Dr. Randy Schekman

2013 Nobel Prize in Physiology or Medicine

Professor of Molecular and Cell Biology
University of California, Berkeley

ISTeC Distinguished Lecture

In conjunction with the
Electrical and Computer Engineering Department,
Computer Science Department, and CSU Libraries

"Publishing Your Most Important Work"

Monday, March 24, 2014
Lecture: 4:00 – 5:00 pm
Location: Behavioral Sciences Building Rm. 131

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Electrical and Computer Engineering Department, Computer Science Department, and Biology Department Special Seminar *Sponsored by ISTeC*

"Genes and Proteins that Control Secretion and Autophagy"

Monday, March 24, 2014
Lecture: 11:00 am – 12:00 noon
Location: LSC Theater

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Abstracts:

Publishing Your Most Important Work

The assessment of scholarly achievement depends critically on the proper evaluation and publication of research work in scholarly journals. Investigators face a dizzying array of journal styles that include commercial, not-for-profit and academic society journals that are supported by a mix of subscription and page charges. The Open Access (OA) movement, launched in Britain but greatly expanded by the Public Library of Science (PLoS), seeks to eliminate the firewall that separates published work from public access. OA journals are funded by a mix of page charges and philanthropic or foundation support. Most OA journals embrace a more liberal licensing agreement on the use and reuse of published work, favoring the creative commons license rather than a copyright held by the publisher. Some publishers, particularly commercial firms, view the OA movement as a threat to the viability of their business plan. Major commercial publishers, particularly Elsevier, have fought against government mandates for OA publication of publicly funded research.

The most selective and successful journals, Science, Nature and Cell (a life science journal owned by Elsevier), maintain a firm hold on the high end of the scientific literature by appealing to investigators to submit only their most important work. Typically, these journals publish only a small fraction of the papers they receive and for the most part they rely on professional editors rather than active scholars to make key editorial decisions. These publishers, particularly Nature and Cell, reinforce their high standing by relying on a metric, the impact factor (IF) that computes the average number of citations of papers published in the journal during the preceding two-year period. As a consequence, many investigators, who quite naturally seek career advancement, strive to publish in these journals even at the expense of repeated cycles of review, wasteful additional experimental work and ultimately lost time. I will argue that it is time for scholars to reassume authority for the publication of their research work and to eschew the use of IF in the evaluation of scholarly achievement and favor OA publications over what I have called the “luxury” journals.

Genes and Proteins that Control Secretion and Autophagy

The broad outlines of the secretory pathway were established by pioneering EM and cell fractionation experiments conducted by George Palade in the 1960s. Beginning in the mid-1970s and early 80s, my laboratory isolated a series of conditionally lethal, temperature sensitive mutations that block secretion at one of several sequential stages along the pathway established by Palade. Concurrently, James Rothman’s laboratory established a cell-free reaction that reproduced vesicular traffic within the Golgi apparatus, and several of the proteins he isolated with this functional assay matched the Sec proteins we identified. Using a cell-free vesicle budding reaction, my laboratory isolated a complex of Sec proteins that comprise a coat, COPII, responsible for cargo vesicle traffic from the endoplasmic reticulum.

Autophagosomes mature by the addition of membrane material from various intracellular sources and the attachment of peripheral proteins that remain bound through a covalent lipidation reaction. However, the origin and the mechanism of generation of the pre-autophagic membrane are poorly understood. We addressed this question with the development and analysis of a cell-free reaction that reproduces the lipidation of a major peripheral autophagosomal protein, LC3. A crude membrane fraction isolated from cells deficient in lipidation was mixed with cytosol harvested from normal cells that were untreated or subjected to a stress regimen known to induce autophagy. On addition of ATP, incubation of the mixture resulted in the formation of lipidated LC3. The reaction requires both membranes and cytosol and is stimulated 2-5 fold when the cytosol was taken from stress-induced cells. Autophagosome maturation requires a class III PI-3 kinase (VPS34 homolog); LC3 lipidation in our cell-free reaction is inhibited by inhibitors of this kinase, and by the addition of a peptide containing a PI3P-bnding sequence, the FYVE domain. Using cell fractionation techniques we have identified the ER-Golgi intermediate (ERGIC) compartment as the major site for lipidation of LC-3. This cell-free reaction may now be used to understand the molecular mechanism of autophagosome maturation.

Speaker Biography:

Dr. Randy Schekman is currently an investigator of the Howard Hughes Medical Institute and a Professor of Cell and Developmental Biology in the Department of Molecular and Cell Biology at the University of California, Berkeley. He was awarded the Nobel Prize for

Physiology or Medicine in 2013, together with Thomas C. Sudhof and James Rothman, “for their discoveries of machinery regulating vesicle traffic, a major transport system in our cells.” Other notable awards include the Albert Lasker Award for Basic Medical Research and the Louisa Gross Horwitz Prize for Biology or Biochemistry, both of which he shared with James Rothman in 2002. In 2010 he was awarded the Massry Prize, and in 2013 was elected a Foreign Member of the Royal Society of London. Dr. Schekman received his Ph.D. in biochemistry from Stanford University in 1975. He is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, the American Society of Cell Biology, and the American Philosophical Society. He is also a Fellow of the American Association for the Advancement of Science. Dr. Schekman is the editor-in-chief of eLife, a peer-reviewed open access scientific journal in the biomedical and life sciences.

To arrange a meeting with the speaker, please contact Steven, Patrick.Burns@ColoState.EDU 970-491-1833