CHEMIST HONORED FOR INNOVATIONS IN RECEPTOR IMAGING

IF THERE IS ONE SENTENCE TO describe the driving motivation behind the work of John Katzenellenbogen, PhD, recipient of the 1995 Paul C. Aebersold Award, it would be: He likes to take things apart to see how they work. Perhaps he should have been a mechanical engineer, but—luckily for nuclear medicine—Katzenellenbogen decided to figure out the nature of things by becoming an organic chemist. His insatiable curiosity has carried him through 25 years of work in receptor-based imaging and earned him the Aebersold Award, which is given for outstanding achievement in basic science applied to nuclear medicine.

His colleagues describe his most notable achievement as his defining the concept of a binding selectivity index in 1980, which rates a potential receptor-imaging compound on the basis of its receptor affinity and nonspecific binding activity. Katzenellenbogen was the first to note that these two factors are both crucial determinants in evaluating whether a radionuclide would make a good receptor imaging agent. "His development of the binding selectivity index was a key that showed that receptor imaging was possible," said Michael J. Welch, PhD, professor of radiology and director of the division of radiation sciences at Mallinckrodt Institute of Radiology in St. Louis who has collaborated with Katzenellenbogen on receptor research for the past 20 years. "He's a world class organic chemist."

What does Katzenellenbogen view as his greatest accomplishment? "Getting the first really good image of a receptor-positive breast tumor using 16-alpha-fluoro-estradiol (FES), the PET radiopharmaceutical Mike Welch and I developed," he said. "It was the culmination of the whole rationale for the development of receptor-based imaging agents and won the award for image of the year at the 1984 SNM Annual Meeting."

Inspired by his wife, Benita, a cell biologist who was doing research on steroids for her postdoctoral work, Katzenellenbogen became intrigued by steroid receptors and their relationship to cancer during the 1970s. He and Welch spent years designing the FES imaging agent that effectively measures the uptake of estrogen receptors in breast cancer patients. "It can potentially be used to tell whether the anti-estrogen therapy, tamoxifen, will work in a particular patient," said Welch. The PET image is more indicative than a pathology report, which only measures the percentage of estrogen receptors—not whether they are indeed functioning in the uptake of the hormone.

No Shortage of Grants

Earning his Bachelor's, Master's and Doctorate degrees from Harvard, Katzenellenbogen began an assistant professorship at the University of Illinois, Champaign-Urbana in 1969. "I was given a lot of freedom in my research and was in a department that had an early appreciation for the fact that chemistry was going to extend itself to biomedical applications." As a young researcher, he was awarded thousands of dollars in grants from the American Cancer Society and the National Institutes of Health. "On my grant applications, I looked like a worthwhile outsider," said Katzenellenbogen. "I was someone who knew more chemistry and more receptor biochemistry than most of the others in the area who had mainly come from medical imaging backgrounds. In fact, many of my chemistry colleagues had no idea what nuclear medicine was in the early 1970s." He became an associate professor in 1975 and a full professor in 1979 and remains at the University of Illinois as the Roger Adams Professor of Chemistry.

With more than $1 million in grants in his current research budget, Katzenellenbogen continues at a feverish pace his work on estrogen receptors and breast tumor imaging agents (*J Nucl Med* 1992;33:558). He is also attempting to develop a compound that hides a technetium atom within a steroid-shaped complex to give a compound that mimics a steroid and binds with high affinity to steroid receptors.

Although funding for his research has never been scarce, grants from radiopharmaceutical companies continue to elude him. "Industry reps have often found what I've done to be interesting but were uncertain if they could make a product from it," explained Katzenellenbogen. "As an academician who works on long-term projects for years, I would find it difficult to refrain from publishing or discussing my work before it is completed, which a company would require of me to maintain secrecy." As a scientist who has spent half his life unraveling how steroid hormones interact with their receptors and as a man who would take apart a friend's broken watch to search for the glitch, it's not surprising that Katzenellenbogen wouldn't want to wait to share his new-found knowledge with others.

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