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The Journey of a Researcher: An Interview with Guido Guidotti

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In a back office room of a quietly busy laboratory on the first floor of the Northwest Building, Professor Guido Guidotti sits with his MacBook Air in his lap, thoughtful. When I knock on the door, he looks up cheerfully and calls out, "Hi there! How do you do?" "I'm well, thank you, and you?" I respond. He flashes me his bright smile: "Well, I'm still here!"

More often than not, Guidotti's radiant energy and constant enthusiasm belie his advanced years, 50 of which he has dedicated to teaching and researching at Harvard. Now the Higgins Professor of Biochemistry, Guidotti teaches "MCB 176: Biochemistry of Membranes," "Freshman Seminar 26z: What is Life?," "MCB 178: Biochemistry of Protein Complexes," and "MCB 391: Biochemistry"; in the meantime, he focuses his research on the structure and function of membrane proteins.

A Winding Path to Harvard

Guidotti describes his education background, with a laugh, as "a story with no object in sight." Growing up in Naples, Italy, Guidotti first came to the United States as an exchange student in 1950 (Johnson 2011). He attended high school in Decatur, Illinois, for one year, after which he accepted a scholarship to attend Millikin University in the same city. Wanting to pursue a medical profession, Guidotti applied to several medical schools in the United States, including Harvard Medical School. On his decision to apply to medical school, Guidotti says he thought, "I'll apply now and see what happens. I didn't expect anything to happen." In the end, he was accepted to Washington University, "and so I went to Washington University! It was very easy!"

However, according to Guidotti, towards the end of the 1950s when "Sputnik had just gone up," many people became interested in scientific research. He says that everyone, including medical schools, got "psyched up about science" and "how everybody had to be a scientist." Told that he needed to learn how to do research in order to "have a career in medicine," Guidotti took an opportunity to attend the Rockefeller Institute in New York, and ended up completing a graduate degree there. However, by the time he was "ready to come back" to Washington University, the school no longer had a spot for him to complete his residency in medicine. "So I had to look for someplace else to go," says Guidotti. A protein chemist at Harvard had asked two other protein chemists at the Rockefeller if they had anyone to recommend for a "position in protein chemistry in the Committee of Higher Degrees in Biochemistry" at Harvard; they recommended Guidotti. So, Guidotti was invited up to Harvard to see if "they were interested in me and I was interested in them. And so I came up and eventually it worked out…So rather than going back to Washington to do my residency…I came [to Harvard]."

Sequencing his own Hemoglobin

Before coming to Harvard, Guidotti had been part of a lab at the Rockefeller Institute that was working on the amino acid sequence of hemoglobin, which was one of the largest proteins being sequenced at the time. However, due to the limitations of technology at the time, a project of such magnitude also required much larger quantities of substances on which to perform experiments than would be needed today. Says Guidotti, "In those days, to do chemistry, you actually needed gram amounts of stuff, rather than micrograms." In this case, Guidotti's lab required large amounts of one particular substance: blood.

Rather than obtaining "expired blood in a blood bank," Guidotti explains that he offered to donate his own blood to his lab. "When I was [working at the hospital], every six weeks or so, I gave blood to the blood bank…So I said, I can give blood, I'm used to it! So I got somebody in the lab, we boiled a syringe, and I helped the person put the needle in the vein and draw out the blood. And then we

got 50mL at a time…and put it through the machine, the countercurrent distribution [which separates the two chains of hemoglobin], and we got several grams of the [hemoglobin] chains. And then when we needed it again we'd do the same thing all over again." His selfless donation in pursuit of scientific progress is unusual and commendable, but Guidotti tells the story as if it were just a routine part of his life. Even after many years of formidable research, he remains remarkably humble.

Further Research at Harvard

After coming to Harvard, and ten years or so of working on hemoglobin, Guidotti's research migrated from proteins inside the red blood cell to those in the membrane. Eventually, he came to focus on other cells' membrane proteins, such as the insulin receptor and the Na+/K+ ATPase. As Guidotti's research shifted, one thing has remained constant throughout his years of research: his passion for proteins. It was not known "in the early times," says Guidotti, "that proteins could change conformation, and have a behavior depending on conformational change." To this day, Guidotti is still fascinated by the unknowns in protein chemistry: "How can a protein, that seems to be sort of fixed in its arrangement, end up being so flexible and do so many things? How does it manipulate that? We have a protein that sits in the membrane with transmembrane domains. The transmembrane domains you'd think would be there holding the protein in, but they're moving around all the time, and they flip back and forth. Why? I mean, it's completely crazy business!"

A Legacy of Humility

When asked which aspects of his career he is most proud of, Guidotti makes no mention of any research achievements he and those in his lab have made (such as successfully sequencing hemoglobin and being the first to isolate the sodium pump), or teaching awards he's won, such as Harvard's Phi Beta Kappa Prize for Excellence in Teaching in 2000 (Johnson 2011). Instead, he humbly highlights his passion for his work, and the contributions of others to his career: "All the research has been interesting…and I was glad that the graduate students in general did well." And on how his graduate students were able to perform such great work? Guidotti cites the fact that his department, with powerhouses like James Watson and Matthew Meselsohn, "was a very eminent department and students came and flocked in." According to Guidotti, when other labs in his department were full, students ended up asking him to join his lab. "And so I got lots of great students," he says with a laugh.

It's not just through his words that Guidotti under-credits his work; in fact, he is well-known for having a small bibliography that is largely misrepresentative of all that he has contributed to the scientific world, because he refused to take credit for work that he didn't put as much manual work into (ASCB 2009). Says Guidotti, "I wasn't even on the papers [my graduate students] published unless I had worked manually in the operation. Because I mean, advice is easy to give, but the work is tough. Unless you work, you shouldn't, in my opinion, get your name on the paper." In a setting where publishing is key to academic survival, such a view is rare and unique. Yet, perhaps it is a simple demonstration of Guidotti's pure drive and energy to perform good scientific work regardless of credit, and further, what he believes should be the emphasis in research: the fascinating process of discovery, not the accolades and recognition that may result.

To Prospective Researchers

According to Guidotti, research is all about asking questions, and then searching for the answers to these questions in order to find out more about the unknown. "Research is [done on] something that is not known, and [when] you think you have a way of answering that question, you go ahead and do it, and if you get an answer of course it may be wrong, because you don't always see the whole picture. [But] at least you got an answer to something, and usually when you get an answer, it opens up another view of what you might do next."

Aside from emphasizing the question-and-answer aspect of research, Guidotti advocates for basic science research. According to Guidotti, applied research is important, "but if one wants to do it with knowledge, one has to understand what one is doing…Curing cancer doesn't mean just making drugs and applying them to cancer and seeing if you can kill the cancer. You have to understand what the cancer, what the cell is doing." Ultimately, Guidotti advocates for medical research methodology that does not attack disease before achieving a careful, rigorous understanding of its foundations. He emphasizes that curing cancer, for example, should not be "a war on cancer…Science doesn't work by wars. Anytime you make a war on something, it never works…Because one has to understand the physiology, the behavior of a cell." Guidotti concludes: "People who are interested in research…have to think about what the normal behavior of the system they are looking at is."

References

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