taiwan's highest academic institution, in 1976. His father was president at the time and had twice before convinced his fellow members to vote against his son. "He did not want me to get the advantage of him being president, so he blocked it for four years," Chien says. "I have never seen anyone with higher integrity. People finally convinced him to withdraw from voting and not influence other people. I feel very happy because when I was elected, it really meant that it was not because of my father."

In spite of a career packed with accomplishments and awards, his father's example has reminded Chien to maintain a level of humility that sometimes surprises his colleagues yet garners their unreserved admiration and respect. "Two years ago I [saw] Shu, then 78 years old, running across the campus with his heavy briefcase," says Bernhard Palsson, professor of bioengineering and one of Chien's first departmental recruits at UCSD. "I said, 'Shu, why are you running?' He said, 'I'm late for a meeting.' And I said, 'Shu, I think they will wait for you.' He believes that he's no different than anybody else. He hates to be late because he doesn't want to inconvenience others."

Chien respects everyone around him regardless of their status. As a new freshman, Thomas Chew attended a departmental event, feeling a bit lost and unsure how to break into conversation with the groups of faculty or students. "Dr. Chien and his wife approached me. They asked me where I was from and what I was studying. For him to come up to me, in his position, to talk to me as a person without knowing who I am, he stood out to me," Chew says. Chew soon joined Chien's laboratory as one of ten undergraduate researchers. "I like to chat with students," says Chien. "They are our future. They always have such new ways of looking at things and are not already locked into fixed ideas."

Student mentoring is a part of Chien's job that he takes very seriously. He fosters their individual interests even when their personal development may not immediately benefit his laboratory. He encouraged Dayu Teng, one of his six postdoctoral students, to enter a medical training fellowship even though it would take him out of the laboratory for six months. "He has taught me to have a balanced life of personal interests, family, and the interests of society and how to achieve that through various academic studies," says Teng. "He's shown me how to be a good person through doing cool science."

The advice he gives to students about finding balance in their lives and work is something that Chien himself follows diligently. Family is very important to him and he makes time for them. In Chien's 70th birthday tribute book, May Chien Busch wrote about often barging into her father's study as a girl. "I would ask him, 'Are you busy?' He would say 'no,' but of course he was." Chien and his wife have been married 54 years, and he credits her with unflagging support and encouragement throughout his life. "She almost puts me before her," he says. "And I feel the same way toward her."

Chien's friends and colleagues use superlatives not only when speaking about his contributions to bioengineering but also about his character. "With some people you get the sense that their ego drives them to do what they're doing. With Dr. Chien that's never the case," says Knowlton. "The reason he's doing this is to contribute to our knowledge of medicine and science. He's a role model and an outstanding leader—probably beyond compare."

In June 2011, Chien turned 80, and was once again presented with a book of tributes. If anyone had illusions about his plans for retirement at his 70th birthday, it is unlikely that they have them now. "I have never heard Shu talk about retiring," says Palsson. "The only thing he said to me a few years ago was, 'It's probably not right for me to be the chair of the department anymore,' which I took to mean, 'I have bigger fish to fry'." His colleagues are looking forward to what Chien will produce in the next decade.

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