Following your interests: The importance of good mentors

Daniel J. Klionsky

This is not a tale that starts out with great scientific insight or well-engineered plans. Rather, it is one of happenstance and following one's interests. But it is also a story of talented instructors and mentors who led me in the directions that ultimately resulted in my current position. I wish I could say that I knew very early on that autophagy was going to be a great topic to pursue, and that it would develop into this tremendous field with hundreds of scientists following up an incredible diversity of connections. However, that would simply be a lie. In fact, when I was an undergraduate student at UCLA, I did not even realize that cell biological research would become the focus of my career.

At that time getting a position in a lab was not very easy, as few labs took undergraduate students, at least in my experience. So, other than the standard laboratory courses that I had to complete during my degree, I had essentially no idea of what real laboratory work was about. I had entered college with many advanced placement credits, and was thus able to replace several required courses with a number of electives. I chose animal behaviour and animal physiology, and spent an entire ten-week quarter on Catalina Island learning about marine biology, but did not know much about molecular biology (perhaps it is worth noting that I started out as a history major). One course that ended up playing a pivotal role in my career was a speciality course on electron microscopy taught by Fritiof Sjöstrand. There were at least two aspects of this course that I found fascinating. First, it was my initial detailed exposure to electron microscopy, and Sjöstrand made it clear that interpretation of the images had to be very careful. Second, and more importantly, one of the main topics we covered was the mitochondrial H^+-translocating ATPase. Thus began what would turn out to be a long-term fascination with this enzyme.

When the time came to apply to graduate schools a year later, I still did not have a very good idea of what I wanted to do, and applied more or less equally to marine biology and biochemistry programmes. I was very close to choosing the Scripps Institution of Oceanography and the lab of Victor Vacquier, when I interviewed with Robert D. Simoni at Stanford University. After talking with Bob, I knew without a doubt that this was the person I wanted to work with. In part, I also found the project attractive, as it was on the assembly of the H^+-ATPase of *Escherichia coli*, which reignited my dormant interest that had started with Sjöstrand's course. I never regretted my decision to forsake marine biology to join the Simoni lab. Not only is Bob a wonderful person, but he remains a mentor for me.

I had a fantastic time in graduate school and after obtaining my PhD I decided to continue my training as a postdoctoral fellow. During this time, I was fortunate to have another wonderful mentor, Scott Emr. One of the projects in Scott's lab involved identifying targeting signals for the mitochondrial ATPase subunits. Because of my background I felt very comfortable with this topic, and I also wanted to work on protein targeting. However, I wished to try something new and elected to avoid the ATPase project, focusing instead on identifying the targeting signals in vacuolar proteins. But I did work for a while with another postdoc, who had joined the lab before me and was analysing the targeting of the β-subunit of the F_1-ATPase, thus satisfying my desire to keep my research somewhat connected with this complex.

When I started my own lab at the University of California, Davis, I initially pursued an analysis of the targeting signal and pathway used by the vacuolar alkaline phosphatase, Pho8. While I was still in Scott's lab I had discovered that the vacuolar delivery of Pho8 occurred by a mechanism that was somewhat distinct from that of other proteins targeted to this organelle, such as Pep4 and Prc1. In particular, Pho8 delivery was not affected by bafilomycin A1, a vacuolar ATPase inhibitor whose use in experiments was relatively new at the time. Thus, at Davis, I reconnected with my earlier interests by starting to work on the V-ATPase, initially as a collaborative project with another mentor, Nathan Nelson, and later independently.

How all this work on the ATPase led me into autophagy will have to be another story. I will end by saying that although I certainly hope that my science will have an impact, I think that my teaching and mentoring will probably affect a much larger number of people. I am glad to have had such fantastic mentors during my career, including Bob, who has been my role model for setting up my own lab. Finally, I find it very difficult to answer when students ask me what would be a good direction to pursue in their career. Follow your interests and work with people who inspire you, is the best advice I can offer.

COMPETING FINANCIAL INTERESTS
The author declares no competing financial interests.

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