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## 2001

### Jennifer Lippincott-Schwartz

Jennifer Lippincott-Schwartz grew up on a horse farm in Northern Virginia. Her father was a physical chemistry professor at the University of Maryland, while her mother stayed at home and kept the family of seven running smoothly. Through her father, Lippincott-Schwartz was exposed to science early; the Periodic Table hung in the kitchen, and the five sisters competed in memorizing the elements.

As a child, Lippincott-Schwartz loved the outdoors and spent many hours riding horses, exploring the woods and frequenting her tree house: in response to her letter asking a local construction company to donate discarded wood, they built the structure instead. Lippincott-Schwartz followed her passion for the outdoors through high school, when she served as an instructor at an outdoor leadership school in the summers.

Raised as a Quaker, Lippincott-Schwartz chose Swarthmore for college. The school had an important influence on Lippincott-Schwartz's interest in biology as well as the history of science and philosophy.

While at Swarthmore, Lippincott-Schwartz met and married Jonathan Schwartz. Upon graduation, recognizing their opportunity for adventure at that stage of life, they set out for a rural village in Kenya to teach high school. There, Lippincott-Schwartz taught biology, physics and health sciences in an all-girl school, with no electricity in classrooms, dirt floors and few books. The students surprised her almost every day. They would have trouble drawing simple three-dimensional objects on paper yet were able to learn complicated knots with rope in a single demonstration. When Lippincott-Schwartz took a group of students on an overnight hiking expedition to some local caves, the students balked at crossing a river (they could not swim and were frightened of the water), but when a pack of 30 baboons aggressively surrounded them, the students bravely stood their ground. This experience and her extended trip back to the States through Pakistan, Afghanistan and remote areas of central Asia provided Lippincott-Schwartz with a broader outlook on the world and a confidence and commitment to contribute to its development and understanding.

After returning home, Lippincott-Schwartz taught science in an all-boys high school run by Benedictine Monks. While her husband attended law school, Lippincott-Schwartz earned her master's degree in biology at Stanford University. When he took a position at the U.S. Department of State in Washington, DC, Lippincott-Schwartz pursued her doctorate at Johns Hopkins. She studied under Doug Fambrough at the Carnegie Institution for Embryology, where the "laboratories were small, the equipment was shared, and PIs performed experiments alongside postdocs." Fambrough tells of presenting Lippincott-Schwartz with the famous U.S. Army recruiting poster, "Be All That You Can Be." Fambrough gave her the "award" as "representing how you approach science, and life."

The high standards set by scientists at the Carnegie and their broad integration of techniques provided a model that Lippincott-Schwartz later aspired to follow in her own work in intracellular trafficking of a lysosomal membrane protein, incorporating biochemistry, cloning, fluorescence imaging, electron microscopy and mathematical modeling.

At the National Institutes of Health, Lippincott-Schwartz was a postdoc with Rick Klausner when he was just setting up a group to study the membrane trafficking pathway of the T-cell antigen receptor, which he had found was targeted to lysosomes when missing its zeta chain. The group found that when subunits of the receptor were expressed individually, they were retained in the ER and rapidly degraded. The finding was significant because it indicated that the ER has the capacity to dispose of unassembled protein subunits within cells, which helped establish the picture of the ER as a quality-control compartment in the assembly, retention and degradation of proteins.

While still a postdoc in the Klausner group, Lippincott-Schwartz also investigated how the drug brefeldin A (BFA) affects membrane traffic and organelle identity and helped to demonstrate, together with other groups focused in this area, that BFA inhibits protein export from the ER and causes the redistribution of functional Golgi enzymes into the ER. These findings created the possibility of using BFA to selectively block intracellular traffic patterns to manipulate the transport of molecules through the membrane systems of the cell. Lippincott-Schwartz's work further showed that the disassembly of the Golgi complex during BFA treatment occurred through a unique, retrograde membrane transport pathway: Golgi-derived membrane was carried on long membrane tubules that migrated along microtubules to the cell periphery.

Transport of membrane components back to the ER along the retrograde pathway is normally selective, but in the presence of BFA it becomes nonselective. The finding that the Golgi complex completely disassembles during BFA treatment was the first example of a drug causing an organelle to disappear rapidly within cells. This finding indicated that organelles such as the Golgi complex are not static, unchanging structures.

Head of the NICHD's Section on Organelle Biology since 1993, Lippincott-Schwartz has devoted herself to the exploration of green fluorescent protein (GFP), found to be useful as a reporter molecule within living cells. She recognized its potential for visualizing complex membrane dynamics within cells, which the then current static morphological approaches could not adequately address. Together with NIH colleagues Mark Terasaki and Carolyn Smith, she began visualizing intracellular membrane transport pathways that previously had only been subject of speculation.

The enormous influx of data has led Lippincott-Schwartz to new collaborations to obtain diffusion coefficients, rate constants and residency times for proteins in different subcellular compartments. Applying these biophysical concepts to their imaging data has given support to the view that subcellular organelles like the Golgi complex are steady-state systems of membrane input and outflow rather than stable, unchanging structures. Lippincott-Schwartz notes with characteristic enthusiasm that "because scientists now can directly visualize dynamic processes in living cells, areas of cell biology that were once studied in isolation of each other, including the cytoskeleton and membrane transport, have become intimately connected." This has stimulated tremendously the activities of researchers in these areas, resulting in major new ideas about cellular organization and function.

Lippincott-Schwartz has two daughters, Leana, 12, and Samantha, 16, who fill up most of her limited free time, along with Jonathan, who, as Deputy Legal Advisor at the U.S. Department of State, participates in negotiations of global issues as central and diverse as Mideast peace and AIDS in Africa.