Interviewer: Hello and welcome to Annual Reviews Audio, a podcast from Annual Reviews where insightful research begins. I'm your host, Mia Lobel. On each episode of our show, we'll speak with a top scientist in fields ranging from astrophysics to sociology. Today, we'll talk with Susan Gottesman, Chief of the Biochemical Genetic Section of the Laboratory of Molecular Biology at the National Cancer Institute and editor of the Annual Review of Microbiology. Dr. Gottesman thanks so much for joining us. So before we get to what you're working on now, can you tell me what first got you excited about science?

Susan Gottesman: Certainly, I was given a book called Microbe Hunters to read by my father when I was in about fifth or sixth grade, I think? It's a book that was, I think, a best seller maybe in the '30s or '40s, so this was a number of years after that, but it was a very accessible look at how people first were able to look at bacteria, how they were first able to understand that bacteria caused disease. It had a combination of enough science to really appeal to me and enough drama to make me think that that would be an exciting to do, and so
I became very interested in bacteria.

*Interviewer:* So was this like the Nancy Drew of microbiology?

*SG:* Well, so this was a non-fiction book with chapters on Pasteur, chapters on the first attempts to make vaccines, on the first evidence of that Yellow Fever was caused by a microbe, had the first attempt to make a microscope—but Nancy Drew was something I was reading at the same time, no question about it. So you know the idea of solving puzzles was something that I really liked and that combined with how you could even isolate a single bacteria—they described how somebody learned to spread it out on a slice of potato and so colonies would grow up, and that was the first time anybody had been able to sort of get isolated a kind of bacteria separate from everything else to study. And so something about all of that really excited me.

*Interviewer:* So when you got to Radcliffe in the early ’60s, did you then know that you wanted to be a scientist as a career?

*SG:* Well, that was what I had in mind, yeah. So I mean, after, when I was in high school, I was able to do some summer programs that put me in a lab. Mostly lectures, but also some experimental work and I really enjoyed that. So that was, I certainly applied to college with that in mind, although other things interested me also. So whether I would have necessarily stuck with it if things had gone another direction, I don’t know. But that, I applied with the idea that I would be a scientist and that I would work on bacteria.

*Interviewer:* Was there a particular class or a teacher that really inspired you on that path?

*SG:* Well, you know I think more than a class. I took a lot of classes and I enjoyed some of them, some of them I wouldn’t say—the science classes weren’t always the most exciting. They had what was called a tutorial system in which I was paired with a senior scientist, well, I mean some of them were graduate students, but actually my tutor was in fact, a full professor at M.I.T., and who tutored a lot of undergraduates. And so I met with him regularly and we read papers and we discussed science, and then I did research in his lab. So all of that was very appealing. In fact, I met him very early on because my freshman year, I was in something called, the freshman seminar, which was again, lab based. And I just liked playing in the lab. So any chance I got to play in the lab, I did. And that’s what kept me very interested.

*Interviewer:* Was that unusual for a woman back then?

*SG:* Well, yes and no. So classes at Radcliffe were totally integrated sex wise at that point, so my classes were with the men. The woman who ran the freshman seminar that I took was actually run by the woman, Mary Bunting who was then President of Radcliffe. And she was actually a microbiologist, so there were a few people around. There were—none of my professors were women. And certainly, Radcliffe, in terms of telling me what courses to take or advising me hadn’t a clue. But there were certainly other women interested in science and doing science around me and I’m not sure it occurred to me that it was unusual. I actually had a very good time. I was in a physics class, which was mostly men. I met my husband there. I met other people that I went out with. You know, it was a lot of fun and I got to do the science too.
**Interviewer:** Can you point to a specific moment that you got really excited about biochemical genetics?

**SG:** Well, so, you know, to some extent biochemical genetics is a made-up name because these sections have to have some combination of names that are unique. And I actually inherited the name of the section from the previous person, so—but genetics was what appealed to me and probably, I got into that as, mostly when I was a graduate student. So it was in the lab of John Beckwith at Harvard Medical School and he’s a superb geneticist. The way one thinks about solving a problem with genetics is figuring out how to get the bacteria to do the work for you and tell you what’s going on. And then you want to take it to the next step and find out whether what’s going on, what you’re inferring from the way a colony grows or doesn’t grow under various conditions. How that, whether that’s really reflected in what’s happening at the level of the DNA, so then you have to go into some biochemistry or at least some molecular biology and be able to look at what’s being expressed.

So that combination—having the genetics tell you where to look and then looking—opening up the cell and looking and getting the answer that you expect is really exciting. And that’s what was going on in Beckwith’s lab when I was there. And then one of our first projects here, we made some predictions from fairly complicated genetics, we went and did the experiment, and sure enough the protein we were looking for was doing exactly what we expected, so that, there’s nothing more fun than that.

**Interviewer:** What would you say is the most significant incident or occurrence in your research so far? Was it there at Harvard?

**SG:** No. I mean, my proj—in terms of the weight of the results or the importance of the results?

**Interviewer:** Kind of the thing that just made you go, “Okay, this is why I’ve been doing this kind of work for my career.”

**SG:** Well, you know I’m not sure that I ever thought anything else. As long as I was in the lab playing, even the day-to-day stuff that can be boring a bit is fun; figuring out the little problems along the way. I think what we all need in terms of going forward with a career is that we can do it; that is we can actually figure out something of worth and have it come out right. And that probably waited until I was here on my own a little bit—or no—let me back up. I had, I sort of started a new project while I was at M.I.T. for a couple of years and made some predictions. And they checked out and it sort of opened up a whole new field that I then started to pursue. That probably gave me the feeling for the first time that I could develop something de novo, by myself, and get it somewhere, you know, achieve something.

**Interviewer:** Was there ever a point where you doubted what it was you were doing and your choice to sort of dedicate your life to microbiology?

**SG:** Not really, partially because it worked out pretty easily for me. I think when I was in college, when I went into college the courses that most interested me weren’t the science courses, necessarily. I mean I was interested in history and sort of political science; I took a lot of courses of that sort. And if I hadn’t ever been in a lab before I got there or while I was there, I might have been tempted to sort of leave the science behind because the courses weren’t so exciting, but I
couldn’t imagine not playing in the lab, and I couldn’t imagine a career in which I read and wrote and didn’t do other things. So it just was something that always appealed to me and I was able to do it without a lot of suffering.

I mean, I got to do what I wanted to do at each stage, which made it particularly attractive. I think the things that frustrate people are difficulty with funding, difficulty finding jobs in good places, difficulty with who’s around them, their interactions, and I’ve really been very fortunate in having wonderful colleagues and wonderful support for most of my career.

*Interviewer:* To what do you attribute your success in that when it is so hard for some scientists to get the funding they need to do the work they want to do?

*SG:* To some extent, pure luck and serendipity. I mean, we first came to the NIH as postdoctoral fellows because my husband had an MD and he would have been drafted otherwise. So I don’t know that I would have ever thought of coming to NIH otherwise. We came, we had a good time here, we left for a couple of years, and when we were looking for jobs we knew we liked it here, and we got offered jobs back here. And I have to tell you, NIH is really heaven in terms of doing research in a way that takes away all of those distractions. We’re supported without having to write grants. Space is tight, there are little annoyances now and then, but basically it’s a wonderful place to be. So we ended up here partially by accident and you know, we have thrived here, and there was also a very strong community of people doing things that were related to what I do. So that makes it all a lot more fun when there are people who are interested in what you are doing that you can talk to, argue with, hear what they’re doing, hear about the latest things that are going on; all of that makes it easier to do good science.

*Interviewer:* How important has that community been in the work that you’ve done over the past couple of decades?

*SG:* Oh, critically important. I can’t imagine—I don’t know of scientist who can invent everything themselves and figure out how to do everything themselves. We get ideas from everybody we talk to, everybody we hear, everything we read, and we integrate it into what we do and try to adapt it to what we do. And having a really active group of people that you can bounce ideas off of that will tell you that they don’t believe what you’re saying, that you better get better evidence. What’s interesting, what’s not, and just hearing what gossip they gather about what’s going on in the scientific world and what might be interesting directions; all of those are really critically important, and make it—aside from being a lot more fun—a lot more productive.

*Interviewer:* Can you tell a little bit more about what’s so great about the lab? I mean, you’ve talked about that from your first days of Radcliffe all the way through. What is it that’s so interesting, and fun, and exciting?

*SG:* Well so, so I can do an experiment one day, put my petri dishes in the incubator overnight and in the morning I have colonies growing up that are different colors that tell me something new about my bacteria. So I can basically do an experiment quickly. I can come in and look at it the next day, so I come in and, well, I don’t get to do experiments as much anymore as I did when I was earlier in my career. You come in and it’s like you know something exciting is waiting there each day. And I like the little problem solving, I mean, that’s what I like to do. So even the trying to make an experiment work that should be working and figuring out why it didn’t is a challenge.
And it’s different every day. I mean there’s nothing repetitious about the kind of science we do although some of the procedures might be repetitious, but there’s always something new. So that keeps it interesting. And I like to puzzle at things, so even when I’m doing something that’s relatively repetitious, I’m thinking about, “Well, if I did this a little differently or if this works, what will it mean about how the bacteria’s working? How it’s responding under these conditions?” So I can sort of worry around it in different directions while I’m sitting there with a toothpick streaking out a bacterial colony or streaking out 50 of them. So it’s the combination of, and I just like, I guess just the, it’s restful to do some of those tasks. It’s not just sitting, it’s standing and pipetting and doing other kinds of things that are, that I find very restful.

**Interviewer:** Where do you see microbiology going in the future, in the next say, five years, ten years?

**SG:** Well so, so the big change that’s happening—and it’s already started to happen—is that I work on a bacteria called *E. coli*. It’s the basic model system or one of a couple of models systems that we’ve been able to manipulate and understand for years. We learn things in that organism, but now we’re getting the genome sequence of many, many other organisms, we’re understanding how those other organisms interact with each other. There’s a huge attempt to get all of the bacteria, the sequence of all of the bacteria say, in the human gut or on the human skin, or in various diseases. It’s never just one isolated kind of bacteria doing something, it’s a whole set of them interacting in complex ways.

And we’re starting to have the tools to try to dissect that much, much more complicated business. And so that’s going to be happening for sure over the next many years. And our ability to sequence as well as our ability to analyze in new ways are opening up all kinds of possibilities.

**Interviewer:** How does it feel to think back to the lab that you started in when you first started in this field to where things are now? What stands out as sort of the most noteworthy event?

**SG:** Well, I mean, I think it’s the change in technology and what we can do. Somebody just asked me about a strain I had made where I had mutated a gene and we did it probably 20 years ago. And I pulled out the paper to look at how we had done it and realized how hard it was to do something like that then. It took us weeks and we didn’t get exactly what we wanted. And now we can manipulate the organism in days in any way we want so the advent of recombinant DNA technology, the advent of PCR, all of these techniques for manipulating DNA, the advent of sequencing what we have very quickly—they’ve changed what can be done so that, it used to be, you had to think hard about how to do it. Now you have to think hard about what it means after you’ve done it. The time isn’t spent with just trying to get there. Things go very quickly.

**Interviewer:** I know you’re quite modest in attributing a lot of your success to luck and your colleagues and all of that, but what would you say is the achievement that you’re most proud of?

**SG:** Well, I think we were the first to show that protein turnover, that the ability to grade proteins was important for regulation of how genes are expressed and how functions are expressed in all organisms. And we were doing it in bacteria before it really became important anywhere else. It’s probably the major thing that our lab was first at. And we were sort of following the genetics and then going back to the molecular biology to do it. Other, more recently, we’ve gotten into these
small RNAs that also regulate gene expression; that’s been very exciting, but certainly a number of groups were doing it in parallel and we all interact and our lab plays an important role there, but I certainly wouldn’t take primary credit for that.

Interviewer: What does it mean to be selected as the editor of the Microbiology Review for Annual Reviews?

SG: So it’s a challenge, but it’s really an exciting job in the sense that’s it’s a way to look at the whole field of microbiology from a bit of a distance. What the job really consists of is sitting around a table with a lot of other microbiologists once a year and coming up with every idea you can think of about what would be good to have reviews written about and then convincing people that they should really write these. So thinking about what needs to be presented, how to get people to present it well, trying to see ahead two years because it’s a book rather than something that comes out very frequently. We’re planning well in advance. It’s a little humbling when I realize how many of the articles in the Annual Reviews educated me over the years, but that’s where we tend to go first to find out.

You know, you’re starting a new field, you want to find out what’s known about it, you go there and find out who’s written what and what they had to say, and then start thinking about it from there. So it’s important to remember who our audience is and try to find people who will speak to those audiences. But it’s a lot of fun and it’s not actually a whole lot of work because the staff does a wonderful job.

Interviewer: What would you say to someone getting started in microbiology, who’s looking at this review, or someone who’s beginning their graduate work, and is sort of looking at the field as a whole?

SG: So I mean, the thing I say to all young scientists is that it’s not worth doing unless they really love it because it’s a pain in the neck. I mean, it’s not like you’re ever done, it’s not like—you’re always feeling like you need to read more, you have to keep up with things, you have to—it’s not a relaxing kind of lifestyle in that sense. But if you love it, it’s exciting from beginning to end. And I try to tell people not to get too narrow I mean, we all work on what is our own stuff and we need to know that intensely. But if you can at least listen and read more broadly, you’ll be surprised at the connections you can make and the directions you can go.

So there are things that I learn in seminars that I didn’t think there would be anything for me, but I learned something that helps me make my research better, and the same is true for reading review articles or reading other kinds of articles. You pick up things that you don’t know you needed to know, and so if you keep your mind a bit open and have at least some of your time free enough to listen more broadly, your science will be better, and you’ll find new directions to take things.

Interviewer: Wonderful. Dr. Gottesman, thank you so much for joining us.

SG: It’s been my pleasure.

Interviewer: You’ve been listening to Annual Reviews Audio. Next time we’ll speak with Sandra Faber, coeditor of the Annual Review of Astronomy and Astrophysics. For over 75 years, Annual Reviews has guided scientists to the essential research literature in the biomedical, life, physical,
and social sciences. Learn more at Annual Reviews.org. I'm Mia Lobel. Thanks for listening.