# **BIOPHYSICAL SOCIETY**

JULY

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# Biophysicist in Profile

*Walter Perkins* often jokes that his career—research and development of anticancer agents and treatment for pulmonary conditions—is his way of "making amends for [his] involvement in perpetuating the use of tobacco." Raised on a Virginia tobacco farm, Perkins recalls taking his grandmother's alarm clock apart to see the mechanisms, converting an old barn into a chemistry lab—not a good location when using an open flame—and serving as the president of his high school's Future Farmers of America chapter. He credits his father, a farmer and a self-taught musician, for teaching him patience and a dogged work ethic that has carried over from the field to the lab.

After earning his BA in chemistry, Perkins went on to PhD studies in biophysical chemistry, both at the University of Virginia (UVA). With adviser *David Cafiso*, Perkins worked to explain the differences in proton/hydroxyl permeability across different model membrane systems and to evaluate the contribution of the membrane's interfacial dipole field in proton/hydroxyl (H<sup>+</sup>/OH<sup>-</sup>) conduction. "I primarily credit Dave for sparking my interests and guiding me into the world of

# Biophysics is the crossroads where all the interesting science intersects...

lipid assembly and interactions," said Perkins. "Dave started at UVA during my senior undergraduate year. I took his physical chemistry class, and then became his first PhD student." Perkins' experiences in Cafiso's lab learning about membrane properties and liposome formation would serve him extremely well in the next leg of his career.

- Walter Perkins

Perkins knew he wanted to enter the pharmaceutical industry after his postdoc, but did not realize that there were industrial postdocs available until attending the Biophysical Society Annual Meeting in 1987, where he pursued both academic and industrial postdocs. "Job searching was contained primarily at meetings in the early days," he said. "Today, the Society's website to connect job seekers and employers is very impressive; back in 1987, I posted my resume and was approached by a scientist from The Liposome Company (TLC)." After weighing the pros and cons of academia versus industry, he decided to head to TLC, and as Perkins put it, "the rest is history."

*Andrew Janoff* was the head of Liposome Research at TLC when Perkins started. "Walter was our first postdoctoral scientist," said Janoff, "and he went on to become one of the most important and productive members of the group." Describing his time at TLC as "a lipid biophysicist's dream," Perkins reminisced, "they had literally every technique and instrument that one could imagine, except x-ray diffraction, which we were able to do through collaboration with Dr. *Sol Gruner*." In those early days of biotechnology research, scientists at small companies had the flexibility to do extensive mechanistic work and off-product research, as long as it generally increased the targeted knowledge base.

With this flexibility, Perkins' time at TLC was extremely productive. Working on a project to determine why multilamellar liposomes made from powder exclude solute, Perkins realized and proved that the captured volumes generally

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reported for most multilamellar vesicles had been underestimated by a factor of two. "Many of his observations have been codified into standard operating procedures necessary in all facilities that produce liposomes commercially," explained Janoff. Perkins' model that amphotericin and phospholipid were combining in a one-to-one ratio to form unique complexes that assembled to form membranes was a key factor in the development of the drug ABELCET®, which treats life-threatening systemic fungal infections, and is still on the market today. His contributions were also essential to the development and regulatory approval of the drug MYOCET<sup>®</sup>, as well as many other Investigational New Drug applications for the company. "Walter is the embodiment of Szent-Gyorgi's ideal biophysicist," said Janoff. "He sees what everybody else has seen, and thinks what nobody else has thought."

Over the years, his career has covered many topics. "I think of myself as a liposomologist," Perkins explained, "but I really have been a biophysics jack-of-all-trades, and master of none." Focusing on drug delivery using liposomes and lipid-based complexes, he has employed techniques from electron paramagnetic resonance to circular dichroism spectroscopy and more. "One of the great things about Walter was that if you had a reasonable idea, he would let you pursue it," said *Don Hirsch*, who worked with Perkins at TLC. "Collaboration was encouraged and there was a sense that we would sink or swim together."

Today, his specialization lies at the intersection of liposome/nanoparticle technology and inhalation delivery. As the chief technology officer at Insmed Incorporated, a public biotech-pharmaceutical company, Perkins heads the research team, working to develop pharmaceutical therapies for rare diseases where there is high unmet medical need. His current work includes an inhaled liposomal amikacin drug, currently in a Phase 3 clinical trial and a Phase 2 clinical trial. "If it is approved, it will be used to treat Pseudomonas aeruginosa lung infections in cystic fibrosis patients, as well as patients with nontuberculous mycobacteria lung infections," Perkins explained. This treatment, as well as others that he is working on, focus on inhalation as a route of administration, expanding his knowledge base to include a "reasonable understanding of aerosol delivery, aerodynamics, and airway deposition."

Through the years, his biggest challenges have come not from the science, but from the supporting framework. Financial support, even in the pharmaceutical industry, is not unlimited. Perkins worked at a small venture capital funded company for several years, where pursuing research questions was limited to those that had potential to advance drug candidates down the pharmaceutical development path.

Time management is also a challenge for Perkins. With career advancement came additional administrative responsibilities, limiting his time even further. He describes the pharmaceutical industry as seeming on occasion akin to an old-west cattle drive, saying, "You gather the herd, head toward your destination and start pushing forward; if you discover new geography or a beautiful landscape, you make note of it but keep pushing forward." Time to investigate those beautiful landscapes—or dangling questions in research projects—is limited, "and often you aren't able to return to explore further."

Despite these limitations, Perkins finds his work extremely rewarding. Solving the mystery of what appeared to be a new phase transition in saturated chain phospholipids was a personally satisfying puzzle to solve. Additionally, the improvement in patient's lives brought about by new therapies, and the interesting science employed to generate the therapies, keeps him pushing forward. "I really love what I do," Perkins confessed. "I'd like to keep doing it until I can't, even expanding my group and doing more mechanistic work into basic interactions."

Perkins would like to examine more closely the role of epithelial cell responses to certain mediators affecting changes in the pulmonary vasculature, and to watch and wait in awe as the endless possibilities of biophysics move the field forward. "In my career, I have seen computers move from simple data crunchers to indispensable tools," said Perkins. "The possibilities 25 years from now are hard to imagine."



Perkins with some of his research colleagues (left to right): Franziska Graf, Walter Perkins, Pallavi Venugopal, and Jane Ong.