# People & Ideas

## Suzanne Pfeffer: Sorting through membrane trafficking

Pfeffer is writing the rulebook for membrane trafficking and protein sorting.

Suzanne Pfeffer always wanted to know what makes the human body tick. In many respects, we're still working on deciphering the first page of the body's operating manual—which Pfeffer says is fine, since it means there's plenty of room for new discoveries.

Pfeffer had her first publication as an undergraduate at UC Berkeley (1), which got her hooked on the spirit of scientific inquiry. Following stints studying synaptic vesicles as a graduate student with Regis Kelly at UCSF (2), and Golgi transport as a postdoc with Jim Rothman at Stanford (3), she developed her own research program studying the proteins and processes that govern intracellular transport of proteins and membranes (4). Her work documenting the mechanisms of mannose-6-phosphate receptor transport from endosomes to Golgi has established some of the fundamental principles of membrane trafficking (5, 6).

Pfeffer's contributions to cell biology don't end in the laboratory, having served the scientific community as president of the American Society for Cell Biology. Pfeffer was also the first female faculty member appointed in the biochemistry department at Stanford. She talked with us about the story of her career and what she expects to find on the next page, as new technologies open up fresh chapters.

### PAGE ONE

***When did you first become interested in science?***

Even as a child, I was always interested in human physiology. I went to UC Berkeley for college, and as a freshman I learned what biochemistry was: trying to understand human physiology in terms of what molecules are involved. I knew immediately that I wanted to do that as a career, so I got involved in some research there. I was very lucky to have a dedicated mentor, Michael Chamberlin, for my research at Berkeley. He worked on bacterial transcription, and he really took the time to show me how to write a protocol, how to design an experiment. Basically, I became a graduate student while I was an undergrad. I was in the laboratory every day doing experiments after class, and I just loved it.

I think every scientist has this experience, when you come out of the darkroom and the film has the answer that you wouldn't have known five minutes earlier—an "aha!" moment. Once you have that experience, there's no turning back. I had my "aha!" moment, and was able to publish a paper on it. I wrote the paper and drew the figures. It was very exciting—the culmination of a lot of hard work—and I was hooked.

> "There are so many unanswered questions in the field of membrane traffic... we are still writing the rules for how things work today."

***With a publication as an undergrad, you had a ticket to any graduate school you wanted.***

This was the time when DNA sequencing had just been established, and the first genes were being cloned. The insulin gene had just been cloned at UCSF, where they also had this brand new graduate program in cell biology, which seemed perfect to me—if a little bit risky, since it was so new. It seemed like the place to study gene regulation, and I thought it would be interesting to go from prokaryotic to eukaryotic gene regulation. When I got there, Bruce Alberts (one of my graduate advisors), encouraged me to try something completely different. I will always be grateful to him for that because it led me to work with Regis Kelly, who was a molecular neurobiologist. He was using biochemistry to study synaptic vesicles and membrane trafficking. I knew absolutely nothing about membranes.

Suzanne Pfeffer

### THE PLOT THICKENS

***What attracted you to the field of membrane trafficking?***

I think that even to this day, people don't understand that there are so many unanswered questions in the field of membrane traffic. People read the textbooks and think that the problems are all solved, and yet we are still writing the rules for how things work today. It's at such a basic level, sort of like discovering the process of protein translation. We are working out what molecules do at the most fundamental level. There is so much room for discovery, but there are very few laboratories that study membrane traffic, so the opportunity to discover new mechanisms is just tremendous in this area.

***So you decided to pursue these problems in your postdoc at Stanford with Jim Rothman.***

Actually, things almost turned out differently. I very much wanted to work in Jim's laboratory, so I applied there, but he wrote me back saying that unfortunately his laboratory was full and he couldn't take me. I was very disappointed

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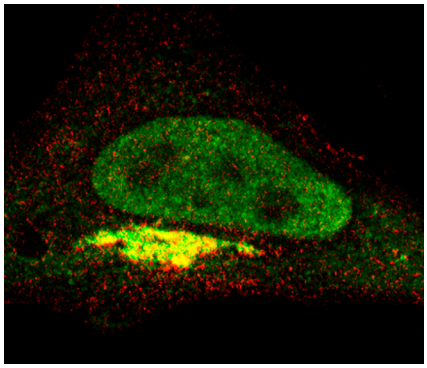

**Tracking transport: a vesicle tethering protein (green) colocalizing with a marker for Golgi (red).**

and applied to another laboratory in the Bay Area, and I got a fellowship to go there. Some months later I needed some frozen brain for my work. In those days we went to slaughterhouses to get cow brains, but it was Christmastime and the slaughterhouses were closed for the holidays. So I called up Jim to ask if he had any in the freezer, and he said yes, I could come down and borrow some cow brain. I went there and we got to talking, and he said, "By the way, now I have space, and if you'd like to come to my lab, it would be fine." I was thrilled, and I applied for another fellowship to work in his laboratory. So the story ended happily.

***Why did you choose to stay at Stanford to start your laboratory?***

It's a wonderful place to do research, and I just thought it was an incredible opportunity. But it presented a challenge: that I was going to be in the same department as my postdoctoral advisor. I felt that as a new faculty member, it would be important to go my own way and lay my own path, so I decided to pick a part of the cell that he wasn't studying, and initiate a different program related to that. That's what led me to study the mannose-6-phosphate receptor and how proteins are transported to the lysosome. I took advantage of what I'd learned as a postdoc to set up a novel in vitro transport assay, and began to study all the proteins that were required for that transport step.

## THE NEXT PAGE

***In what direction are you headed now?***

We make great use of siRNA technology, which allows us to do genetics in human cells. The field has gained some very valuable insights from studying these processes in yeast, but we know that human cell pathways are more complicated, so we're really grateful for this new technology.

We're taking our work in high-throughput directions to get a fuller picture of the membrane recycling pathways that we study. We've discovered a lot of new molecules that participate in endosome-to-Golgi transport, and we're now working on understanding how they work with each other. It's really four-dimensional biochemistry because we have to track how things interact between multiple compartments, in space and time. We're very excited about that.

> "The tools we have now make discoveries possible on a scale that's really unprecedented."

***You've had an accomplished career already. What are your professional goals now?***

I'm looking for another project that will enable me to continue contributing to the scientific community in a positive way. At the moment, I'm serving on the Cell Structure and Function Study Section for the NIH. I also help the Burroughs Wellcome Fund on their Scientific Interfaces career panel, which awards fellowships to senior postdocs transitioning to their early faculty years.

I wish it was easier for young scientists right now. I think science is an absolutely wonderful career, and I feel very lucky to be a scientist, but I know that a lot of young people are becoming discouraged by the funding situation and job freezes resulting from the bad economy. Whether they're considering a job in academia, industry, or some affiliated activity, I hope that they won't be too discouraged, because the tools we have now make discoveries possible on a scale that's really unprecedented. It's such an important time, and I hope that young people won't be put off by the temporary challenges we face this year. We've had rough times in past decades, but things eventually turned around, and I feel confident that they will again.

***What do you do when you're not in study sections or in the laboratory?***

In the last few years since I stopped being department chair, I started playing tennis seriously, which keeps me healthy. I also enjoy scuba diving. Every year in December, I go on a scuba diving expedition—I'm just back from two weeks in Indonesia, where I scuba dived off of Sulawesi. I do underwater video photography and I was able to film one of my favorite creatures this year: this beautiful flamboyant cuttlefish. I have a special affinity for this creature because its Latin name is *Metasepia pfefferi*. JCB

1. Pfeffer, S.R., et al. 1977. *J. Biol. Chem.* 252:5403–5407.
2. Pfeffer, S.R., and R.B. Kelly. 1985. *Cell.* 40:949–957.
3. Dunphy, W.G., et al. 1986. *Proc. Natl. Acad. Sci. USA.* 83:1622–1626.
4. Goda, Y., and S.R. Pfeffer. 1988. *Cell.* 55:309–320.
5. Barbero, P., et al. 2002. *J. Cell Biol.* 156:511–518.
6. Burguete, A.S., et al. 2008. *Cell.* 132:286–298.

**Catchy name: *Metasepia pfefferi* (the flamboyant cuttlefish) filmed by Pfeffer on a diving trip in Indonesia. (*view video footage at www.jcb.org*)**