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Guido Guidotti

"The first thing Guido Guidotti taught me about doing science was that little things matter," says John Pringle, who was one of his first graduate students at Harvard University in 1968. "Early in my graduate studies when Guido was still working on hemoglobin and the binding constants of oxygen, I went up to his lab and found his technician doing the experiment while Guido was over by the sink washing the glassware. Later, I asked him about this and he said that the experiment was interesting enough that he could trust the technician to do it right, but he just couldn't trust her to get the glassware clean enough."

But what matters to Guidotti is not always what matters to others. For example, Guidotti's CV lists a modest number of publications during the 1970s and 1980s, a time when his lab was making major advances on membrane protein transport. "That's this business of his not taking credit on papers," says Pringle, who is now at the University of North Carolina at Chapel Hill. "That's why it's so hard to figure out what he's done over the years. If you do a search for Guido, you don't find as much as you should," says Pringle. Guidotti's name was neither on Pringle's first published papers nor on other major papers from early Guidotti graduate students and post-docs who launched their careers from his lab. "Guido just wouldn't take credit unless he'd been actively involved in the creative part or had put in a lot of other work himself," Pringle recalls. "For a while, everyone knew about Guido's not taking credit. We all thought, 'this is cool.' Then everyone forgets what Guido actually did."

Lewis Cantley, now at Harvard Medical School, corroborates Pringle's assessment that Guidotti's impact far exceeds his bibliography. As a post-doc in 1978, Cantley says he only managed to convince Guidotti to add his name to papers on vanadate as a NaK ATPase inhibitor by arguing that the Guidotti lab itself deserved the recognition. Guidotti is well-known for turning out extremely confident and well-trained people who go on to major careers. A partial list of Guidotti students and post-docs might include Eva Neer, Jack Kyte, Steven G. Clarke, Kurt Drickamer, Anjana Rao, Marilyn Resh, Michael Forgac, Daniel Jay, Robert Bloch, Gilbert Chin, Betty Eipper, James M. Anderson, Jonathan Lytton and Chung Wang. Their mentor shrugs off any undue credit. In any case, Guidotti says his days as an unacknowledged collaborator ended abruptly in 1985 when he was called on the carpet before an NIH study section. "They said I was plagiarizing by using these articles that were published without my name on them," Guidotti recalls. "So now I put my name on all the papers, even the ones I didn't work on."

Even today, papers may not be the best way to follow the life of Guido Guidotti. Despite his name and the faint trace of an Italian accent after more than fifty years in America, Guidotti admits, when cornered, that his grandmother was "a lady from Boston," a Brahmin by birth, even if she was born in Tokyo. Her father (that is, Guidotti's great-grandfather) was George Adams Leland, Sr., a distinguished Boston ear-nose-and-throat specialist who was teaching in Japan by invitation of the Imperial Court, when she was born there in 1880. At the suggestion of a Japanese princess, the baby was named Jiun, supposedly "obedience" in Japanese. After three years in Japan, the Lelands returned to Boston (via Germany where her father stopped to study new surgical techniques). In 1907, Miss Jiun Leland was seated next to a young Italian naval officer, Salvatore Casano, at a formal dinner in Boston to honor the arrival of his warship on a goodwill mission. One thing led to another and they married and moved to Italy in 1908. Salvatore Casano rose to the rank of admiral in the Italian Navy, according to Guidotti, before he was forced out during "the fascist time." Jiun Leland Casano lived in Italy to the end of her life in 1975, speaking English to her daughter and grandchildren, and Italian (with a pronounced Boston accent) to everyone else.

Guido Guidotti first came to the U.S. in 1950 as an American Field Service exchange student bound for a final high school year in Decatur, Illinois. He was born in Florence in 1933 but weathered the war with his mother and older brother at his Yankee grandmother's home in Naples. His father, an officer in the Italian Army, was captured by the British in North Africa in 1941 and held as a POW in India until 1946. Even with the return of peace, Decatur seemed like welcome relief. "Naples was a chaotic large city with over one million people," Guidotti recalls; "Decatur was a town of 50,000. In Naples, the war hadn't really gone away.

The port of Naples was completely destroyed by the bombs so that by 1950, things were just getting back to normal, although life in Naples is always different from any other place."

Guidotti found Illinois "very different and very cold but the people were very cordial and friendly." He was taken in by Ralph and Dot Williams with whom he remained close ever after. It was the Williamses who arranged for Guidotti's admission to Millikin University in Decatur. After two years at Millikin, Guidotti was "miraculously" accepted into the Washington University School of Medicine, earning his MD in 1957. He served a residency in Internal Medicine, and was looking toward a career in academic medicine when Sputnik shook up American science. Suddenly a stint in basic research was de rigeur for a would-be medical academic and Guidotti was advised to join Lyman Craig at the Rockefeller as a way of adding a little hemoglobin research to his resume. After two years in New York, he was so engrossed in the

problem of identifying the amino acid sequence of the beta-chain of hemoglobin that he thought he might as well finish his doctorate. (He had also become the personal source of the lab's beta-chain hemoglobin).

In 1963, Guidotti was of- fered a faculty position at Harvard University under the "Committee on Higher Degrees in Biochemistry," which also included James Watson, Matthew Meselson, Walter Gilbert, Konrad Bloch, Paul Doty and John Edsall. The name and orientation of his depart- ment has morphed several times over the decades. These days, the sign outside says "Department of Molecular and Cellular Biology." As the Higgins Professor of Bio-chemistry, Guidotti is highly regarded by Harvard students, who voted him the 2000 Phi Beta Kappa Prize for Excellence in Teaching.

In 1990, Guidotti married molecular biologist and Harvard colleague Nancy Kleckner. They live in Newton. Guidotti has a son, also named Guido, by a previous marriage. The younger Guidotti is 34, married, and an MD who is a consultant in the Boston area. Guidotti has been a member of ASCB since 1992 and an Associate Editor of the Society's journal, Molecular Biology of the Cell, since its inception.

In forty years of research, Guidotti has watched an entire field—membrane protein transport and signaling—coalesce before his eyes. The work he is most closely identified with is the characterization of the NaK pump and the inhibition of NaK ATPase, work credited with explaining the mechanism behind the clinical use of cardioglycosides to control heart failure. Yet Guidotti is no longer sure his old molecular explanation is complete. "The NaK ATPase has been a major actor in the control of the force of cardiac contraction, but the more I read about it, the more difficult it is to understand how it works. There is a quandary emerging in more recent work that shows the concentrations of cardioglycosides used to treat heart failure would inhibit only a small fraction of the sodium pumps in the body. So it isn't clear how this would affect the heart un- less there were special high affinity receptors there," he says.

The idea of a hypothetical secondary receptor that might undermine one of the major discoveries of his lab seems to delight Guidotti. "Nature teases you. It makes you think you know something whereas you don't know the whole story. The first time you make a discovery, you think you understand everything, but as you do more work on the subject, you realize that there are more and more actors involved in this business. When you collect all the actors together, you realize you don't know who has the principal role."

Says Guidotti, "The reason cells work is that they have enormous back-up arrangements so that any perturbation that comes along can be dealt with. You have to be ready for this change and that change so you can escape one way or another." And so, says Guidotti quite cheerfully, "you solve one problem and that always brings up another."