NIDCR Oral History Project

Interview with Dr. Lawrence Tabak

Conducted on September 7, 2023 by Kenneth Durr

KD: This is an interview with Dr. Lawrence Tabak for the NIDCR Oral History Project. Today is September 7, 2023, and I'm Kenneth Durr. Dr. Tabak, last time we ended with your coming into NIDCR, talking about some of the strengths and weaknesses of the Institute that you inherited. I want to start today with going back a bit and talking about something else that you inherited, which was the Surgeon General's Report that came out in 2000. It's lauded as being the first report that covered dental science. Tell me about the significance of that report, and particularly how it developed into this call to action that came out three years later.

LT: First, full disclosure, I take zero credit for that report. All of the work was done by colleagues prior to my arrival at the Institute, Dushanka Kleinman, who was the Deputy Director of the Institute, and Caswell Evans, who had some affiliation with the Institute (I don't recall exactly what it was) but the two of them really were the leaders. And I remember vividly joining the Institute basically the day of, or the day before, this report was being released. And I was at a townhall meeting with NIDCR, and I was asked to comment on it. And I had read it, but my strength was not public health, and I trained, really, as a basic scientist, and it was a bit of an unnerving situation for me.

But I will say the report was substantive and, as you said, several years later, again, my colleagues, I don't take any credit for it, were able to build upon that report to turn things into an action plan. And it really put dentistry in a different light. It helped connect the mouth to the rest of the body, and I think ultimately paved the way for greater coverage for kids, maybe not so

much for adults, but certainly greater coverage for kids. And really, on the public health side and on the community level side, formed the basis of what the Institute engaged in for many years after its release.

And it was out of the desire to update that, that my successor, Martha Somerman, decided to put together this next iteration of the Surgeon General's Report. And Dr. Somerman decided to step down as Director. There was a change in administration, and so it became a little, awkward I guess would be the word, to have the new administration embrace something which was fine, but because it was from the previous administration, it became a little awkward, and so it was left to the current NIDCR Director, Dr. D'Souza, to navigate that. I helped a little bit with the department, but I think what ultimately emerged, and I know it's because of a lot of hard work that Dr. D'Souza personally put into it, and some of her team, what emerged was a really good update on that Surgeon General's Report which went much further than the original report, but that's fine. I mean, that's the whole point, is to build upon.

So yes, I do remember that. I do remember speaking to it the like the very first day I arrived and feeling incredibly ill-prepared and uncomfortable doing it. And it was not the last time I felt ill-prepared and uncomfortable. But I was very fortunate in having colleagues who metaphorically took me by the hand guided me and so forth.

KD: This is a messaging exercise; it's distilling a message and getting the message out who was the audience? Was it Congress? Was it interest groups, universities?

LT: All of the above. And that was the beauty of that report and I hope the most recent iteration is that every stakeholder, Congress, patient groups, academia, the dental profession, every stakeholder group saw something in the report for them. And I suspect that will be replicated

with this most recent report, because the feedback I've gotten is extremely positive. So it was it was for all of the stakeholders.

Congress, I think for the first time, began to understand the intimate connection between oral health and overall health. At the time, Surgeon General Satcher was a tremendous spokesperson and was a brilliant speaker and really helped us back then. And I think subsequently Surgeon General Murthy has helped in his way in amplifying the messages in that report, which strictly speaking, was not a surgeon general's report but it was commented upon by him and his team.

And I think Surgeon General Murthy helped a great deal as well, because if you if you look at oral health in its fullest dimension, many parts of Health and Human Services have equities. It's not just NIDCR, there are CDC, and FDA, and AHRQ, and there were different parts of the Department at play. And this, both the most recent report and to some extent the first one, I think provide some guideposts for people.

So when you have such a big department as HHS is, and then you have something which is really, really important but maybe not necessarily as visible to everybody as cancer, cardiovascular disease, and so forth, it helps to have something like this. So again, I take zero credit, but yes, very important, very, very important materials.

KD: Okay. Something that fits into that area as well is Friends of NIDCR, which was a fairly new organization at this time. Clearly your relationship with that group had to have been very limited, but talk to me about the role that it played and the things that you were able to accomplish with help from that organization.

LT: Well, I have to say, if I'm being honest, the relationship was mixed. I think that the folks who created the Friends organization were very well intended, and they really wanted to help the

Institute in, frankly, any way possible. but there's a dividing line between what a friend's group should be involved with and what they shouldn't be involved with. And so surely if they are so disposed, they can advocate for NIH, for the Institute. That's all fine because we can't lobby Congress, obviously.

But when it came to programmatic decisions, that's where I drew the line. And I think for some members of the Friends group, they may have been a bit disappointed that their influence was not more extensive in that domain. The other thing was—so I'm not a social butterfly, and I'm being charitable here—and so I have always avoided the rubber chicken dinners as much as humanly possible. I mean, there are certain things, of course, I have to attend, but I really—

And unfortunately, the Friends group made a habit of honoring their own, and it just didn't seem reasonable to me for so much energy to be expended on taking turns honoring each other. Now, I'm a curmudgeon, and I'm anti-social, and I understand all of that. and so, I'm sure somebody else would look at this in a very, very different way.

But the good news is the organization did advocate on the Hill for NIH as a whole and NIDCR, and it formed the basis of what was a renewed Friends group when other people got involved in terms of its management. And again, I had zero to do with any of that and I haven't really kept up with it, so I really don't know but I've heard second, third hand that things are on a much better course now than perhaps they had been in terms of expectation and so forth.

But again, I want to emphasize the Friends group, from its earliest inception, only with the best of intent. I mean, people were donating their own time, their own energy, in some instances their own resources. They really wanted to see the Institute succeed. I think they were a little taken aback when I was chosen as the Institute Director, but that's all fine. But I do think that over time it did lead to some really good things.

And other institutes have modeled groups after that Friends group. The Eye Institute, for example. I think the National Library of Medicine was another example. NCATS may be a third, I don't remember. But several other institutes and centers used the NIDCR Friends group as a model. And people only do that as a sign of flattery. They thought what the Friends group was doing was good, and maybe they also like rubber chicken, I don't know.

KD: We talked last time about the changes that you were making in your first couple of years in the extramural, intramural programs. At the same time, there's a lot of changes going on at NIH itself, culminating in the 2006 Reform Act. But Dr. Zerhouni's got the Roadmap happening, which I've discussed with other folks in other divisions, that really people at your level that would have involved a good bit of time in figuring out how to participate in that. Talk to me about how you participated, your people, NIDCR in general.

LT: Yes. So I resonated very strongly with the Roadmap, because at some level it was what a research dean does. You have a central set of resources, and you allow everybody to contribute and collaborate. What the Roadmap did is it allowed small institutes and centers to basically team up and do things that only the large institutes had been able to do on their own.

And so NIDCR was all in in terms of the Roadmap. We participated a great deal. I personally co-led with Pat Grady, who at the time was the Director of the nursing institute, the team science Roadmap. And we had a number of initiatives that were launched from that.

Dushanka Kleinman, who I mentioned earlier as the Deputy Director at NIDCR, ultimately went to the Roadmap office to help lead certain aspects of it. Back then it was called the OPASI. I have no idea what the acronym stands for, but I am told by people who speak Serbo-Croatian that it means look out. I don't know if that's true or not, but it was a transformative approach and I give Dushanka a great deal of credit.

So in addition to Dushanka's presence in a leadership role, I personally was very involved. It was the opportunity for me to work directly with the Director, with Elias, which was a great opportunity for me. Because we had different backgrounds, but both knew how to run large things across an academic center and so we just applied those principles here in NIH together with many other people, obviously.

And I think some of those relationships that I made across the board at all levels of the organization, from very junior people to very senior people, actually some of those persist to this day, although sadly, a lot of those folks have now retired. But I thought it was just a great opportunity for the small ICs to be able to do larger types of efforts that their budgets just wouldn't allow for.

KD: What's an example of that?

LT: So for example, we did a lot of work on putting together centers of interdisciplinary research. And the inside joke was any time somebody tried to do something that was interdisciplinary, the first line of the review was "This is an overly ambitious, unfocused application." And there is some truth to that because of the way the institutes and centers are organized.

What this allowed you to do was to combine cardiovascular research with dental research, with cancer research, with basic science, and do it in an integrated way, but in a new way. Probably the poster child was the microbiome project.

Now as an aside, dentists had been doing the microbiome research for years (we called it dental plaque) and in fact led the way. We were one of the first to do this. But what the Common Fund allowed us to do, or this approach, this Roadmap, it allowed us to get all the institutes together and say, okay, which part are you interested in? And so the GI tract, urogenital tract, the skin, the

mouth. And what emerges is the birth of a brand-new field of how microorganisms interact with and influence the host cells.

It's not scientifically correct, but the tagline was "You're born 100 percent human and die 50 percent microbial" because you get all these inhabitants of your body. If you fast forward, we now know that the microbiome influences just about every physiological process in the body, sometimes in a deleterious way, sometimes in a very positive way, and so people—

There are now fecal transplants in order to enhance one's intestinal microbiome. We now know that certain cancer drugs don't work as well because of the nature of the gut microbiome. There's some evidence now that the microbiome can influence cognition through neuroendocrine circuits and so forth. I mean, all of that never would have happened if not for the playing field of allowing every different discipline to come in and play.

So you needed genomics because you had to identify in silico all the different organisms, many of which, over half of which, were never cultivated. The old-fashioned way was you cultivated the organism and then you followed Koch's postulates, and you figured out what organism caused disease and so forth. This was all identified in silico through different phases of genomic sequencing.

It got better and better and better as time went on, but at first, they were just sequencing transfer RNAs, and now of course, you just do shotgun whole genome because it's become inexpensive and fast and so forth. So you had the genome institute, you had the various clinical sub-specialties of medicine, and dentistry included, and everybody was at the same table.

You had people who were interested in skin disease. Whoever thought that skin disease was going to be a thing when it related to the microbiome? But it is in a very real way. So I thought

Elias's approach was brilliant. And I thought what emerged—and this is only just one example, there are many, many, many examples of outstanding things that were developed that we never would have had without that opportunity.

KD: The microbiome project, for example. Where did the initiative come from? Clearly, there's some research supporting this, but was it one of the institutes driving it?

LT: Well, it was several institutes driving it. It was genome, it was dental, and it was NIDDK. It was the three of us. Genome brought the horsepower of the methodology, dental brought the historical understanding that, yes, these communities live on the surface of your body, and DK brought the gut, where there's just an extraordinary diversity of microorganisms, although I have to say the mouth can give you a run for your money. It's pretty diverse.

And then other groups came in and everybody sat at the table as equals because it was nobody's money; it was the house money, so to speak. And it was very empowering.

KD: Excellent. Something else that was happening in the mid-2000s. You undertook what was referred to as a program to accelerate clinical research, moving from small, single-center trials to larger, multi-center trials. What was the genesis of that initiative?

LT: When I came to the Institute, everybody was worried that I was going to turn it into a basic science institute, and mostly what I focused on were things like clinical trials. I was alarmed that so many of the publications of NIDCR trials ended with "Future studies that are of higher power will be needed to definitively answer the question."

And when I asked staff why we funded trials that were underpowered, I was given the wrong answer. The answer I was given was, we can't afford to run a properly powered trial, because if we did that, we would only have money for one or two trials a year. And I felt that was the

wrong answer. Because to run underpowered trials just made no sense for me. I thought it was a waste of resources.

I was also told that, well, we have all these trialists out there and if you only fund one or two trials, what are the other people going to do? I also thought that was the wrong answer because I didn't view NIDCR or NIH as a whole a jobs program for researchers. So I took steps to bring in people who actually understood how to run proper trials, because I'm not a trialist, it's not my expertise.

And so I was initially able to recruit Bruce Pihlstrom from Minneapolis, who had a long track record of running trials. He recruited some folks who had run big trials at some of the other institutes. And it was through their efforts initially, and then subsequently Pamela McGinnis was recruited from NIAID to continue in that way, who had run very, very big trials at NIAID, to get the Institute into a more modern framework where, step one, power the trial to give you a way of answering your null hypothesis. And if you can't afford to do that, then don't do it at all.

I told everybody at the Institute they shouldn't worry about the money, they should just worry about queuing up the very best trials. And if we can only do one a year, then that's what we'll do. And if we could do two a year, then that's what we'll do. And I did shift some resources around to allow us to fund a few a year.

But they were right, it meant that we were funding fewer trials, and we had to do a very detailed training, if you will, of some of our extramural Investigators who were not used to the rigor needed to do trials of this type. Some were, of course, but some were not, and we didn't want to leave anybody behind, so to speak. And so we did do workshops. I mean, it's before webinars, but the early day equivalent of a webinar. We did workshops and at national meetings we did

presentations, and when I say "we," I mean my colleagues, because they were the experts. I could tell them how to do an enzyme assay, but I couldn't tell them how to run a trial.

But I think the Institute found itself in a better place after that. Now I confess, I haven't really kept track of the types of trials that have been funded since my departure, and so whether they re-equilibrated to some happy medium or whether they stayed only funding well-powered, larger trials, I don't know.

KD: Okay. I want to turn to something that in some respects could be considered a signature of your time, which is the Practice-Based Research Network. And I want to get to where that came from. It's an old concept that goes back to primary care, that sort of thing, but this is something very different. Tell me where that concept came from, what the challenges were of implementing it.

LT: Well, it came from group discussions with my team. I was concerned that when I would go to a meeting—when I went to a research meeting the usual suspects showed up and we talked about the usual things. When I went to a more clinical meeting, like an American Dental Association meeting, basically nobody showed up and so we didn't talk about anything and that disturbed me.

And so I had some discussions with people at the American Dental Association, the American Dental Education Association, discussions with people who are running practice-based networks in their institutes, and said, "What if we made the Institute relevant to the community practitioner of dentistry? Because after all, most dental care is delivered," at least at the time, "in community-based practices." Now today economics is driving it to a slightly different model, practices are being bought up and so forth, but basically, it's community based. I mean, that's the point.

And so we collectively came up with an idea: could we empower practices to do simple observational studies and then ultimately simple interventional studies to answer practical

questions that dentistry wanted answered? And so it required a tremendous amount of socialization, because most practicing dentists want to deliver what they view as the best care to their patient, full stop. And they didn't want anybody, least of all somebody from Bethesda, Maryland, telling them what to do.

Now of course it was voluntary. They didn't have to participate. But when you laid this out and you said …Well, so observational studies people understood, and they were okay with. But interventional stuff, like should you use a plastic restoration or an amalgam restoration, that got tricky because people wanted to deliver the care that they thought was best for their patient, and so we had to modify things.

Now, as it turned out, if you fast forward (although you'd have to ask Dr. D'Souza because I'm a little fuzzy on what happened during her tenure) so COVID hits. I think the practice-based research networks was the first place they went to begin to get a better understanding of how practices were dealing with the pandemic.

Now, it was a different practice-based research network. It had evolved and I'm sure got better over time, perhaps more sophisticated over time, but for the first time, dentists in the community kind of cared about the dental institute because … And the questions were largely submitted by the practitioners themselves through their groups, so they were very practical things.

I don't remember the specifics, but they were very practical kinds of questions. And again, the most successful, at least at that time, were observational things. Perhaps it's now evolved to where they are more successful doing things that are a little bit more challenging, but you'd have to ask Dr. D'Souza.

KD: So in one respect this was a good transmission belt between the Institute and practitioners. And information was coming back to the Institute, I guess. You were getting results from this.

LT: It was good data. They were publishing work as a consortium, and so it was a two-way type of thing. Now, the people in academic health centers were critical, unless they happened to be one of the coordinating centers, because "Oh you're spending all this money and you're not getting a whole lot out of it, and it's not very sophisticated."

Dr. Mandel used to tell me proving the obvious is sometimes the hardest thing to do. And I think some of these things were proving the obvious, if you will, so I thought (and again, I don't take credit for it) it was a collective idea, and as you point out, the concept has been around for a long, long time.

But again, if you think about it, dentistry is so community grounded, it made sense. And it would be interesting to know what the latest iteration is, because I think they recently recompeted these things.

KD: Right. There was a big reassessment a decade later under Dr Somerman. Let's move on to some other big projects. There was a TMJ study.

LT: Yes. This was a really, really important moment in the Institute's history. For years and years, people with TMJ dysfunction, or TMD I guess they prefer, reported problems and had nowhere to go. And many practitioners and many academicians concluded that because they couldn't see something on a radiograph, or fast forward, using MRI techniques and other sophisticated imaging, that it had to be psychological.

And patients would descend upon us and basically say, “Look, don't tell us we're crazy. Our lives have been destroyed. We have been mistreated, over-treated, and we in many instances are worse now than when we started.”

Now as it turns out, I have a very close friend of many, many years, atypical because this individual is male not female (most of the TMJ sufferers are female), but this individual happens to be male, and I watched his life deteriorate because of this. And because of what I know about the individual, this “I'm not crazy” resonated very strongly with me. We tried in vain to get other institutes and centers interested, and unfortunately at that moment in time they said, “Nope. TMJ is yours. Good luck.”

So we were able to fund the OPPERA trial, which in principle was simple. Let's round up a bunch of people who have no symptoms, who have no problems, and let's, based upon available data, get enough of them so that we'll have incidents of conversion to TMJ problems, and we'll follow them longitudinally, before and after, and figure out what the heck is going on.”

And the late Bill Maixner was the PI. Unfortunately, Bill passed away a few years ago, but it was he who put together this amazing team of people. And they looked at everything. They looked at biopsychosocial parameters, they looked at genetics, they looked at endocrine function, they looked at cardiovascular function. I mean, they just looked at basically everything.

And as has been proven true subsequently for many other chronic conditions, there is definitely an axis in behavioral issues that is cognitive and so forth. But there are also genetic underpinnings. There are also some physiologic underpinnings in some instances. And so what was, “Oh, you're just crazy, go away,” we learned, and again this is now in common with other very complex chronic pain conditions, is that it is multifactorial and needs to be treated by a multi-disciplinary team of practitioners.

For example, there are certain gene variants where somebody is much more sensitive to certain types of pain which are very common in TMJ patients, who would have known, right? Well, it was because of this that we began to learn this. And the other thing that this study proved is "Doctor, do no harm." And we worked with the dental profession, and I give the ADA a lot of credit because there was pushback at one time, to point out where sometimes palliative care—hot compresses, cold compresses, jaw exercises to slowly open the mouth wider and wider, are far better than the more irreversible procedures such as occlusal equilibration and surgery.

Now that's not to say that some of these more aggressive or irreversible treatments are never needed; there are some circumstances where they are; but for the most part, people who present with TMJ problems, it's reversible. So if the dentist or physician does no harm and is supportive, over time it can be reversed. And that's what the study showed. So I think that was a very, very important study, and it set up the Institute with that knowledge and with the understanding that there are other chronic diseases like this also that are painful. It set up the Institute now to truly partner with other institutes and centers in NIH.

And so at the most recent iteration, and again you'd have to ask Dr. D'Souza, but I believe they now have a Coordinating Committee that consists of several institutes and centers including NIMS and NCCIH. So there's now this consortium, and so the whole field is in a much better place. And again, I think the current efforts building upon the stuff that we started back then, but obviously building to where it is now, which now it's the idea saying mainstream medical dental practice, which is so far ahead.

I will tell you that the person who deserves a tremendous amount of credit is Terry Cowley. Terry Cowley is a patient, but also an advocate. She runs the TMJ Association. Her husband is

actually a very well-known cardiovascular physiologist, and he helped her as well. And they kept at it. They were in my face without let up.

And together with my personal experience with my friend, with their getting Congress to give me a kick in the backside a little bit, and also then subsequently partnership and working together, I think Terry is an example of a patient advocate who's done amazing stuff for people who are afflicted with a disease or condition. And I think the Institute and I think all these patients owe her a great deal; I really do.

KD: Yes, it's good you pointed that out. I noticed that by your time and definitely afterwards the advocacy groups have a seat at the Advisory Council. They're coming. And you mentioned when your group first came up with this idea, the other institutes were like, no, you go ahead, we're not interested. Was that a resources issue? Or was it the fact that they didn't want to get involved with one of these fuzzy chronic illnesses?

LT: I think more of the latter. They wanted a test. they wanted a blood test. They wanted something that was pathognomonic on an MRI. They wanted it to fit neatly into the medical coding, and it doesn't, but neither do many other chronic painful conditions. And if you fast forward to the HEAL Initiative, which I played a pretty major role in, TMJ people are at the table with people with many other chronic painful conditions—phantom limb and pelvic pain, and the list goes on and on. And there are many more commonalities than differences.

KD: NIDR was very strong in pain research for years and years. Was that still the case when you were Director?

LT: It was, but they were not keeping up with the times. but it was the same group of people doing the same experiments over and over again. They were very strong at peripheral pain, but most of

them—not all, most of the Investigators didn't think about the brain as the center of the pain response. And so one of the things that I did was I reached out to the then Director of the neurology institute, Story Landis, and invited her to one of these workshops on TMJ.

And I said, "Story, how do we convince neuroscientists to get involved in this painful condition?" And we talked about it and agreed that you have an acute situation with TMJ, and most people it resolves, and everything is copacetic. For a small subset of people, that acute situation transitions to a chronic situation.

This is exactly what happens in all the other pain conditions that I referred to, and so it's likely, and there's now evidence to support this, that that transition from acute to chronic pain involves a rewiring of the brain synapsis so that now the pain becomes hardwired. And so a call goes out to neuroscientists who are interested in neuronal plasticity, and of course they're all studying memory, but we're trying to get them to study pain now. And some took the bait and became engaged in this. And so the level of conversation and the diversity of thought among the investigators who are now beginning to study this condition just became much greater.

And the same is true for the other pain conditions. But it all started with me being so frustrated with the same people getting funded over and over again to do the same experiment. And it's not their fault. Because they kept getting funded, so why shouldn't they keep doing the same experiment? So finally I said, "No, we shouldn't do that anymore. We need to bring in new people."

And when I was challenged, "Well, what new people," that's when I went to Story and I said, "Okay, tell me about the brain. Because to me it's just like it's up there but that's about all I know about it."

So that really, I think, set up future engagement. And now when you go to a chronic pain conference, you would think it's a neuroscience conference.

KD: Yes, so you went to the neurology institute. Did this become a matter for them? Does NIDCR say, "You do the brain research and get back to us with what you find out"? Or does NIDCR put out FOAs for brain researchers?

LT: I think both models were employed. We wrote funding opportunities to entice neuroscientists to play with us, and again, it wasn't so much a resourcing issue as it was, "Well, I don't want to do that. I'm a neuroscientist, why would I want to study that? I'll get laughed out of my department."

And so it had a you had to do a little education, a little socialization. But today chronic pain is just a horrible thing and so much of the opioid crisis was initially fueled by chronic pain. And so now I think people think it's quite acceptable for neuroscientists to engage in these types of inquiries.

KD: Another big initiative is the FaceBase consortium.

LT: Yes.

KD: Was that similar? Did that come out of your group brainstorming? Did that come from the activists?

LT: So here I do think that the patient groups helped recommend that we move in a certain direction. But there had been a long history. And of course, the antecedent to this was Hal Slavkin, who was a craniofacial scientist. And so he already, under his leadership there was already a substantive portfolio of craniofacial research in the Institute. And what occurred to me and the investigators themselves was that each group was doing their own thing, but there would be

obviously a great deal of power and leveraging if we could bring it all together. And so that's how that consortium idea began. It was group thing.

But I think it's in some ways the patient groups, people interested in clefting, people interested in some of the craniofacial dysmorphologies, and the investigators themselves all arrived with the mindset that we would do a lot better if we if we pulled it together.

Now the early approaches were quite rudimentary. I think what they have today is much more sophisticated, and Dr. D'Souza is a craniofacial biologist herself, so I think probably it will now take on an even more important role going forward. And I think there have been a couple of evaluations in between.

The cancer institute had been doing this stuff all along, for years and years and years. The heart institute had some stuff. But the smaller institutes tended not to have these kinds of things. And so for us it was sort of this experiment, and how much money would it sop up and so on. But the idea was that if you had a one-stop resource you would further research and you would facilitate more collaboration. And I think that's all borne out.

Groups maintain their individual identities, but there's also a lot of groupthink now. and I think as a result the field has moved ahead much further than they would have. We don't have to catalog things anymore. We can begin to think about ways we might want to intervene. But at the time, for a small institute it was "Gee, what is this crazy guy doing?"

KD: Because there was concern about the resources.

LT: Resources and will people play together.

KD: Speaking of playing together. Late in your tenure you reorganized extramural. I realize reorganizations are always happening, but you reorganized extramural, and the quote was "to

reflect the current NIH model." In what respects was NIDCR extramural not in the NIH model—What did you do to fix it?

LT: First of all, the review and the program were mixed together, lumped together, and so we separated those out. It's like the fox watching the hen house. I thought we needed to separate that more formally than it had been. And also, we had a pretty decentralized model, and every Program Officer had his or her own mini fiefdom if you will. And I don't mean that pejoratively, but they had their own little … and we wanted to break that up a little bit so that there would be cross fertilization among the different disciplines.

And so we combined a lot of things, rather than keeping individual little areas. And I think that helped, because NIH by that time was all about multi-disciplinary, interdisciplinary team research. And I think that helped our investigators moving forward to accomplish those types of things.

And in so doing, it allowed them to attract investigators from outside our traditional field, people from particularly the medical schools, or the schools of public health, or the colleges, chemistry department and so forth, to begin to take their expertise and bring it to bear on the questions that we have.

Whereas if you have this narrow narrowly defined focus, a chemist doesn't see what's in it for them. A cardiovascular physiologist doesn't see what it's in there for them. But if you do it more broadly, it becomes more apparent and obvious what the opportunities are, and of course there are many. And so that's why we did it that way. And I think most of NIH went in that direction.

KD: Okay. Anything else we should talk about as far as initiatives, big changes?

LT: Well, the only other one that comes to mind is the sialochemistry initiative. This was actually the only natural one for me because I grew up with the godfather of spit, Irwin Mandel, although Hal Slavkin had started it. I didn't start it, he started it. But I certainly foot stomped on it because I thought it was important to see what the possibilities were, what could we use saliva for, both in terms of a diagnostic for systemic diseases and conditions as well as diagnostic for oral, local conditions and what could technology bring to bear.

So I always had this vision of a little sensor put on a tooth surface that would be continuously bathed with saliva and that by telemetry it would feed into a computer which would give you real-time values of whatever analyte it was that you were interested in. There are things like this now, although they're not being used in the mouth, and I would say that a lot of cool technology was developed.

So the whole HIV detection with a saliva-based kit came as a result of some of these efforts, although NIAID was involved as well because it was about AIDS. And then, of course, during the pandemic, salivary diagnosis of COVID became a thing. Many, many people gave saliva samples as opposed to the nasal swab. And all of the principles of that were built off of the work that was done related to sialochemistry.

So that one was natural. I knew all the players in the field, both within the traditional dental world as well as outside the dental world who are more the engineer types who didn't really care what they were analyzing, they just wanted to make it smaller, faster, more robust. And so we were able to connect oral scientists, people interested in sialochemistry, with bioengineers. And companies were formed and also all sorts of interesting things happened. And I think there's a lot more that can be done here, but I think now that it's in the commercial sector, I think companies

are driving a lot of this innovation now and less so in academia, which is not a bad thing. I think that's a good thing.

KD: Right. and one of one of the tried-and-true functions of NIH to pioneer something and—

LT: Exactly.

KD: You had had a lab going the whole time.

LT: I didn't start the lab the first year I was here on purpose because I wanted to get myself organized a bit. But starting in 2001, my lab began, at NIDDK because you can't have a lab in your own Institute, and that's where it remained until 2010. And then I moved my lab when I came over to the Office of the director to NIDCR because my main collaborators were at NIDCR, although even though my lab moved to NIDCR, it's never been paid by NIDCR. It's paid by a tithe of all the institutes and centers.

And my lab review has never been conducted by NIDCR; it remained in NIDDK because the dental oral science community is pretty small, and initially the first review it wouldn't have been appropriate because a couple of the people had been former trainees of mine, and I had appointed all the other counselors, so that was a conflict.

When it came up for the next one (these occur every four years) there was an obvious conflict, and I said let's just keep it at NIDDK. What difference does it make? And they've been very gracious. And in fact, I recently had one about quite not quite a year ago and still at NIDDK. So yes, I've had a lab all this time and have really been very privileged to be able to do that.

KD: What kind of work? Have you continued in mucins and salivary?

LT: What we did was, I left behind a lot of stuff when I left Rochester, including a lot of grants and so forth. And I didn't want to compete with the people I left behind, so we really focused our

attention on how the mucin is synthesized and how it acquires its sugar coat. And to do that, we focused our attention on one of the enzymes that does the first committed step in mucin biosynthesis.

And we had just done some of that work in Rochester, so when I came down here, I focused all of my energies on what that enzyme does and how it does it. And I was able to take advantage of the unique community here of structural biologists to express, purify and crystallize one of these enzymes.

And we were able to solve the first crystal structure of this class of enzyme. And that was a big deal actually for the field. And subsequently we've continued to be able to make contributions like that both with structural biology as well as understanding what the substrates are of these enzymes, because it turns out it's a family of 20 enzymes and subsets of them have unique mechanisms of how they recognize the part of the mucin or other molecule that they're going to decorate with these sugars.

And so what started out with like three or four publications in the 70s, our group started in the early 80s on, now there are thousands of publications about these enzymes, which is great. And interestingly enough, the other one of the first people who got into this field, a guy named Henrik Clausen, is also a dentist. He's at the University of Copenhagen and we have been … He has a massive group of people and has gone way beyond what we've done, but he and I were competitors, but in a friendly way.

And then one of my former colleagues who came through my lab but then got her own tenure track position and is now tenured at NIH for a number of years Kelly Ten Hagen, so we continue to collaborate. And she's lapped me like five times over. She's so far and away… In fact, she's getting the preeminent award from the glycobiology society at this meeting coming up I think in

November, and something that I never, ever would even be nominated for. So it's so wonderful to see how amazing she's done.

So we really reinvented ourselves, taking advantage of the unique attributes of the intramural program where it's really easy to collaborate with everybody. And most recently, mostly Kelly, although we've gotten involved a little bit, we've started to look at some of the clinical issues related to this enzyme family.

So if you're lacking this enzyme, you have a congenital disorder of glycosylation. And there are at least two known examples of that with this enzyme family, one of which we have a mouse model that mimics the human condition. And among the presentations are craniofacial dysmorphology, so it's actually quite interesting.

KD: We have about 25 minutes to cover your time as Deputy and then Acting Director, so we'll hit the highlights here. And it appears that the first thing you did was went and led, speaking of fun acronyms, something called DPCPSI.

LT: I think there's one key thing before. I was the Acting Deputy Director between Zerhouni and Collins. I worked with Raynard Kington. Raynard Kington was the Acting Director of NIH at the time. He had been the Deputy. We had worked on several things over the years. We got along very well. He said, "Will you be my Acting Deputy?" I said, "Sure." He said it would be no big deal "You can keep the dental institute. Just help me out here with some administrative stuff."

And then the Recovery Act occurred. And so overnight we got $10 billion dollars to spend. And he said to me in the hallway right outside my door here, "Oh, and by the way you are going to coordinate the entire Recovery Act. Good luck." And basically, that became my job full time was doing Recovery Act.

So Francis is confirmed, Raynard goes back to being the Deputy. They asked me to stay on briefly to become the Acting Director of DPCPSI because I had been so involved in the Common Fund it was a natural thing that I could do. But it was only for a few months, it was like four or five months.

And then I'm back at the dental institute and I'm doing what I do there, and Raynard is back here being the Deputy for Francis. And then Raynard decides that he wants to go into academia, becomes the president of Grinnell, and so Francis does a search for the new Deputy. I'm invited to apply, I apply, and I get the position.

KD: Yes. how big a jump was it? Before, you at least had one foot in dental science, and at this point you're just an administrator.

LT: Well, it was a big jump, but not one that I hadn't had before because I was a research dean of an academic medical center. So as I break up my career, I'm a dentist, I'm not. I'm a dentist, I'm not, and so here I am again with nothing out of the ordinary to do with the dental institute other than what I do with any other institute.

And because I had been the Acting Deputy, the transition was a little bit easier than perhaps if I hadn't been. Because at least on some level I knew what to expect, although obviously Francis is a different cat from Raynard.

KD: Right. Yes. and I get the sense that Francis Collins would tend to give you projects and that you'd really hold down a pretty large chunk of those. Was that the case?

LT: Yes. And of course I have teams who work with me, of course. Francis had a very, very clear understanding of what he wanted and was very precise in defining what his hoped outcome

would be. And in many instances, yes, I was one of the folks who helped him with that thing, although there were other people as well, obviously.

KD: Right. One of the first ones that came up was the reproducibility controversy as far as scientific research was concerned. And this was something that NIH had to respond to.

LT: Right, and I think we did so well with a whole series of workshops and new approaches to peer review and new approaches to guide people for writing grants and how we do things in the intramural program to heighten awareness. Because everybody says science is self-correcting, but in this era of multi-disciplinary research, sometimes it's hard to know, if you're not an expert in whatever it is that the person is doing, to really understand whether things look the way they should.

And so it's incumbent upon investigators and particularly members of the team to ensure that everything they do is laid out in a way that will allow others to replicate what it is that they're doing. So in this space we're not talking about malfeasance or anything; we're just talking about doing whatever you can to ensure that the next person who wants to replicate your work has all the information they need so that they're able to do that. And if they can't, then you've got to figure out why they can't because that might be telling you something that's very important.

KD: Yes. So you said that you had working groups. things like that?

LT: Yes. We would have working groups across the agency, and I would either lead or co-lead those. We would get involved with our Advisory Committee to the Director, get their input on some things. We reached out to the community. Francis and I put together a commentary about this which was taken up by the community in a very significant way. And I think we were able to

make some improvements in the clarity with which people were putting together papers and grants and so forth.

But I think we still have to be vigilant. It's not a solved problem, because as science grows more and more complex, you've got to become increasingly complex in how you deal, to ensure that you're publishing replicable results, that you're putting into your preliminary data, data that is solid and can be replicated.

KD: Another thing that's happening during the 2010s is an emphasis on diversity and it takes place in a number of steps, including the creation of an Institute. Can you take me through that, maybe taking us up to the UNITE Initiative?

LT: Well, yes.

KD: Just the highlights.

LT: It's a lot. So the Institute came from a center, which came from an office. So that one was percolating along all the time. Where the Office of the Director, I think, really became engaged was a parting gift that Raynard Kington gave to the agency. And that was a paper that he was the senior author on by Donna Ginther, published in *Science*, which basically said if you're African American or Black, you have less chance of receiving an NIH grant. And that was after they had accounted for every possible parameter you can think of. And the only one that was left was because the person is Black or African American.

OK. So we had a problem because here we are, an agency that prides itself on being fair and equitable and so forth, and basically this publication and prestigious *Science* magazine says, "Well, actually no you're not."

So we started by socializing this and discussing it with many leaders around the country. And people from the traditional African American community had only one message for me, and it was you didn't need to do a study about that; we could have told you that a long time ago. And so that began our attempts at figuring out what the heck is going on.

And it's very complicated. Part of it has to do with who your network is. Do I know who you are as an Investigator? Well, I'm important. If I don't know you, you can't be important. And sadly, many people of color who are in research are not well known to mainstream, majority scientists. So there's that. Some of these investigators are at institutions that have lower resourcing, and so despite the attempts at normalizing the data, perhaps they didn't completely succeed, I don't know.

There was a whole myriad … The things that you're interested in may go to institutes and centers that have less resources. And if the institute or center has less resources, then you're less likely to get funded. So you talked about the new institute, NIMHD, which had been a center, they had modest resources. And if everything related to the health disparities research, or much of what we were doing in health disparities research, goes to that institute and their success rate is lower than most, ergo, you're not going to get funded.

And it turns out that people of color tend to be more interested in community-based research related to health disparities, health equity, and so forth. It's not that they're not interested in other things; of course they are; but just on average they're more likely to be interested in those topics. And so it's not the topic that's bad, it's they go to an institute that's lower resourced. Now, we actually tried to redress that over the last several years and NIMHD got quite a bit more money as a result to help balance that. But it's not completely in balance.

So that started everything. And then along the way as we were doing more and more outreach, we began to realize that we were listening but not hearing. And I have to say that was a particularly complicated thing for me to understand. Because I always thought I understood this stuff. I'm not going to bore you with my background, but by any measure, I came from a family, a single-parent family, under resourced, complicated things.

So I thought I understood this, not realizing that rich African Americans suffer just as much discrimination as poor African Americans. It's not about SES, it's not about education, it's about racism. And that was very sobering for me to learn because I truly thought I had this figured out and tried to be a champion, but frankly only understood a portion of the story.

And so that's how we started, we created the concept of UNITE because we wanted more feedback from our own staff. We wanted to empower them. We wanted to engage them. There was a group of African American staff at NIH, some extramural scientists, some intramural scientists called 8CRE, Eight Changes for Racial Equity (I may not have the acronym exactly) who reached out to Francis and me and said, “We need to talk.” And we agreed to, and they hit us over the head with a 2 x 4. No punches pulled. They just laid it out.

There was also another group of African American and Black scientists a bit more senior in terms of their tenure at NIH who also came to meet with us. They didn't use a 2 x 4, but the message was the same. Asian American scientists came to see us. And so through these various interactions—people representing the sexual and gender minority community came to see us. Through these various interactions, UNITE became fleshed out and has become, to my mind, the most important thing that the agency has done in many years.

Because if you can't have equitable treatment, how the hell are you going to achieve your goal of keeping people healthy? So it's on many levels, internal to NIH, external to NIH. The groups

continue to work strong. Many initiatives have come out, many, many advances, and I'm incredibly proud of our staff, who, they've mostly volunteered to do this, and they put tremendous time into it.

Even simple things. It sounds simple but it's really complicated. The great white wall. Have you heard about the great white wall?

KD: I haven't, no.

LT: So the great white wall are pictures of all the people who have won the Lasker Award at NIH, and with one exception, a white female, everybody's an old white guy. And so one of our scientists, a pediatric neural oncologist, wrote this essay about the great white wall, wanting to know why there's nobody who looks like her anywhere.

And that led to a whole portraiture effort so that we now have portraitures of a much broader range of our staff all over the place so that people feel more welcome in the environment. So you say, “Well, why is that important?”

It turns out it's really important. And it's like the first thing that visitors comment about when they show up. If they take the Metro, it's right in front of them. And various Funding Opportunity Announcements. And I’ll give you another example which it's like one of these, “Well why didn't I think of that?”

So we have all these amazing training opportunities for staff so that they can get ahead and get higher administrative-level positions both on the science as well as the strict administration. Except we had nothing for lower grade levels, nothing for GS 8, 9, 10, 11. It was all for 13 and higher. Well guess what? when you look at the demographics, guess where most of the African

Americans and Hispanics are? It's all in the lower grade levels, so they were getting frozen out due to a structural defect that we had in our system.

We just opened up a program now for 9, 10, 11. Overwhelming response, people clamoring to get into those types of training programs. Simple fix. I never figured it out myself. Somebody had to say, "Hey, what are you guys doing?"

KD: Excellent. I don't want to wrap up without talking about COVID. And you'd also mentioned the HEAL Initiative. Francis was still director when COVID hit.

LT: Oh yes, very much so. So the way we worked it out was Francis wanted to devote as much of his time as possible on COVID. So he did two things. He said, "Larry, to the extent that I can delegate things to you, you worry about NIH. And I'm going to put my full attention on solving this pandemic crisis."

So the only place that I personally touched in COVID was our internal response for our own staff. I was very involved with that, but all the external stuff, the Active Initiative with the pharmaceutical companies, all the work with the Department, all the work with the White House, Francis did all of that. I was an observer, but Francis did all of that,

I think Active was one of the most brilliant decisions he ever made among many brilliant decisions. I have zero credit for it. I had nothing to do with it. I was just an observer. And it was brilliant because we had all the great minds at the table together.

Now, what was good for me was when Francis finally decided to step down, because I had been an observer in all of these things that he was involved with, it made for an easier transition for me because I was at least familiar with many of the things.

Of course we're in a new administration now. We go from Trump to Biden. And the other good thing was I had been responsible for many of the ongoing day-to-day operations of NIH because he wanted to be freed up (he must have been working 100 hours a week on the pandemic) I was doing the same but for NIH and so forth, and so it made for an easier transition for me in all honesty. I don't think that was the intent but just how it worked out.

But I think Francis's leadership was exemplary. I think Tony's leadership was exemplary. I thought that every institute and center director did an amazing job helping us keep this place together. We did not miss a beat. Grants were all reviewed on time, grants were all funded on time, intramural research continued. The hospital never missed the beat. I mean the numbers were down, but we kept going what we had to do. And so I think as a community NIH responded in an amazing way.

KD: You also ran NINR for a little while.

LT: For like a day and a half.

KD: It was longer than that.

LT: That doesn't count. Here's what happened. Unfortunately, the bench in NINR was not very deep, and I had previously run NIMHD for a little while because when there's no obvious person, I would step in. I stepped in at NINR, and something like two weeks after that decision was announced Martha came to me to tell me she was stepping down as NIDCR Director. So then we had to do this somewhat awkward pivot from a dentist to a biologist. Actually, Tara Schwetz is a biophysicist, she's not a biologist. She's trained in biophysics.

And so Tara wound up running NINR for a while and then I went to the dental institute for a while until a permanent director was selected.

KD: And you've mentioned that you missed a lot that's happened at the dental institute, at NIDCR, but just to wrap up, your perspective on how things have changed big picture from when you first got involved to now.

LT: I think under Martha's leadership, under Rena's leadership, the science has become so much more sophisticated. When I first arrived, there was like dental research, and that's not to say that everything in the portfolio was not quite as sophisticated as the rest of NIH, but there were subsets of things that were not as sophisticated.

Under Martha's leadership, under Rena's leadership, you can't tell a difference between NIDCR and any other institute or center at NIH. And that's the way it should be. Because as we said in the Surgeon General's report 23 years ago, the mouth really is connected to the rest of the body.

KD: News flash for everyone.

LT: News flash, exactly.

KD: That's great. Anything else we should touch on that we haven't?

LT: No. I appreciate the opportunity to remember some of these things. It's a remarkable place, NIH, and initially I came down here because it's one of the few places where a dentist can come and actually be like a real scientist. Of course, that all evolved and I think the future is so incredibly bright for biomedical research and for dental science as well. I just hope that relations with the Congress can be normalized over the coming years, and we get back to a place where the Congress views NIH as an important asset for the nation.

KD: Right. Well, thank you so much. It's been great talking to you.

LT: My pleasure. Take care now.