Interview with Linda Birnbaum, Ph.D., D.A.B.T., A.T.S.

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JM = John Maruca, interviewer
LB = Linda Birnbaum, interviewee

JM: We have Scientist Emeritus and former director of NIEHS and NTP, Dr. Linda Birnbaum. To get started, let's talk about your role as a scientist. Have you always been interested in science, and how did you get started?

LB: Well, it's kind of a story going back to when I was a kid. I did always like science, but it wasn't something that girls did 60 years ago. When I was in junior high school, I was a cheerleader and I had a science teacher who was young and peppy and married, and she made it okay for girls to like science. I then proceeded to take lots of science. I enjoyed the fact that I was always one of the only girls in the class at the time, and I was successful in what I did. So, I actually won the New Jersey State Science Fair in about 1961 and was sent as the New Jersey delegate to the Youth Conference on the Atom, which was in Chicago. That was very exciting. There were Nobel Laureates. There were scientists from all over, you know, representatives from every state who had won their science fairs. And it was just an exciting, energizing thing. I did well in science. I think it made me a little different.

JM: From that point on, tell us about your academic background.

LB: Well, when I graduated high school, I went to the University of Rochester, and I graduated in three years there. My husband and I had met when we were in summer camp, and we planned to get married as soon as we graduated college, and that's where he was going to college. So that's where I decided to go. We knew that once we were married, we'd be on our own. So, I decided I would just graduate in three years. And I was lucky. I had several advanced placement courses in high school that I got a credit for, and then I went to summer school, actually at Columbia in New York, two different summers and got all the credits I needed. So, graduated in three years and my husband and I were married three weeks after graduation. We both were going to go to grad school. He was in mathematics, and I didn't really know what kind of biology I wanted to do.

So, I applied to six different universities, the same ones my husband was applying to in math, and I applied to a different biology department in each one. So, one was zoology. One was [inaudible]. One was physiological psychology. Physiology. You name it. And we ended up going to the University of Illinois Champaign-Urbana because that's where we both got in and got the most money. And I ended up initially in a cell biology training program that was run by the microbiology department, and I ended up majoring in microbiology. But at that point in time, to kind of call yourself (that you majored in microbiology) was you took one course and you taught one course. And that was kind of my qualifications. Most of my coursework as a graduate student was in biochemistry and physical chemistry. And I loved what I did. My lab work was in

the microbiology department, and I was actually the first person to map the genes for ribosomal RNA in E. coli.

And then I was actually able to transcribe those genes, using an RNA polymerase that I isolated into the RNA. So, it was pretty exciting. It was a lot of fun. What I did that took me, I would say, over three years of lots and lots of scutwork could probably be done in a matter of a week, maybe less today, because this was before we had all the technological developments and knowledge that we did today. When I finished, I actually finished a semester before my husband did at Illinois. So, they asked me what I'd be willing to teach, be a sabbatical replacement, really, for the second semester of 1972. And at the time I was teaching molecular genetics. So that actually had somewhat of a genetics background, as well, at that time. When we left Illinois, we had decided that we would follow my husband's career at the beginning because I was pregnant with our first child.

And so he got a position at Amherst College in Amherst, Massachusetts, and I wrote a Damon Runyon Postdoctoral Fellowship and got awarded one. And I was doing that in the biochemistry department at the University of Massachusetts. So, we stayed there two years. Then my husband moved to Hamilton College, which is in upstate New York. And I was able to get a position at a girl's college that was affiliated with Hamilton called Kirkland. I was kind of excited about that because I loved teaching and I loved being with students. I learned pretty quickly that at a small college where you had a very heavy teaching load, there was no time to do any research. I had thought that I would be able to get my students involved in some kind of relatively modest microbial or molecular genetics work, but there just wasn't the time. We also had our second baby at that time.

So now I had two kids, 2 and under. Hamilton announced about halfway into that year that they were taking over Kirkland. And the idea that a faculty wife could be faculty was something that they were not willing to consider. And you need to realize this is in the mid 1970s. So, I was kind of up a creek without a paddle in a sense. We were living in an area that there wasn't a lot around. There was a small branch of the State University of New York in Utica. And I taught a basic genetics course there for a semester. And then I was able to get a research position at a laboratory on the grounds of the Masonic Home for the Aged in upstate New York. And the focus of this laboratory was to solve the problems of aging. And there was a group there that was looking at the biochemical changes associated with aging.

And that is kind of the winding road that eventually led to my getting involved in toxicology, because I wrote a NRSA, which is an NIH postdoc and was awarded one to study the age-related increase in cancer, using the hypothesis that our ability to handle carcinogens, our metabolic capability, changed as a function of age. So, I worked at the Masonic lab for four years, but I would say after about three, my husband and I both said we didn't think that that's where we wanted to spend the rest of our life. Now it was my turn to be the leading spouse to find a job. And we started looking, and there was a lot going on in North Carolina. Several of the enzymes that I was looking at, the cytochrome P450s, for example, there was a group at NIEHS that were kind of the leaders in the field.

And there were some also great work going on, both at North Carolina State and at UNC Chapel Hill in the area of drug metabolism. So, I kind of was interested in this area. And then, my sister and her husband moved to this area because he was doing his residency and fellowship at Duke

University Medical Center. So here was a great opportunity. I was brought down, I applied, you know, one of those things where I just answered a job ad from NIEHS. I was asked to come for an interview, which I happily did, and the person who interviewed me was Skip Matthews. And some people may remember Skip, who retired, I want to say probably in the early 2000s from NIEHS. But anyway, that's how I came to NIEHS, actually, in August of 1979, as a senior staff fellow, which at that time was essentially a tenure-track position. So that's how I got to North Carolina and never left.

JM: So, tell us about your research here then from then on.

LB: I realized when I got here, I was in the novel new National Toxicology Program, and I didn't even know what toxicology was. I literally went to the dictionary and looked it up to find out what it was, and my first day or two at NIEHS, Skip gave me a project to work on, which was to look at the pharmacokinetics of the chemical, that it was very closely related to TCDD, the contaminant that caused agent orange problems. So, this was a chemical called TCDF, and there was a scientist at NIEHS named Jim McKinney, who had done a couple of studies with TCGF with Guinea pigs and it looked like it should be equally toxic in the Guinea pig to TCDD. And that was the assumption we had. So, we knew that one of the reasons TCDD was such a problem was because it had such a long half-life in the body.

So, Skip to helped me to design my first pharmacokinetics study. We assumed that it would have a half-life of somewhere between 10 and 20 days, and we designed this study that would go on for a couple of months. Well, to our surprise, within two days, well over half of the TCDF had left the animals. And that was the beginning of my work with TCDD and all the related dioxin-like compounds that I spent the 10 years that I spent at NIEHS from 1979 to 1989 studying. So, I got very interested in these dioxins and related compounds. They're highly toxic. The dioxins and the furans are never intentionally produced. They were unwanted contaminants of different industrial and combustion processes. In addition to doing the kinetics, I worked on a scheme to look at the relative potency of these different chemicals, which is driven both by their binding to a specific receptor, which was really first identified at NIH in the 70s, but not isolated until the 1990s. The basis for what we worked on to understand relative potency was the kinetics and the binding to this age receptor.

So, I did a lot of work in that area, and I helped develop what was really a bioassay where dioxins caused a very explicit syndrome of birth defects in mice. So, at very low doses, it affected kidney development and it caused cleft palate. I did lots of developmental toxicity studies in mice, looking at a range of these compounds. And we were able to actually use that as the basis for the relative potency. This led into much of the work that we do (had a huge impact actually) on risk assessment, because the relative potency scheme of which this played a part is how EPA and much of the world actually regulates the dioxins that are present in soil and sediment and food, and even evaluates what's present in people. And it actually ended up being kind of set in stone by the World Health Organization at a series of meetings that we had looking at the relative potency of these compounds.

So, I was doing development. I was doing mechanisms of toxicity. I was doing the kinetics. Sometimes we had surprising things. The first thing when I first came on board, and this TCDF came very rapidly eliminated from the animals. We never expected that. Then we had an interesting related compound called hexabromonaphthalene, which did have dioxin-like effects

in Guinea pigs, and I was going to study that. Well, we expected it to hang around a long time. Again, about 60% of it was very rapidly metabolized and eliminated. Twenty percent of it stayed in the animal. And that was the basis for its dioxin-like toxicity. Other scientists at NIEHS had published papers saying it was only one isomer of this hexabromonaphthalene. And it turns out it was two, but the methods they had used were not sensitive enough to detect it. The animals could tell it, but the chemistry at that point in time couldn't. So that was kind of an exciting happening that we found.

JM: What scientific advances would you like to see in your field in the next five, 10 years?

LB: My career now spans over well over 40 years. And I think there have been tremendous changes in how science is done. So, there are all kinds of new techniques and new tools that we can ask different things about. I really believe that all the answers are not found in genetics, certainly not genomics. That may be the groundwork upon which the environment acts. And the environment acts by many different ways. There's also different kinds of environment that we need to talk about, but the environment can cause changes, not in the basic sequence of our genes, but in how genes are turned on and turned off. I can remember when the genome was first sequenced. Before it was sequenced, I think most people thought that humans were going to have a 100,000 genes, maybe more. And it turned out that they weren't that many. And we understand why now.

And it's because genes are expressed in different tissues in different times. For a long time, we always said, "Oh, you've got the same DNA in your skin cells, and your lung cells and your bone cells." And then we'd wave our hands and say, "So why are lung cells not skin cells, not bone cells, and so on." And we now know that it has to do with what genes are turned on when and where. And I think that that whole epigenetic understanding is huge. We understand that not only is the epigenome controlled during development, and if you mess it up, you're going to have developmental problems. Whether they are structural changes or functional changes, what happens in development doesn't reverse. It doesn't go away. But we also understand that the environment can modulate the epigenome. In a sense, it's something we've known for a long time. Certain cancer drugs are actually epigenetic agents, which turn on genes and turn off genes, for example, in tumors.

And many environmental agents can also alter the epigenome. And I think that's really been an important understanding. Now, the kind of data that you generate today in many ways can be very different from what we did. I was one of those people who liked to instant gratification. So, I loved when I could say, do something in the test tube, or do something in cells and look under a microscope and see things happening right away, or at least get data coming out of the centrifuge or the scintillation counter, you know, within a couple of hours so that I could see what was happening. Today, the amount of data that's generated is tremendous. And it's not something that you can frequently analyze yourself by just looking at a graph. I've never been very good at saying, "Where do I want to be in five years or 10 years?" But I think it's very, very important that we understand that our health is not just our genes and not just our environment. There's always an intersection between the two. And I know we're developing CRISPR-Cas9 and other methods to modify genes, but it's still a lot easier to change our environment, if we know what in our environment is causing a problem.

JM: Alright. Name one skill that you think every scientist should possess.

LB: Communication. Number one. Maybe I'm not being fair here because communication — there's both written communication and oral communication — but you need both. And I would say that one thing that has evolved, at least while I was director, there was more and more attention that was paid to giving our scientists and our non-scientists communications training, especially oral training, and a lot of opportunities, especially in the younger scientists, to practice what was so important to learn, because people have to understand what you do. When I tell kind of a funny story, my kids know a heck of a lot about TCDD and related compounds, because I used to practice my talks on them from the time they were in about fifth or sixth grade. And what I learned is that you need to be able to speak a language that people can understand. And all too often as scientists, we speak our own language, and it's important to be able to speak so that people can understand. I am a big believer in engaging communities and engaging citizens in the work that we do, especially environmental health. I don't think you can do it unless you work with communities, because they're the ones who often know that they've got a problem, and they often have some idea of what may be causing that problem, and getting them involved from the beginning, from problem formulation, through conduct of studies, through evaluation of data, and then communication, is absolutely essential.

JM: If you hadn't become a scientist, what career do you think you would be pursuing?

LB: First of all, I might have been a medical doctor, but I kind of have had been thinking about that lately and feeling I probably would have ended up conducting research, but I probably would have been doing maybe more clinical research rather than the more basic science. The other thing I might have been something like an archeologist, except I don't think I would've had the patience to be a field archeologist where I was very carefully on a dig where you have to use a paintbrush and very carefully look for things. Because as I said, I like to get results more quickly. So, I'm not sure; I'm sure I would not have been in English. I would not have been in languages. Languages were always a challenge for me. I would not have been in mathematics, because I'm not that good in math. But I think maybe something in the social sciences, maybe history, archeology, which in some ways is ancient history. I think those are, kind of, some of the areas I might have enjoyed.

JM: Finally, what advice would you give to young people who are interested in a scientific career?

LB: Love what you do. Absolutely love what you do. If you're not, you know, you'd spend every day for most of your life at work. And if you don't have passion for what you're doing, try to find something else. I think it's really, really important. Again, it doesn't mean that you won't have bad days, but if you're not enjoying, you know, if you put things and you put the scales there and the scale that of being happy doesn't go towards the bottom, you may want to look for something else. So, I think that's really important. I think a couple of other things that I would urge people to do is be willing to take a chance. Change is difficult, but change is good also, and it helps you grow. I think that that's extremely important. I think maybe passion and change are two of the most important characteristics. I think other things is be willing to compromise and be flexible, and maybe the compromise and flexible all goes into the willingness to take a chance and change. But I really think it's important that you love what you do.

JM: Well, Dr. Birnbaum, this has been wonderful. Thank you so much for participating today.

LB: It's a pleasure for me to be able to reflect somewhat on my being a scientist and my being director of NIEHS. It was a wonderful time. Truly an honor. I actually spent 40 years as a government scientist, 21 of them at NIEHS; 19 at EPA, but I certainly consider myself an NIEHS-er.