



Breaking Depression's Icy Grip

You could make a good argument that Kenneth Koe '45 is one of the great liberators of the 20th century. Thanks to his work on the antidepressant Zoloft, millions of people around the globe have been freed from the shackles of despondency. But Koe, a Reed chemistry major who made vital contributions to the pharmacology of neurotransmission, would never put it that way.

Now 83 and long retired, Koe spent 40 years developing drugs at Pfizer, concentrating on compounds affecting the neurotransmitter serotonin. He will talk about his accomplishments on a molecular level—if he's pushed—but only in the manner of a careful clinician.

Sitting in his home in Ledyard, Connecticut, Koe describes the breakthrough that last year won him the Vollum Award for Distinguished Accomplishment in Science and Technology.

"Two compounds with chlorine [atoms] in particular positions had very interesting properties," he says of the family of compounds he worked on in the late 1970s with fellow chemist Willard Welch. "I tested every one of those isomers—one turned out to be a selective serotonin reuptake inhibitor [SSRI], and that compound became sertraline hydrochloride, which developed into Zoloft."

Koe published the first paper on the new compound in 1983, but it wasn't until 1991, more than a dozen years after the initial testing, that the drug hit the pharmacy shelves, becoming an overnight blockbuster.

Paul Currie, associate professor of psychology at Reed, says Zoloft is one of the most effective of the SSRIs, which increase serotonin availability in the brain's synapses, thereby alleviating depressive symptoms. Zoloft is particularly effective in the treatment of obsessive-compulsive disorder, bulimia, and other pathologies.

"This is a compound that has gone far, and will continue to go far in terms of its clinical applications," Currie says.

Since its introduction, more than 115 million people have been treated with Zoloft. In 2005, the last year Pfizer held a patent on the drug before it could be manufactured generically, sales hit \$3.3 billion.

All of which seems a long way from the grimy wharves of Astoria, Oregon, where Koe was born in 1925. During those years, the coastal town had a booming population of Chinese laborers, including his immigrant father, who filled shifts at the salmon canneries. After an unsettled stretch moving around the Pacific Northwest, the family settled in Portland's Chinatown and was eventually able to buy into the C&H laundry on NW Sixth Avenue; Koe, his parents and sister lived in the back of the shop.

After graduating from Lincoln High School, Koe received a scholarship to Reed—tuition was then a hefty \$250 a semester—and he joined the ranks of wartime commuter students, or day-dodgers. On weekends, he washed dishes and waited tables at Hung Far Low, then a bustling fixture in Chinatown, decades before its migration to the neon-lit strip of SE 82nd Avenue.



Kenneth Koe '45 receives Vollum award

"I didn't absorb much of the campus life," he says. "I never got involved with the social functions—I never really had that chance."

Koe wrote his thesis, *An Apparatus for the Porous Disc Method of Determining Osmotic Pressure*, with adviser Fred Ayres. After Reed, too skinny for military service, Koe headed for graduate school, first at the University of Washington and then Cal Tech, where he received his doctorate in chemistry.

In 1955, he headed east with his wife, Jo Ann, and joined Pfizer's laboratory in Brooklyn. Koe arrived on the scene during an era when companies like Pfizer encouraged research and development work in a setting more like a university than a high-pressure corporate environment.

"It was pretty free and open," Koe says of his early days at Pfizer. "You had to look for certain things, but how to do that was pretty much unregimented. We had lots of chances to do things on our own. It was a different atmosphere in those days, it was a smaller company, and everyone knew that research was the only way to get to those big products."

Koe thrived in the collaborative atmosphere—his name is on more than 100 scientific papers and articles. While he downplays his own contributions, his colleagues are quick to give him credit. "When I was very young and starting my career, he was very engaging and open and friendly to a young person he didn't even have to acknowledge," says Irwin Lucki, a professor in the departments of psychiatry and pharmacology at the University of Pennsylvania. "The willingness to engage in discussions and talk about science was kind of what those pioneers in that type of research were like."

Koe still attends professional conferences and maintains an interest in the latest developments in a field he pioneered. He also enjoys singing with the choir in the United Methodist Church of Gales Ferry and the chorus of the Eastern Connecticut Symphony Chorus and is active on Ledyard's planning commission.

Every once in a while, he stops to contemplate a memento outside his study, given to him by his colleague Welch. It's a blue and white license plate that reflects anything but vanity, and it reads: "Zoloft."

—Will Swarts '92



Listen to **Kenneth Koe's** acceptance speech for the Vollum Award at Convocation '08.