

George Vann Bennett

Vann Bennett stood out in the 1970 entering class at Johns Hopkins Medical School, recalls his longtime friend, sometime collaborator, and Hopkins classmate Peter Agre. Agre remembers meeting the dark-haired surfer from Hawaii who had the compact physique of an ex-wrestler from Stanford but somehow spoke with an accent straight out of *Gone with the Wind* Atlanta. Agre, a self-described tall, pink-faced Norwegian from Minnesota, says he and the Hawaiian with the drawl hit it off at once. They ended up sharing a seedy apartment off-campus and a body in gross anatomy class. “We were the Cadaver Brothers,” Agre reports, adding that they were equally inept at dissection.

But whatever his struggles with routine coursework, Bennett stood out for his ahead-of-his-time grounding in molecular biology at Stanford and for his mind set, says Agre. “Vann was the most interesting person in our class and I think universally regarded as the smartest. He’s always had a way of looking critically at information.” Take the time the lecturer in obstetrics posed a trick question to the class: “What is the growth hormone responsible for fetal growth in utero?”

Agre describes the scene. “All the aces sitting in the front wave their hands and say it’s human growth hormone. The lecturer grins. And then there’s a voice from the very back row. It’s Bennett, saying, ‘Insulin.’ Someone knew! It almost knocked the lecturer off his podium.” Agre continues, “Vann didn’t know. He just figured it out. Insulin was a polypeptide with metabolic activity. He’s always been an insightful biologist and that’s followed him through his career.”

Academic Geography

That career has covered a lot of academic geography. After a Ph.D. and then an M.D. from Hopkins, Bennett went north in 1976 to

Cambridge for a postdoc with Dan Branton at Harvard. A year later, he went south to North Carolina’s Research Triangle for a staff scientist position at Burroughs Wellcome under his Hopkins mentor, Pedro Cuatrecasas. Then it was back to Hopkins in 1981 to join the cell biology faculty. Finally, Bennett went back to North Carolina, where he was appointed one of the first Howard Hughes Medical Institute investigators at Duke University Medical School in 1987.

Yet to a remarkable extent, Bennett’s career has followed a single protein. Working on red blood cells (his own), Bennett used careful proteolytic degradation in 1978 to pick out a fragment of an unknown protein that bound to the cytoskeletal protein spectrin. He called it ankyrin. It was known that in red blood cells, spectrin served as a cytoskeletal tent pole holding up a membrane canopy. But no one knew what was actually pinning the canopy in place. Bennett believed that in ankyrin he had identified the membrane anchor. The following year, Bennett purified the other end of the ankyrin protein and found that it bound to an anion exchanger in the cytoplasmic domain.

It was and remains a revolutionary discovery, according to Agre, because it showed for the first time the localization of transport molecules at the site of their function. “It’s the kind of work that’s tough to do. Those first purifications were heroic—big centrifuge rotors going all night in cold rooms. Vann is a workhorse for this kind of thing,” Agre explains. “This [ankyrin] was a unique kind of binding protein, never before purified or characterized. And Vann did it all. It’s really a fundamental breakthrough in biology.”

From Erythrocytes to Neurons

Ankyrin has become the Swiss Army knife of membrane binding proteins, at least in most



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animals. Over time, Bennett has revealed ankyrin to play key roles in human cells from erythrocytes to neurons to cardiac myocytes. He has discovered three human ankyrin genes, A, G, and B.

Through a variety of alternate splicings and foldings, the ankyrins are now believed to bind 14–15 different families of membrane proteins in addition to spectrin, according to Peter Michaely. A Bennett graduate student now on the faculty of the University of Texas Southwestern Medical Center in Dallas, Michaely says that ankyrin is still gaining connections as it emerges as an essential part of the genetic kit for nearly all metazoans.

“It’s a new class of protein,” Bennett explains. “Recent findings suggest ankyrins are not only required to localize proteins within membrane domains such as epithelial lateral membranes and the sensory cilia of rod photoreceptors, but they also are required to form these domains.” It’s an intriguing combination of functions. “How would you describe something that both stabilized and helped form the structure?” Bennett asks.

A PubMed Search

“Adaptor protein” is the best anyone can come up with now, but ankyrin continues to lead the Bennett lab in unexpected directions, many with clear connections to human health. Bennett has published on topics as diverse as electrical regulation of photoreceptors, defects in skeletal muscle organization in muscular dystrophy, mechanisms of cell junction formation, protein structure, mechanisms for arrhythmia and senescence, neuronal migration, and design of nanodevices.

“Perform a PubMed search on Vann,” suggests Peter Mohler, a former Bennett postdoc who now runs his own ankyrin lab at the University of Iowa, “and you will see all sorts of high-profile manuscripts. This guy’s on a whole different level.”

The Bennett level began in Morganton, NC, in 1948. “I do tell people that I’m a native,” Bennett explains, “but they don’t believe me because I am this bearded academic type.” Bennett left North Carolina soon after he was born as his father pursued a successful practice as an ear, nose, and throat surgeon, first in Atlanta and then in Honolulu. His son was 14 when they arrived in Hawaii.

“We moved from Atlanta, which at this time was very segregated. Suddenly I went from being in a white majority to being a member of a minority group. It was fascinating, seeing all the races, ethnicities, and backgrounds.”

Bennett learned to surf, breezed through high school science, and transferred in his junior year to the Punahou School, which is now more widely known as Barack Obama’s alma mater.

He chose Stanford because it was a good school and on the Pacific Coast. “After that,” Bennett observes, “I seemed to be migrating east.” He was influenced at Stanford by John Brauman’s organic chemistry course and by the famous introduction to biochemistry at the Stanford Medical School, which was team taught by Paul Berg, Arthur Kornberg, I.R. Lehmann, George Stark, and

Dale Kaiser. The experience made Stanford his first choice for medical school, but he didn’t get in. Johns Hopkins Medical School did take him, though. “In the long run, it was good for me to move out and get exposed to the East Coast,” he says.

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Molecular Thinking

In Baltimore, Bennett was impressed by his new friend Peter Agre and unimpressed by the Hopkins medical curriculum. “I’d been infected by the science virus [at Stanford]. I didn’t realize how deeply it went in until I was sitting there during [medical school] lectures and worrying that the lecturers didn’t understand how things were really working. They were not thinking on the molecular level.”

His medical training and the physiological slant that it gave to his thinking were powerful influences, Bennett believes, but he realized during clinical rotations that his talents lay elsewhere. “There were superb clinicians at Hopkins and elsewhere, so I thought I should concentrate on the basic science end.”

Bennett found his own mentor in Cuatrecasas, a young Spanish-born, American-educated pharmacologist who developed affinity chromatography as a breakthrough drug-discovery tool. Agre remembers Bennett’s “discovery” of Cuatrecasas. “It was Vann who identified Pedro as a really exciting and creative scientist,” Agre recalls. “How did Vann do it? He heard Pedro lecture. The rest of us were there too, but these people are all so brilliant, who’s to

know who is the most brilliant? But Vann knew. He said, ‘Pedro’s the one.’”

Finding Ankyrin

Cuatrecasas left Hopkins to direct basic research at Burroughs Wellcome, the first of many high-level posts he would hold in pharmaceutical development. He quickly recruited Bennett. It was a fateful move both for Bennett, who first purified ankyrin there, and for Agre, who was doing a clinical residence in hematology nearby at the University of North Carolina (UNC) medical center. Agre was still torn between bench and clinical research.

Agre says straight out that he owes his own scientific career to the direct influence of Vann Bennett. That career includes winning the 2003 Nobel Prize in Chemistry for the discovery of aquaporin membrane channels. “I would never have become a basic scientist without Vann,” Agre declares.

It was Bennett who got Agre a summer place in the Cuatrecasas lab at Hopkins when a clinical research fellowship fell through. It was Bennett who took Agre into his Burroughs Wellcome lab to study the role of ankyrin and spectrin in human hemolytic anemias. Later when they both landed back at Hopkins, Bennett offered Agre bench space while Agre scrambled for research funding to pursue the basic work that would culminate in the aquaporin channel.

“Maybe I would be practicing medicine in northern Minnesota or working as a missionary doc,” says Agre, “but I would never have had the confidence (for basic research). Vann made me change my career plans.”

Bennett has had a huge impact on others. Velia Fowler, who is now at The Scripps Research Institute in La Jolla, credits Bennett’s example as an industrious postdoc when she was a green graduate student in the Branton lab. “Vann was just so full of energy that he inspired me,” Fowler recalls, particularly for his wisdom on experimental design. “He’d be working late and I’d be sitting there like a puppy dog asking him all sorts of questions.” Later, Fowler sought out a postdoc position in Bennett’s lab at Hopkins.

Why This and Not That?

“Vann still has great intellectual influence on me,” Fowler explains. “I still read his papers and think, ‘How did he put this together? Why did he conceptualize the problem this way? Why did he put it together this way and not another way? And most of all, what can it tell me?’”

Mohler says he was extremely naive when he started his postdoc in 2000, and still laughs at himself for missing the whole point of the Bennett mentoring technique. “Every morning we’d sit down and talk, just the two of us, for 20–30 minutes about experiments, data, and manuscripts. At the time, I thought, ‘I am offering this great scientist some wonderful ideas that will change the way he thinks about science.’ In hindsight, I realize how ridiculous that was. He was doing it all for me. He was the ultimate mentor.”

Despite Bennett’s status as a great mentor and inspired scientist, Mohler still says he would never step into a canoe with Bennett on one of his famous northern wilderness river expeditions. “He’s too dangerous,” says Mohler. “I couldn’t handle it. Vann comes across as this totally reserved guy, but just under the surface he’s super intense.” From opening champagne bottles with a saber to paddling down arctic rivers in bear country, “He’s off the bell curve,” says Mohler.

Boundary Waters

Bennett has always had a taste for high-misery athletic performance. Back in their Baltimore student days, Agre and Bennett used to ride bicycles long distance on the hottest, stickiest days, their tires sucking on the melting asphalt with Agre growing pinker and Bennett sweatier, both of them grinning from ear to ear.

In respectable middle age, Bennett and Agre discovered their mutual interest in wilderness kayaking, exploring together the boundary waters of Minnesota and the arctic-running rivers of northern Canada and Alaska. “There’s something about the northern environment that I really like,” says Bennett.

At home, Bennett lives in the country outside Hillsborough, NC, with his wife, Bernadette Pelissier, who was just elected on the Democratic ticket to the Orange County Board of Commissioners. Born in Senegal of French parents but raised in New Jersey, Pelissier recently retired as a sociologist for the state prison system. She is a legendary cook. Bennett says that since they married in 1996, “My greatest challenge is not to double my weight every three years.” In his turn, Bennett is a legendary gardener and poultry raiser on what he insists on calling a “farmette.”

From his first marriage, Bennett has three grown children and a new grandchild, Arabella. Her mother is Bennett’s eldest daughter, Patricia, an artist who lives in Baltimore. His second daughter, Lisa, is a writer who just moved back to Chapel Hill. His son, Davis, is graduating this year as a philosophy major from UNC.

“That’s so Vann Bennett,” says Fowler of Bennett’s approach to programming the ASCB Annual Meeting, meaning understated and self-deprecating, but with sharp, strong opinions about what makes good science just millimeters beneath the surface.

High-Profile Programming

Bennett is vice-chair of cell biology at Duke and has served on his share of academic, editorial, and meeting committees. But this year he has taken on the high-profile position of program chair for the ASCB Annual Meeting to be held in San Diego. In typical Bennett style, he credits his committee, the ASCB Council, and ASCB meeting staff for the excellence of the resulting program. “I just looked at the [final] program in the *ASCB Newsletter* and I can’t believe that I had something to do with this,” Bennett reports. “I mean, it looks really interesting.”

“That’s so Vann Bennett,” says Fowler of Bennett’s approach to programming the ASCB Annual Meeting, meaning understated and self-deprecating, but with sharp, strong opinions about what makes good science just millimeters beneath the surface. His work on the ASCB program this year, says Fowler, may mean that Bennett “is going to get a little more visibility, whether he’s ready or not.”

Agre agrees. Ankyrin was a discovery of historic importance, Agre declares, and the scientist who so painstakingly unfolded the ankyrin story will become far better known as its connections to diseases are traced. When deserved recognition finally catches up with his friend, Agre says he has no expectation of any change. “Vann’s always kept this kind of boyish inquisitiveness like the student at the back of the class who comes through with the brilliant observation. Vann is still doing that.” ■

—John Fleischman

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Deadlines:

Travel Award	July 8
Abstract	July 22
Registration	August 20 ■