Perspectives on Research
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jur: What are you currently doing in your field of research?

Culver: In general, I’m looking at the factors that are inside the protein coding sequence that influence the amount of protein that is made. In particular, I am interested in how the genetic code itself, the synonymous codons that are chosen, affect the amount of protein. I got there in a circular way, doing an experiment with Eric Prakash and Stan Fields in a functional genomics experiment, where we made a library of every yeast gene fused to a purification tag. We did that because we had a set of 6,000 strains, and each one expressed a particular polypeptide. We could use that to assay for a biochemical activity and then know what gene caused it because you could purify every one of those genes by an affinity method, put it in a pool of 100 proteins, assay for a biochemical activity, and get right back to the strain that was responsible for it. So, that was called biochemical genomics. That was where I started making genomic libraries. And then, I made [a genomic library] with Eric and Mark DuMont and Mike Snyder at Yale. The weird thing is that you have a thousand-fold difference in expression in this library where you have the same promoter, same terminator, the exact same context, and the only difference is the protein coding sequence. That meant that the protein coding sequence has a lot to do with how much is actually made. We weren’t the first people to know that codons affect things. So that’s what I study now; how the actual genetic code that codes the proteins affects how much is made.

jur: Education-wise, how did you become interested in your current field?

Culver: I went to an all-female Catholic high school, and at the time I attended, not that many people went on to college. A few people were going to the University of Illinois, and other people were going on to two-year colleges. My mother had gone off to St. Louis, and she was one of the few women in her generation who had gone to college. She then went to Johns Hopkins to get her bachelor’s degree. My dad was a doctor, so my parents were encouraging. I went to a small college in Appleton, Wisconsin, called Lawrence University. From there, I had classes with all of the biochemistry majors. It was amazing. It was great because it was a real confidence builder. I left there, went to Cornell, and worked with Jeff Roberts. Then I worked on bacteriophage lambda and the Q protein. I wanted to move on to eukaryotes, but onto something that I can grow quickly. I moved on to work with yeast at the University of California at San Francisco. Because of the combination of the two people I worked for, I was really lucky. Both [researchers] were fantastic and very different. Jeff was extremely smart, very analytical, and really deep. I learned a lot from him. Ina, who died a few years ago of cancer, was very creative and imaginative; so, it was like a study of contrasts. But I just thought I got really lucky that it worked out in both labs I was in. The people there were smart; they were fun. The whole field was also smaller. It was much easier to imagine yourself solving great problems.

jur: Why do you think research is important?

Culver: Basic researchers are the prospectors, finding the areas that people who do translational research later on might in fact find interest in. We contribute [to the fact that there’s information] there for manipulation. It changes the spectrum of drugs available. I think that both types of [research] are very important, but they are fundamentally different. I think there are people whose research is directed at problems that they know impact health, and there are people who are interested in addressing questions that have potential but need to be figured out first. Basic researchers also develop the tools. An example is the genome sequence – when a genome was first sequenced, in a sense, you could say it was a string of A, G, C, and T. You need to figure out how you’re going to make use of that information; there’s no guidebook.

jur: Are there any roadblocks that you have faced?

Culver: There are huge roadblocks. There are times when you’re doing research and you have to rethink yourself. Sometimes you have to go a different way than you might have thought, and find something to do in there that works.

jur: You mentioned earlier that you were part of a few chemistry students – that was hard for you?

Culver: That was actually easy. The Biology department had a lot more students. I had actually taken college chemistry and never taken any high school chemistry, and when I went into it, the professor said that the last five students who did this failed it. He said that if you get into any trouble and don’t understand the lecture, come in and ask me. And I did that. And I understood it all, but that kind of attention was really good. And in graduate school, there was one other woman in my class. So, I wasn’t completely alone. I didn’t really encounter any sexism in graduate school or as a post-doc I did on the job market—that was the first time—in that somebody said, “Our wives are good biologists, but we husbands have the jobs.” I’ve never quite forgotten that.

jur: Do you have any advice for students who are pursuing something similar to what you are doing?

Culver: I think students and all young people should do what they love to do, but the other part to that is that you don’t always know what that is. So, in the end, you pick something and try it, and you can’t afford to pick. And if you pick something that’s not right for you, don’t be afraid to change. My dad told me that you’re going to spend a lot of your life working, so you have to like it.