Introduction and guest background

it's possible to regain cognitive function even in an Alzheimer's patient. There seem to be variations. I'm not an expert on it, but these multimodal treatments or multi-domain treatments seem the real key.

Not only can you find the inflection points, but they should be able to guide treatment. You can find out what it is that's changing at that time and you can detect it the network methods, dynamic network biomarkers I'm really interested in that use, they measure multiple things and how they're correlating together.

I am definitely a network person and not a single biomaker person, but I I m interested and there are Those have been shown in some experiments with other conditions that they can predict proximity to a tipping point, you know, so they're really good for they not only predicting proximity, but they kind of detect what's going on.

Welcome back to the Think Well, Age Well podcast. I am your host, Dr. Heather Sandison. And today, I'm joined by Dr Stephen Chamberlain, a truly interdisciplinary physician scientist and assistant professor of neurology at Oregon Health and Science University.

He brings together a rare mix of naturopathic medicine, acupuncture, computational biology, and more than two decades of data science experience across multiple industries.

At OHSU, he completed advanced training in bioinformatics and complementary medicine research. He's contributed to studies on botanicals for cognitive resilience and serves as the geneticist at the Oregon Alzheimer's Disease Research Center.

he's also the principal investigator on a five-year NCCIH grant studying salutogenesis, how health is restored, using multimodal non-pharmaceutical interventions for age-related cognitive decline.

He teaches AI and machine learning, continues a clinical acupuncture practice, and is working to build whole-person models that help us understand why some people decline and others age well.

So Dr. Stephen Chamberlain, welcome to the show. Thank you. Thank You. I want to dive in to first, you know, how you got into this. How did these two paths of data science and naturopathic medicine and I mean, it's more than two pads, right?

Acupuncture and traditional Chinese medicine. So that goes really way back to my dad, who was a physician and a psychiatrist. And he worked at a hospital called Menager Foundation in Kansas, of all places.

But he was really early. He was involved in the American Holistic Medical Society. So he a very early holistic sort of MD in their late 60s and early 70s.

They were doing really interesting thing that things are like early psychedelic therapy and things like that. And so he was, I always think of him as like a pioneer in that area.

He was my inspiration. So I wanted, when there was a lot of study of consciousness and so that was why inspiration I went away to college thinking I want to be a doctor.

I wanna be like and I got to school. It's like, well, nobody's teaching this. I just ended up in research and was kind of drawn to stats and programming.

You know, after I did, I was a biology major. And then that sort of led to a career just in data science in multiple places. I always thought, you know I wish there was way to get back to what I saw then.

Then I started developing an interest in trying to go to acupuncture school, trying switch my career. Lots of big corporations for years. And then I moved to Oregon and I went to this conference at NUNM, the naturopathic school here.

And I knew I shouldn't go because it would make me want to go to the school. But I did. It was called Transforming the Mind and they talked about it. They had a biostatistician and he was applying physics ideas to consciousness and to studying natural medicine.

And that hooked me. And then I volunteered at their research center at the HealthCOT for a couple of years to decide if I wanted to go.

Salutogenesis and health restoration

Then I decided, and I love natural medicine. I like naturopathy and Chinese medicine because I liked the integration of the old and the new, but it's also like you study every major health system on the planet with those two degrees put together.

So for research, it's really good too. And I, you know, from the beginning of my decision to go back to school with naturopathy, I wanted to integrate, wanted do research.

I want to do clinical work too, but I really wanted research so I could draw on all my computational experience. Talked to Heather Zwicky there quite a bit in the begin and she was a big guide for me.

And then I took six years off and went to school, got both of the degrees full-time. And I wasn't sure exactly how the research would open up. I came to OHSU, to their Department of Medical Informatics here and did a fellowship in computational biology and biomedical informatics.

It was the National Library of Medicine. So I had been talking to them too for a long time. and I was able to get in and they accepted a naturopath. It's pretty, I think it's fairly open here at the school.

So, and then, from there I just, first it was natural products and cancer was my interest and Solutagenesis, I heard a talk given by Helene Langevin at the NCC IHIN 2021, where she gave a really nice, easy to understand description.

It was actually a grand challenge. They wanted people to study that. That's how I switched from natural products and cancer to solutogenesis and switched my focus to cognitive impairment.

Let's dive deeper into salutogenesis. This is health restoration. We're both naturopaths. So in our language, this is like the vis medicatrix nature, right?

Like this the healing power of nature. There's fundamental belief system, that the body has the ability to heal when we use a whole person model. And I think that was the belief.

It was living in that truth with a capital T that made me open to Dr. Bredesen's approach that maybe think like, maybe this might work because I fundamentally believe that the body can heal itself, the brain not being an exception to that, right?

So I'm curious how, you know, can maybe take us back to talk where you were turned on to salutogenesis. How do you define it in a way that makes sense for patients and clinicians?

How did she explain it that day where had that aha moment? She used a lot of pretty pictures, like simple graphics, and one of the things she showed was that health is a continuum and it has two directions.

Instead of like a binary, sick or healthy. So there's a Continuum and you can get less healthy along that Continium and then eventually end up in a disease state.

And that if you know where you are in that continuum, it's easier to reverse the health and that there are, it goes in both directions too. And so it comes from, the term was originally coined by a psychosocial researcher in Israel in the seventies named Aaron Antonovsky.

He actually studied survivors of concentration camps from World War II. So he was really interested in why are there people that are resilient in that horrible, you know, that really unimaginably horrible situation and some people aren't.

So his focus was more on what are the factors that created that resilience. And then so one of the things I like is oftentimes people compare it to the pathogenic approach.

There's the salutogenic orientation and the pathogens orientation, and they're complementary. They're not one is right and one's wrong, but the orientation is all about like what are disease processes and then the pseudogenic is what our health processes.

And then I like there are tables, you know, what is, comparing the two, but one of the things I liked is that in pathogenic orientation, there're risk factors and you're mostly trying to avoid those risk vectors.

You know you like living so and in that, in the sleutogenic orientation, risk factors aren't necessarily bad, and in fact, they might make you stronger.

So there's that idea that a risk, so they can actually be salutogenic. What I like about that is that you're not hiding from the world. It's like you are building your own health resilience.

It's like the hormetic effect, essentially. Exactly. Yeah, I like that. Yep. That's the way I think of it. So that's one. And the other is, you know, that I already mentioned that it's a continuum.

It looks at health as a continue. I'm really interested in, so I got really interesting in computationally that continuum, what is it like? A lot of people think that there are tipping points along that continuum, like you're sort of in a stable dynamic state, and then there's a tipping point into a disease state.

You can detect the tipping and things are more reversible for a dipping point. And I'm also interested in models that look at the whole person along the trajectory.

You know, it's interesting as you say that I am thinking back to probably a meme I saw somewhere or something I read in someone's email newsletter, but it was this aging continuum and how at 44 and 77 it seems like people kind of fall off a cliff.

For some reason. And you mentioned this in the context of a disease state and we certainly see that like around a MOCA score of 16 or 18 gets a lot harder to bring someone back.

So I'm curious, how do you apply this whole person model, this salutogenesis, health restoration model to aging and to studying brain aging, and neurodegeneration?

So I'm working my current researches with a lab model. So, I actually work with mice and they have cognitive decline too. So I will say that one of the ways that I work with this is I either find or create populations that have the health restored already.

So that's the way I'm working with it right now. I've been working on interventions. In a saluted genesis research model, I am not really studying whether this thing restores health or not.

It has already been shown to restore health. But I have been studying what that trajectory looks like. create that trajectory so that in the lab, I can set that up and I create mice.

There are lots of things that have already been shown to restore cognition in mice, and so I'm doing that.

Whole-person trajectories in aging and cognition

And then I have the side-by-side aging model. One of the things, I do a lot of molecular omics with different tissues, and so I'm looking at what all is changing along that trajectory, that health trajectory and the trajectory of getting less healthy.

And one of questions the NCCIH has is, are you reversing things? Whatever you're looking, at are, you just reverses the decline or is it a different process altogether to restore health?

And once your health is restored, Are you healthier? Is it stronger than it was before your What's the answer? I don't know yet. I just finished my experiments and I'm working with the data right now.

But the other place to do that is with data repositories and real live data, clinical data that people have, which is one reason I reached out to you.

So I am kind of looking for people People that are experiencing this, seeing this in clinic, there are a lot of, we have a repository here for Alzheimer's people, just clinical and tests and all these different things.

And there's some big national repositories. So that would be another way. I'm just looking at longitudinal data, but the main thing is that I might have primary outcome of cognition.

Either that's getting better, that getting worse, whatever it's doing. But I want to track the whole person, what is changing along that. So it's not defined by all of the other systems necessarily.

It's defined the condition of interest, which is cognition. But how do all those other things change? And I do a lot of network analysis. How do they change together?

How are they changing together and then multi-scale? If I can get omics data, I'll use that along with. you know, any data that I can get, but really trying to represent the whole person is the idea.

Okay, so you are setting these trajectories of cognitive health, really whole-person health that both improve and decline. They go in both directions for mice and humans, right?

So what have you learned so far? I think some of these big questions you don't have answers for, But what has this taught you so for about aging and the possibility for improvement?

Well, so I'm new still to this, and so, I haven't analyzed the data from my experiment, but I know one of the things. So, cognitive non-neurodegenerative cognitive decline is more acceptable that you can reverse that.

And as you know, it's not really believed that, you could reverse Alzheimer's cognitive as much. It's changed quite a bit in the last couple of years.

And that's what's drawn me in. The interesting thing is that all of these clinical repositories with human data, they have reversion rates. So they certain rates like the ADNI, the Alzheimer's disease, neuroimaging.

repository is a really big one used for research, a national repository, and it has like a 15% reversion rate. And I'm not sure from what age to what stage.

Can you define reversions? Reversions just that their cognition is improving, you know, so I've been, Looking at the research and most of the researchers interested in, I mean, there's a lot of interest in predicting these trajectories, especially for Alzheimer's, but the interest is when are they going to hit dementia?

Or when they're going decline worse? And they always throw out the people that get better. Not always, the ones that I've looked at, they exclude them.

And I know that that's not the focus. There's a lot of question. People don't know why that is. I mean, because this is observational data mostly. And so we don' know what people are doing, but they think that it will, you know, it's not what they're interested in.

So, and we have that here in our data. The OADRC that I work in has a data repository. It's part of the national network. We have data for Alzheimer's people that can be used for research.

We have them here too, and everyone knows about it. We even have names for them. Nicknames are called the bouncers or the wobblers because they go back and forth with their cognition.

And there's a need to study those. People feel like there is a… And that's how I got started. To study solutogenesis, like I'd said before, you have to have a population that gets better and a population gets worse.

And so that's easy to do in the lab with age-related cognitive impairment with mice, and even age related cognitive decline in people is, I guess, more acceptable to be restored.

But I started out thinking, well, I started off wanting to study, apply seletogenesis to Alzheimer's and like, well, there's not supposed to be any population of anybody getting better.

And that's what led me to looking into these databases and finding… And then you and I know Dean Ornish and Dr. Bredesen and then Dr Isaacson and Florida.

So that's one of the reasons I've reached out to you. There are people that are publishing these results, and then these repositories have people who also get better that no one really studies.

Well, even the pointer trial that was out recently also showed that. What patterns or hypotheses are emerging from these cases where people on the path to dementia are improving?

So most people, when I talk to people and I haven't dug into the data yet, the human data, but most think it's an error. Like it, you know, that's mostly, or it like they, they just didn't do a good job at, administering the tests that day or something.

Oh, good days and bad days. Right, and people do go up and down. Yeah, so nobody really knows, but it's ignored. That's pretty certain that they ignore that group of people.

So that's the niche I want to work with. But that was required to study pseudogenesis. Like we just said, there are people like you that are reversing cognitive impairment and Alzheimer's.

And before we hit record, you mentioned a personal friend of yours who you know had recovered some cognitive function. So what do you think is driving an ability to recover function?

So you agree, like you're part of the reason we're having this conversation is because you agreed this is possible. It's possible to regain cognitive function even in an Alzheimer's patient.

Maybe not all of way after a certain point, it's not guaranteed certainly. But what do you think drives that potential ability to recover function? I think it's the multi, you know, there seem to be variations.

I'm not an expert on it, but there are these multimodal treatments or multi-domain treatments seem the real key. And I thought I'd heard like the finger people are starting to do that combined with the new medications.

But so I think that's really key. But I you know, you'd know more than me. I there's a belief that those multi-domain approaches are not just working on the neurology.

They're working multiple systems that restore cognition. And I'm really interested in, I've mentioned this before, tipping points in neurodegeneration and resilience and all of that.

There are papers about that, And then would you venture to guess what early signs or biomarkers seem most promising for understanding where that inflection point would be?

So that's my area of research. That is the core of my research, so that would require… I don't know yet. So I mean, I know people say, you know, cardio metabolic issues are going on too, but I'm new at it.

Reversal cases and tipping points in dementia

But my interest is using, complex network models to find those points. And then those point, not only can you find the inflection points, But they should be able to guide treatment, like if you can find out what it is that's changing at that time, and you could detect it.

There are methods, there are network methods. Dynamic network biomarkers I'm really interested in that measure multiple things and how they're correlating together.

I'm definitely a network person and not a single biomarker person, but I am interested in there are, those have been shown in some experiments with other conditions that they can predict proximity to a tipping point, you know, so they're really good for, they not only predicting proximity, But they kind of detect what's going on because they are usually based on omics data, So they can guide treatment and guide their experiments which show that things, you know, conditions are more reversible before the tipping points, which is just sort of common sense.

So that's my interest. It's not exactly what it is as much as it's like characterizing that trajectory from a whole person perspective and in a sort complex multiscale, multi-omics, maybe omics, but a So there's something called network physiology which this intersects with, which is kind of new.

And then NCCIH has just funded another project at Stanford, started in August to define the physio, m which has a model of the entire physiological system in a person and how it interacts.

So it's a dynamic model. That intersect. My thought is, I mean, I'm doing a, call it a poor person's version of that, just doing correlations, but the idea is like, how does this thing change over time?

And can you detect- Multiple inputs and like just, yeah, innumerable variables. We do this at a… It's costly, it's expensive, right? But we do it at one-on-one level where we get tons of data about people.

And then we look at it at multiple points over time. We're talking toxin data and inflammatory data, nutrient data infectious burden, full immune function, understanding, you know, like all of these things, I've listed these in the book and also on this podcast before.

But then as a provider, I'm going to put all that in my brain and kind of make sense of it and then create a treatment plan. As you're describing this, it sounds like, you know, sort of leveraging that sort idea, this complex system science approach with lots of data, but essentially plugging it into like an AI model.

I have to imagine that this all gets a lot easier, a lots less expensive to use this whole person multi-scale model to transform how, not only how we study cognitive decline, but then how test interventions, certainly, and then we deploy them at scale so they can really have an impact.

Yeah. I mean, that was one reason I reached out to you because I don't have clinical experience with this and I have computational… I had my friend who I've seen do a lot of this, and have a miraculous result.

But I wondered, I know I read your book and know that I'm familiar with all of the things you look at, the approach you use. Yeah, and my question was, is there a need for a complex model or do you do well just kind of evaluating the data clinically?

And then, of course, the way I see science is you have the luxury of building these complex models that of, course aren't practical in clinic. And you then have to figure out how to translate those, which usually means finding a

subset of those things that are easy to get in a clinic or collect in clinics.

Um, but yeah, that was a question. I mean, uh, That was one of the things I wanted an opinion from you who does this kind of thing. You know, is there a need for a complicated model which puts all these things together and looks for tipping points, you know?

Or are you already doing that? I think the need, and we're in some ways trying to respond to this, but the needs is to make this accessible because it's $1,000 to see me as a doctor, right?

It doesn't, I can only see eight people a day and that's a full day for me because It takes 90 minutes to sit down and learn about someone's health and it takes another 90 to go through all this data with them and describe it in a way that makes sense so that it is motivational to And that is not accessible to everyone.

So how do we create a tool, and how to we leverage the technology so that this can be accessible for anybody who is Medicare eligible? Because it's so expensive.

It's such a horrific disease. And it is so costly to care for people. I know very well how much memory care costs. How much it costs to deliver, how it cost for patients.

But that's the financial cost. Now the burden to caregivers, the cost that doesn't get counted as often, The burden of caregivers. The absence of that grandparent in the lives of the grandchildren.

the absence Of the mom and the, and The lives Of her children because she's in that sandwich generation, having to care for her mother or her father. There are so many costs to this disease that yes, I think any effort.

to scale what Dr. Bredesen has created to make it less expensive, more accessible, easier to deploy is a very worthy endeavor. Yeah, that helps. Yeah, we are starting to offer the guide, guide helps a little bit.

Guide is basically some care management, some through, it doesn't have to be through a clinic, but we'll have a nurse practitioner joining us who does bill Medicare and she'll be deploying the Bredesen approach.

Plus, will have this additional care team basically clinical coordination happening to support with respite care and Meals on Wheels. And, you know, it's so challenging to have dementia, to be elderly, and then to navigate the healthcare system, even if these resources are out there for you.

Just getting them, getting access to them doing the paperwork, and getting through that process can feel insurmountable, especially when your partner has got diabetes and is in pain or can't hear.

They might have full cognitive capacity, but they've got these other issues that are going on. So it can be really challenging. I do think that we desperately need solutions that leverage technology and computational analysis.

Tell me how, tell me when. One of the things I'm doing now, which I mean, of course, the stuff I am doing with animals, that is not translated yet. I means, some of things that we're working with, with the biomarkers with mice are translatable and clinic like CRP and I work with 8-OH-DG and the plasma too.

But I also trying to do, I trying get some money now to work with our data repository here, our people data, I don't like the word human, like it sounds like people, or I dunno, people repository.

So, and that's to work to do untargeted, either proteomics or metabolomics in their plasma, you know, which is clinically available and maybe not too expensive, to-do and might capture a broad range of things, so that might be a translatable thing.

I'm not sure. I mean, I know what we pay, it's $200 or $300, something like that. And it can be pretty holistic. So that's kind of what I'm working with right now with our data repository.

You teach machine learning and how to interface with AI. How do you see these tools helping us to understand these complex interventions, complex system science, recovery patterns, the trajectories, and these tipping points?

Network biomarkers and AI for early detection

Not all of these things are linear. No, they're not. They're no linear at all. Yeah. So that's why Dr. Langevin put that grand challenge into 2021 because of AI.

She's like this, you know, it's always been and I You know, I, did research when I was in school, which was 09, you know to 2015, health care research Institute.

And it was always an issue. Like, well, our medicine has multiple interventions and everybody's like, You can't study that with a conventional, randomized control trial.

why it took so long for Dr. Bredesen's first trial to happen. Yeah, you've heard that story. It's such a breath of fresh air, right, that the trend has really shifted, everyone is accepting now.

No, we actually don't want to limit the variables. We want the synergistic effect of multiple interventions. The work I'm doing right now with the animals, that's one aspect of it, is it has multiple interventions.

I mean, I am trying to restore health and study that, but I also do it with multiple intervention and look at how they interact. Anyway, the AI is just the compute power is there now and the ability to handle very large quantities of input variables.

That's why You know, she put that grand challenge forth and we, we got, my department actually got a grant on that grant challenge, which is different from my grant, All of the data they can think of, this is for people with diabetes, but collect that data on them for a year.

Just everything, lifestyle, lab tests, imaging data, wearables, all of that. And now AI can handle it. I mean, there are methods out there, deep learning and all that, so AI means a lot of things.

Chat GPT is kind of AI people think, I think. Yes, that's certainly my experience. Like you say AI, and I think of my relationship with Chad GPT. Yeah, so that's generative AI.

So that is the kind of AI that will answer questions and things like that. But the other kind, anything that machine learning and predictive is technically AI, artificial intelligence.

Machine learning has been around for a long time. There are simple logistic regressions or simple methods that have been round. Support vector machines, all of that, is AI and then neural networks.

They've been around a long time too, but they didn't work very well. And then, then when the compute power got better around 2010 or 11, they were able to build much bigger neural nets with lots more, a lot more connections.

and that's when deep learning came and deep Learning is where everything changed. So deep-learning are just really gigantic neural networks with lot of layers and lots of connections in the model.

and they can pick up all these nonlinear relationships. And then deep learning can be predictive, and it is in healthcare a lot of times. So you can feed in image data where a variable is a pixel, like in an image.

Or I work a little with RNAseq, which has 15 or 16,000 genes expression level. You can fit all of that in, that's 15,00 variables. And then there's multimodal where you put the imaging and the RNA-seq and clinical data from the notes.

And there is mining of clinical with AI to get concepts out of complex. But the AI, even like chat GPT, and that's considered natural language processing, those are large language models.

Those are deep learning neural nets. They're all deep-learning neural net. That came, you know, that was, like I said, the compute power got to where it could handle creating larger neural networks, and that's when everything changed.

And so do you see that playing a role in like, what stage, early detection, personalized protocols so that we can be more precise? Do you that in helping us predict who's most likely to respond to different interventions, whether it's a medication or a lifestyle intervention?

Yeah, all of them. All of that and more? Yeah, all of that. So I think definitely early detection. One thing that does really well is it takes in more data.

You can take in a lot more and get more accurate at detecting. I know in Alzheimer's, I've been interested in trajectories, and those are really long as you know.

People are interested at predicting what trajectory you're going to go down or what path from a point for years out in the future. So they're good at that.

So there are levels of models. There are predictive models, which risk is a really common prediction in health care. But you don't really know what to do with that, so that's one of the things that I teach in my class.

I'm really interested in decision science. How do you make a decision from a model? Okay, it's great, you can predict all this stuff. And people get all caught up and, oh, I can't predict this and that, but it doesn't ever solve a problem.

There's an actual problem in healthcare with people building models and they don't get used because people are so fascinated with just predicting something.

But then there's beyond that is a prescriptive model and a prescription model tells you what to do, recommends a treatment. I did all of that. Actually, before this, that was one of my industries and we did that kind of we at the time were considered ahead of healthcare as far as our sophistication.

And we, we did all of that. You know, he would predict, you know what's the net income from all these different options and things like that? So, but that's going on now.

But, I mean, so I think, clearly a model in my mind would identify early detection, But beyond that, where are you on that trajectory? Are you near a tipping point?

Or are about to tip? And what you need to reverse that proximity, you know, and so the model should be able to, if you're doing omics and things or even proteomics from plasma, that should give you, there are ways to like see what groups of proteins are sort of changing together and what function that might belong to.

And then that may guide what treatments would be appropriate. I mean, I know. Oh, it's just the multi-domain. It's like, well, everybody should exercise an ether Well, this is my next question.

Based on everything you've learned from your acupuncture background, your naturopathic background. All of the computational data analysis that you have done.

What are the lifestyle factors that seem most impactful for maintaining, optimizing, restoring cognitive health? Like what are top things that would suggest someone do?

Yeah, I'm still, like I said, new to that. I know I am doing exercise and a botanical with the mice. Does it work for the mouse? Yes, it does. There's a huge body of evidence that both of those work for the mice.

Nobody's ever tested the two together, so I'm still in the process of seeing what my data said, but that's why I chose those two, because there's already a big body.

We do here, we do a lot of Centella research here in Ashwagandha. And very much so. Even if there's an Alzheimer's mouse model called 5X FAD, which we use a lot here.

And it does so with them too. It reverses their cognitive decline. So exercise and herbs, you heard it here first. Yeah. Well, yeah. They haven't been tested together as much.

They have, I mean, like my friend did, my friends who you had mentioned who has miraculously reversed her cognitive decline and held it stable as a huge exerciser.

Lifestyle, herbs, and multi-domain interventions

And she continues, she's very motivated to exercise. I think that's got to be one of the number ones. But again, that I don't have any answers yet for my own work.

But what I think is that it's the combination of things. That's always what i put in my grants and that's what… I've heard that from our vice chair of research here that they're very much open.

People here in our neurology department are very into the multi-domain and very on board with that, but they don't study it. know how because it needs new methods and it's not.

But he'd mentioned at one point that the problem with that is you see these effects with multi-domain and then everybody goes out and studies the single intervention and they don't work when they look at them individually.

So I'm really big on synergy. I've always been a synergy when I first came here. I did cancer research and I didn't just study, I was trying to predict synergies between natural products and cancer drugs, so I wasn't trying just to find a new drug from a natural source.

I really was interested in synergies because there was evidence in cancer that certain lycocumin, when it's taken with a cancer drug, makes the drug more effective in the cancer tissue and protects the healthy tissue at the same time.

There's amazing things in plants. I studied the effect on neurons of centella in vitro. It looks like centellae is anti-inflammatory and also works on reducing oxidative stress, but centelle is also a It's also used in derm applications.

And when I treated these neurons, their collagen turned on like crazy. No one's looked at that as far as is that affecting cognitive impairment. But we have seen that Centella increases the density of dendrites.

So it's actually changing the shapes of the neurons. It seems like the neuron might want to restructure the extracellular matrix. I actually get it. Our listeners might know centella asiatica as good cola.

Yeah. And this is an often used herb in, in Ayurvedic medicine and traditional Chinese medicine throughout Asia. We know that it's very helpful for wound healing, skin health, antioxidant, anti-inflammatory.

It helps with like microvasculature and potentially vascular support with mood and then cognition because it's supporting BDNF is potentially one. I mean, certainly if you have better circulation and less anxiety and inflammation and oxidative stress, you might get downstream effects that include cognitive support, but it also directly impacts BdNf.

One of the things I was interested, so I really focused on the interactions between the compounds in the plant, because it's got hundreds of compounds.

The whole plant rather than… Yeah, the whole plants. Yeah. And we did both. There's a few triterpenes, which they think are the active ingredient in centella, and there's capyloquinic acids.

So we looked at those separately. We combined just those, then we look at the entire plant. Then we got an idea of

some of these interactions. But one of things that I did was It seemed to me like, because I did RNA-seq, I looked at sort of untargeted, like all of the gene expression going on.

And then I mapped that to pathways and kind of figured out what are some of functions that might be activated. It looked to be like some those functions were working together.

So I thought, well, how? Is there a wisdom of the plant? And so I did statistical tests of randomness to see are all these things that are being turned on by this plant just randomly happening and they weren't.

The chance that those all happened by random chance was less than 5%, something like that. So that was another thing I thought was cool. So yeah, so I, you know, at least at this point, my whole thing is like the interaction, the synergies between things is what really works.

And that's why I think, doing multi-domain lifestyle stuff with a medication might be okay, or might actually make… I'm all for like, if somebody has to take a meditation, can you make it work better and have less side effects?

Of course. Yeah, same. What gives you the most hope right now in the Alzheimer's research landscape? Oh, the multi-domain treatments by far. Yeah, I'm aware of the drug things.

Nobody seems happy with the development, actually, that I know. I mean, no matter where you come from. But maybe if you combine some of those with a multi domain, they might work, really.

I really think, you know, the amyloid, I mean, at least my framework is that amylol tau, these are there to protect the brain, right? They're antimicrobial, they engage metals in interesting ways.

They are their to the protect brain. And so if we just take them out without addressing the toxic exposure, or the oxidative stress, that infectious burden, then we end up with a less well-protected brain But if we can first kind of do our work, clean up the messes, stop the exposures and the burden, then what we do is we turn off that microglial activation, right?

And then if get the amyloid out and there's not as much to protect us from, fantastic. Maybe we're in a much better place. I think that there could be wonderful synergy between those things.

But, if you just go in and rip the Amyloids out, Yeah. And that doesn't seem to help most people. I agree. That can actually be really harmful. Yep. No.

Yeah, I know. I hear that, and I agreed with you. They seem so complimentary, unlike the neurogenic effect of exercise. Like if you, you know, getting them out is great, but then repairing everything, it seems like the two would go together really well.

Is there a diet that you see work best in mice? That's a good question. If I do more mice work, I might do the diet. I haven't looked into that as much.

And so that's a really, yeah, I am really interested in that and diet is definitely something that is not too hard to do in the lab, you know, in an experiment like that.

Exercise has turned out to be much trickier than I thought in a lot of ways. I don't know because it affects a lots of things. It definitely, so we put the centella in their drinking water and it effects how much they drink.

The ones that are for some reason, so the mice that exercise tend to drink a lot less of the water, the centella water. And we do, from memory, we did something called the Morris Water Maze, which is a swimming test.

So the exercise mice are in a much better shape, theoretically, for that swim. They're natural swimmers and they float. It's like it's not a risk to them to swim, But they, but so, and there's, you know, exercise is not a linear dose effect, either from what I can see in the literature with mice, like there is a sweet spot in older mice.

If you exercise them too much, it actually hurts, so. Yeah. And then, the neurogenic effect can take, be delayed. So when do you test? So I've run into some issues with exactly how do, when you do test them and how does it, I just learned it's Interact, you know, studying interactions even in the lab is very complicated, much more complicated than I thought.

And because you just have to know like how do those mechanisms interact with each other and when do you test and what's the right length of time. I think Centella, I mean, we've done other dose testing with Centell and it's more linear, like the more they drink, the better their memories.

But it's also interesting. This is a tipping point. We've done tests where we've given Centella at different ages, throughout the age of the mice, and it doesn't do anything before about 12 months.

Before middle age, it does it make a younger mouse smarter.

Hope, accessibility, and closing reflections

It only does that once they've started to decline. I've seen other researchers that have seen that with other natural products they're using for memory with the mouse.

That's interesting. Like it's almost the antioxidant. It's the anti-inflammatory process that's actually beneficial. And if you don't have a bunch of inflammation or oxidative breasts, then it doesn't Yeah, and that's a total tipping point.

So to me, that would tell, you know, if you can, I'm sure you could pick that up somehow, what is it that is telling you, okay, Centella wouldn't be worth it to give right now, or maybe it would be.

Steve, so I ask everyone this, but what brings you joy at this stage in your life? All of what I do. So I am 67 and just kind of at the beginning of a career.

It's taken a while. Like I went, you know, I've been in school and doing post-docs and stuff for like 15 years, maybe now. But I always, You know I just got married.

I got into a relationship with a lady in life. And I love meditation, and I I loved nature. You I'm here in Oregon, it's unbelievable. We go all over.

We travel, we camp, and we hike a lot. I do all of the multi-domain things. You know, I box. And I like martial arts and boxing. This isn't a boxing accident.

Okay, you're not getting traumatic brain injuries, are you? No, no. No. Not that kind of boxing Yeah. What's your routine? What do you do for your brain health based on what you wear?

I do. I take supplements. So I just took the supplement designed by Dr. Bredesen for the last month. The NeuroQ? Yeah, and we had our top like Centella researcher here did a grand rounds and she was talking about She was doing just talking about the literature with centella and ginkgo and then coffee fruit and curcumin.

She's talking by the research and at the end she showed that supplement, she said she kind of picked it out as what she thought might be the best supplement for me.

And so I tried it and it really made a difference. And I do supplementation, but I'm not a fan of just doing supplementations with everything else. I exercise, I box, hike, lift weights, and I keep my mind active.

You know, really try to study, love to learn, keep studying and learning new things, which my job is really good for. And I get up in the morning and I meditate.

I sometimes do pretty intensive mindfulness retreats, which are very good for that. And, I love music. So I exercise and do meditation, spiritual connection, aside from religion, but just that connection to everything.

Nature is one place I really like. I live on the edge of a forest in Portland, you can live downtown and be on edge before us. And yeah, exercise though I have to say, I'm pretty good with my diet.

I've learned not to be too strict. That's part of it. When I first got into naturopathic school, drove myself crazy about being strict, but I do. You know, try to do smoothies, trying to get, you know a bunch of veggies in every day as their core and protein.

And I do do better with low carbohydrate, diets, leaning towards the diets. Yeah. Steve, it's such a privilege to have you here and I'm just so grateful that you brought such clarity and curiosity and scientific depth to this conversation around like AI and the data and what it means for cognitive impairment as people age.

It's really fun to talk to someone whose work sits at this intersection of data science, natural medicine, neurology, human resilience, aging. And really, I think that what you've illustrated is that there's this potential for understanding cognitive health in a really new way right now.

Your focus on pseudogenesis and this whole person modeling, and again, this possibility of cognitive improvement rather than inevitable decline, it's so refreshing to hear and to know that this is being represented in the research world.

And there's this reminder, I think, throughout our discussion here that the brain is dynamic, it's interconnected. It's far more complex than we might realize.

I have a reverence for it certainly every day, but also far capable of repair than what we've been taught to believe. And so I hope that everyone who's listening, this encourages you to think differently about how you're aging and to question the assumption that decline is unavoidable and really to explore what the possibilities are when we think about the entire system and we do exercise and think these herbs and how we can leverage them to really optimize as we grow older so we could think well and age well.

So thank you. Thank you, thank for joining me today, Steve. Is there anything that you want to leave our listeners with or any way that they can learn more about your research or about you?

I think if there's anyway, I don't know how many people have. I've had several people with dementia that I, you know, in one way I had to care for and I know about the resources.

If there is anyway, to support resources for people that do have cognitive impairment and might not have anybody, like family, don t have family around or they family, you know, doesn't want to deal with them or something, do that.

There's a need for that, to really support people that don't have anybody with cognitive impairment. That would be my urging for people. Yeah, what a compassionate answer.

Thank you for the work that you're doing. And thank you, for helping us to just illustrate and illuminate that there's a future where cognitive resilience isn't just the exception, but the expectation for everyone.

Thank You, thank You Steve, such a privilege having you here. Yeah, Thank If you enjoyed today's conversation, please take a moment to subscribe, leave a review and share this episode with someone you care about.

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Until next time, keep thinking well and aging on purpose.