

## **Randy W. Schekman, PhD**



### **Current Position**

**Professor of molecular and cell biology at the University of California, Berkeley**

**Investigator at the Howard Hughes Medical Institute**

**Editor-in-Chief, *eLIFE* Journal**

### **Education**

BA, molecular biology, University of California, Los Angeles

PhD, biochemistry, Stanford University

### **Awards**

Nobel Prize in Physiology or Medicine 2013 (shared with James E. Rothman and Thomas C. Südhof )

Albert Lasker Award for Basic Medical Research

Eli Lilly Research Award in Microbiology and Immunology

Lewis S. Rosenstiel Award in Basic Biomedical Science, Brandeis University

Gairdner Foundation International Award

Louisa Gross Horwitz Prize, Columbia University

2008 Dickson Prize in Medicine, University of Pittsburgh

E.B. Wilson Medal, American Society for Cell Biology

### **Memberships**

US National Academy of Sciences

American Academy of Arts and Sciences

American Society of Cell Biology

American Association for the Advancement of Science

American Philosophical Society

## **Biography**

Traffic inside a cell is as complicated as rush hour near any metropolitan area. But drivers know how to follow the signs and roadways to reach their destinations. How do different cellular proteins "read" molecular signposts to find their way inside or outside of a cell?

For the past three decades, Randy Schekman has been characterizing the traffic drivers that shuttle cellular proteins as they move in membrane-bound sacs, or vesicles, within a cell. His detailed elucidation of cellular travel patterns has provided fundamental knowledge about cells and has enhanced understanding of diseases that arise when bottlenecks impede some of the protein flow. His work earned him one of the most prestigious prizes in science, the 2002 Albert Lasker Award for Basic Medical Research, which he shared with James Rothman. In 2013, Randy Schekman, together with Thomas C. Südhof and James E. Rothman, were awarded the Nobel Prize in Physiology or Medicine for their discoveries of machinery regulating vesicle traffic, a major transport system in our cells.

Schekman's path to award-winning researcher began with a youthful enthusiasm for science and math, which he attributes to his father, an engineer who helped develop the first online program for real-time stock quotes. High school science fairs—and winning them—further whetted his appetite for competitive science. Biology's power hit him more personally, though, when his teenage sister died of leukemia.

He considered pursuing medical school as an undergraduate at the University of California, Los Angeles. But after spending his junior year in a laboratory at the University of Edinburgh, his path to graduate school became set. He obtained a Ph.D. in biochemistry at Stanford in the laboratory of Arthur Kornberg, who won the Nobel Prize in 1959 for identifying a key enzyme in DNA synthesis. Schekman first became interested in how proteins move within cells during a postdoctoral fellowship between 1974 and 1976 with John Signer, who was studying the outer membranes of mammalian cells. At the time, though, scientists couldn't easily study the steps of vesicle movement in mammalian cells growing in culture.

So Schekman, who moved in 1976 to the University of California, Berkeley, as an independent investigator, decided to use yeast, a one-celled microorganism, to determine how vesicles containing proteins move inside and outside the cell. Scientists can easily genetically manipulate yeast, which have membrane-bound organelles similar to those of higher organisms. Organelles, such as mitochondria or the Golgi apparatus, are structures within cells that perform specified functions.

When Schekman began his yeast studies, scientists only had a general sense of the cellular traffic patterns that proteins follow: Ribosomes manufacture proteins, which enter the endoplasmic reticulum, a membranous network inside the cell. Vesicles carrying proteins pinch off from the endoplasmic reticulum and travel to the Golgi apparatus, which further processes the proteins for internal or external use.

What Schekman, using genetic methods, and Rothman, with biochemical approaches, working

independently did, was dissect in meticulous detail the molecular underpinnings behind vesicle formation, selection of cargo, and movement to the correct organelle or path outside the cell.

Ultimately, he identified 50 genes involved in vesicle movement and determined the order and role each of the different genes' protein products play, step by step, as they shuttle cargo-laden vesicles in the cell. One of the most important genes he found, Schekman says, is the SEC61 gene, which encodes a channel through which secretory proteins under construction pass into the endoplasmic reticulum lumen. When this gene is mutant, proteins fail to enter the secretion assembly line. Another significant set of genes he discovered encode different coat proteins that allow vesicle movement from the endoplasmic reticulum and from the Golgi.

Although Schekman's research was done in yeast, follow-up studies confirmed that higher organisms, such as humans, share the majority of the genes in the yeast secretory pathway. Such knowledge provided a foundation for understanding normal human cell biology and disease states. In fact, as the study of the genetics of mammalian cells has become easier, Schekman has been characterizing human diseases that arise from secretory pathway problems. He has identified the structural basis of a rare craniofacial disease that disrupts the construction of a coat protein complex essential for transport vesicle formation. He also is studying whether the accumulation in the brains of Alzheimer's disease patients of the protein amyloid is due to a secretion pathway roadblock.

While many steps in vesicular trafficking are now known, some have evaded discovery. Schekman continues to look for receptors in the endoplasmic reticulum membrane that find appropriate protein cargo for transport to the Golgi. He is also trying to identify molecules that help protein-laden vesicles move from the Golgi out of the cell. Schekman, with as much passion for science today as he has had throughout his career, is confident he can persuade Nature to reveal undiscovered routes in her traffic patterns.