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## 1998

### Randy Schekman

Randy Schekman was born in St. Paul, Minnesota, where he and his siblings grew up in a Jewish neighborhood there before moving when Randy was ten to Los Angeles. Their father, who had grown up in the twin cities, was a mechanical engineer and decided in his mid 30's that "there must be something better out there." After interviewing for a job in Southern California in the middle of winter, he returned to his family and declared, "we're out of here." The senior Schekman entered the burgeoning software industry, becoming an early designer of the first on-line program for instant access to stock quotes. Schekman attributes his interest in math and science to his father.

Schekman recalls the moment in seventh grade when he knew he would be a scientist. "I went to a science fair and a whole world was opened up to me that I had not seen before. That is the first moment that I remember falling in love with science," Schekman recalls. His interest in biology and medical science was sadly solidified when his teenaged sister died of Leukemia.

Through high school, science and science fairs were Schekman's passion. He saved money to buy microscopes, using them to examine pond scum while other kids were busy with typical teenage activities. Although the trophies he won built his confidence and he relished the experience, he realized in retrospect that even so, he didn't learn science rigorously, knowing nothing about designing proper experimental controls.

Schekman chose to go to UCLA for college in large part because it was what his family could afford. But as fortune would have it, UCLA was a "great" experience. As a freshman he was accepted into an honors chemistry course taught by Nobel Laureate Willard Libby, inventor of Carbon 14 dating. At that time, Schekman had thought he would go to medical school because he wasn't aware that there were other outlets for his interest in biology. But after working the lab of Dan Ray, he realized that graduate school was the better fit and mustered the courage to tell his dismayed parents that their son "was not going to be a 'real' doctor." In his sophomore year, Schekman faced the typical undergraduate frustration as a student of science surrounded by pre-medical classmates. Patience never being one of his strong traits, Schekman escaped to spend his junior year at the University of Edinburgh, where he arranged to work in a lab. When Schekman arrived, he was surprised that they thought he was a visiting scholar and gave him his own lab. (He quickly disabused them of the misunderstanding.) Schekman's transition to graduate school at Stanford was circuitous: Reg Kelly, the brother of his lab partner in Edinburgh, was working with Arthur Kornberg on DNA replication. Schekman returned to the States, determined to join Kornberg.

He succeeded, entering the Bio-chemistry Department at Stanford to work in Kornberg's lab in 1970. Even today, Schekman marvels at the opportunity he had to join the small, distinguished department to be guided by the leader of his field. Schekman describes Kornberg as "demanding and with the highest standards that you can imagine," whose approach was to "define a problem worthy of study, pick the simplest system in which one can study that problem, and unremittingly attack it." This experience committed Schekman to the reductionist approach. While the immediate payoff may not be apparent, he is convinced that, "in the end the payoff is much greater." He is surprised that more scientists don't subscribe to the approach of taking things apart, purifying the gene products implicated and concentrating them in pure form. Schekman reflects, "when someone tells me that all the interesting problems have been studied, I think 'nonsense'. There are all sorts of problems that are just waiting to be attacked."

While at Stanford, Schekman married his wife Nancy, whom he met through the intervention of his lab partner Bill Wickner. The newlyweds moved to San Diego where Nancy finished her bachelor's at the University of San Diego while Randy took a postdoc with Jonathan Singer. At the urging of Wickner, Schekman became interested in the area of membranes, realizing that one could study a membrane as a macro-molecule and that its subcomponents are subject to study themselves. Wickner calls Schekman, "one of the most creative scientists of our era," particularly remarkable when also recognizing the "time and energy he gives to his colleagues, his department, grants and fellowships, and national organizations."

Ultimately, Schekman came to focus on yeast as the model in which to study growth and division of the cell. Admitting that he "may have been young and naive," Schekman thought the subject of yeast membrane assembly was ripe for investigation and perfect for him. He took the yeast genetics course at Cold Spring Harbor at the end of his postdoc, which enabled him to meet leaders in the field, such as Lee Hartwell.

Schekman was appointed Assistant Professor at Berkeley in 1976, based, he believes, more on his graduate work than on his postdoc. He naively approached his work on yeasts assuming that the NIH would happily support him on the basis of his past productivity. So he was taken by surprise when his first grant application to the NIH was "roundly trounced," which was less common at that time. He was able to get some support from the NSF, and with a terrific graduate student, Peter Novick, and technician

Charles Field, who knew more yeast genetics than Schekman, they isolated some mutants. Out of the first 100 mutants that they found, one, called Sec 1, blocked secretion. Schekman recalls, "you could see in the electron microscope cells that looked like they had measles because they were filled with vesicles." Schekman's work for many years to come would be to clone these yeast genes, but most of the sequences were not instructive. As a result of his early work, students were attracted to Schekman's lab to study yeast genetics, so Schekman encouraged one of them, David Baker, to establish a cell free system, which he did at the same time as Hanella Rouholla (a student of Schekman's former student Susan Ferrow-Novick) at Yale (through a series of coincidences Baker and Rouholla were married years later.)

A recent scientific interest of Schekman's came from his work on COPII, a novel coat protein complex that is responsible for forward membrane traffic. This year his lab reported that the coat proteins will bud vesicles from synthetic membranes. COPII is responsible for deforming the membrane to create the curvature of a transport vesicle, but it also serves as a scaffold to attract and cluster proteins that have to leave the ER to go to the Golgi. Other proteins seem to need adapters, which may be fairly specific in the molecules for which they are responsible. This work suggests disease states in which only a certain kind of secreted protein fails to be transported. In fact, Randall Kaufman in Michigan has shown that a rare form of hemophilia in which patients are missing two different blood clotting factors are also missing a protein that is an important linker. Schekman thinks that this idea could explain the effects of mutations that cause forms of early onset Alzheimer's disease.

Schekman became involved with the ASCB early in his career when it became clear to him that it was an avenue for his interests that were not satisfied by other societies. Those who were calling themselves 'cell biologists' were doing interesting things that he also wanted to do. Over time, he became an editor of both the Journal of Cell Biology and Molecular Biology of the Cell. Schekman continues to be impressed that the Society "brings young people in at the very earliest stages of their careers." He recognized early that "this is a Society that is doing important things not just for cell biology but for science." Schekman served on Council from 1991-1994, and was elected President for 1999. He has also become deeply committed to Molecular Biology of the Cell, and has watched it grow in stature.

Schekman has gained the respect of his peers by combining exacting, demanding standards with loyalty and self-sacrifice, exemplified not just by his Society leadership but also his leadership at UC Berkeley where he serves as Co-chair of the Department of Molecular and Cell Biology in a sort of job-sharing arrangement with Jim Allison. Schekman looks forward to consolidating the considerable strengths of the ASCB during his presidency, and also hopes to establish a young investigator award to recognize an outstanding researcher making the transition between junior and senior positions. Schekman admits that despite the time burden, he is eager to take on the leadership of the Society. He hopes to establish the tone of his term as inclusive, making people comfortable participating, and ensuring that people have a sense of belonging. He is already working with David Drubin, Chair of the Program Committee for the 1999 Annual Meeting. Schekman recognizes both the scientific and financial importance of the Annual Meeting to the Society, and plans to focus on attracting the attendance of people who have not yet identified themselves with the ASCB, or even as cell biologists.

Despite his commitment to his own science as well as the community of scientists, Schekman's top priority is his family. He explains that one of the ways his family connects is through music, although he himself is not musically inclined. "Music has become our spiritual life. My wife is very musical and that is where our kids get their talent." Their son, Joel, 20, is studying to be a classical musician at Indiana University, and their daughter Lauren, 16, is in an international touring choir. For better or worse, neither child is interested in science. Schekman feels he has learned an enormous amount about classical music from both his children. The Schekmans have a second house on the ocean in Sea Ranch, north of San Francisco, where they "recuperate" from the pressures of their daily lives.