[<< back]

2001

Merton Bernfield

The best plans of Mert Bernfield went awry in the fall of 1961. He'd thought his next step was all set: He would finish his pediatrics residency at Cornell Medical Center in New York City and then take up the postdoc that he'd all but sewn up at the NIH. But at the eleventh hour, the PI took a position in Boston. "I was devastated," Bernfield recalls, "all my NIH contacts were lost." In Bethesda, he started over interviewing with NIH lab chiefs. There he ran into Don Summers, an old friend from the University of Illinois Medical School in Chicago.

"Who's your next appointment?" Summers wanted to know.

"Marshall Nirenberg," Bernfield read the strange name aloud. "Who's he?"

"Who's he?" Summers exploded. "Marshall Nirenberg is going to win the Nobel Prize. He just broke the genetic code!" "The genetic code?" Bernfield asked. "What's that?"

Nirenberg would indeed win a Nobel Prize, in 1968, for decoding the very first code word ever read—UUU for phenylalanine—but in 1961 the vocabulary of DNA was still exotic, even to pediatrics residents. With only five minutes to spare, Bernfield dashed to the NIH library and pulled Nirenberg's groundbreaking paper. "I didn't even understand the title," Bernfield recalls rue- fully. Undeterred, he raced to the interview, pumped Nirenberg's hand, and said truthfully, "I've seen your work. What are you going to do next?" The great man talked for the next 59 minutes straight. Bernfield got the job.

It was a classic Mert Bernfield moment—standing at the leading edge of science, wondering what comes next, and making the most of it. That's Mert's style, says Ralph Sanderson, a former Bernfield postdoc: "in terms of day-to-day experience, Mert was very hands-off. He was always sure he understood what everyone was doing. He made suggestions and he gave very good advice on how to think scientifically but basically he gave people the opportunity. He helped them to make the best of it but he didn't coddle them by any means."

The opportunities were certainly there in the early '60s. It was a dizzying time in cell biology with people and money pouring into research and astounding results pouring out. When Bernfield took the position with Nirenberg, he expected to be one of three postdocs. By the time he reported for duty, Nirenberg had about 20 postdocs. Bernfield fondly remembers the special opportunities at the NIH in those days. "If you couldn't do research at the NIH, you couldn't do research anyplace," he says. "You could get anything you wanted at that time. It was a government bureaucracy but it was an intellectually stimulating place."

After a then-typical two-year placement, Bernfield took an "intramural" investigator's position well outside the NIH walls with Clifford Grobstein at the University of California, San Diego. It was in Grobstein's lab that Bernfield first took up the problem that still enthralls him— how what's outside the cell affects what's within. Among the chief characters of the extracellular matrix were proteoglycans, a little understood family of proteins with devilishly long heparan sulfate (HS) chains. The proteoglycans were difficult to manipulate and difficult to characterize but Bernfield was convinced that they were key players in many cell functions, including morphogenesis. "I thought they were im- portant because they were made by every cell and because they were the most acidic molecules made by any cell," he says today. "It was a guess but it turned out that they were." Proving that guess took years.

As much as Bernfield liked the San Diego lab, he remained committed to pediatrics. In 1967, Stanford offered him the post of Chief Resident in Pediatrics along with a research lab. Bernfield blossomed at Stanford as a medical educator who tirelessly preached the importance of research to young clinicians and as a clinician working in birth defect and premature infant follow-up clinics. He was also pressed into service by Stanford's innovative Human Biology Program for undergraduates. The program recruited the university's top researchers to address the swirl of social, political, and environmen- tal problems of the late 1960s from a scientific viewpoint. When the program's director, Donald Kennedy, left to become the head of the Food & Drug Administration in 1977, Bernfield stepped in to run it for three years. In the meantime, his lab was getting results that showed cell surface proteoglycans directly affecting the shape of developing cells.

Don Ingber remembers those papers well. "In the mid-to late-'70s, Mert had a series of papers that to this day I think are fundamental to our understanding of epithelial morphogenesis—how tissue patterns develop in epithelial tissue through branching." Cell surface proteoglycans, though, remained maddeningly difficult to work with in hose days, says Ingber.

Finally, in 1988, Scott Saunders, a MD/PhD student in Bernfield's lab at Stanford, cloned the first

proteoglycan. It needed a name and so Bernfield took a colleague on the Classics faculty to lunch to get one. Bernfield told him how this new molecule seemed to affect what went on inside the cell by assembling other extracellular ma- terials on the cell surface. The Classics professor suggested the Greek verb “syndein,” meaning to bind together. Bernfield combined syndein and glycan to create “syndecan,” which became syndecan-1.

Eventually four syndecans were cloned in mammals and one in Drosophilia, suggesting that it is a highly conserved mechanism. In 1990, a former Bernfield postdoc, Guido David, cloned the first of a second family of proteoglycans, the glypicans. There are now six known glypicans in mammals and two in flies. Today the list of cell behaviors that the syndecans and glypicans are known to control or influence is growing rapidly—tissue repair, energy metabolism, tumorigenesis, and immune response development. In the post-genomic era, the syndecans and glypicans offer another layer of control by their ability to bind and modulate extracellular matrix components. “That’s the fascinating thing about proteoglycans,” says Don Ingber. “They explain how tissues are really built. They are not just gene switches that click on and off and miraculously you have an organ. I think gene switches are impressive but they don’t tell you enough about how you build something as complex as an organ.” In 1989, Bernfield was recruited by Harvard Medical School to direct the Joint Program in Neonatology, the department responsible for care of sick newborns at three Boston teaching hospitals. Such a program was a longtime dream but it led to one of the greatest disappointment of Bernfield’s professional life when after nine years, the hospitals pulled the plug, citing costs. On reflection, Bernfield believes that it was probably the best thing that ever happened to his lab career. It freed him to hone a new tool for probing the proteoglycans, knockout mice.

Throughout these transitions, Bernfield was making important contributions to the ASCB. He had been a member for decades, serving as Treasurer of the Society from 1990-1995, and was through the ‘90s a member of the Public Policy Committee.

Most recently, Bernfield and postdoc Ofer Reizes came up with a mouse mutant deficient in syndecan-3 which turned out to be critical to appetite control. The mutants that did not express syndecan-3 did not perceive hunger normally, even following an overnight fast. Their wild type cousins finished their fast ravenously hungry with a 3-5 times increase in syndecan-3 lev- els in their hypothalamic centers. The implications of this work in a country where 50 percent of adults are considered overweight and a third obese is not lost on Bernfield.

For all his evident passion for the lab, those close to Bernfield say it is just one part of his life. “There are people in science who get totally lost in the science and don’t have a life,” observes Ingber. “Mert is not one of those. He can be as passionate and as lost in proteoglycans as anyone but he also has strong interests in theater and art. Most of all, he is extremely proud of his family.”

His greatest pride is his wife Audrey, who runs the office of enrichment programs for medical students at Harvard. Their three children, now grown, are all in the arts: Susan is the founder and artistic director of an Off-Broadway theater company in New York; James is finishing an MFA in film at Columbia, and Mark is a computer trouble-shooter by day and a jazz drummer by night in Oakland, California.

Does it ever bother Bernfield that his children had no interest in following their father into biology or medicine? He lights up at the question. “I am thrilled with their choices. Thrilled. They are following their dreams and succeeding.”

Bernfield is afflicted with Parkinson’s disease and struggles today with the physical limitations imposed by its symptoms. But his science, his intelligence, and his wit are in their prime. He brushes aside self-pity. “I’m a lucky guy,” he says. “They let me work with young, smart people. They still pay me for this. It’s amazing to me.”