Interview with Thomas Kunkel, Ph.D.

Conducted on August 9, 2017 by John Maruca
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Research Triangle Park, NC

TK = Thomas Kunkel, interviewee
JM = John Maruca, interviewer

TK: Hello, my name is Tom Kunkel, and I'm a member of the laboratory called the Genome Integrity & Structural Biology Laboratory here in the Division of Intramural Research at the NIEHS.

JM: Tom, thank you for joining us today on our history of NIEHS. To get started, have you always been interested in science?

TK: Yes, I've always been interested. I got started, I guess, when I was in the seventh and eighth grades taking science courses, and I did very well in them and became interested in science. I didn't actually know what I was going to be at that moment, but we did the kinds of things that seventh and eighth graders do at that time, including chasing butterflies around fields and thinking about the way the world works. I enjoyed that very much, and I was actually pretty good at it. So that was my first encounter with science.

Then I got more interested as a freshman in college when I ran into a particularly talented teacher and things just grew from there.

JM: So, tell me a little bit about your academic background.

TK: Well, I went to a small liberal arts college, and I studied everything basically. But included in that was scientific studies in liberal arts-type science classes. Again, I was very good at that. I actually wanted to be a farmer, but my family situation didn't work that out because my father had health problems, and we had to sell the farm. So, I started looking for alternatives, and since I was always interested in science, I picked up on that. I got my undergraduate degree at a small liberal arts college, and then I went to the University of Cincinnati and obtained a master's degree. Wasn't sure whether I was interested in a career in science.

So, I taught high school for a little while, and then I got a job and I realized that I was, in my own opinion, more intelligent than the person I was working for. So, I decided to give graduate school another go. I went and got my Ph.D., and I switched from what I had done for my master's to biochemistry. So, I got a Ph.D. in biochemistry from the University of Cincinnati, and that was sort of the beginning. I really enjoyed that very much.

JM: Is biochemistry your main field of research here?

TK: It was for the first 25 years I was here. But then about 10 years ago, we got interested in knowing what we had defined biochemically would also be seen *in vivo*, in cells. So now I would say we are about two-thirds genetics and one-third biochemistry in my research group here at the institute.

JM: And how does your work have an impact on human health?

TK: Well, we're interested in the biochemistry and genetics that underlies the accuracy with which DNA is made, and that has lots of implications for human health. So, we've studied the basic mechanisms responsible for high-fidelity DNA replication. That's interesting to human health because the processes that allow DNA to be replicated with high fidelity are what becomes perturbed in human diseases. So, our research has implications for the origins of human diseases, like cancer or neurodegenerative diseases.

We have a combination of research that studies the normal processes that achieve high-fidelity replication. And then we look at environmental insults that perturb replication, fidelity-caused mutations, and those mutations lead to human diseases.

JM: Is there one discovery that you made that was most surprising?

TK: Yes, several things over the years. Currently, the most interesting one to us is while we've been studying the fidelity of DNA replication, one of the sort of general rules of that research is that DNA polymerases do not readily incorporate ribonucleotides, the moieties that are responsible for RNA. But, in 2009, I had a Summers of Discovery student in the lab working with a postdoc who discovered that that isn't quite true, and the consequences, eight years of work so far, describing the incorporation of ribonucleotides into DNA during DNA replication and the consequences of that kind of aberrant synthesis. That has several implications for human diseases as well.

JM: Think about the next few years. What kind of scientific advances would you like to see?

TK: The biggest one has already occurred and is in a constant state of improvement, and that is the ability to sequence huge amounts of DNA, including the whole genome of a cell. We have been, in the last five years, heavily involved in that effort. So, for years, it's been possible to analyze the accuracy with which DNA is synthesized by using specific genetic tests that monitor one 10,000th of a genome.

In the last 10 years, the technology has arrived where we can now ask that question for the whole genome. So, you get a 10,000-fold better view of the fidelity of DNA replication of a cell. That's still in its infancy, but it's rapidly advancing our understanding of replication fidelity across a whole genome instead of just one tiny little one looking under the lamp post idea. So, we anticipate, and, in fact, we can see in the scientific literature many advances that are being made from using whole-genome sequencing technology to the kind of research that we do. So, we're heavily involved in that, and it's like a lot of modern technology, the cost keeps going down and the throughput for the number of nucleotides that you can sequence keeps going up. So as the technology improves, we anticipate that we will learn a lot more about replication fidelity than we ever knew before, and we're heavily involved in that effort.

JM: So, what brought you to NIEHS?

TK: Well, when I finished my postdoctoral research and started looking for a position, I interviewed at seven places, and the NIEHS was the only one that offered me a position. So, when I first

came here, I really didn't know that much about the institute, but it was one of the more fortunate events in my life, because when I joined here, I joined a collection of scientists who have become very close friends, but have also been as intelligent or more so than I am. So, I learned a huge amount of information from working here at the institute and that continues today. I've had a number of offers of positions elsewhere, and none of them have ever gotten me nearly as excited as the opportunity to come in every day and continue to work with my colleagues here who are very, very bright.

JM: Tell us one skill that you think every scientist should possess.

TK: Curiosity is the most important attribute that any scientist needs to do the kind of work that I treasure. It motivates asking good quality questions, and it never goes away.

JM: If you hadn't become a scientist, what career would you have pursued?

TK: I would have tried to be a farmer. I grew up with eight brothers and sisters in a very low-income family. Most, not all, but most of my brothers and sisters and relatives are blue collar workers. We treasured education mostly from my mom. My dad never finished the eighth grade and never made more than a few thousand dollars a year. But in that large of a family, we lived on a very small farm, and we loved it. I would have tried to be a farmer, but then we had to sell the farm, and my career took a different path. I've never regretted that. But if I wasn't a scientist, I would have at least tried to be a farmer.

JM: You have any advice that you would give young people who are interested in becoming scientists?

TK: In my opinion, the most important criteria for any person deciding what they want to do as a scientist is very personal, and they need to give that a lot of thought beyond what they're doing at that moment to try to have a five-year plan, which can evolve and often does, and is very, very different. I had postdocs join my lab who tell me what they want to be, what they want to do when they leave the lab, and about half of them changed their mind before they leave.

So it's okay to adjust your plans based on what it is that you find interesting to do, but if you don't at least think about what it is that you want to do three, five, 10 years from now, then the chances of you achieving that goal are much less, so you need to think ahead. I've had postdocs who have chosen to do very different things from what they told me when they first came, and I'm perfectly fine with that. I've had postdocs who have switched their goals halfway through, and then came to me and said, "I have to apologize for this." I tell them, that's ridiculous. In your planning, it's your life, not anybody else's, and you have to take advantage of your strengths in deciding what it is that you want to do.