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The laboratory of David Epel at Stanford's Hopkins Marine Station in Pacific Grove, California, sits on a rocky promontory covered with ancient wind-sculpted cypress trees jutting out into Monterey Bay. It is one of the most celebrated seascapes on Earth and one of the most historic, at least in biology. Hopkins Marine Station is the oldest marine research station on the West Coast, and the third oldest in the U.S. after the MBL at Woods Hole and Cold Spring Harbor. It owes some of its fame to its spectacular location and much to novelist John Steinbeck's Cannery Row and other works which features marine biologist Ed Ricketts. In the study of sperm-egg interaction, it is known for Epel's work exploring the intricate signaling of metabolic activation at fertilization using sea urchin eggs.

When David Epel first arrived at Hopkins to set up his lab in 1965, Ricketts was only a memory and Cannery Row an industrial ruin, but Hopkins Marine Station was the ideal location for his work using marine organisms. Nearly three decades later, a redeveloped Cannery Row is filled with boutiques, Ricketts is enshrined in the nearby Monterey Aquarium, and Epel is still engrossed in the mysteries of embryo activation. But in recent years, Epel has opened an ancillary branch of inquiry. He wants to know how marine embryos cope with the stresses of the real world outside his lab window.

"Stress on organisms is probably the most important evolutionary force in the world — physical stress, pathogen stress, parasite stress. That's what's driving evolutionary selection," says Epel. "People are realizing that you have to go into the real world to understand what development is about. Working on well-known lab models is not going to tell you everything."

After fertilization, marine invertebrate embryos must survive without physical or parental protection in an environment that teems with natural and manmade dangers, including UV radiation, pathogens, and natural and manmade toxins.Using molecular and cellular approaches, Epel is discovering that these organisms cope in surprising ways. For example, sea squirt embryos generate their own cellular sunscreen to block UV radiation in the shallow waters where they mature. Epel is also looking at multidrug resistance (MDR) transporters in sea urchins, mussels and mudworms. All eukaryotic cells have MDR genes and turn them on when the environment becomes noxious. Epel's mudworms seem to have super MDR capabilities. It's what enables them to thrive in grossly polluted substrates. Epel also notes that MDR transporters are also what enable some human tumors to resist chemotherapy.

David Epel's ability to link molecular events to the larger world is a hallmark of his work, says Victor Vacquier, a former post-doc and longtime collaborator now at the Scripps Institution of the University of California, San Diego. "In the last ten years, Dave has become interested in the mechanisms that marine invertebrate embryos use to protect themselves from environmental harm," says Vacquier. "Dave is interested in their ability to grow in polluted environments and also how they could be used to monitor pollution levels of small organics. But MDR transporters are also a big issue in chemotherapy. Cancer cells select for the ability to exclude anti-mitotic agents by overexpression of MDR transporter genes and get around cytotoxic molecules. Anything that's hydrophobic and over 60 in molecular weight gets tossed out."

"David is that rare cell biologist who is answering fundamental questions of both medical and environmental importance," says Gerald Schatten, who heads the Pittsburgh Developmental Center at the University of Pittsburgh School of Medicine. "David continues to make pioneering discoveries on the origins of embryonic life using sea urchin eggs and yet in this most recent work he's extrapolating to issues of truly global proportions," he adds.

First at Hopkins Marine Station and then during seven years at UCSD's Scripps Institution, Epel's marine animal models led him to three important discoveries: the "slow block" against polyspermy through the egg's release of cortical granules containing a protease that elevates the fertilization envelope and degrades sperm receptors, the role of free calcium as the primary activator of the dormant egg cell, and the rapid rise in intracellular pH following fertilization. "All of this work came from the eggs of these wonderful marine models," says Epel. "That's the beauty of them. Everything that takes place in the first 30 minutes after fertilization is a microcosm of cell biology. It's what goes on in the entire life history of a cell right up to cell division."

Beyond these discoveries, says Vacquier, "I think Dave's major contribution was the idea that there's a program of metabolic activation of an animal embryo, a stereotypic activation of different metabolic reactions that takes the egg from being dormant and puts it on a path leading to mitosis. It's like a computer program where you press the 'start' button, and it reads it out stereotypically. The sequence of events (of embryo activation) has the same timing and all the events have the same relationships. Dave didn't discover all the steps of this himself. A lot of people did various pieces, but it was Dave who put the concept forward so forcefully."

The road to Monterey Bay began for David Epel in Detroit where he had the good fortune of an older brother interested in science, a younger brother interested in whatever David was doing, and a basement. His brother Joseph passed along a chemistry set, a photographic darkroom, and a microscope, all of which David took downstairs with his younger brother Bernard. “That’s why I was fortunate in growing up in Detroit,” Epel says. “I had a basement to putter around in. California homes don’t have basements.” The puttering had its effect. Today Bernard is also a cell biologist, studying cell communication in plants at Tel Aviv University.

David Epel took his undergraduate degree at what is now Wayne State University but was then a much smaller and more intimate place that allowed him to do undergraduate research in the laboratories of parasitologist Dominique De Giusti and cell biologist Lawrence Levine. It was Levine who pushed Epel into the problem of calcium’s role in cell motility and onto graduate school at UC Berkeley under Daniel Mazia. “I’d never heard of Berkeley before,” Epel confesses. “They didn’t have a good football team then and I thought I would go to UCLA. Then Dan Mazia came to Detroit and I heard him lecture.” Working primarily with sea urchin eggs, Mazia, who served as ASCB President in 1972, was best known for isolating the structure that became known as the mitotic apparatus. But Mazia was also interested in unraveling the oscillations of ionic energy that seemed to drive the cell cycle. Epel was drawn into that side of the work and pursued it, first with Mazia and then as a postdoc with Britton Chance at the University of Pennsylvania.

From there, Epel went to Hopkins in 1965 and to UCSD in 1970. In 1977, Epel was invited back to Stanford and to the Hopkins Marine Station as part of the university’s commitment to revitalize its role in the Department of Biological Sciences. He’s been there ever since, running a yearround research lab with grad students and post-docs, and teaching undergraduates during the winter and spring terms. Epel remains deeply committed to biology education at all levels. In 1996, Stanford students voted to award Epel the Cox Medal for Faculty Excellence in Fostering Undergraduate Research. With NSF funding, Epel, technician Chris Patton, and high school biology teacher Pam Miller opened a web site in 1998 on using sea urchin fertilization in high school and freshman biology labs1 . The site has received 10 million hits.

Even though his wife, Lois Epel, has recently stepped back from her psychotherapy practice, David says he’s never been happier or busier with his research, his students, and his writing. The Epels have three grown daughters—Andrea, who works in alternative medicine for Kaiser-Permanente; Sharon, who is a freelance magazine writer who is studying to become a family counselor; and Elissa, who is an assistant professor at UCSF in health psychology—plus four grandchildren.

Close friends and colleagues can’t imagine a retired David Epel. Says Vacquier, “he always has high energy and is always in a good humor. If Dave were all alone on an iceberg, he’d be smiling. Either he’s full speed ahead or asleep. I was his roommate a couple months ago at Woods Hole for the sea urchin meeting. We’d get back to our room at the end of the day and I’d be ready to go to bed, but then Dave would start talking. We’d go on for hours. It was awful,” says Vacquier with a laugh. “I wasn’t getting enough sleep.”