NIDCR Oral History Project

Interview with Dr. Lawrence Tabak

Conducted on August 24, 2023, by Kenneth Durr

KD: This is an interview with Dr. Lawrence Tabak for the NIDCR Oral History Project. Today is August 24, 2023, and I'm Kenneth Durr. Dr. Tabak, thanks for talking to me today.

LT: Pleased to be here.

KD: Let's go back to the beginning and talk about how you developed your interest in dentistry, and more importantly, in research.

LT: Well, my interest in research preceded my interest in dentistry. I became interested in research in high school and carried that through into college, where I worked as a part-time lab tech in one of the professor's labs and then started to do some independent research with him and his spouse—they were a husband-and-wife team.

When I graduated from ... I went to the City College of New York, and so when I graduated from City College I failed to gain entrance to medical school and decided to matriculate at Hunter College, which is another part of the CUNY system for a master's degree, and presumably leading to a PhD eventually, and I worked at a biophysics lab, working on a very esoteric scientific topic.

And while it was intellectually stimulating and I enjoyed being a teaching assistant (I taught evening class while at Hunter) I realized that in terms of the science, only three people in the world really cared about what I was doing: my mentor, a person who worked with him at Hunter,

and some guy in Australia. And so I decided I wanted to do research that had more of an effect on people.

And just by serendipity I was introduced to an individual who had graduated from Columbia many, many, many years ago who said, "You're interested in research. Why don't you think about dentistry as an option?" And so I literally applied to one dental school, Columbia, in addition to a number of medical schools I reapplied for a second time, and failed to gain entry into medical school again. But late in the admissions season I was admitted to Columbia.

Kind of an odd story. This was back when I was young and knew everything and was interviewed by the then-dean of the school. I hadn't realized it was the dean of the school when I was being interviewed by him, and it was very late in the admissions season, so obviously somebody had dropped out and they were trying to fill the class. And he looked at, presumably my folder (I had no idea what was in there) and dramatically threw it on a table and said, "We're not going to accept you, Tabak."

And because I knew everything, I stood up and said, "Well, that's your mistake," and I walked out of the room. That was my auspicious beginning of my dental career.

Anyway, they must have really been trying to fill that slot, because less than a week later I received a letter (back then things were sent by registered mail, no emails) admitting me to the class of '77, so I started dental school in 1973 and really immediately secured a job as a technician part time working in the lab of Irwin Mandel and that began a lifelong relationship that I had with Irwin and his partner in crime, Dan Fine. And Danny is still with us and I still speak to him every once in a while and he's still going strong. He's still a professor of dentistry. Irwin, sadly, passed away a number of years ago, but had an amazing career and amazing life.

So I really started with research as the premise and then the clinical degree, which turned out to be dentistry, came after the fact.

KD: Tell me about working with Irwin Mandel. What kind of a mentor was he?

LT: He was the quintessential mentor. He was incredibly supportive but he would give me a kick in the behind when I needed that. And we were all from Brooklyn, so punches were never pulled. He was, in a true sense of the word, a renaissance man. Extremely well read, not only in science but also all forms of literature. His wife, Charlotte Mandel, is a noted poet; she's published a number of volumes; so they were just a remarkable family.

He was sort of the consummate biologist. He thought very, very broadly about science and would read voraciously, constantly sending me, in those days, hard copies of journal articles. And it was not just dental journals. He would read all the medical literature. He would read all the basic science literature. And it was really with Irwin that I gained an enormous appreciation of the very rich biology that one could study in dentistry.

And Danny Fine, Dan Fine, was the most enthusiastic human I'd ever met in my life (he still may be the most enthusiastic human I've ever met in my life) because everything was interesting. There was never a question that was not interesting to him. And although he was 10 or 12 years older than I was, we were sort of like more like big brother/little brother than professor/student, whereas Irwin was Dr. Mandel for many years after I graduated because I had such extraordinary respect, and I still have extraordinary respect for Danny as well.

And the other thing about Irwin was, he was not afraid to say that he didn't know something, which was such a valuable lesson for such an immature person as myself. And because he went to college (City College, by the way) with Elvin Kabat and Bernie Erlanger, who were two giants

at Columbia at the time, I got access to the best-equipped laboratories in the entire Columbia University.

Because the dental school had nothing in terms of equipment, but between Dr. Kabat's lab and Dr. Erlanger's lab, there was nothing that I did not have access to in terms of equipment. So actually when I went to graduate school it was sort of like a step down because where did all these instruments go? It was kind of a funny thing. So it was just a spectacular opportunity for me.

Now the problem was I spent all my time in the lab and very little time learning dentistry, a fact that was not-so-gently pointed out to me on multiple occasions during the 4 and 1/2 years I spent there. When I finally graduated, Irwin told me—and he was actually being serious, he wasn't trying to be funny—that he now had two extra hours in every day of his life.

And I looked at him sort of quizzically and said, "Irwin, what is that all about?"

And he said, "Well, I used to spend one hour a day out of talking you out of quitting dental school. And I spent one hour a day talking them out of throwing you out of dental school."

And all of that was true, by the way. So I was just so incredibly fortunate to have Irwin and Danny as mentors.

KD: Let's talk about what you were doing in the lab all that time. Did you develop your interest in mucins early?

LT: Well, it's kind of an interesting story. The short answer is yes. I actually worked it out two ways. I worked for Irwin and did certain lab procedures for him and other members of his group, but then I was allowed to have a project on the side, and I had one with Dan and I had one with

Irwin. So I effectively had a full-time job there, even though I was supposed to be in dental school at the time.

The first presentation I ever gave at a national meeting was the AADR meeting I believe in ’75 or ’76. I don’t remember, I’d have to look it up. And it was about a very small molecular weight protein that had the unusual property of being highly charged. It was very, very, very negatively charged. And we defined this based upon the way we separated the protein, which was in an electric field through an inert polyacrylamide support, a gel electrophoresis, and the title of the abstract, the title of the presentation was, “The Most Anionic,” meaning negatively charged, “The Most Anionic Protein in Human Submandibular Gland Saliva.” Pretty pretentious title, but that was what we put in.

And I gave the talk, and I was, of course, scared out of my wits because I’d never given a scientific talk before at a scientific meeting. And in the back of the room, this 9-foot-8 giant stands up, a fellow named Gunnar Rolla from Scandinavia, who said, “Nice talk, but it is not the most anionic protein in human saliva, that’s mucin. And the reason you can’t see the mucin in your acrylamide gel system is it’s so large it cannot penetrate the pores of your gel.”

I was devastated. I thought my career was now over. I was just a puddle. But Gunnar Rolla did a remarkable thing, and he did it not so much because of me but he did it out of respect for Irwin, because Irwin was beloved by everybody. And he came up to me after the session broke up, I mean, I was like pasted to my seat with perspiration. I couldn’t move. I couldn’t breathe. I didn't hear anything.

And he approached me, and he said, “Would you like to go for a coffee and let’s talk about mucin?” And that’s when I became enamored with mucin is we sat for over an hour, talking

about these strange high molecular weight gloppy, sticky, viscoelastic proteins. And Gunnar was able to put it into not only a biological context, which Irwin was so fabulous at, but also a very strict biochemical context. And so for the first time I really saw, okay, biochemistry can really tell me a lot about these molecules that I care about.

And so it was on that basis that when I finally was released from dental school, I went on for a PhD in Buffalo to work with a guy who was specifically interested in mucins, Mike Levine. So it really started at that very, I think, second year of dental school working for Irwin.

KD: You've talked about the fact that with mucins there was this debate at the time between specific and nonspecific. Where did you come down in that?

LT: We were specificicists. Gunnar Rolla was a nonspecificicist, which was also fascinating, and we spent a little time talking about that as well. And of course the answer is yes, we were all right. All of us were right. But when you are young and immature, you're dogmatic because that's what young, immature people do. And so we had these raging debates about whether it was or was not specific.

We came down on the specific side because we were able to inhibit mucin bacterial interactions with very discrete, defined sugar structures, carbohydrate side chains of known sequence. And because we were able to prevent those interactions from happening by swamping out the ability of the microbe and the mucin to combine to one another, so in effect we were using the sugar side chain as a decoy, we said, see, we proved it, it's specific.

Now, it turns out that fast-forward to today, both claims were correct. There are many interactions that are quote, "nonspecific," electrostatic and hydrophobic in nature, and then there are others which are incredibly specific in terms of protein-carbohydrate recognition. So proteins

that recognize sugar are known as lectins. At the time, everybody thought lectins were only found in plants (parenthetically, Elvin Kabat made an entire career of isolating lectins from different legumes and showing how they interacted with blood group substance and so forth).

What we didn't realize at the time but subsequently did when we were in Mike Levine's group is that we showed that actually bacteria do have lectins. And it was almost impossible for us to get that work published because the reviews all came back saying, and I'm paraphrasing, "Everybody knows bacteria don't have lectins. What are you people talking about?"

Of course, within a year there were many, many reports of bacterial lectins, with sort of a simultaneous discovery. So we wound up publishing it in a sort of third-tier journal, *Biophysics, Biochemistry Research Communications*, because nobody else wanted it. But yet it turned out to be one of our most important works. So yeah, so both were right, which is so true all the time in science, right?

KD: Yes. Was Mike Levine a coauthor on that paper?

LT: No. Mike was the senior author. Patty Murray was the first author. It was part of her thesis work. And I did quite a bit of the work, so I was one of them. There may have been one other author but I don't remember. It was a group effort. Mike had a very large group, and at that time, I was still very much a member of his team.

KD: Did you have an ability to direct your research into something that you were personally interested in while you were at Buffalo?

LT: So when I got to Buffalo, there were two graduate programs in the country at that time for people with dental degrees to get a PhD, Buffalo and Seattle. And Seattle's program director wrote, saying, "Now remember, you have to maintain a B average to stay in the program," reflecting on

my outstanding grades in dental school. And the Buffalo program director wrote, said, "Irwin said you're going to be okay. I'm sure you'll be fine." And so guess what? I went to Buffalo. And I teased the program director at Seattle about that for many years to come, a woman named Pat Keller, who was an outstanding biochemist, by the way.

So here I am in Buffalo. I was there about one year and most of my colleagues were moonlighting, doing some dentistry a half day a week on weekends. And that was not an option for me. As you may have already inferred, I'm not the strongest clinical dentist in the world. And so I asked the departmental chair at the time, a fellow named Bob Genko, Robert Genko, what did I have to do in order to get a raise? And he said, "Well, write your own grant. If you get a grant, then we can make you a research assistant professor and we'll give you a raise."

And I thought, okay, I can do that. And so I wrote a grant to the Cystic Fibrosis Foundation to study human tracheobronchial mucins. So you might wonder how I'm going to get access to tracheobronchial secretions. I reached out to the New Voice Society, which were individuals whose voice boxes were removed because of carcinoma. And they all had stoma and they could aspirate tracheobronchial secretion on a pad through their stoma, which they had to do, they had to clear their lungs of this stuff. And so that was the whole thing.

I had already shown people I knew how to purify mucins. I was going to purify these from human tracheobronchial secretions from this sort of unadulterated source. And so I got the grant from the Cystic Fibrosis Foundation, went to Bob Genko and said, "Okay, good news. I got my grant. You've got to make me a research assistant professor and I want a raise." And he looked at me like I had four heads because he had forgotten all about it.

And I said, "Bob, don't you remember you said if I got my own grant ..." Anyway, so I got a raise of $10,000. Excuse me, I got a raise of $8,000. I was earning $10,000 as a postdoc and I got an $8,000 raise to $18,000 as a research assistant professor, which I was paying for with this grant. And that was very, very fortunate. The first of a number of grants I was able to get.

So even though I was still a graduate student, I was already funded, and I was a member of the faculty. Kind of a weird thing. And that was decidedly my work because I'd gotten the funding for it and I was doing the work and so forth.

And then Mike and I had this sort of great divide. And he at the time was sort of the premier salivary protein person in the universe, and he had many, many people working with him. And so at some point I started kvetching about my independence and he said, "Okay, you want to be independent? There's a room down the hall. Go over there and that can be your lab, but don't come in my lab and use any of my equipment."

So we had this divorce. And of course, reverting to my immature roots, I said, "Okay, I'm going to show that son of a something," and refused to enter his lab for about a year and sort of toughed out a couple of projects where we just used what I had in my little lab, my one-room lab. And after I published the second of those papers, we had a thawing of relationships and I was invited back to use the equipment. But eventually, for all the right reasons, I decided to leave Buffalo and join the University of Rochester.

KD: Right. But you did get your PhD at Buffalo.

LT: I did get my PhD at Buffalo. And I also received my certificate of proficiency in endodontics. So this is a weird thing. Michael's first wife, Ming Shi Levine, was the chairman of the endodontics program, and she encouraged me to take endodontic training part time in lieu of faculty practice,

because by that time I was already appointed on the faculty. And if I did that, I could have a state line, I could have a hard-money position. And that was a big deal, obviously, with a young family and so forth.

So I did that. And I took—in those days, the endodontic training was a two-year program. So I took that over the course of four years, part time, and so I had the unusual experience of giving a lecture, listening to a lecture, getting a test, giving a test, because I was both on the faculty and I was a graduate student at the same time. And then when Ming went home to Taiwan for a little while, I was also the acting director of the department while I was a graduate student in the department. It was very strange.

But yes, I got both my PhD and my certificate of proficiency in endodontics, and I gave up all of that to move to Rochester because it was just sort of time for me to move on.

KD: At some point in there, you were a visiting fellow with Bruce Baum?

LT: I was a visiting investigator with Bruce. What I did was I cobbled together my vacation time and other things to come down to NIH for about five months or so I guess it was. I was still in Buffalo and I really wanted to see how the other half lived. I wanted to see what it was like to be in a high-powered environment.

And one of the people that Irwin introduced me to, in addition to Mike Levine, who was a spectacular scientist, was Bruce. And the thing that distinguished Bruce and Mike from virtually everybody else in the field was they published in mainstream biochemistry journals. Their work was no less rigorous than anybody else from a biochemistry department and so forth.

And of course Bruce was here at the NIH and was involved in so many different things, and it was sort of like back in Elvin Kabat's lab, a kid in a candy shop. And so I actually shared a bench

with one of the people in Bruce's lab. And the deal was I was a very early riser and so I would get on campus by 5:30 in the morning, have all my experiments done by noon, by which time the person whose bench it really was would show up and then she would work until 9:00 at night. And we sometimes saw each other during the switch-overs, but not too often.

And then in the off-hours I would be in the library, or I'd be going to seminars. And I sort of laid out what I thought would be the future things that I'd want to do well beyond the kinds of approaches that we were doing. And when I returned to Buffalo, Mike was a little critical because he thought that it was all fantasy. "You're never going to be able to do this. You're never going to be able to do that."

And we sort of did it. And as it was, ironically, in part with his help. Because he was this really outstanding scientist, and it wasn't like "You can't do this and I'm not going to help you." It was, "I don't think you're going to do this, but yeah, if you want my help, my advice, I'll give it to you," which I took gratefully.

So yes, it was a really important time in my life to be here because I needed to fully immerse myself with no teaching responsibility, just being able to think about science, do science. I actually toyed with the idea of coming to NIH because it seemed like life as an intramural investigator was a good one, but the opportunity never really came at the time when it was reasonable for me to relocate.

KD: You said you wanted to see what it was like. What was your impression of NIDR in that would have been the 1980s, the mid-80s?

LT: They had some powerhouse people in the program then. And it was all people who I had read about and had read their papers. They were not particularly strong in biochemistry. Vince Hascall

was a very good biochemist. He was about the closest to the sort of stuff that I did. And Bruce, of course, was trained as a biochemist. His PhD is in biochemistry.

Most of the other people's strengths were in microbiology and immunology and pain. Those were the three areas that were most represented at that point in time. And then there was also a bone biology program which was well-thought of. But it wasn't so much the people within NIDR, although obviously I thought very, very highly of Bruce, as it was everything else about the place.

Because you could hear seminars from the leading scientists in the world because everybody found their way onto the campus eventually. And what I realized was the best scientists do the science that's the most easy to explain. They did it in a way where the scientific proofs that they provided were unambiguous, clean, and not contrived.

And I have to say so much of science now has become muddled with sort of what I call cartoon biology, where people make a bunch of stuff up and then they figure out crazy, cockamamie model systems to prove what they're trying to prove. Nature's much smarter than us, and if we would just be true to nature and let nature be our guide, I think science would be in much better shape. Anway, that's an aside.

So it wasn't so much NIDR per se, although the people in Bruce's group were obviously impressive, but I really ... just the whole vibe of the place where so many giants were running all over the place and giving talks. And I took advantage of all of that. I don't think I slept very much the whole time I was down here.

KD: Was Harald Löe there at that point?

LT: You know it's funny, yeah, Harald I guess would have ... No, was that before?

KD: David Scott maybe?

LT: It may have been David Scott at that time. I had no engagement with any of the administration. It was strictly a deal I made with Bruce. And he insisted that I fill paperwork out so that I was legal. I wasn't even going to fill out paperwork because it was like ... I'm still wearing my torn jeans and ripped sweatshirt. I'm a lab rat. I'm just going to do science.

It must have been Dave Scott at that time, and it must have been Marie Nylen must have been the scientific director. And then Abner came in, and I don't remember if Abner was already there or if Marie was still the scientific director.

KD: Did you have any interaction with Marie Nylen?

LT: Not at that time. It was only after the fact that I did. And as I hope you know, she's a giant. First female scientific director, outstanding investigator, and sort of really outstanding mentor. Brought the best out in people. She was instrumental in Bruce's career, I know. She was the one who recruited him back from NIA, from the National Institute on Aging, which is where Bruce was, to the dental institute.

And ironically, a lot of the dentists never did well at NIH, but Marie sort of turned that corner. She made the environment more conducive and laid the foundation for a lot of things that occurred subsequently.

KD: Why did you say that a lot of the dentists didn't do well at NIH?

LT: They just didn't. They struggled in this environment. Their work, you know, people didn't think their work was as strong as it needed to be and so forth. Maybe some of that was true and maybe

some of that was just a sort of inherent bias against dentists that some of our physician colleagues harbor. I would like to say, "used to harbor," but it's not necessarily in past tense.

KD: So you took five, six months down here in DC and then back to Rochester.

LT: Back to Buffalo, and then in '86 I left for Rochester.

KD: What was the opportunity there? What were you looking to do?

LT: I really wanted to be my own person. And even though Michael and I had divorced and reconciled, I was always going to be *et al* because Mike was such a giant in his field. And the other thing was, even though I had a career development award, which ostensibly is to free you up from teaching, I was sort of teaching four half days a week and really didn't have a whole lot of time to do the kinds of things that I wanted to scientifically.

And then at one point, people sort of said to me, you know, "you're one of the best molecular biologists on campus in Buffalo," and that scared me. I thought, Oh my God, if I'm one of the best, this place is in deep, deep straits. So frankly, I wanted to go to a place where I was the dumbest person in the room because I wanted the opportunity to really learn more stuff.

And so Bill Bowen, who was the chair of the Department of Dental Research in Rochester, had been trying to recruit me for a few years, and finally in '86 I agreed to go. And so it's a medical school without any dental students, but it's a school of medicine and dentistry, for historical reasons. And many, many people came through the graduate dental programs that they had at the Eastman Dental Center and many, many people got their PhDs through the Department of Dental Research, but in collaboration with traditional basic science departments. In fact, at one time, every dental school in the country had at least one person who trained at Rochester. That may not

be true anymore because we have all these new dental schools, but it was one of the places to train.

And so I came to the medical center and was able to get a joint appointment in the Department of Biochemistry and teach biochemistry formally, and was able to set up a lab myself, a real lab, and was then clearly independent of Mike. And Bill's interests were so different than my own that there was never any ambiguity there.

And so, yes, it was really a very, very important move for me, and honestly, if Ruth Kirschstein hadn't called me one day to recruit me to NIH, I'd probably still be in Rochester because just as we loved Buffalo, we loved Rochester also. And it was an outstanding environment and so forth.

But Rochester really gave me the opportunity to collaborate with and engage with people much, much smarter than me. And I sort of learned a lot of the stuff that I never did learn. Because, I mean, my PhD was really more of a hands-on "do your research project and you're done," and so I learned what the environment could give me, but not much more than that. I mean, it was substantive at the time, but science moves so fast.

And unfortunately, at least at the time, I don't know how it is now, the dental school environment in Buffalo just wasn't conducive to keeping up with the most modern approaches. As I say, it's probably changed today, but back then, it really hadn't. And so I was in a medical center where the newest, latest and greatest everything was there at your fingertips, and there was an expert down the hall. And I enjoyed talking science and I enjoyed doing science with others and so yes, it was a fantastic move.

KD: Given that, where were you able to take your research during your years at Rochester?

LT: Well, what I did in Rochester was I decided I was going to leave all the mucin biochemistry biology behind me, because Mike's group was just so extraordinary, there was no way I was going to compete with them anyway. And I decided to look more at the biosynthesis of the mucin, which was some work that I began when I was with Bruce Baum during that interlude.

And then as a side project, which is ironic, I came up with this idea of why don't we go after the enzyme that initiates mucin biosynthesis, the enzyme that puts the first sugar on the protein core of the mucin? And it's got this horrible name UDP-GalNAc, polypeptide N-acetylgalactosaminyltransferase, GalNac Ts for short.

And I hired a postdoc from Calgary, Canada, who had been working in Z DNA and he was a really good biochemist. He really knew how to do biochemistry. A guy named Fred Hagen. And I said, "Okay, look Fred, I've got this easy project for you. Purify this enzyme, we'll get some sequence on it and protein sequence and then we'll clone it and then we'll go on to other stuff."

It took Fred about 19 months to purify this enzyme. He purified it almost 2 million-fold. We did, in fact, get some sequence the old-fashioned way, by Edman degradation. He did, in fact, clone it, and we were the first to report the cloning of this enzyme, although we subsequently learned that another group in Copenhagen had done it earlier but they hadn't published because they were patenting everything. But we and a group from Kalamazoo, Upjohn, simultaneously published it first. And we didn't know of each other's work, but there it was in the same issue of the *Journal of Biological Chemistry*.

And then in the next study, which was a simple study to figure out where this enzyme was expressed at the basis of the mRNA transcript, we did—the scientific procedure's a so-called Northern Blot. So you probe RNA from the different tissue sources and then you probe it with a

radial-labeled DNA which would be complementary, and it will light up where the mRNA is, and that will tell you which tissues have it.

And it was amazing that one tissue that we thought had to have this enzyme had a very, very faint signal—lung. And we said, look, we knew lungs had mucins because my first grant was to purify mucins from lungs, so you did something wrong. So we berated the technician, "You don't know what you're doing."

So then Fred did the experiment and it still didn't work So then I did the experiment, much to the dismay of everybody in the lab, because by then my hands had started to shake a little. And it still didn't work.

And then I said, "You know what? We're looking at this all horses backwards. There's more than one enzyme, and lung has a different type."

And sure enough, 20 enzymes later and hundreds and hundreds of papers from around the world, maybe thousands by now, no doubt thousands by now, we realized that this was a very robust family of enzymes all doing ostensibly the same thing, taking this one sugar and decorating the protein backbone at the cerine and threonine amino acids.

But it turns out, fast-forwarding, lots of work that we started in Rochester, and this is where Kelly Ten Hagen came in, who was another brilliant biochemist who came as a research assistant professor. She came right from her graduate program, from Stan Cohen's lab, from Stanford. So it's Cohen and Boyer. These were the people who patented gene cloning. So Kelly really knew how to clone, okay?

So she comes, and using at the time a very novel approach of using degenerate PCR primers, which basically means you can cast a very wide net for anything that looks kind of like what

your original probe was, she pulled out many, many different isoforms of this. And so thus began the isoform race. We would publish one, the group in Copenhagen would publish one (Henrik Clausen). We'd publish one, they'd publish, and then a group in Japan got in the act, and so we were all racing, racing, racing.

So when the dust settles, there are 20 different isoforms and as it turns out, they each have exquisite nuances of specificity, and that's where the story ended in Rochester because now it's time for me to go to NIH as Director of NIDCR.

KD: Now if you'd just remained a lab rat and shut up in your lab, you never would have made that change. Let's talk about how you moved into administration and what the challenges were.

LT: Well, when I went to Rochester, Bill had the plan of me becoming the chair of the Department of Dental Research because he wanted to step down. And I told him that if he insisted I would leave and go back to Buffalo, because I could never imagine myself as an administrator.

Two years after, he asked me again and I agreed to do it because I saw the handwriting on the wall. Things were getting a little more competitive at the medical center and we were essentially a soft-money institution, and I was beginning to worry a little bit about the sustainability of what we were doing and knew that we had to do some additional things in order to be sustainable, for the whole group to be sustainable, not just my lab.

So I decided to become the chair of Dental Research, and the then-dean Marshall Lichtman, brought me into his office and said two things. "Congratulations," and "You're $80,000 in the hole."

And I said, "Excuse me?"

And he said, “Oh, didn't Bill tell you?”

So I go upstairs and I say, “Bill, I had this interesting conversation with the dean.” And Bill was a crusty old Irishman in the truest sense of the word, and what emerged were many words that you would hear at the pub in Dublin. And anyway, when he calmed down. It turned out the dean was right, we were $80,000 in the hole. So I was able to figure out how to deal with that.

And then we got a new administration at the medical center, and a fellow name Jay Stein came to us from Oklahoma, and he was going to shake the place up. He was going to turn the place upside-down. And in speaking to colleagues at Oklahoma and Minnesota and San Antonio, where he had been previously, I learned that the guy sort of had an approach which he used in each new place. And he was one of these guys that got stuff done, but there was often collateral damage.

So he kind of ignored me for the first few months that he was installed as the new Vice President for Health Affairs and whatever other titles he had. And he finally called me into his office one day and didn’t even invite me to sit down and just said, “What do I need a Department of Dental Research for?”

Unfortunately, I reverted back to my immature, arrogant days and I said, “Well, what’s your current endowment, Dr. Stein?”

And he proudly said whatever the endowment was, I don’t know, $300 million. I’m making it up; I honestly don’t know.

I said, “Well that’s great, but you do know that half of that endowment is mine.”

And he looked at me and he said, “What are you talking about?”

I said, "Well, when the school was originally created, it was created as a school of medicine and dentistry because the guy who gave the money, the guy who founded Kodak, was saved by a dentist, and he wanted both a medical and dental school. But they were way ahead of their time, because in those days, dentistry was sort of a you just worked with a dentist for a few years and then became a dentist. There was no formal schooling. An apprenticeship, I suppose, is the word I was looking for.

So as not to lose the money, the dean, the guy whose name was Whipple, who was many things but smart, Whipple said, "Look, we'll create a graduate program in dentistry and train people who can be educators to form dental schools around the country."

And so they agreed to that, and so technically half the endowment belonged to dentistry. Anyway, he sort of poohed me out of the office. Two weeks later, he calls me back. Cup of coffee, sit down, let's talk. And he basically said, "Well, strictly speaking, Tabak, you're not legally correct, but I do admire your testosterone," and he used a different phrase. And from that point on we got along pretty well. And I was one of the people who helped him as he tried to reimagine what the medical center could be.

And I have to say Jay did a lot of really amazing things at Rochester. So the Department of Dental Research was dissolved. We became the Center for Oral Biology, which I thought was the right thing to do. I still think it was the right thing to do because it got us integrated in every single traditional department in the medical school. We got new space out of the deal. It was all really exciting stuff.

But he also wanted to merge hospitals, and hospital mergers are complicated things, and there's collateral damage and so on and so forth. I was one of the people who worked well, I thought,

with Jay, and he actually, at one point (I think it was in a moment of insanity) asked me to become the dean of the medical school.

And I said, "Jay, you do realize that I don't have a medical degree."

And he goes, "No, I know that, but you're the leader here and everybody knows that." Because along the way I'd become the research dean for the medical center and so I really was part of all the decision making at the medical center and learned a great deal about how medical centers run, how hospitals run. And so all of that prepared me to come to NIH.

KD: What were some of the things that you were putting in your toolkit in these years as far as administration and leadership?

LT: Well, I guess to start with, why did I actually do it beyond just being the chair of a little department? As I became more and more aware of what was going on in the medical center, I realized something really important: I'm a good scientist, I'm not a great scientist. You become depressed a little bit for a while, but after you get over that, you realize, okay, good scientists can make contributions. I did good things.

But what I did much better than that was I was able to enable great scientists. I was able to identify who they were. I was able to figure out what resource they needed. And I was parsimonious, but I was able to figure out just what they needed to move forward.

And so, becoming research dean made a lot of sense to me because then I could then control a pot of money that I could use as seed money for all these up-and-coming great scientists, and I didn't care if they were women, and I didn't care if they were not old white guys. And so I was able to build in diversity before it became a thing, which obviously has changed a bit over the years. And I realized that I derived a lot of pleasure from that.

So I was always trying to find people much better than me and always trying to figure out ways of furthering their careers. And at one time I figured out that for every dollar I spent on these folks, I got back $9 in grant support that they ultimately generated using the seed money that I had provided. Now, I'd be long retired if my own portfolio did 1 for 9, so it was a very, very good bargain.

And of course, as you do more and more things in that sort of space, and dealing with more and more people, particularly on the hospital side, on the clinical side, other institutions. We set up an early consortium across New York state to leverage some equipment that we had to do microarray analysis of gene expression, so we got everybody across the state to buy in. And so I had a chance to learn how to do all those things. And I didn't take management courses or anything like that, but it was all sort of on-the-job training.

KD: I wanted to talk about the anti-disparities training program that you put in. It sounds like that sort of sprung naturally out of the hiring that you were doing.

LT: Well, that program actually started in Buffalo, very early on in my career. In the 80s I guess, early 80s, I realized ... You know I went to Columbia, and New York City, next to D.C., is probably one of the most diverse cities in the world. And I had one African American in my class and one, no two Asian Americans in my class, and nine women. A class of 51 people. And realized when I looked more into it after graduating from dental school, that that wasn't just unique to Columbia—in fact, Columbia was good compared to most schools.

And so I realized that part of the problem was that young people from typically marginalized communities had no role models. They didn't see anybody who looked like them. I never had an African American professor in dental school. I think I had one Hispanic professor.

So we started this program in Buffalo, and then I ported it to Rochester, so it began with NIDCR funding (back then NIDR funding, I guess) but then when I got to Rochester, I was really able to kick it into high gear because the problem was, and this should be no surprise, people from the these otherwise marginalized communities didn't have the resources to travel anywhere to afford the luxury of these programs.

And so in Rochester what I did was I went to Kodak, and I went to Bausch and Lomb, and I went to Xerox, and I said, "Have I got a deal for you. You guys all want to recruit people from diverse backgrounds. I will have a group of young people here every summer with your support and of course they will be allowed to visit your facilities, learn about the science you do, and you can recruit the hell out of them if you want."

And so they did. And they supported travel, living expenses, added to the stipend that we could give the kids, and it turned out to be a really important program. And among the people who participated was Jennifer Webster-Cyriaque, who is now the Deputy Director at NIH, as well as others who have gone on to academic careers.

Now truthfully, it may be in spite of and not because of, because Jennifer is enormously talented. But it did give her an opportunity to see these kinds of things, and others opportunities like that. And it turned out to be a very important feeder program to other graduate programs that we had, particularly in Rochester.

While I was in Rochester, I wound up running four training grants, and the whole way we did the training grants were we recruited faculty from the entire university and the trainees could go wherever we thought the best fit was. And so we didn't keep all the slots to ourselves. We had

only a few that we actually used. And that brought tremendous good will and additional collaborations between our little oral group and the whole rest of the world.

In fact, the first person who I supported on an oral cell and molecular biology training grant was a woman named Gloria Culver, who was studying tRNA splicing, and they were aghast that I was going to support her. And I said, "Look, don't we have tRNA from here to here?"

And they said, "Of course you do." And I said, "Then what's your problem?"

Gloria went on to become—fast-forward many years—to become the graduate dean of studies at Rochester. After doing her PhD and her postdocs elsewhere, she came back and just recently stepped down as dean but remains on the faculty there as a professor. So all kinds of good things happened from those training programs.

KD: During this period (we're getting into the 1990s) I notice that you were an ad hoc reviewer for the intramural program for a little while? This would have given you a perspective on what was now NIDCR.

LT: Yes, it was an interesting view. The intramural program was sprawling. It did a lot of things in a lot of different areas. But with the exception of Bruce's program, which was both broad and deep, many of the programs were sort of one-offs. And so my favorite was they had a program that was run by Steve Leppla, who was a brilliant microbiologist who studies anthrax. Okay. Anthrax is not a common oral pathogen. It has nothing to do with oral health.

And so I wondered out loud, on more than one occasion, why our precious resources that could be used for things that are related to oral health, are being used for things that are decidedly not. Now, if you're doing fundamental biology, okay, fine, I get it. Basic science is basic science. But

this was—and I don't mean to pick on Steve because he really is an outstanding scientist. I don't know if he's still active or not, but he was an outstanding scientist.

But in his case, it was really directed to understanding bacillus anthracis and the toxin and so forth. But the quality was I thought very good but uneven and it sort of formed the bases of my own later view of the need to kind of prune, if you will, some of the weaker labs, which led to a lot of angst but I think was justified because what was left was much stronger in the end.

KD: There have been—I mean, this wasn't a new thing. There was a blue-ribbon commission some time in the 90s, I believe, looking at the program and saying, "Hey, we've got to be more." Do you remember that period?

LT: Oh yes. Well, I contributed to that. I don't think I was a member of the group, but I think I wrote a letter or something that they published, something like that. Yes, no, I remember it. And part of it was, the scientific director at that time was an individual named Abner Notkins, an MD, and unfortunately, he really had a disdain for dentistry. He embraced microbiology, but he was much more interested in diabetes. He thought that AIDS research was really important and if it manifests itself in the mouth, then that was important (and he was right about that). Pain research, which was so important to dentistry and other fields as well, eh, he wasn't so hot on that either.

He really had a somewhat narrow view of what the organization should be. And I think as a result the program didn't flourish. Some subprograms did, and that's fine, but overall, I think the program just didn't flourish as much as it could have.

KD: No strong, central guidance in the intramural.

LT: Not really. And no real encouragement. No resource allocation to make sure your stars were doing well. No sort of "this lab really isn't making it and it's time to fold" and so forth.

KD: Interesting. Well, let's take you to NIDCR. You talked about that call from Ruth Kirschstein. What did she want?

LT: Well, I kind of was set up. The chair of the search committee was the late Steve Katz, who had been a long-time director of NIMS. Steve was a dermatologist. He coauthored the definitive textbook in dermatology with Lowell Goldsmith, who was the dean, at the University of Rochester, of the medical school. So I think what happened was Steve called Lowell and said, "Is this guy Tabak for real? He's your research dean? He's a dentist."

And Lowell, I'm surmising now, I honestly don't know what was said, probably said something like, "Oh yeah, he's real," or something like that. Because Lowell used that phrase. And so when Ruth called, she said, "Look, there's a consensus that you'd be the right person for this. Do you want the job?"

And I said, "Let me think about it a little bit." And so of course I called Irwin, and we had a very long conversation. And it was one of those times where I needed a kick in the behind, because I was trying to rationalize why it was a good job. And I was focusing on the fact that I would be able to set up an intramural program for my own research and I wasn't saying very much about the Institute.

Now, you have to know Irwin, just a brilliant writer, a brilliant speaker, never used profanity ever in my presence, ever, and basically what he said to me was, "Larry, it's not about your f-ing lab." And to hear him use the profanity for the first time ever in our relationship just jarred the heck out of me. And of course he was right; it wasn't about my lab, it was about the institution. And so

that led to a lot of soul searching, and basically what I had to decide was did I want to go back to being a dentist again. Because in Buffalo, of course, I had to be a dentist because I was teaching dentistry. In Rochester, I stopped being a dentist because I was teaching biochemistry, I was the research dean. Yes, I happened to have a dental degree. But if I went to NIH, I have to be a dentist again because I was going to be *the* dentist.

And so a lot of conversations with Irwin. A lot of conversations with Bill Bowen, who was extremely supportive of me going. He said, "This is the next logical step for you. You've outgrown this place. Get out of here. Enough already." A lot of conversations with Bruce Baum, which was sort of awkward because I then became his boss. But we had a close enough relationship that we could put things in little boxes. And decided that it was the right time to come down here. And yes, became a dentist again.

KD: So once you stopped thinking about your own lab and started thinking about NIDCR and the path forward for dental research, what were some of the things that you put on your agenda? What were the strengths that you wanted to build on and the weaknesses that you wanted to mitigate?

LT: I knew what the strengths were, at least extramurally, because I was pretty plugged in to the extramural program. And I also knew what the weaknesses were. Because in Rochester, they had a very, very, very strong trials group, clinical trials group, and they were doing a lot of trials in neurological diseases. And as research dean, I had to provide some initial resources for them as they were building this thing up.

And I knew, even though I'm not a trialist and was not a clinical researcher and was basically a basic scientist who happened to have a dental degree, I knew that their clinical research was not

up to the cutting edge and thought that as a basic scientist everybody would assume that I would focus only on basic science and everything would sort of go along the way it had been. But instead, my real first agenda was to figure out how to reimagine how we were doing clinical trials, and in particular, clinical research and clinical trials in the Institute.

When I questioned staff about this, as to why we were doing all these small, underpowered studies which all concluded with the praise, "Future studies that are properly powered will be required," I was told that, well, we would only be able to afford only one or two such big trials, and then what would all the trialists do?"

And that didn't seem reasonable to me, and I spoke to several colleagues, new colleagues at NIH (they didn't know me from Adam) and I came asking this sort of dumb question, "Does this make sense to you," and was told emphatically it's the dumbest thing they'd ever heard. So I then needed to recruit somebody who knew a lot more about clinical trials than I did, and that's when I recruited Bruce Pihlstrom to the Institute to take on that responsibility. And Bruce really worked very, very diligently to get the Institute to the next level in terms of how they were thinking about clinical trials.

And so that was sort of my initial concern. I also wanted the intramural program to become more focused because by that time there were I don't remember exactly how many, it was well over 40, approaching 50 investigators, but a lot of these folks were grandfathered in from a time before sort of more rigorous criteria were used to appoint people to positions where they had independent resources.

And so there needed to be some rejiggering and rethinking about who had independent resources and who had sort of passed their time where they were being productive and so forth. And which

individuals might find better opportunities being program or review people in our extramural program and so forth. And so over the course of four or five years, we dropped that number of people in the intramural program to a much more manageable number, and that allowed us to recruit some new talent, which I think was critically important.

So yes, I guess it was counterintuitive to what people assumed I was going to do, which was going to be to turn the whole thing into a biochemistry institute or a saliva institute, and we really did focus more on trials. We also really launched major efforts in tissue engineering. We had a very, very clever program officer, Eleni Kousvelari, who was really one of the leaders at NIH in that space, and she was able to recruit outstanding investigators from outside of the traditional dental universe to form the basis of our first cohort of extramural investigators.

Ironically, a lot of those grants ultimately ended up going to NIBIB when it was formed, but that's just the way it had to be. But it was and it still is a very important portfolio for the dental institute. So that was the other thing. Clinical trials and tissue engineering we really pushed.

And of course, that was the time when biofilms and the sort of microbiome became popular, way before everybody else discovered it. So people in the dental institute, mostly Dennis Mangin, I give a lot of credit to, working with extramural people as well as a few of the intramural investigators, decided to sequence all the microbes in dental plaque, which is, of course, the prototypical biofilm. Dennis called it plaque many, many years before everybody else discovered it.

And of course, they weren't sequencing the whole genome of the bacteria because the technology wasn't available yet. They were sequencing tRNA markers which served as surrogates. And so the first real microbiome description, genetic microbiome description, came

out of work from the dental institute. And rarely do they get credit for it, but that's where it as originally done. And of course that whole field has exploded in a remarkable set of directions.

So those were the kinds of things that we got engaged in, and I made some decisions that people to this day are critical of. I stopped program project grants. I didn't think that the Institute could afford them. I cut way back on the number of center grants we were doing because they turned into entitlements, and I thought that was inappropriate.

I tried really hard to bring in people from outside of the traditional dental schools to try and up some of the science. That's not to say that some of the people from dental schools weren't doing great stuff, they certainly were, but it's a big world out there. And I think with tissue engineering, with clinical trials, we also started in earnest something that Hal Slavkin started related to the use of sialochemistry.

Irwin sort of invented all of that back in the 60s, so I was very, very familiar with sialochemistry, and indeed, some of my very first publications with Irwin were on distinguishing oral diseases by analyzing the saliva, so I have a series of papers on that with Irwin. And Hal sort of started it and we just jumped on it.

KD: Was that grants, or was that intramural?

LT: That was all outside. The sialochemistry was all outside. And the craniofacial biology was mostly outside, although there was a presence intramurally, Ken Yamata's lab in particular. The bone people, Pam Robey, Marian Young, Larry Fisher doing a lot of work in bone and cartilage. But I just built off of things that Hal had started in those one or two places.

KD: Let's step back and talk about something contextual. At this point, there's a lot of studies coming out linking periodontal health to things like pregnancy and problems with pregnancy, heart

disease, diabetes. So I get the impression that this would have been an opportunity, a way to think about dental research in a broader fashion.

LT: Yes, well, the first big trial that was properly powered that we supported was one that showed periodontal disease was not linked to heart attacks, much to the dismay and chagrin of all the periodontists in the world. There had been many underpowered trials that had suggested that they were, and when you did the trial properly powered, the answer was no, it's not.

Now subsequently there have been many, many, many studies. Most of them are association studies that are under powered. And I fear that at least a subset of the discipline continues to fall in that trap. They make a sort of preliminary observation; it doesn't really prove anything because it's underpowered; and then the next headline is "floss or die" or some silly thing like that.

I have no doubt that there are linkages related to the inflammatory state of the body, and there is not doubt that periodontal disease in particular contributes to that inflammatory state. But whether that inflammatory state is the major contributor in these various conditions that people find associations with, I think the jury is still out. Now, I confess to not being completely up to date in this literature anymore because 13 years ago now I stopped being a dentist again to assume my current role as principal deputy is my position of record.

But I fear that the field in their excitement continues to fall in the trap of looking at observational studies. Association doesn't mean causality, and I can't tell you how many times I've said that at how many meetings. But hopefully by now there is firmer really solid evidence *vis a vis* causality that has emerged from properly trialed studies.

KD: That's really interesting, because at the time, in the journals, this was written up as this is why we're important. This is our reason to be. But it sounds like there is a vulnerability, a flip side.

LT: I remember the first meeting that I presented the Michalowicz trial, which was the one. The "New England Journal of Medicine" published this trial that had a negative finding, but it was done so well that they published it anyway. And I mean people didn't talk to me the rest of the meeting. I had killed their golden goose. I kept looking at them and saying, "If you wanted to be a cardiologist you should have become a physician and taken your cardiology residency. You're a periodontist; get over it." That's too narrowminded. Okay, fine. But until you show me some data…

So I was not very popular, particularly with organized dentistry, people in schools of dentistry, because they felt that I was not sufficiently supportive and was not putting enough resources to find out these associations in terms of causality. With the benefit of hindsight, maybe they were right; maybe I should have put more resources to it. And I suspect that my successors, both Dr. Somerman and Dr. D'Souza, have or may be doing that. Again, I honestly haven't kept track of it.

But no, I was subject to quite severe criticism, but I just didn't buy in. And I have to say what they didn't understand was around the Institute, Center director's table these "floss and die" headlines made the Institute a little bit of a laughingstock. And it was only until properly powered trials were done, at least during that nascent stage, began to sort some of this stuff out that people said, "Okay, they're trying to do this the right way. Everything will be fine," and we re-normalized things.

But it was the thing. It was the *raison d'etre* to be a periodontist or dentist in general. And there's lots of good reason to deliver dental care. Preventing heart attacks may not be one of them. Now again, there may be newer data that I'm unfamiliar with and I completely concede that point if that's true, but at the time there was no solid evidence for that.

KD: That's great. We've set the table, we've brought you into NIDCR, talked about the things that were on your agenda. Anything else we should touch on up to this point that we haven't hit yet?

LT: I hope you are getting the sense that I am probably one of the luckiest people in the world because so much of what happened to me was serendipity. And amazing mentors. You know Bowen was a great mentor to me also. He would tell me things in a very unvarnished way, as you might imagine as I've describe him, but he was a tremendous mentor. When I got to NIH, Ruth was a tremendous mentor. We sat in this room, this very room, and talked about all manner of things and she was really very, very helpful during my sort of nascent time here. So I mean if you're going to sum me up in one word, "lucky."

KD: Fortunately, I don't have to do that. This has been an excellent talk. I know we've got to wrap up here. Thank you very much for your time today. I appreciate it.