

TINNITUS TALK

PODCAST

EPISODE 24



INTRODUCING
Tinnitus Quest

0:00:00 Introducing Tinnitus Quest

Hazel: Hello, and welcome to the **Tinnitus Talk Podcast**. I'm Hazel, your host, and I'm here today with **Dirk de Ridder**, neurosurgeon and famous tinnitus researcher, who has been on the podcast before, and also with **Sven Köllmann**, a German entrepreneur who came up with an idea to revolutionize tinnitus research, and Sven I'm going to start with you because our listeners probably don't know you. Could you start by just talking a little bit about yourself and why the topic of tinnitus is important to you?

Sven: Sure. First of all, I'm a tinnitus patient. I have, I would say a classic tinnitus career, getting tinnitus from sound blasts or music and discotheques when I was young. And I've had several spikes in my life, things that I could have avoided, and some things I just couldn't, and over the time it got worse. I can manage it, like probably a lot of tinnitus patients can. Some days are stone, some days are diamond, it always depends. My background is, I have a Bachelor's degree in Economics and a Master's degree in Real Estate.

I studied in Germany at the University of Bamberg and University of Regensburg, and I also had a year abroad as a student at the American University in Washington, D.C., and today I'm an entrepreneur in a family business and we're doing real estate development, hotel management, and a couple of other things that are not really related to the topic, but that's basically my career.

Hazel: Thanks, Sven. The idea we're talking about today, it's called **Tinnitus Quest**, although the name came later. I think that's when you approached us, Tinnitus Hub, and asked if we wanted to be involved in this, and we said yes, I think we came up with the name at that point, but your idea predated that.

Can you talk a bit about the idea, where it initially came from?

Sven: It initially came from the general situation that we're having as tinnitus patients. First of all, not having the possibility to speak to doctors that understand the situation. So the classic ENT in Germany is, I would say, not as well educated in the topic as most patients are, because they do self-study online and try to educate themselves on what are possible treatments and of course they will very quickly come to the point where they say, okay, there is no real treatment available at the moment besides, of course, Tinnitus Retraining Therapy and CBT and so on. I was very lucky that, during my time in Regensburg, I met Berthold Langguth, who you will hear at a later stage.

And then actually through the Tinnitus Talk Podcast I went through the episode of a guy who donated 1 million dollars to tinnitus research. This is how I got to meet **Hamid Djalilian** and his project. And then I thought my professional background as a developer is bringing good people together, or the best people together on the table to be able to get a project done in time and on budget. This is what my profession is. I did some online research and I knew Dirk de Ridder from his names and papers before. I think I saw the paper or the website, I'm not sure what was the first thing, where I saw his War on Tinnitus concept, which was really a revolution to my mind how to approach this situation because I think that those big multi-center studies with a lot of patients, is not the way probably to address this topic.

I think we need a very new approach, more aggressive approach. I actually thought about that a couple of days and I just put in my mind where is the situation today and how can we ensure financing in the future? And this is one big thing because of course financing today is on the big topics like cancer or Alzheimer's, but tinnitus is a topic which is really just under the table more or less. But if you ask in your surrounding social network, and how many people are struggling with it, it's amazing, and the harm that it does economic wise is amazing. My idea was, how can we ensure financing in the future? So I came up with the idea of this foundation and the idea to link the patient to the research because the problem today, as we see it, is that there is research and there are many scientists worldwide working on the topic, but nobody's really informed about what's going on.

I just want to generate hope. And hope always comes through education and knowing what's going on. The idea that I presented. Then, I contacted Tinnitus Hub, you and Markku, and Dirk de Ridder, and Hamid Djalilian, and Berthold Langguth and tried to give you guys my idea. And this is how I came up with the **Tinnitus Quest** idea.

Hazel: You made a very compelling pitch, I must say, which got us excited as well. We'll talk a bit more in a moment about what's really new or different about **Tinnitus Quest** compared to other research efforts. But first, I want to know from Dirk, and Dirk, welcome to the podcast, by the way. Good to have you back on. How did you react when Sven approached you about this?

Dirk: I was, of course, very happy that there was somebody who had not only the financial means, but also the spirit to drive tinnitus forward. Now, there is a lot of tinnitus research going on, but it's slowing down somewhat. The reason being that after 20 years of doing tinnitus research, we're not really advancing to a stage where we can be really happy that we're silencing the sound. There is some improvement with improving the suffering, but not the core business, which ultimately should be silencing the sound. And what we needed was a new wind, a new dynamic, and this is what I could hear immediately from Sven's very positive energy into driving the activity in tinnitus research again.

Hazel: So what do you think, Dirk, I will ask Sven as well, but what do you think is really new or different about this project?

Dirk: We already have had the **TRI (Tinnitus Research Initiative)**, which was sponsored by **Matteo de Nora**, a single person donor. But the moment that the money finished, basically the TRI shifted from being a research driving organization to just a research promoting organization because there was no money to be donated.

So whereas it was a very good start, it gave us a lot of unified people around the world to combine research and initially there was a lot of money to do research and it set the first stage. But once these financial means ran dry, basically research slowed down as well. And I think the difference is that Sven wants to not be a single person donor, but unite multiple donors so that there is a more long-lasting steady stream of financial means to support tinnitus research. So the difference, it might just be a little bit more in long-term stability. I think what Matteo de Nora had envisioned is that, as many entrepreneurs and businessmen, is if you put enough money into it and you have the right team, you come to a quick solution.

But unfortunately, the quick solution did not arrive in the time frame that Matteo had envisioned. And therefore it needs some revitalization, and I think it's not just revitalizing, but it's also a somewhat different approach. Although TRI was very aggressive in the beginning as well, it mellowed down, with the bigger the group of researchers became, the less aggressive the approaches became, which is fairly normal. And so I think that a lot of good organizations like ATA and BTA, they do support tinnitus research, but it is more on the safe side where the idea is more, look, we have to account to the donors that something is done that has some positive result, even though it might be a small incremental benefit of what we already know. I think what's different now is, and Sven has clearly stated that to us as well, that there is no need for yet another trial to show a difference between Cognitive Behavioral Therapy and Tinnitus Retraining Therapy, that we really need something very different and that's where my idea of War on Tinnitus came into play and that's how Sven and I met.

0:09:09 War on Tinnitus – a New Approach

Hazel: Can you tell a bit more about the War on Tinnitus and also explain that is this now subsumed by **Tinnitus Quest** or does that still continue on its own or how will that work?

Dirk: No, the War on Tinnitus is just an idea.

Hazel: Okay, it's a concept.

Dirk: It's a concept. The concept is different from the War on Drugs. It actually has nothing to do with the War on Drugs. The philosophy is more that just like in warfare, in combined warfare, what you have is that you've got the air force, you've got the navy, you've got the ground troops, and you can never say, okay, the navy won the war. No, it's the combination of different approaches that in a combined way result in a positive effect if you talk about a war. So this being said, from a scientific point of view, we tend to study one thing. We'll study one little drug and see does it do anything for tinnitus. We'll test one neuromodulation device like rTMS on the auditory cortex and see whether it does something.

And this is easy to do from a scientific point of view. However, if we really want to follow the philosophy of War on Tinnitus, then we have to start combining. We have to combine medication with neuromodulation, with psychotherapy, with hearing aids, and it's the combined effort that should lead to a benefit.

That being said, this is slightly more difficult to study in a strict, scientific perspective. And therefore, we might have to accept that the scientific proof might be more difficult to get,

but ultimately the goal is to have a clinical outcome first. And if we can have a good clinical outcome, then the science can come afterwards to prove which of the parts are essential. And this goes into detail, for example, with medication, ultimately the brain has an accelerator and a brake like in a car, and then you can shift gears. We know the two, we know the accelerator is glutamate and the brake is GABA, and all the other products that we use that work on dopamine, serotonin, et cetera, they're like shifting back gears. So if we consider tinnitus as a hyperactivity, then it makes sense just like when we stop our car, we will do all together. We will release the accelerator, press the brake and shift back gears, which means that we have to use a cocktail of pharmacology in order to block this hyperactivity, just like we would block our car. We're not just gonna let the accelerator go because before we stop, it will take quite a bit of time.

And so the same philosophy occurs within pharmacology, but also within rTMS. We know, for example, that in neuromodulation, if you combine rTMS with tDCS, that the combination is stronger than just using rTMS, it can last longer, the effect size is bigger. Furthermore, we know that if you combine medication with, for example, rTMS, that the combination is better than the medication by itself or the rTMS by itself.

So then you go one step further. That's the concept of, or the philosophy of War on Tinnitus. It's a combination of different approaches that individually might have small effect sizes, but if you combine it should have a good effect. We know this can work, for example, pharmacologically, when in the 1980s AIDS was discovered, there was only one product, **zidovudine**.

And with zidovudine, people would live five years and then the effect would disappear. Then the virologists thought, what if we combine it with a drug that works on a different mechanism, but that helps the zidovudine and then people with this combination would survive for 20 years. Adding a third drug, they survive for 40 years. And now the standard treatment is four different drugs that each work on a different mechanism of action. And people that are seropositive live as long as people who are not seropositive. So we know it can work. And that's why I think we should also apply this to the field of tinnitus.

Hazel: Dirk, one more scientific question before we get back to the sort of organizational aspects of **Tinnitus Quest**: We need a combination of treatments or approaches, it's not going to be one solution, it's going to be a combination of different things, but let's say we find this magic cocktail of things, would it work for everyone, or would it have to be a different cocktail for different types of tinnitus patients?

Dirk: That's a very good question. You can approach that from two sides. On the one side, you can say, there should be some kind of final common pathway that results in the creation of a sound in the brain. So we could still focus on this final common pathway, but just like there are multiple ways that lead to Rome, there might be multiple different means to modify this final common pathway, and indeed, I do think that we might have to adjust it, we might have to individualize it to the people.

If somebody has a severe hearing loss, or no hearing loss at all, that might already trigger a different mechanism of generating the tinnitus in the brain. I think we should do both. We should focus on what's the final common pathway, and this we could do by, for example, looking at EEGs and using artificial intelligence to find the pattern, the brain signature of tinnitus.

But then that signature might be triggered by different causes and it makes more sense to then attack the cause, because if we only are going to attack the final common pathway and we leave the cause as it is, then it will return. We might treat it, it might disappear, but then it will come back. Yes, you will have to look for both. The individualized treatment related to the likely cause of the tinnitus, and that's more maybe as a preventive way of preventing it from coming back, and then the final common pathway to try and silence the sound.

Hazel: Sven, you're a layperson, you're a businessman, but you've looked, I think, quite deeply into tinnitus research. What are your thoughts on what are viable avenues of research?

Sven: I think that the points Dirk had, those are very valuable. I don't know today if there is a magic bullet because, as Dirk mentioned tinnitus patients are quite heterogeneous. For example, in my case, I have no detectable hearing loss whatsoever, but I would say I have a quite severe tinnitus, and there are other people who have hearing loss, some people are somatosensory driven. So there are many different aspects, but if I look at all the research at the moment, then I think there has to be a common pathway.

The second point that I would like to mention is that if you would ask me today, not as a professional researcher, just as an educated patient, and maybe an educated person, I would say that we should also have a look at a technological solution. We know today the best treatment that probably exists today is a cochlear implant. So for most people, who have a severe deafness and tinnitus and they're provided with a cochlear implant, then, for most people, it gets better or in an ideal situation, it will disappear completely.

And I think we should have a look at cochlear stimulation by implants and I think, if I look into the research world, there are a couple of universities at the moment working on such an implant. Actually, one university in the U.S. has already implanted, I think, ten implants at the moment, that's a current study. And, this is something we should have a look at. Maybe it's not the finest solution, but could be something that fills the gap, until a better solution is found. This is just something I want to point out that there's still a technological advancement, especially on the development of micro-implants.

For example, in Germany, there has been a great program, actually financed by the government or by the German state, that is working on the development of micro-implants. It's called INTAKT, and it was financed with about 17 million euros. And there were three things that were a possible first use for those micro-implants, and one of them was tinnitus. I think this is something we have to have a look at.

00:17:59 Tinnitus Quest – Structure & Funding

Hazel: Sven, can you talk a bit more in detail about **Tinnitus Quest** in terms of what are the plans now? So what's the plan for the organizational structure? What's the plan for how research will be funded, how researchers will be involved, how patients will be involved? It's a lot, but if you could try to summarize that.

Sven: Our idea as a team is that we want to connect science and the patient; and how we want to do that is that we would like to trigger researchers to speak more about their research. I think this is crucial. And not just because it's interesting for the patient, but it's in

general important that people have the feeling that progress is being done. And that's the first thing.

The second thing, I think, which is very important, is that we talk about failures and not in terms of, oh no, another study has failed and we're not coming to the point, but failure is so often the pathway to progress and this is something I miss a little bit in the scientific community. Today, trials, especially if they're phase three trials, they're only made if you already know the outcome, because a lot of money is in the game, I understand the hustling there, but, in the end, that's something I want to reorganize, and that's very important. And, of course, I want to use the huge, heterogeneous crowd of patients in the world. Today they have no hub and no real information source where they can see what's being done at the moment and also who are the worldwide specialists, and that's very important.

We tried to gather a group of brilliant researchers, and this is also where **Dirk de Ridder**, **Berthold Langguth** and **Hamid Djalilian** come into the game, where we tried to find them. And I always thought that my basic question for them would be, what was in your mind, what did you always want to try, but you couldn't do it because it wasn't financed? Because maybe the idea was too crazy, and we have a lot of those obstacles and this is something I want to diminish.

And the second thing from the organizational part is that the foundation should be organized quite simple. This is very important. So we'll have an executive committee, with probably three people coming from the patient world, two from the scientific world, and then we'll have a scientific committee, also around seven people. And we will organize basically two meetings every year, so one meeting, I hope, will be in Germany, so it's more or less in the middle of the planet and we're close to Frankfurt and it's a big airport, and we try to create three days, in a very nice atmosphere, and not in this typical medical congress atmosphere, with poster discussions and so on. What we want is that those people connect and brainstorm and have the time to think and speak.

And out of those discussions, we hope that projects will emerge, with new ideas, and those ideas will at some point be reviewed, and I hope that we can set up a donor crowd, that will fund as much as possible and donate as much as possible so we can fund those projects. And, which is very new, with this donation and with the financing of such a project comes the responsibility for the researcher, not of course just do his research, but also to communicate in a regular way, and we can use that on our website, **tinnitusquest.com** and we will try to communicate this research. And this is very important. This is the crucial factor. And what we also want to do, of course, in terms of putting or spreading the word into the world is, we try to connect the foundation to many groups of interest, for example, musicians. We hope that we can, of course, gather one or two celebrities, if we're lucky, who are supporting the matter.

And this is what we're working on at the moment, as a team. And we'll try to set up this foundation and the next step will, of course, be creating the scientific program for those meetings twice a year. We're actually at the moment having the discussion if we arrange the second meeting around the **Tinnitus Research Initiative** conference because people are already there. Most of them are probably there. So we try to connect this and, what we'll do this year, as a first meeting, but Dirk can probably say a little more about that, what the scientific idea will be, that we do an online meeting in June and we try to explain the first steps to the scientific community.

And, of course, we hope that many patients will join as listeners and get the idea what we are trying to do.

Hazel: So where will the starting capital come from and how will the funding grow from there?

Sven: The starting capital will come from me or from me and my family, we will try to set the brick of the foundation, and then we will see how it will develop. I think within the team working, at the moment, we struggle to have a feeling what the amount of donations will be. I think this is something that we have to work with and see how it develops. We'll do everything that we can to get as many donors as possible. And what's very important to mention today is, we are relying on the little donors. 5 euros, 10 euros, whatever you can afford as a patient and makes you feel good is great. We will not rely probably on the big donations. Of course, we hope, to attract them. But very important is that every patient who is really into the topic and wants progress, and wants to be part of it with 5 euros or 5 dollars, you can be a part of it, and that's a crucial factor.

00:23:52 Why Funding and Breakthroughs Have Been Lacking

Hazel: Dirk, what's your experience with fundraising for tinnitus? Because in my experience, it's a particularly difficult condition to get people excited to donate for.

Dirk: This is true. If we do research for pain, if we do research for depression and anxiety, it's always easier to get funding than for tinnitus, even though tinnitus is the biggest problem, for example, for soldiers who come back from the war. Bigger even than PTSD. It's highly associated, of course, also with PTSD, but it's the most common complaint, yet the problem is that, analogous to pain, you cannot see it, you cannot see whether somebody suffers from tinnitus or not. Whereas, and it's, strangely enough, maybe it's not a sexy research topic. Cancer in children, of course, should be studied tremendously because it is a horrible pathology. Alzheimer's disease, cancer, etc. These are sexy research topics, but unfortunately tinnitus is not. And therefore, a lot of big money goes to those sexy research topics, where there is also lots of researchers doing it.

And you also need a critical mass of researchers that exist, in order to create those brainstorm meetings where you can develop maybe crazy ideas, but a crazy idea does not mean that it cannot work, and, in reality, what you need to get a breakthrough is not a lot of money. You just need knowledge and luck. And with this combination, and sheer dedication, of course, you can develop maybe a prototype of a stimulator that Sven has talked about earlier on. Then, of course, to develop it into a commercial product, that's where the big money is needed. But this big money then usually comes from commercial enterprises that want to build a device and sell it and make money with it. But often, the initial breakthrough doesn't require a lot of money, but it does need a minimum of money. And I think this is where **Tinnitus Quest** is going to be very important because when we apply for money for, call it high risk, high gain studies, there is no funding agencies that are interested in that.

Hazel: Is that why we haven't had the breakthrough yet? Because you say we don't need a lot of money to get a breakthrough, is it because, like you said, researchers haven't

been, let's say, adventurous enough in their studies? Is it because of that fragmentation we discussed; that someone's working on a piece of the puzzle here, someone's working on a different piece of the puzzle, and the bigger picture is lacking? What do you think is the main reason?

Dirk: I think the TRI had a very similar philosophy to **Tinnitus Quest** in the beginning. But the difference was that none of us knew anything about tinnitus, there was nothing known. So we really still had to find out the very elementary things like, is tinnitus related to the brain or not? Can we modify it in whatever way? So all these steps have now been kind of found, but like you said, the putting all the pieces of the puzzle together hasn't been done. And the pieces of the puzzle are just like in the War on Tinnitus are the ground troops and navy. So we still have to bring all of that together.

Yet, I have to be honest, we don't know yet for most drugs, for example, what they exactly do. And this is, a little bit to come back to what Sven said earlier on, and this goes back to, for example, Winston Churchill said that success is stumbling from failure to failure without a lack of enthusiasm.

And this communication about failure is what we don't do for a couple of reasons. One reason is that it's very hard to publish negative results. Journals are not interested in negative results. Furthermore, if you have a negative result, writing a paper on takes time, and it won't be cited a lot, so also for the researcher it's of no benefit. But yet it is extremely important, and I'll give you a practical example. This year we tested a new kind of neurostimulation, where we combine infraslow with pink noise, it doesn't matter what it means, but we thought we will attack the tinnitus core, as was described by Jae-Jin Song from Korea, who wrote a publication saying is the posterior cingulate cortex, a part of the brain, the on off switch? And he found a core, so we said, okay, we have to dissolve this network, this core network. And we developed a new stimulation design because of it. That took a little bit of time, but we finally managed it. And we thought we will now finally have the solution.

And it didn't, it worked, but the placebo worked equally well, which means that it was not what it was supposed to be. So then, this failure taught us, however, maybe we should combine it with a drug that helps to dissolve strong connections in the brain and we used Ketamine as a dissociative drug to disrupt it.

And on top of that, we used the stimulation, so a preliminary approach of the War on Tinnitus. Again, we failed. But then we had to think, why do we fail? Now we failed for the simple reason that there was a problem in my thought process that the infraslow activity on which on top we put noise, actually, was the same in the three areas, which means it probably strengthened the network because these areas were going in synchrony. And so now we're going to do yet another study where we remove this and just use noise because noise can break connections. With hopefully in the next stage, if that would show a partial benefit, then we would add Ecstasy, for example, because that can break the connections even more.

So from every state, every study that fails, we learn. But yet, as Sven said, if we do not communicate it for patients, it comes across like either they are doing nothing, or they have no clue what they're doing, which, of course, is partially correct. But it is important, just like Churchill said, that we stumble from failure to failure by learning, and that's ultimately going to lead to success.

But in order to do this kind of research, where you have to develop new tools, whether it is for intra ear stimulation or whether it is for brain stimulation, this costs not enormous amounts, a device. Once you have the device, you pay for software, and the software can cost, that has to be specifically made for you, that can cost five, six thousand euros, it's a lot of money, but not in the setting of research.

But for every study, you need these kinds of relatively small investments. But the essential point is, yes, we do stumble from failure to failure and we need to be able to communicate the failures, but also what we've learned from it. And this is where **Tinnitus Quest** will be very important. And maybe if we show the way we work, it will progressively make the field also more sexy because people will understand that it's actually very, it can be very rewarding, even though we fail, most often that can be very rewarding because slowly but certainly we zoom in to what will lead to success.

And it is a field where still a great breakthrough can be made so that should be very attractive for young researchers as well, on the condition that we can make it more sexy.

00:31:37 Getting Researchers Together

Hazel: So the importance of failure, the importance of communication, open and honest communication, which, like you said, for patients often, you hear nothing for years and years, and so you just assume nothing is happening; that very much resonates. I want to zoom in on another element though, which is that aspect of getting researchers together, because my impression is still always that the field is very fragmented. And there's something that Sven said that really resonated with me because I've been to a lot of research conferences and it is always the same structure, right? It's person A presents on his or her study, person B presents on his or her study, but the bigger picture is just lacking. And also often the dialogue itself is lacking, maybe you have time for one or two questions at the end, but that's about it, right?

Sven, maybe can you talk a bit more about the meeting and how we want to structure that very differently from these traditional conferences.

Sven: I think we're talking about two different things. I think the first online meeting will be more about, first of all, just getting to know the researchers. And the second thing is showing the patients by documenting it, how much is out there, and we talked about luck and I'm the person that is working a lot with luck, but what I learned in my career is that if you bring the right people together on the table with different professions, then you can enforce luck.

It's possible to enforce luck. And this is so important, I think. This is my core idea about those meetings is to create an environment where those people have the time, and also the fun to speak together about projects and how can we emerge those projects and bring them to a certain point, where we can test something. And this is my personal idea, how those meetings should be structured and what, for example, Dirk and I had a long discussion is, how can we provide incentives? So I think competition is a good thing. Competition has always brought progress. And, of course, we want to create a healthy competition. We will create some kind of ongoing competition between different projects. At the moment, we're not 100 percent clear how we will reward them. Of course, there will be a financial reward system that we would like to set up for ongoing science.

I think we will learn in the process. We will learn what works, what doesn't work. Maybe the first meeting will look totally different than the second one, we don't know, but everything has to be based that we create an atmosphere of open brainstorming, that people have time to speak together in a nice environment. And, in the end, we hope that those events create specific projects that then will be addressed to the scientific committee and then in the end decided and financed by the executive committee of the foundation.

Hazel: Dirk, what's your experience with research conferences and do you have tips for how those could be made more productive?

Dirk: It depends on the size of the conference. If you have a big conference, like some of the medical conferences have 40,000 participants. This is very difficult to organize in a brainstorm meeting because you can't have 40,000 people all saying what they want to say. But if you have smaller groups of highly dedicated people that are not afraid of saying something stupid, or that might appear stupid, then, and in an open atmosphere where people are not afraid to share their ideas that somebody else will run away with a good idea.

That's the most important aspect, I think. And this is where some people might not fit in this kind of approach. You need people who basically are not afraid that their ideas will be stolen. But if you have a hundred new ideas a day, it doesn't matter whether a couple of ideas are being tested by somebody else because you don't have the time. If you only have one idea in your whole life, then you might want to protect it. What is required for this kind of approach with **Tinnitus Quest** is that you have creative people who come up with lots of ideas and are not afraid of sharing it. And when I was watching the America's Cup in New Zealand, a couple of years ago, I was very surprised to see on a Toyota car, a Japanese car, which is normally made very meticulously in a very structured way, and it said "in crazy we believe", which was very non-Japanese from my point of view.

But I liked the idea and it actually has become my personal motto in research is that in crazy I believe, but in science I trust. The ideas can be crazy, but they have to be shown to work or not. Otherwise, there is no difference between science and quackery. And we want to make sure that what is being tested has some rationale or can be explained at least. And for this you need small research settings, not those big conferences. I think these big conferences are very good to show small incremental improvements and a slowly going research, but the **Tinnitus Quest** is more for what I would call exploratory neuroscience.

So **Thomas Kuhn**, in his book *The Structure of Scientific Revolution*, has described two different kinds of science. On the one hand, the exploratory neuroscience or exploratory science, where discoverers like Stanley and Livingstone walk around in Africa following rivers, following hints, but they don't do that in a very detailed way. Then that's what the solidifying scientists do. They come then afterwards, they follow the traces that have been laid by people like Stanley and Livingstone. And then the next generation like Darwin and Von Humboldt came and they brought botanists, geologists. And then everything was developed in detail.

I think **Tinnitus Quest** is probably more akin to the explorers like Stanley and Livingstone. And then you need a small venue where people can really brainstorm. I did this, I tried this, and I went there. Whereas the big conferences are more for the solidifying neuroscientists that then come with more filling in the details.

So there is a necessity for both, yet funding, up to now, is more for the solidifying neuroscientists and less for the solidifying, whether it's neuroscience or auditory science, it doesn't really matter, for science in general. And this is lacking.

Hazel: It's less for the exploratory, you mean?

Dirk: Yes, because the explorers are considered non-scientists, really, by the solidifying scientists. They do these weird things that nobody really understands, but that's not true, because even Stanley and Livingstone, they didn't wander just around, they were following hints that were given to them by the local people, they were following rivers, there is a certain structure in what appears to be somewhat chaotic behavior.

And this is where we know - because that's also how the brain works. If you look at brain activity, it appears, if you record it, as very chaotic. Yet there is a clear structure. There's a clear pattern in it. And that's what the explorers also have. But that requires trust from the founders, from the people who donate money that it's not just chaos, because in chaos there is zero information, there will be zero output, but there is a structure in the noise. Then there is, that's where the information comes from. So also the information that will lead to a solution for tinnitus.

00:39:53 Why a New Foundation?

Hazel: Sven, this lack of funding for exploratory research that Dirk talks about. Is that also the reason that you didn't want to, for instance, just donate a large sum of money to an existing tinnitus organization? It's a bit of a leading question, sorry, but I don't know how else to formulate it. Because if I'm playing devil's advocate, I could say, why create your own new foundation? You're just splitting up even more the already scarce resources and funding for tinnitus.

Sven: No, it's a very good question. The basic problem is that all of us tinnitus patients, we have seen so many discussion forums and so on and I saw that the people are always fighting with the lack of information. And if you look at the sources that are out there at the moment, like the **American Tinnitus Association** or the **German Tinnitus League**, those informations are, how can I call them? This is just basic stuff that there is TRT and nothing else. So I always had the feeling that those organizations, they somewhat manage the current state of knowledge, but there is not enough drive to improve the situation and improve the biggest problem, which is financing.

I'm, of course, not saying that they're doing nothing. This is absolutely not my point, but I know as an entrepreneur that it's very important to push it as much as possible and this is, I think, the core difference between those other organizations. And I think Matteo de Nora, when he set up TRI, he had the same idea. He had the idea that with a large sum of money, as a lump sum investment, you can get to a solution. But I think this was probably way too early because, as Dirk said, the foundations in research about tinnitus were so low, you had to start from the very beginning.

And my idea was that, especially if you had a look at the COVID-19 research, and especially the research about the drugs that were used, which showed that if there is a problem that is addressed to many people and is a problem to many people, then a lot of

money goes into that research. And I think it was a great example that a lot of money combined with a lot of smart people and the pressure, the positive pressure, in the end showed that we as human beings, we can develop a vaccine against such a big worldwide global problem within 24 months. Of course, there has been a lot of ground or basic research in this field years ahead.

And this is the second thing that I thought about; the woman who got the Nobel Prize for the mRNA development. She was basically, she had this research topic over her whole career, and so many times, it turned out that it didn't work, it didn't work. She was downgraded by her university, she was put in a small office. She was basically punished for having failures all the time. In the end, the development of this mRNA technology will probably lead a huge progress, not just in that field, but in others in the future. And, actually, this was one thing I was thinking about when I read about this woman, this researcher, that I don't want to have this person who might have the answer to tinnitus in his head or her head, to be sitting in a small office and being punished because her research doesn't work. I want to get her out of the office, into an environment where she knows that somebody is on the other side of the table, us as patients or me as founder or the team that says, okay, this is an idea we, maybe we don't understand it, but it sounds, it sounds aggressive, new, creative. What do you need to try to test the basics; if it works or if it doesn't work?

And I think this is the groundbreaking difference between my idea and the idea of classic organizations such as ATA or Tinnitus League or something of that kind.

Hazel: I think it would be wonderful if we could get those researchers out of the woodworks, let's say, that might be out there, that might have an interest, that might have an idea, and definitely also younger researchers. I've heard a lot of young researchers say that they were actively discouraged from pursuing a career in tinnitus because they were told it's a dead end. So hopefully we can change that perception as well.

Sven: Maybe, I think, a good example is always HIV or AIDS. I think this was a dead end in the 1980s. It was something that was so complicated to address that it was not just an easy thing that we are tackling, and I think there are many things in, of course, in medicine, that are complex and very complicated to tackle, but we will always have to start at some point, and I have the feeling that a good amount of basic research has been done, but now it's the time to aggressively tackle a solution.

And as I said to Dirk and he mentioned before, we don't need the 127th trial about CBT or TRT or something like this. This is something that we know works, and for some it doesn't as often, and this is an important thing. And the second thing I really liked about talking to Dirk was the problem also with tinnitus is, as I said, some days are diamond, some days are stone – the high amount of placebo that we are facing within this problem.

So if tomorrow we would do a trial with Greek olive oil, then probably 20 percent of the people would have some benefit of the Greek olive oil, but if you would ask them a couple of months later, then probably diminished. This is not easy, but it's something that can be managed and what we try, as a team in **Tinnitus Quest**, is to manage this environment, to manage the communication, the ongoing communication. And, of course, we try to advertise this idea as much as we can through professional PR strategies all over the world and we have somebody on the team who's working on that. And I think he had a very nice saying in the last meeting we had. He said it was the first time in his life that he addressed so many people with an idea or a problem, and the idea how to solve it, and it

was the first time in his life, he only got the answer, yes, we will support it. And I thought, this is very nice. And this is something, we should ride the wave now.

Hazel: Guys, I feel like we've covered most of the ground here, but I will ask you both if you have any final remarks and maybe, so I'll start with Dirk and you give me any general concluding remarks that you want, but maybe you also want to do a kind of call to other researchers to get involved?

Dirk: Yes, I think for those researchers who are young, and have good ideas, but who might be afraid to phrase them because they could be considered as crazy ideas or stupid ideas. There is no stupid or crazy ideas, it's just a lack of understanding, and so if as a researcher you have a very good idea, or as a patient you have a very good idea that says, I've tried this and this seems to work, but I have no clue why, these things can be investigated, and I think **Tinnitus Quest** should be open for crazy ideas that will be tested scientifically to show whether it is crazy, it can be crazy, or whether there is a golden pearl hidden in the idea. We start from the ground, we have to accept that only in 2021, so only a couple of years ago, we had a definition of tinnitus that was more or less generally accepted, so before then, everybody had their own definition, which meant that we were not even working on the same topic, so we need some standardization, but then I think, if you're young, if you're bright, if you have good ideas, don't be afraid to come out with those ideas.

And that's where I think **Tinnitus Quest** will be a haven for those young and creative people.

Hazel: Wonderful. And Sven, what would be your concluding remarks and do you have a particular call to action for tinnitus patients who might want to get involved?

Sven: If you want to change something, you have to be part of something and do it yourself. Of course, everybody can do it in a certain level that he's able, but if you complain about the current situation, that's totally fine, but then be part of the solution. And being part of the solution means to donate, ideally on a regular basis, and see what comes out of it, and be part of the communication process.

I think the team around **Tinnitus Quest** will think a lot about how we can integrate the patient into this whole setup. I think this is very important. We will try to not just document those meetings, but also document as much as we can about the research process. I think this is crucial. And I also want to point out to the researcher side, especially to young researchers who have great ideas, that we're not talking about a very limited case of a very rare genetic disease that is one in a million times.

We're talking about one of the biggest health issues in the world. We're talking about the number one invalidity reason in the United States Army. We're talking about something that covers between 715 million to a billion people worldwide. And, of course, with increased aging, hearing problems will increase as many other things do, but we're talking about a severe health issue that is not being addressed properly.

And I think that's a great motivation to be part of a research project that not just helps a very small amount of patient group that unluckily got a rare disease. But we're talking about a solution for a huge amount of the world's population. , and I think this is something where we want to motivate patient side and research side.

Everybody should stay tuned. We hope that from this part and from this day on, we can gather funds and set up the project and have our first annual meeting early 2025 here in Germany.

Hazel: I want to thank you both so much for being here today and speaking so passionately on this topic.

I hope you've both convinced a lot of people out there. If people want to know more, they can go to TinnitusQuest.com. But as Sven mentioned, the website at the moment is very rudimentary, but we'll be building it out over time and have a fuller version in June. Here's to hopefully a very successful quest with no doubt a lot of twists and turns ahead, but hopefully with a pot of gold at the end.

Thank you, Sven. Thank you, Dirk.

Dirk: You're welcome.

Sven: Thank you so much.