

## Michael Shelanski



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Mike Shelanski got in on the proverbial ground floor of cytoskeleton proteins while he was still an MD/PhD student at the University of Chicago in the 1960s, and he likes to say that the cytoskeleton has been pursuing him ever since. “I’ve enjoyed changing what I’m doing, several times in my career,” says Shelanski, who has been Chairman of the Department of Pathology at Columbia since 1987, “but somehow I keep returning to the cytoskeleton.”

Shelanski’s latest cytoskeletal encounter comes from new work on how amyloid beta, which is the active principal in Alzheimer’s Disease (AD), modulates the formation of the memory trace by impeding proteasome function. Shelanski believes that A-beta has a very early effect on the proteasome. By studying changes in dendrite spines, the little spikes composed largely of actin bundles that mark synapse entry points into the dendrite’s long shaft, his lab has been able to closely monitor proteasome function in response to the presence or removal of A-beta.

Joel Rosenbaum has known Shelanski from their “ground floor” days as grad students and post-docs at the University of Chicago. Says Rosenbaum, “As an MD and a neuropathologist, Mike always had a deep interest not only in normal filamentous conditions, but also in the abnormal conditions in neurodegenerative disease like Alzheimer’s which are characterized by masses of filamentous proteins. As Mike’s career progressed, he became more interested in the pathology of those filamentous masses. He’s been well-positioned to apply all that basic information to neurological pathology.”

Former post-doc Dennis Selkoe agrees. “You can read his seminal papers on the cytoskeleton and microtubule polymerization, but Mike has also done amazing work in signaling and neurodegenerative disease. He’s just very eclectic and catholic in his scientific interests.”

Rosenbaum says that in their early years, he and Shelanski were among about a dozen people at the University of Chicago who were “interested in the cytoskeleton but at a time when no one had successfully isolated their proteins.

At the time, it was not widely accepted that that colchicine-binding protein was the microtubule subunit. Shelanski did one of the key studies that showed that this was really the building block of microtubules, studying sea urchin (sperm) flagella. Mike was able to demonstrate using a combination of electromicroscopy and tritium labeling that as those central microtubules disappeared, more and more colchicine-binding protein became solubilized.”

Michael Shelanski is very much a “city guy,” a product of Philadelphia and especially of the city’s Central High School, which in those days was all boys. Shelanski recalls, “We were taught science by people who very well trained. Many came into the public school system during the Depression with advanced degrees. I was taught physics by Fred Hofkin, an MIT graduate. He led our science project, which was to build a little cyclotron in the basement of the school. We got it to work, much to the horror of the Board of Education.”

Shelanski’s father was a parasitologist and toxicologist in Philadelphia who died when Mike was 12. One of his father’s professors, Louis Heilbrunn, stepped in as Mike’s education mentor and advised young

Shelanski that if he was truly interested in basic biology, he should study physics instead. So Shelanski attended Oberlin College in 1959 as a physics major and found himself two years later deeply interested in biophysics, but restless in small-town Ohio. He enrolled in graduate school at the University of Chicago after less than three years as an undergraduate.

Without a Bachelor’s degree, Shelanski was accepted as an MD/PhD student in the Division of Biology, which included the College of Medicine. Shelanski tolerated his med school classes but saw his future in experimental biology, especially after joining the lab of the charismatic physiologist, Julian Tobias. After a year in the Tobias lab, Shelanski abandoned medical school to concentrate on membrane potential experiments. “We were working on the cardiac ganglion of the lobster,” Shelanski remembers. “You could open up the lobster, remove the ganglion and then wrap up the animal in seaweed before putting it in the

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refrigerator. By the end of the week, you had six or seven lobsters. With some beer, you had all the ingredients for a blow-out party.”

When Tobias died suddenly of a heart attack, Shelanski was left without a lab, a mentor or a clear career path. He returned to his medical studies but later borrowed bench space in Ed Taylor’s biophysics laboratory to finish some membrane potential experiments. His own work was going nowhere, Shelanski realized, but all around him, Taylor’s post-docs were working furiously to purify a mysterious colchicine-binding protein that supposedly formed the mitotic spindle. Taylor asked Shelanski if he might be interested in joining the group. “I told him that I knew nothing about protein chemistry,” Shelanski remembers. “Ed said, ‘Go ask someone.’” Shelanski asked Gary Borisy.

Borisy and Taylor’s working hypothesis was that if this protein made up the mitotic spindle, then the higher mitotic index, the higher the colchicine-binding rate should be. This worked until they got to the squid giant axon, which had the highest colchicine-binding rate of all, but no mitotic spindle. Taylor set Shelanski to find a better source for this obviously structural protein. Shelanski tried growing and harvesting (with a secondhand industrial dairy cream separator) *tetrahymen* cilia but couldn’t get them to bind colchicine. Shelanski turned to the next lab bench where Dick Weisenberg was working on sea urchin eggs and asked if he could have the sperm. Forcing them under pressure through a 22-gauge needle, Shelanski was able to shear off the tails and get at their molecular contents. This led him eventually to the breakthrough demonstration that the Taylor-Borisy colchicine-binding protein was the major constituent of the microtubule, the protein known today as tubulin.

Shelanski finished his MD in 1966 and his PhD in 1967. Over time, clinical medicine had grown on him and Shelanski decided to train in neuropathology under Bob Terry at Albert Einstein in New York. While still a resident, Shelanski contrived to get a grant and set up a research lab at Einstein. He has maintained his dual identity as clinical and basic researcher for nearly forty years, while moving through positions at the NIH, the Institut Pasteur, Harvard Medical School, NYU, and Columbia.

Shelanski and his wife Vivien, a lawyer specializing in private mediation and arbitration,

live in the Cobble Hill section of Brooklyn. They both grew up in Philadelphia and went to Chicago for grad school but only met later. The Shelanskis are the parents of three and the grandparents of two. Their son Howard is a professor at Boalt Law School of the University of California, Berkeley; Samuel is an oncologist in Fort Collins, Colorado, and Noah is “a superb bartender and sometime law student in New York City,” says their father.

Reflects Selkoe, “Mike can be somewhat acerbic, but if you get past that, you discover that he’s a very supportive guy. When I got to Harvard, there was no place for me to sit. So Mike moved me into his office. I was a new post-doc sharing an office with this very senior guy who had a lot of responsibilities and was on the phone quite a bit. It was very instructive. Mike had a huge effect on my research. He set me off on what I wanted to do and toward everything I’ve done since.” ■

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