Interviewee: Dr. Samuel Frank
Interviewer: Alison White
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Abstract:
Resilient is a term Dr. Samuel Frank uses to describe the Huntington's Disease community—a trait he has obviously inherited through his close work with it. In no-way an outsider to the HD community—Dr. Frank expresses his research and personal interests in working with Huntington's Disease in this jovial and laughter-ridden interview. From his first run-ins with HD through the affects of the HD community on his day-to-day life Dr. Frank takes us through his goals, his aspirations and frustrations as a researcher and clinician working with Huntington's Disease.

AW: It is April 17th, and we are here with Dr. Samuel Frank to interview him about Huntington's and his relationship working with Huntington's Disease.

How did you first hear about HD?

SF: How did I first hear about HD? Well, I first encountered HD as a medical student here at BU [Boston University], and we brought in a gentleman who had HD, and was at home and wasn't doing very well, and . . . so, as third year medical student I saw my first case. Because there were—this was in the mid 90s—and so there was a relatively large population of patients that were followed here, and there was just someone that came through. That was my first experience actually seeing someone. We learned about HD in medical school. It's one of the classic diseases that we learn about because it has so many applications to some of the other diseases as well, as not an autosomal dominant disease.

AW: Was that something you learned about more with the direction you took in medical school, as a movement disorder specialist?

SF: No. Everyone needs to take genetics in medical school. When I was going through med school—it was only two weeks. I hope that it's a whole lot longer than that now. But as part of that genetics course, we learned about Huntington's Disease. So that was everyone. And I don't know if that's specific to here as an institution because we had people who were doing research and were interested in it, or if that's nationwide. And again, in the mid-90s, that's what was done. So, everyone learned about HD as part of a genetics course. I don't know

that everyone saw a patient in medical school, but . . . but I happened to. So that was my first exposure for, to Huntington's.

AW: Ok. What about HD sparked and retained your interest?

SF: So I did do a movement disorder fellowship. But, it kind of evolved. I actually didn't—I wasn't even sure I wanted to go into medicine to begin with. And then when I was in college I spent some time and the University of Chicago, and I decided I did, want to go into medicine. And then I spent a year, also at the University of Chicago, studying circadian rhythms and fluctuations in hormones over the course of the day, and what happens with aging as well. And then I went to med school; and I was thinking when I went to med school I wanted to do something with sleep or endocrinology or something like that. But then in the summer between first and second year, I spent some time interviewing people with Parkinson's to find out what kind of sleep problems, they had. I am getting to Huntington's . . .

AW: Oh no! That's fine!

SF: . . . and I found that rather than the sleep aspect, which was interesting, I was really interested in the Parkinson's Disease. It was such a fascinating aspect: to watch people change over time, and to see the fluctuations. So that's when I decided I wanted to go into neurology. And I was so struck with Parkinson's disease, I was pretty sure I wanted to go into movement disorders, not just neurology. So then I did my internship/residency, and residency, at the University of Rochester. And toward the end I had to make a decision about what I wanted to do, and so I stayed at the University of Rochester for a two-year fellowship and did movement disorders. And actually, it was actually experimental therapeutics, which is clinical trials and . . . but the clinical side of it was about two days a week. That was all movement disorders. And, that's where I really got hooked on Huntington's Disease. Because I hadn't seen a whole lot before then. I thought I was going to spend most of my time doing Parkinson's, maybe some Dystonia and Botox clinic, and . . . and . . . a little bit of other things like Tourette's Syndrome and tics. But I really was struck by HD clinic, which was a very full day at least once a month . . . we . . . saw a ton of people through that clinic. Not all the fellows did Huntington's Disease clinic, but I choose to, and was just, completely . . . I know this sounds . . . I-I-I was bit by the HD-bug. I really felt a need to be involved with this community—right from the get-go. There were so many myths that people, that people would come in and they thought something was true because they had heard about it and, or a family member read about it on the internet, or whatever it may be. So, just from an educational standpoint, I felt that

there was a lot that we could do . . . Sometimes it was just knowing about the disease and what not to do that helped people out. I was really struck—there was one woman who I took off of a medication and she started walking again. I mean, that's clearly somebody, as a provider, wasn't doing her a service. So, just knowing about the disease I was able to help a person out. So, there's a lot we can do just by knowing about the disease, and education the community. And then, to see the multiple generations that it impacted. It just, you know, I felt like I could do something for the patients with Parkinson's, and with Dystonia. It was medical treatment that was there that we could help them, and improve their quality of life. And we could do that to some degree with Huntington's Disease, but not nearly as much as we could with other populations. So, I felt like there was someone who needed to, to be involved with them. I felt that could be me.

AW: Awesome. So, how has your relationship to Huntington's changed how you view yourself?

[5:28]

SF: . . . How I view myself? . . . I don't know that it's changed how I view myself so much . . . I really truly felt like that from the beginning, and I feel like that now, and I feel like the only difference in the past 12 years is that I've seen a whole lot more people and families, and I've had a whole lot more experience. And we've come a long way—but in terms of how I view myself? . . . I guess from an academic perspective, I just see myself as a more experienced person, versus a less experienced person.

AW: Ok.

SF: For example, I had someone from a pharmaceutical company who came to see me earlier this week. It's from a company that had not yet been involved with HD; they're just getting involved with HD now. And she was asking around to say, well, you know, if you want to find out about HD, or you want to find out about patients, or the community, who would you go to? And she kept hearing my name. And to me that was a surprise. A nice surprise. But I think that just means I'm someone who's vocal, who's experienced, who knows about HD, and is out there. I guess I'm only now beginning to, I guess, recognize that I'm one of the more experienced people out there in terms of HD.

AW: Ok. Well, congratulations to that!

SF: Thanks, I think!

AW: So, how do you involve yourself with the Huntington's community? Aside from . . .

SF: I'm quite involved. So, seeing patients is how I got started. And, when I came here in 2004 I did the same thing—I started seeing patients. I was also involved in the local support group, gave talks at the annual education day. So I've done the same thing. I give talks to the community, I give grand rounds at other academic facilities, and then I got more involved with HDSA at a local level. And . . . I think that they recognized that there was a young physician who was interested in HD and they wanted to take advantage of it—so I kept doing more and more. Finally, for the past three years I've been on the national board of trustees for HDSA. Basically, being the medical voice for the board. Just recently . . . I was elected to the Huntington's study group executive committee, so from a scientific and research perspective, I've gotten more involved, as well. I anticipate responsibilities for that organization are going to grow. So, I see patients; I am a site investigator, so I do research here. We do some local studies as well as regional or international. And I'm involved with the HDSA, some of the affiliate organizations.

AW: Ok. I'm going to switch gears just a tiny bit. What do you find most challenging about working with Huntington's Disease?

[8:38]

SF: Most challenging . . . Everything is a challenge. From the time I lay eyes on a person, whether it's a follow up or a new person—in terms of clinic—I guess . . . I guess the challenge . . . well, right away I'm thinking about clinical responsibility, and what we can do.

AW: We can answer it in parts.

SF: I kind of think about this as: what can I do from an education standpoint? From an advocacy standpoint? From a clinician's standpoint? And from a research. So, those are kind of, I guess, the four buckets—in terms of an HD, from my perspective, in terms of HD.

From an education standpoint, what's the challenge? Getting word out there. Both to the HD community as well as the provider community, about HD, and it seems like it's never enough. Everywhere I go there's always somebody who doesn't know enough about HD. Yet, they have one or two people, or sometimes more than that. But there's always some misunderstanding—always a question that they have. These are

people who are not necessarily involved with HD. So that's from, from an education standpoint.

Advocacy . . . I think that we have a long ways to go to help out with our community and challenges are pretty broad. I think that under that is caring for our patients with advanced disease. I have a patient in one long-term-care setting, the family wants to move him to another and I can just see the rejection letters the rejection phone calls coming, because, that kind of ties in with education . . . but there's just a lot of work to do from a patient level, but also disability. We still have a lot of ways to go there to get our patients who are symptomatic with HD and can no longer work, how can their families survive? So . . . I think that we have, as a community a lot of challenges there.

I'm going to skip to research, and then come back to clinician.

AW: Ok.

SF: But, research-wise, there's so much that's going on—which is great. It's really exciting. There's so much that's in the works from a clinical research standpoint. But our dollars for research are shrinking, and have been for a while, and smaller diseases like HD tend to get dropped first. So, I'm concerned about that. I think that's a real challenge as a community—that we need to advocate from within the community, and to the, NIH, they fund a lot as well as pharmaceutical companies, FDA, they all can fund research. They need to have Huntington's Disease in mind because they may say, "Meh, smaller disease, orphan disease, we don't need to do much research there." In fact, if you use HD as a model for other neuro-degenerative diseases, like Alzheimer's Disease, Parkinson's, ALS—now we're talking 6-8 million people who are impacted?—rather than just a couple hundred thousand. And we know HD so much better than some of those other diseases. So I think that we have a real, funding challenge, when it comes to research and HD. That's . . . that's from the bigger picture side.

From the community side: we don't participate enough in research. So, if you have Alzheimer's for example, there are 5 million Americans, over 5 million Americans that have Alzheimer's. If the average amount of people that participate in research is about 1%, you're still going to get enough people to fill a clinical trial—to get that information that you need. IF you have 30,000 people that are symptomatic, and half of those are too advanced to participate in clinical research, we're talking about a very small number of people that are even eligible to participate in clinical research. So we have to be better than average 1% of people that participate in research. So, from a community side,

that's a real challenge, to get people . . . to convince people it's important. That's really what it comes down to. And . . . research that's being done now is all-important. So, there are lots of choices—which is great in terms of research. But, people should choose one—not none.

From a clinical care perspective: there are so many challenges. *So many challenges.* We just . . . we don't have enough tools to work with when it comes to patients. And what I feel like I can do. There are no surgeries. We have a few medications, that can help with the movement, that can help with the mood, that can help with some behaviors. But we're really limited. So, that, I think there are huge challenges there. And I think that all the other aspects of the challenges with HD kind of funnel down, and are shown in the clinical challenges that are there.

AW: Ok.

SF: I hope that answers what you were looking for.

AW: It does! It certainly does, and in four ways. Are there any medical events or legal advancements that you remember affecting the HD community since you began working with it?

SF: Medical or legal . . . There are two that stand out as very significant. One is in 2008, the approval of Xenazine. So . . . the approval of Tetrabenazine to treat chorea associated with Huntington's Disease was huge. Not, not because it changes the course of the disease—but if you treat chorea, you can improve people's quality of life, you can reduce injuries; you can improve the quality of life of those around them. So, caregivers that feel more comfortable taking them out to parties or dinner or whatever because there's less chorea—whatever it may be, I think that you can improve someone's quality of life. And that's important. But, the fact that there was a drug that was approved for HD was huge. And I can tell you—because I sat on the Peripheral and Central Nervous System Advisory Committee of the FDA for a few years—I came on just after Tetrabenazine was approved. And everyone that was on the committee that was there for that meeting said that they were not going to approve Tetrabenazine—but because of the outpouring of the community, because of what the HD community did for the FDA, and the Peripheral and Central Nervous System Advisory Committee, they pushed it along and convinced them that it's important to treat chorea. So, having *a* drug available for Huntington's Disease is a huge step. One, because it gets HD on the map, and two, it opened the door for other pharmaceutical companies to say, "Hey, look, we can develop a drug for an orphan disease and do

ok." So, I think that that really opened the eyes of some other pharmaceutical companies. I think that was one huge medical leap in the past 10 years. I think there have been some significant other, like finding the gene, and things like that—but I think in the past 10 years, that's it.

From a legal perspective, I think the biggest advancement I've seen is GINA—the Genetic Information Non-Discrimination Act—because people really were afraid to get tested because of the fear of not getting health insurance. So GINA, again, I think it applies for a lot of different diseases, but Huntington's Disease was at the top of the list of diseases that can be impacted by GINA. And so, that was legislation that was in the works—12, 13 years? Something like that—and finally got passed, and I think really does benefit the HD community.

AW: Have any of these changes affected your work specifically?

SF: Yes. Tremendously. I should start off from the medical side of things. Well, let me take the legal side. That's easier. I can have that discussion with patients that come in that are at risk. I can say, you can get tested and not be afraid to lose health insurance because of any testing results. They're still at risk for not being, getting life insurance, or disability, or long-term-care insurance, so there are insurances that need to be concerned about. Employment, theoretically, is protected as well—though there's lots of reasons that employment may not be protected. But, at least for health insurance, which is huge. So that's a discussion I have in terms of GINA in the office, and people who are at risk going through testing.

From a medical side of things, I should disclose that I was the medical monitor for the Tetrabenazine trial. So I was very involved in the development of that drug. And, it, through a contract with Huntington's study group did support my salary. And I'm also involved with First[-HD] and ARC-HD, which are due, related (?), to Tetrabenazine which we're developing with Auspex, Huntington's study group with Auspex, for . . . Chorea . . . for Huntington's Disease.

But, that being said, I have a substantial number of patients that I prescribe Xenazine, Tetrabenazine, for, to help with their chorea. And it was . . . more than I anticipated. Let me put it that way. I think its because I saw . . . I was already looking at skin to look at bruises and cuts and scrapes and . . . those types of things. But I think I was, I paid a little bit more attention, particularly in people in the chronic care setting. When people came in, in a wheelchair and they had bruises all up and down their leg and scrapes on their elbows and across their arms, I knew that they were having enough chorea that they were . . .

potentially injuring themselves. I've also seen enough staff that, at places that don't understand Huntington's Disease, that think that the movements are volitional. Which . . . anyone who knows Huntington's Disease says, "What?! How could that be?" But, it's . . . if you're standing next to someone, and you put your hand on their arm and they reach out and hit you—is that a purposeful hit, or was that chorea? And I think that there are some people who are not educated in HD to know enough. I've seen action taken in some patients because of misperceptions. So, I think Xenazine has helped to suppress chorea, and help out people at all stages of the disease. Whether it's early or late. So . . . it's refocused some of my clinical encounters—how's that?—and changed how I prescribe.

AW: Ok. Where do you see research involving Huntington's headed in the future? Or where would you like to see it go?

[19:46]

SF: Well, I'd like to go to see a cure—how's that? But . . .

AW: We all would. What's our first step?

SF: Yeah, so, I think that there are really going to be three steps to getting to that cure. Obviously that's the goal. But I think until we get there, we need to understand Huntington's Disease better. So that is, observational clinical trials. Trials like Enroll HD. I don't know if I can mention specific companies or trials or companies or names or anything like that—but I'm going to. So—Enroll HD, for example, is an observational trial that helps us to understand Huntington's Disease better over time. So I think that we need to understand Huntington's Disease better. As much as we already know the gene, the protein, what it looks like from a cognitive standpoint, and from a motor perspective, the progression of the disease, what it looks like in certain imaging—there's all kinds of stuff that we know about—there's still a lot that we don't know. And we don't know enough to make better treatments or the cure. I think understanding the disease better—both from basic sciences as well as a clinical sciences perspective is really important. So I'd like to see research, I'd like to see more people participate in studies such as Jazz, Enroll, or simple observational studies that don't require a whole lot of effort and produce a whole lot of useful information for the scientific community.

Then I think, until we get a cure—there's care. So care until a cure is really an important concept, because, even people who get diagnosed today—this is a disease process that potentially has been going on for a long time. And, if we find a cure, may not be able to reverse the

damage that's been done in those . . . For example, let's say we find a cure today: those that have it still need care. And a cure is not around the corner. I mean, it's not tomorrow. Hopefully soon, but soon is a relative term when it comes to medicine. So, treating aspects of the disease. And I would like to see more research not just on the movement side of things, but on the behavioral side of things, on the cognitive side of the disease. So I think there's a huge un-met need to address those aspects of the disease.

And then ultimately—a cure. I think there are lots of different strategies that, we're getting there. Cure is a big term. And obviously getting rid of the disease completely. But—how about just delaying the progression; and if we can do that, can we delay the onset? If we can do that, can we delay the onset so that it's so far out that people have to live to 100 to get the disease. To me, that's where I see us going in terms of a cure. Which would be great. So . . . I think there's a lot of exciting work that's going on right now—on all of those fronts, when you look at research.

AW: Awesome. What do you find most inspiring working with the HD community?

SF: . . . Most inspiring . . . there's so much. It's really hard to just pinpoint on one thing.

AW: We used four buckets before . . .

SF: That was all the same thing, just sub-categories!

So . . .

I mean, the one word that comes out is resilience. And I think that's not just as an individual patient living with Huntington's Disease. But families that have been through it. And I don't just kind of mean grandparent to parent to child. I mean cousins, I mean whole communities that work as a family. The fact that there are so many people that . . . still do their best to enjoy life and do everything that they really wanted to do—whether it's travel, skydiving, who knows, whatever it may be—they do everything . . . I think . . . they live with the disease, and have seen it in so many family members . . . I don't know how to . . . I don't know how to put this in words—obviously I'm struggling with this. Just seeing families that have been through this for so long, and for so many different generations . . . that is inspiring to me—to go home and see my kids, and know what my family has been through . . . and whatever it may be is such a small thing compared to what the entire HD community has been through. That it

makes the small things that are tough in my life, even smaller. So, and . . . I've done my best to share that with my family—I bring them to some HD events, and . . . they're . . . it's clearly an inspiring group.

I took . . . it was . . . I have three daughters. My youngest is eight. She had a good friend who, her grandmother was dying of cancer, and I took her with me to the Hoop-a-Thon, the one in Lexington. She said later—she said, "I didn't know what to expect, and I didn't know that I wanted to go to this event (she's not a real big basketball person). She said it felt really good to go there, because I was helping people who were sick—and they were all so supportive of me." I think that kind of sums it up in terms of what inspires me, coming from this eight-year-olds mouth. And I don't know that I can be more specific about it, but that's . . . I guess that . . . I have the same feeling. I feel like I'm doing some good for them when I'm getting out there and talking, and demystifying some aspects of the disease, educating, treating people, addressing symptoms. And I feel like they're giving me perspective on my life. So they're supporting me, and I guess, that's . . . in the big picture, in the grand scheme of things, what inspires me. I guess . . . I don't know. It's hard. I've never really thought about that question before.

AW: Ok. That's actually all I have as far as questions I wanted to ask you. Do you have anything that you wanted to voice that we haven't covered? I imagine there's a lot . . .

SF: There is, but . . . no . . . I mean . . . no. Probably. How's that for waffling?

AW: That's fine, we'll wrap it up than. Thank you very much Dr. Frank. I appreciate you doing this with us.

SF: Thank you for giving me the time.