# Plasmalogens: Key Components in Alzheimer's & Cardiovascular Disorders Transcript

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## Introduction and Guest Background

Hello, this is Doctor Joseph Rafael, your host for the Telomere Summit. Today I'm very pleased to have on the show. Doctor Dan Goodenough, who will talk about his research into plasma allergens and the relationship to many diseases, including Alzheimer's disease.

Doctor good knows research into the biochemical mechanisms of disease. Started in 1990. His curiosity about the biochemistry of life is as insatiable today as it was 30 years ago.

In those 30 years, Doctor Goodnow invented and developed advanced diagnostic and bioinformatic technologies, designed and manufactured novel and natural biochemical precursors, and identified biochemical problems of numerous diseases, including Alzheimer's disease and dementia, Parkinson's disease, multiple sclerosis, stroke, autism, ALS, schizophrenia, bipolar disorder, depression, and cancers of the colon, pancreas, ovaries, breast, and many others.

He is just getting warmed up. Doctor Goodnow is now going beyond disease and the detection of biochemical dysfunctions to diagnose, and the correction of biochemical dysfunctions to treat disease.

Doctor. Good nose. New focus is to defeat the entropy of aging by creating strategic biochemical and bio functional reserve capacity in advance of known disease risks, such that the human body can maintain the physical and biological functions of life indefinitely and without disease.

Welcome, Dan. I am so glad to have you on here. I know we've had lots of conversations about, patients that have done your lab testing, but I don't know that we've actually ever really talked about the journey, that you took to get to this fascinating area of plasma and medicine and cell membrane medicine.

I'm sure that, I would love to. And our listeners would probably love to hear about how you got here. Well, thank you, doctor Rafael. It's a pleasure to be here and talk with you about these things.

But yeah, so my background is actually in chemistry. Okay. So I'm a PhD in, psychiatric medicine's my PhD. My initial training is in synthetic organic chemistry.

And so I look at the world there's three levels. Basically the biological world where we have organisms interacting with each other at a, at an organism level.

And then we chemistry is where actual atoms, the three dimensional molecules interact. And we have that simple first law of thermodynamics that, you know, matter cannot be created or destroyed.

It only gets transformed. So essentially biology is just moving these atoms and electrons around. And then you go deeper into it, you get into the physics and you get into quantum mechanics.

And what is the nature of these molecules themselves and that kind of gets out of reality. And so the core of our existence really, you know, our, you know, reality, existence is is chemistry.

And so that's where I got more and more interested as time went on. So I first started looking at the biochemical mechanisms of psychiatric disease and depression, anxiety, other different, you know, neuropsychological disorders.

And obviously Alzheimer's, Parkinson's and so on. And then as what happens is sometimes when you're doing

your research, the tools don't exist that you need to answer certain questions or trying to understand what's actually going on at the biochemical level in these systems.

And then when the 1990s came around, the genomics revolution started, where people were saying, well, we can sequence genomes and we can start changing the way we look at, science and medicine, where we're going to say, let's, let's collect the data first, generate hypotheses.

After we generate all these large amounts of information and that and that was pretty powerful because then we could we could modify genetic genes and we could say, okay, what does this gene do?

And then we can go beyond that. The problem with genetics is that it's all derived from genetic code. And so your genes get transcribed into transcripts with your gene chips and messenger RNA.

And then they get translated into proteins in the human body. But metabolites is small molecule chemistry that we live in doesn't come from our genome.

It comes from our environment. And our genome basically just moves them around. And we didn't have a technology that could be analogous or complementary to this whole genome sequencing, or gene chip technology.

## Metabolomics and Disease Causation

And so from a chemistry perspective, I started looking at how do we comprehensively measure all of the biochemistry occurring at once. And that's why my first invention was non-targeted metabolomics.

And that's the the core technology platform. This behind proteome scan, which is kind of a mini portion of that. And so that allowed me to measure tens of thousands, probably over half a million small molecules and biological systems.

I've measured over the years using this advanced technology. And it was used for basic research, but it's also used for very extensive, large scale clinical trial research for understanding diagnostics of disease.

And that was great. It was like a little like I was like a little boy in a candy store of metabolomics, right. We're getting all these biomarkers and we could diagnose different diseases.

Basically it is it's a it's a complete diagnostic manual of human health. Like there isn't a single human disease. It cannot be diagnosed using metabolomics.

And that's just a flat out fact. And so when I first started doing that, I was thinking then that these biomarkers were going to be useful for diagnostics.

And that's true. And and I found lots of patents and got a lot of this. You passed on diagnosing multiple different diseases. But what happened over time was that these biochemical changes kind of surprise me.

Okay. I thought, you know, we're going to diagnose the disease and then we'd fix the disease and then these biomarkers would come back to normal again.

And my first major wake up call was in colon cancer. And we did a trial with colon cancer in Japan, in Osaka, Japan. And we have these great biomarkers that were decreased in people with colon cancer.

And then we did a before and after surgery study and after surgery. The biomarkers didn't change. They stayed the same. I thought I was expecting these biomarkers to get back to normal because hey, these obviously the tumor is consuming these biomarkers causing this major depletion.

And so if I fix the tumor the biomarkers should come back to normal. Well, that didn't happen and I didn't really understand it. So we repeated the whole study over again in a different collaborator out of out of, Chiba University

in Japan, northern Japan got exactly the same results.

And then this was starting to show up over and over again, the plasminogen story with Alzheimer's. So we're seeing these situations where the biochemical changes are preceding the disease.

And then as you do more and more of this work, rather than getting more and more complicated, we started getting simpler and simpler because as we started moving up, the causation chain of events, we were getting closer and closer to the most proximate biochemical changes and the diseases that we're seeing really became symptoms of biochemical dysfunction, not causes of biochemical dysfunction.

And then and as that started getting more of a more reductionist point of view. And, so plasma allergies are one of those stories. And so that's kind of how this whole thing progressed, really from, you know, for me, trying to break down my own biases and, and ignorance is in terms of, you know, we think are so smart and that biology has a way of really humbling a person once you get into it and they realize that the, the diversity of, of this world can be really.

So it was interesting you were talking about, first seeing biomarkers that you're picking up in the metabolome of these colon cancer patients. And then you thought that once the tumor was treated, the the signal would go away because the assumption was that perhaps those biomarkers you were picking up were produced by the colon cancer.

But in fact, what you figured out was that they were still there. And then they were probably causing for part of the biological milieu of what was actually causing the cancer to occur.

But before we sort of answer that question, just for our listeners, most people are familiar with the term metabolomics and metabolome, but not very deeply.

How would you define the metabolome that you're looking at with your technology? The human metabolome, is it all the molecules in the blood? Is it certain ones? Is there one?

It's just a, related to metabolism or is it is it all markers in the blood? It's all small molecules that are not derived directly from your genome. And so glucose exactly is a metabolite.

And glucose in a plant and in a mouse and in human is exactly the same glucose as glucose is glucose. And so metabolomics measures all of those small molecules.

And fundamentally the entire study of drug biochemistry is all metabolomics. Okay. Every single drug is essentially a metabolite. And it's a metabolite mimetic.

It's only been in the last few decades that we've been developing what's called biological drugs. And those are drugs that are more derived from the the genome.

And so those are proteins that have sequences based upon human genetic coding. And then they're designed to interact with specific human proteins. But typically if you take an antidepressant drug or you take, you know, for instance, of statin, those are metabolites that are designed to mimic, endogenous small molecule, and it interacts with those are human proteins in their receptors.

And that's kind of how. So our our genetic code translate into it's a it's a, it's a, it's a set of possible reactions to a given circumstance because essentially our, our genome is passive.

Okay. They have no eugenol, has no idea what you're going to do in the morning when you wake up. And so they're, they're they're kind of one step removed from reality.

So they're going to react to whatever happens in your world, whatever you eat, whatever you do. And it's going to adapt to those situations. And and so it's all your genetic structures completely reactionary to maintain you in a living environment.

So it's sort of, your instructions in your DNA produce RNA and then produce proteins. And these proteins are maybe like machines that depending on what raw material you put into them, then produce the metabolome so you can well, they don't produce the metabolome, they interact with it, they transform it.

Your proteins are essentially sensors. Okay. They'll sense am I is is Joseph exercising? Is he not exercising okay. Is he having glass of wine? Is he not having a glass of wine and is saying, okay, based upon what you are doing, the proteins are sensing that, okay.

They're saying, oh, all of a sudden I'm seeing ethanol in the blood. Now. Well, that wasn't there two hours ago. So now I have ethanol. So I have to deal with that. So.

So Joseph doesn't die. Right. And so then it's going to change okay. I need more of this protein now because I'm experiencing this thing okay. So if you get an infection or whatever it is.

So all the proteins in your body are essentially genetic sensors. It's how your genome can sense the world around itself. And as we change with disease or anything else, then your your modifications.

And so a lot of the things that we think about with epigenetics and a lot of things we think about with aging and the genetic adaptations, we a lot has, we have that that sequence events backwards.

We're thinking that these genetic changes are related, are causing our aging. And really what they're doing is they're preventing us from dying of aging.

And they're they're basically sensing that changes are occurring and they're they're trying to keep you alive as long as possible. And sometimes they can be overprotective.

And the best way to tell people and it sounds counterintuitive because when you look at it, it looks so causative, it says, oh, I have a gene for autism or, or the Brackett gene for that to a here's a gene for breast cancer.

Well, no, it's is not a gene for breast cancer, okay. Brac is a is a gene that has a mutated results in a mutated protein. And that protein has causes these your breast cancer cells and ovarian cancer cells to have, a difficult ability to switch into the fasting state.

Okay. And so that particular sensor is now lessened. So the the person with the Brackett gene, the other genetic responses have to adapt to that. And so one of the adaptations is to protect those cells from dying.

You end up it converts the cell to say, I'm going to be more, glycolytic versus lipid filling, because if I don't get enough glucose, because, because a, a breast cancer cell can't it's not getting energy from fat metabolism.

Okay? Because the body is not switching to fasting. So either it's going to die or it's going to switch. Say, you know what, I need to get a larger percentage of my energy now from glucose, and it starts becoming parasitic to the local environment.

And the genes are doing that because it's saying their job is to to survive. Okay. Every single cell of your body has one job is to say, how do I keep this cell alive for as long as possible?

And, and sometimes it gets overprotective. So when you have stressors and you have you have. So the body will say, all of a sudden you get, you know, mitochondrial stress, for example, and you get electron stress on inside of the cell and the body.

The cell is going to start damping down your energy utilization. It's going to protect you from blowing up basically. And then it's going to wait until that stress leaves, and then it's going to let you kind of open up again.

So part of it, the the genetics of aging is learning to be safe to be young again. Okay. So you kind of get protected to death as we get older. And every time you get in your, your, your body feels an insult, ourselfs feels an insult, it

protects itself and it gets slower and slower to open up again.

And I tell people it's almost like social interaction, right? Like you want to be in a, extroverted, non paranoid world where you feel safe, your kids can walk outside and you and you don't have to worry about things.

Right. And that's how you want to be. So you want to be open and and safe. Then all of a sudden, you know, you have a bad event occurs and you say, oh, well, you know what?

I'm not so safe walking around without any protection anymore. Okay. And so you start protecting yourself, you become more introspect. And then the more insults, the more protected you get, and the less likely you are going to become open again.

And so your cells end up suppressing themselves to protect themselves. But that suppression also reduces our function. And as we get older, you get this accumulation of protective mechanisms against accumulation of of adverse stress events.

And that's so that's what your genes are. So your genes are kind of there. They're they're in your nucleus right. They're they're behind this curtain and there.

And you can just imagine that they're like, you're sitting in your little control panel and you have like you're you're in a war. And unless the scouts are coming back and telling you what's going on with the with the with the enemy, you have, I and you have no idea what's going on out there.

So your genes have no idea what's going on until it gets sensors. And your proteins are those sensors. And you'll say, okay, I need more LDL receptors, because all of a sudden I'm not.

For some reason, my cholesterol manufacture is low, so I'm not making enough cholesterol. And the cell will sense. That said, okay, well, I need to get more external cholesterol.

So I'm going to regulate my LDL receptors so I can pull in more LDL cholesterol from the periphery. And that's kind of how it works. And we think about it.

It's anyway, so that's kind of it was a long process for me to get to that point. And the realization that as we move up this causation pathway, there become simpler and simpler, and then, so that's what Proteome Scan was trying to think, that that short list, like membrane biology, electrochemistry, like the mitochondria, are these there's a, there's a, there's a small number of really core functionalities that have to get met.

Then everything else can be built upon that. And that's kind of what we're focusing on. So just getting back to metabolome for a second, the metabolome that would not include those proteins that are translated from RNA, it's just the smaller molecules that you can pick up on, like GC, mass spec kind of.

## What Plasma Allergens Are

So and you said you made a statement that virtually every disease could be or has been or could be, diagnosed or characterized by a specific metabolome.

Absolutely. 100%. So, but that's so sort of big data biology, a little bit bigger data biology to do that. We're not doing currently. Like we're not diagnosing cardiovascular disease.

We're looking for atherosclerosis. But what you're saying or is it the prodrome to that that can be used. Can you pick up on the metabolome and then. Yeah.

So the problem is the cause of all disease, right? I mean, okay, so where do we do that with that for sure. Yeah. And so and so all diseases have to interacting factors one is a degree of susceptibility.

So say the break a gene gives you a susceptibility to breast cancer. But it doesn't cause the cancer. It creates a susceptibility. And then the second part has to be the trigger a triggering event that actually so initiates the pathophysiology cool cascade.

So you can be you can walk around all day long with a risk factor. And it may never translate into a final disease if that susceptibility doesn't happen okay.

So it becomes an odds game. You can you can drive with ball tires all day long and beautiful streets and never get a flat tire. Okay. You can have a brand new set of tires.

And if you drive in the wrong conditions, you'll still get a flat tire. Okay. But the odds are okay if all things being equal, when you have a brand new set of tires, you're less likely to get a flat tire.

It's not impossible because you just need a much stronger nail to pierce that tire. If you have brand new tires, if you have ball tires, just a little rock will give you a flat. And that's how all diseases occur.

And so programs are basically ball tires. They're not a guarantee. But fundamentally virtually all of that disease will occur in that particular group.

And so for colon cancer that molecule was gastrointestinal tract acids from the gut microbiome. And what you can find in is that once you understand the prodrome you can eliminate other risk factors.

For example. So age is not a risk factor for colon cancer okay. It doesn't matter how old you are. What matters is how much your GTA levels are in your blood and what happens as we get older.

The percentage of people who have low gas in their blood increases, and so therefore the increased prevalence of a GTA deficiency is the cause of the age association.

So once you understand the GTA level, your age is irrelevant. You can be €90 if you if you're a 90 year old man or woman with good GTA levels, your risk of colon cancer is the same as an average 40 year old.

And so yeah, it's me it. The GTA will supersede chronological age, but chronological age is a risk factor for lower gta's. Correct. And so the and what's the.

Well we're getting a little bit ahead of ourselves because these are sort of in that family of molecules that we're going to start talking about more about.

But in, in terms of sort of going from metabolome into plasma genes, let's first, talk about what plasma genes are, because I had heard about them until I, you know, sort of heard about your test and then started ordering it, and, and, and what, getting results back and talking to you about it.

But, I'm sure a good portion of our listeners have never heard of a plasma again. Yeah. And also, you know, what role they play in diseases, in aging, and particularly in Alzheimer's disease, which we're going to talk about.

But let's let's start with plasma. Plasma. I'm going to one for about five minutes and day. Plasma engines are like this bad penny that just keeps on showing up.

It's it's one of those molecules you just can't get rid of. So statistically speaking, linear in science, we are trying to find understand, understand the causation of a disease.

Molecules that we see that change with the disease are either symptomatic or they're causative. And the farther you get away from the the causation of a disease, then these symptomatic variables disappear.

You say, oh, okay, that's not really like the aging GTA, for example. So age is really not the important thing. Gta's are the important thing. And so what you can do is you can eliminate biomarkers.

They're saying, oh, that is just a secondary or tertiary effect of the disease. It's not a primary effect. Plasma allergies are one of those molecules you can't get rid of.

So it's always there as everything. So it's a get people confuse. You don't want to go. Yeah exactly. An aging a plasminogen deficiency is a really critical issue.

And so what becomes unique of a plasma allergens. They're a phospholipid. And so as I was telling you earlier there's the human body has two core capabilities that you must meet to live.

One is your mitochondrial function. We take in hydrocarbons, burn them into carbon dioxide and water. We use that energy to charge a battery called the electron transport chain.

And that's how the body the human body is essentially a hybrid electric car. We burn hydrocarbons to charge a battery, and that's our energy source. The second part, and that's all the electrochemistry with lots of native stress and electrons.

The second part of the human body that must absolutely get met at all times is membrane biology okay? What gives the human body structure so that you're not a bowl of soup?

Okay. In a in some yeast that that we're we're brewing okay. What gives us structure is the membranes. And they're the ones that give all of our trillions of cells the three dimensional structure and all the proteins of your body fundamentally either work directly in a membrane or they are influenced by a membrane.

So lipids are the matrix of our life, okay. It's like when you walk, it's a difference between walking on hard ground versus walking in the mud, okay.

It changes how everything works. And so that's the so so lipid membranes are called phospholipid bilayer. And phospholipids are like a soap. They have a polar head group that likes to be in water.

And they have a non-polar fatty acid sidechain likes to be in lipid like in oil like your oil and vinegar mixtures. And what happens with phospholipids is that they create, a phospholipid bilayer.

So the fatty acid sidechains, aggregate together in the center and the polar head groups on the outside. And that's how the body creates a biological wall and creates an impervious wall.

And that impervious wall is allows the body to do compartmentalization. So you have things that can happen in the mitochondria, things that will happen in the endoplasmic reticulum.

Things will happen in cardiac cell that won't happen in the lung cell. And so that gives the body all the organizational compartmentalization capabilities.

But things have to go in and out of these membranes okay. That's where your metabolites go in and out. Proteins go in and out. And so the maintenance of this lipid membrane becomes really, really critical.

Plasma challenges are one of those critical elements okay. They make up 20 to 30% of the entire lipid composition of your brain. Like we're not dealing with small amounts high levels of your heart, your lung, your kidney, the retina of your eye.

Are these molecules called plasma allergens. And what makes them interesting is that you can't get them from a dietary supply because your body makes a lot of them, and your body uses a lot of them.

And the very final step in their manufacture creates this bond, which gives them their functionality is called the vinyl ether bond. And it's designed to be very exquisitely sensitive to acid.

It's one of your major neutralizer of hydrogen peroxide. And we just published this clinical work in Alzheimer's

disease showing how plasma gene therapy, the proton neural, dramatically reduces your maladie aldehyde level.

So it's a very potent antioxidant. And well, and we showed really powerful cognitive improvement and mobility improvement which we'll talk about in a minute.

But so you put your body makes it and you can't get it digitally. So you are constantly making a certain supply. So when we're younger we create these biochemical reserves.

So the myelin sheath, the protective coating on your axons are high concentrations of plasma allergens. And so as we as the course of time goes on, after about age 50 or so, plasminogen levels start to decrease, not in everybody, but as a population generalist perspective.

Right. So the the better way to think about is that the the prevalence of plasminogen deficiencies start to increase. So maybe in people in their 40s or maybe 5 or 10% of people that have low plasma allergies, then it becomes 10 to 15%, then becomes 15 to 20%.

And so as we as that plasminogen deficiency increases, you start losing your biochemical plasma reserves that you built up over your lifetime, and it starts bleeding out of your brain, bleeding out of your membranes.

And this is where it becomes important, because all the cells of your body, it's kind of like a bakery, for example. So people say, well, can it be that simple?

Is it just plasma? Yes. But I tell people, imagine, like your cells are cooking things every day, okay. They're making membranes, they're making molecules.

They're basically a bakery. And you can imagine if you're going to make a cake for Thanksgiving and you have your favorite recipe that takes, you know, two cups of milk and three eggs and 2 pounds of flour or whatever.

Your recipe is. Right. And you're going to go and you're up in the morning to go make your, your cake, and you go into the fridge and say, oh, well, I don't have two cups of milk anymore.

I only have one cup of milk. So are you going to make a cake with all the other recipe ingredients in it and just one cup of milk, and you're going to end up with a brick for for a cake and not an actual fluffy cake.

Or are you going to say I'm going to cut everything down? Instead of three eggs? I'm going to use an egg and a half instead of 2 pounds of sugar flour.

I'm using half 1 pound of flour. So you're going to reduce the whole recipe down so that the cake still comes out. You have less cake, but it's still good quality cake.

And that's essentially brain shrinkage 101 okay. So when we're time at age 90, our brain has shrunk 20% of its volume since we were 50. Okay. And so part of the brain shrinkage problem is that your cells, like I said, are passive.

They can only work with what they have at their disposal. And they will adjust to that, that that environment the best they can. So plasma is one of those molecules and very critical ones.

So and it's involved in your neurotransmitter release like you need to release the circular release of neurotransmitters required. These plasma allergens cholesterol regulation and transport.

Like your HDL cholesterol transport system, is almost entirely driven by plasma allergens. And so those kind of things are really, really critical. So that's kind of where the plasma allergen story comes in.

Let's get a little bit more clarity, because I know this is confusing for me. When I first heard it, I'm sure to a certain extent it's a little confusing to people first hearing you.

So plasma allergens, you can't take it in your diet because that vinyl ether bond gets destroyed in the stomach acid. There's a sort of a reserve that's in the body, in the in the white matter tracts in your brain.

You're saying that that's built up from birth, and then you gradually chip away at that because we ask we should also get into the exact structure. My understanding is that the components of the plasma allergen can be gotten from the diet, like there's the plasma allergens or EPA plasma allergy.

There's choline is part of it. There's ethanol. I mean, is part of it. Putting it all together is what's done. And you have some supplements that can help do that.

## Plasma Supplementation and Structure

But why don't we talk just a little about the structure of a plasma. So the big the big thing bring those, those levels up right from the natural history of losing them.

So the critical component of the plasma allergen is called the the ether bond. So most lipids are on a glycerol backbone. So when you go to your pantry and you get olive oil that's called a tri acyl glycerol.

And when you get fish oil from the market, it's a tri ACL glycerol, which means there's three ACL bonds on a little. It's like it's like a it's like a power strip with three plug ins.

And you can plug in any one of the three components. And that's your classic glycerol molecule because those are called triglycerides that float around. Exactly. And all the things and yeah, exactly.

Triglycerides plasma allergens are an alkyl ACL glycerol. So the SN1 position, instead of being an ACL bond, which is a fatty acid bond, is an alkyl bond, which is an alcohol bond.

And that's what makes it very different. It's manufactured entirely. It looks almost identical, but it's manufactured in the paroxysm. It doesn't fall any of that once.

It once it's made, it'll share with other phospholipids. But it's not digitally involved. And so in order to get exogenous plasma allergens, I'm a synthetic chemist.

So one of my excuse me work was to develop, precursors that could survive the gut. And the way we did that was designing alkyl glycerol that don't have the vinyl ether bond, but just the ether bond.

And then that gets absorbed, and then your body can make the final step in all the cells your body. And so it has two very powerful important issues is one, it'll increase your circulating levels of plasma which is your pool size.

But every day you take the supplement, it pulses into the cells of your body and allows each of those cells to make their own plasma engines on demand.

Which is why, excuse me for the way this works. You get some water, you know, can't, you know, I, exactly didn't have one year with me, so. So the clinical trial.

Wow. My voice doesn't normally do this. We can pause it. You can go ahead and get a drink of water. Yeah. Do that. Okay. Resume. Serve that. So we were talking about the chemical structure of plasma allergens.

And, what makes a plasma marginal plasma is this ether bond. And it's an and it's very if you had to design a planned obsolescence, if you had to design a human body with like a washing machine with a bad belt, you would pick plasma allergens because it's there's a single non redundant biochemical system to make all the plasma allergens.

And there is absolutely no backup plan. It's one of the few systems in the human body that has only one pathway, one system. And if you are born with genetic mutations in your plasma engine manufacturer, there's like three

enzymes that are completely obligate to their manufacturer.

Basically, either you die within a month or a few years of of birth or you have severe, neurological defect, dwarfism. There's a bunch of very significant adverse effects.

So we know plasma engines are obligate to human life based upon mutations or rare diseases that affect plasma engine biochemistry. And so the design of supplements that can survive the gut and to target different plasma allergens was to get these alkyl ACL glycerol.

So it's kind of like L-dopa for Parkinson's, where L-dopa is a biochemical precursor of dopamine. The proteome neuro and proteome glia are precursors of plasma allergies.

And they're designed to by to survive the gut acids. And they're designed to go into each of the cells. The other interesting thing about plasma engines is that they're different types have entirely different purposes, like they're really opposite of each other.

So the plasma mountains for your neuronal synapses and your neuromuscular junctions and the, you know, the HDL cholesterol, transport and your macrophages, those are all your de long chain omega three plasma engines.

And they're involved in the fluidity. And they're also involved in amyloid function in the brain and so on. But the plasma genes that are protective of your neurons, that create that protective sheath in your Schwann cells and your oligodendrocytes, those have almost no omega three.

They're almost all omega nine oleic acid. And that creates a very, very tight, impervious structure. So they're very, very different from each other. And so the challenge is to be able to target those individual cell types.

Because l.q glycerol has been around for a long time. Shark liver oil, for example, is one of the sources that you can get alkyl literals, but they don't.

And you know, the positive effects of shark liver oil, for example, in radiation therapy for cancer has been known since the 60s. And so the the point is that when you take shark liberal, you're going to get squealing.

You can't get the actual plasma that you need, which is either the DHEA version or the oleic acid version. And obviously there's always the, the environmental contamination issues of sourcing issues.

And so we have 100% vegan designed program. So we get our data from an L from LJ, we from LJ triglycerides. We actually process that. We we strip the day off basically like making soap.

And then we purify the VHA from the algae source and we put it on a plasma engine backbone. And that way it's completely purified. There is no chance of any kind of environmental or even allergenic reaction to the source of the fatty acid.

We just use that to get the fatty acid and then gets put onto the backbone. So that's where the Proteome Neuro comes in. And then for the proteome glia, which is designed for stroke, concussions, multiple sclerosis, autism type diseases where you have a white matter major white matter component, we get our oleic acid from, sunflower oil, a high, high oleic acid, sunflower, source.

And again, because the same process, we strip it off, we purify it, and we put it on a backbone. So there's no, like, if you're sensitive to, you know, sunflowers or if you're fish sensitive or not like that, like, this would have none of the product has none of that issue.

And also any there was any kind of contamination in the source. That's all cleaned up in our purification process beforehand. So there's no risk of Mercurys or LEDs or anything like that coming from the source.

So that allows us now to target either the neuronal system, or we can target the glial system based upon the type

of issue that we're dealing with. Now, they're both going to restore all plasma allergies as a general rule, because it's the backbone that drives it.

So that's kind of quick plasminogen 101 story. Great. So, I know I'm going to ask a couple more questions about plasma allergens versus typical fish oil that you get over the counter.

In terms of supplementation, I'm going to know the answers to the, our listeners to here. But first and most importantly, talk about your groundbreaking work in, in sort of a whole new approach to Alzheimer's disease.

These are the, plasma allergen levels and plasma allergen supplementation. Any clinical trial results? You just. Yeah. So we just presented this. And so first of all, let's start with the theory behind it and how you got to the, you know, sort of to the point where you we're going to do a clinical trial and and then we'll talk about the results okay.

So yeah, so using this non-target metabolomics technology, when we're looking at people with cognitive impairment, we found that cognitive impairment was associated with plasminogen that levels in the blood.

People with low levels of plasma allergens had a higher risk of having dementia.

## Alzheimer's Research and Clinical Trial Results

And if you had lower, depending upon the severity of your plasminogen deficiency, it correlated with the severity of your cognitive impairment. And that's at a cross-sectional perspective.

But then as we did more longitudinal studies, it became even more prevalent in a sense that the lower your blood plasma margins were, the faster your rate of decline was, the higher the level the prediction of your, cog impairment was.

And you look at postmortem data plasma, which is in the brain, become highly correlated with cognitive status. More so than anything else, any other pathological feature more than amyloid, more than tau, more than, the, flotilla and raft even even more than the cholinergic neuron density, which we can measure with the choline high affinity transporter.

So the plasma margins became head and shoulders, the most associated brain molecule with cognitive impairment. And this is a mild cognitive impairment or early Alzheimer's.

Later Alzheimer's. I mean, when did across the whole spectrum, you get the signal at, you have cognitive aging well in the brain. It's across all okay in the blood.

You're you're one step removed from the brain. So there's a there's going to be a temporal difference. Basically. How long have you been deficient? And how long has that deficiency.

What's the severity of the deficiency based upon your consumption of plasma allergens. And that'll define your. It's like a it's like a it's like a leaky.

Pail. Right. So it's it depends by how much, how much water is in the pail and how much water is pouring out. And and so and so those two things together will determine how quickly we start seeing clinical symptoms.

And so that's where that came in. And so yeah the the human brain data is pretty well absolute. And it's across all spectrums so completely 100% cognitively normal mild moderate to severe dementia.

It's it's a linear line. And that's all presented in the book Breaking Alzheimer's. We had published a few months ago now and then like that is fully described in the postmortem studies that we've, we've performed who performed.

And so then the biochemical mechanisms like we've used plasminogen precursors, they're, they're completely neuroprotective in animal models, say for Parkinson's disease, if we use MTB to generate Bill Banerjee neurons, if

we treat animals with plasminogen precursors in advance, we get 100% neuro protection.

They're 100% protective of demyelination in demyelinating diseases like multiple sclerosis models. So then very, very powerful preclinical aspect of it and it works like clockwork.

It's the precursors are very simple and clean. They get converted. And so we've known about plasma for 100 years. And we've had some very, very simple calculus rules back in the 60s and so on called battle alcohol and time alcohol and situational alcohol.

These are very simple alpha list rules, but they've never been shown to properly elevate blood plasma margins because you have to take massive doses. And what I discovered when I was doing all the structure, activity, relationship work is that you actually have to put the fatty acid that you want on the molecule in advance, okay, the SN2 position has to have you get the, the De or the oleic acid on it.

And once you do that boom, your body takes it, it gets absorbed, it gets rapidly converted, and it works. And so that's really when the big issue came up on, I think that's where all those my patterns in that area came in, came to be.

So we know from ether lipid deficiency diseases that it reduces neuron transmission. The cholinergic system is is is specifically sensitive to plasminogen deficiencies versus other neuron systems.

And the cholinergic system is a key system involved in in dementia. And so we basically systematically started studying and studying them. And so then finally we you know, I had a bunch of patents on chemical structures of plasma.

But as my earlier story were we things become simpler. Plasma deficiencies are in ALS, they're in Parkinson's disease. Virtually all cancers will have a plasminogen deficiency.

We're just publishing a big paper in breast cancer that'll come out, probably in the next month or so, or in Japan. And so plasminogen, biochemistry is this weak link of health that has consequences in multiple different avenues.

And then your own personal genetic predispositions we're going are going to lay on top of that. So it creates a stress to the system. And then you're going to have the diversity of each individual's environmental, life and their genetic predispositions which can trigger which what potential clinical consequence you might end up experiencing from a plasminogen deficiency.

So that became clear that this one drug, one disease model is not going to work. And quite frankly, as a chemist, I basically did a bunch of medicinal chemistry tricks to create non-natural plasminogen so I could patent them.

But allergies are natural, so you can't technically patent natural molecules. And so I basically just threw that all in the garbage a few years ago and said, okay, we're just going to get a natural supplement, okay.

That can satisfy, you know, Grass regulations. There's no prescription required. You can use it for anything you want. We're going to stay away from actually making medical claims.

We're going to say, you know what? Here's a here's a supplement precursor does exactly this. It it elevates blood plasma allergens. And then we're going to do a whole bunch of clinical trial work.

And we're going to show what plasma engine level modulation can do. And we're going to keep those two worlds separate. So we're not going to make the actual medical claims. But they're supplements.

We're going to let doctors make their own medical claims. We're going to do our own clinical trial research to show the effect, good, good, high quality clinical trial work.

And then we'll be able to do blood testing. And then that way we're going to find out the different areas that it can

work. And be honest with you, that iterative protocol process has been incredibly successful because we're seeing dramatic results in our in our customers.

And then in the clinical trial, which we just announced last week, it was amazing. The small trial. So, so 22 patients complete random. They all had cognitive impairment.

They had either mild very mild. So using the Clinical Dementia Rating scale they had either a 0.5 which is considered questionable, or very mild dementia, CDR of one which is mild dementia and a CDR of two, which is moderate dementia and Alzheimer's.

They go just for it goes from 0.5 to 1 to 2. And then the highest degree is is a three. Okay. So that's severe dementia. So we had yeah. So we had 14 people at baseline that had a 0.5.

So the very mild case we had four people that had mild CDV one and we had four people that had a CDR of two moderate. So eight people, we had very definitive cognitive impairment and 14 had very mild, questionable people at the 0.5 level and bounce back and forth.

But, you know, these are late onset Alzheimer's. What was the average age of the group? We had a the average age was in the late 60s. So but it was not that late.

No, I had even we had some people at age 37 with frontal temporal lobe. So we had some Lewy body. We it was a hodgepodge, the heterogeneous group, very heterogeneous group.

And it was designed that way. And we did no pre-selections this was totally done for pharmacokinetic purposes. It wasn't really designed for cognitive outcome analysis.

What we did is we we did no pre-selection on their baseline plasma levels. So people get high. Low doesn't matter. And the whole point of the trial was to do an escalating dose.

So for the first we did baseline analysis. We did cognition and mobility analysis. And we did biomarker analysis on everybody. And so first month they took one meal per day.

So that'll be one bottle of Proteome Neural for the month. And the second month we doubled the dose. So they took two meals per day. And we did that for two months.

So two bottles a month. And then the fourth month we did four meals per day. So four bottles for the month, one bottle every week. And then we did a one month washout period afterwards.

And so what we found was that we got our dose dependent increase in our target plasma margins. It was beautiful just step by step by step. And there's there's detailed videos that'll be launched within the next day or two on my website.

Doctor. Good Now.com that actually goes through all the clinical trial data so you can show the slides and everything that I presented at the Alzheimer's conference last week is available for everybody.

So anyways, we got very clear pharmacological improvement that the biomarkers improved exactly as design. So we're getting the molecule in as expected.

Then we started looking at cognitive impairment. This is where it got really exciting. So we actually of the four individuals that had moderate dementia they had a CD two.

Three of those four people improved by an entire CDR score in a five month period. Wow. It's really crazy. And then two of the half of the the CDR ones also improved by over a CD five by a full CDR level within five months.

And so when we look at the statistical analysis, if you do a tri square test is too small to look at statistic of, of of the

actual outcomes. But if you, if you group people into responders versus non-responders versus what you would expect random occurrence to be, it's statistically significant cognitive improvement. The second part was mobility.

So we looked at the 32nd sit stand test. And in that situation was that even bigger improvement. So the muscularity the muscle tension the muscle activity improved dramatically.

So actually 14 over half of the subjects had an improvement. So what the sit stand test does is basically you ask a person to sit and stand as many times as they can in a 32nd period, and you count it right.

And it's a measure sarcopenia as well. And so anyone who had an improvement of two or more was called an improver, and anyone who had a decline of two or more was considered a decline or in terms of their, their, their mobility, 14 people improved by two or more.

Many were improved by 4 to 6 Sit stands in five month period. We had four people decline, which we would expect. And then we had whatever the difference was, stayed stable and that was highly significant.

And so the mobility improvements were quite robust and the individuals themselves self-reported feeling better, like their they felt their energy levels were increased and and so on.

And so we're very happy with. But the other thing that was really interesting though was that of the nine clinical responders, okay, that had a full CDR rate change in the five month period, five of them were in the people that had preexisting low plasma engines, and for them were in people that had high plasma allergies.

Okay. So the clinical outcome was not related to the blood test. Okay. So the blood test didn't predict clinical response. The blood test, of course, predicts the clinical decline over time.

But the plasminogen precursors are designed to go in. And actually, not only do they increase your plasminogen levels, but they're actually going rate into your neurons for biological activity.

And, we've had some patients that have, you know, after in the washout period, some of their effects were disappearing. So they've kept on high doses of the plasminogen.

So we're pretty excited. That's the first time in human history that we've been able to target plus management. Okay. We've gone to a place management over a hundred years.

This is the first time that we've been able to target and elevate plasma allergens in humans. And the second thing we did, we looked at oxidative stress biomarkers okay.

So we know plasma allergens reduced hydrogen peroxide. We know anecdotally from what we're doing. You know, C-reactive protein is dropped dramatically when people picked the plasma allergens.

So we measured melanoma aldehyde which is an end product of lipid oxidation. And then we looked at catalase activity, which is an enzyme that's used for hydrogen peroxide.

Neutralization is also a biomarker of aging. And then superoxide dismutase. So we had a very powerful reduction in MDA levels. It's an R 0.5 p value of ten to the minus seven.

So the correlation between blood plasma levels and MDA levels was very very robust. And more importantly when you looked at oxidative stress biomarkers there's a biological flaw like you, if you have good levels, you can't get better than good like so.

So there's so if you take a look at each group of people and say, what about people who just had high aldehyde levels? Those individuals had a disproportionate benefit.

They dropped like 50% catalase levels. People had a preexisting level of a low catalase activity, catalase, which

turned to normal. And what happens is that by reducing the the aldehyde stress or the hydrogen peroxide stress catalyzes a protein protein gets consumed in its activity process.

So by reducing the aldehyde load, we ended up reducing the negative pressure on catalase and catalase returned to normal. And we also got a benefit in people with superoxide dismutase, low superoxide dismutase activity, which is your first line of oxidative stress defense.

So biochemically. So the pharmacokinetic data was robust. The pharmacodynamic in a sense that it's getting in. But it's actually biologically doing something with the MDA.

And then the clinical outcome data was well beyond our expectation. And so we're going to be moving to a bigger trial design, but really focusing. I'll be doing community work.

But the we'll we'll look at MRI data, because I believe that we can actually show significant changes on brain MRI with plasma supplementation. And, going forward.

So that's kind of a quick and dirty of the clinical trial results that were presented. That's that's really, fascinating. And, you know, groundbreaking in early study.

But I was just thinking about a couple of things you said. One was that fixing, increasing plasma allergens can help with neurotransmission because it's involved.

And so that could be a CoQ10 effect. But it seems to me, based on what you're saying, particularly with the oxidative stress markers, that maybe one of the major factors is through a reduction in oxidative stress, perhaps, you know, within the mitochondria, within other, elements of the cell, how does that tie into this sort of more traditional view of Alzheimer's?

And is there any way for physiologically to link that up with the amyloid hypothesis, which of course, is you've been taking a beating? But you know, and then the final question I have, which I know, you know, because I've, I've spoken to other people about is the whole telomere hypothesis of, of, Alzheimer's disease.

## Amyloid, Tau, and Brain Biochemistry

And, you know, it seems to me that there may be a link in that reducing oxidative stress, you know, in is perhaps the, the link in the whole thing, and you're doing it through plasma allergens, you know, mopping up, you know, free radicals increasing, you know, cattle catalase is ability to do its job.

With telomere biology, it could be increasing PGC one alpha and beta, improving mitochondrial health. And, I just wonder if you have any thoughts about, you know, the traditional approach to Alzheimer's, you know, sort of the amyloid.

Abbass. How does help us figure into that? Well, we can turn amyloid on and off the plasma once we published that work. So so I I'm not sure I've not heard that, but I mean, I mean, oh, yeah.

So amyloid biology is not actually that complicated. They've just developing a, a drug is the tricky part on that part. So actually, I'll be launching a series this next week.

I just did the with for people with AP for genotype. So I'm launching what's called the Alzheimer's Breaking Alzheimer's Definitive Lecture series, and it's a series of ten lectures.

Each lecture is like an hour long. One will deal with each aspect of biology amyloid brain shrinkage, tau pathology. And so those two different aspects of brain pathology that are commonly associated with Alzheimer's disease, those are biomarkers okay.

So in terms of cognition okay. The cognitive mechanism is cholinergic neuron transmission. Full stop. Okay. And

then the next question from there is where does that degradation come from.

And how does the cholinergic neurons decline. The oxidative stress membrane hypothesis. It's definitely oxidative stress is related to your inflammation status.

So all inflammation comes from lipid oxidation. Fundamentally that's what activates your your your immune system cells and so it causes autoimmune diseases in its full process.

But in terms of plasma allergens and amyloid and in tau but mostly amyloid. So amyloid comes from a protein called I know let's get some details here.

But amyloid precursor protein ATP is obligate to human life okay. We you cannot create animal models with ATP knockouts. They won't survive. AP is critical.

And when it normally gets processed by alpha secretase, it creates a molecule called soluble ATP alpha. And that is a critical neurotrophic molecule. It involved in nerve neurogenesis neuron growth.

It is very very powerful. It's actually a drug development program in its own right into mimicking soluble ATP alpha. So you don't want to block amyloid precursor.

But biology because it is absolutely obligate to human life. What happens in brain amyloid is it's a membrane structure issue and it's related to cholesterol efflux capacity of the cells.

And that's why the E genotype is associated with amyloid okay. And it's the amyloid association with E4 that gives ape reefer carriers an increased risk.

So an E4 carry that can manage their cholesterol level, their membrane cholesterol has no increased risk. And we published that work extensively. So what happens in amyloid is that there three different membrane regions.

And the beta secretase which is the enzyme that forms the the amyloid beta one 242 peptide that turns into the plaque that's located in lipid raft regions or high cholesterol rich regions.

And the alpha secretase is located in a separate membrane region. You know, in a phospholipid rich region. So when we if we increased de plasma, as we increase, alpha secretase, we increase soluble ATP alpha and we dose dependently decrease a beta 142.

And that's shown in lab, it's shown in humans. So when we do postmortem studies the brain your brain levels of plasma correlate with your amyloid levels.

And so for example, someone who's an E4 carrier that has high plasma mountains will have normal amyloid. So it neutralizes the E4 effect on amyloid. So amyloid chemistry is very highly linked to two things.

One is membrane chemistry. The second is methyltransferase. The homocysteine system. So the other pathway that turns that amyloid formation on and off is the phosphorylation, AP phosphorylation and the De phosphorylation is is linked to methyltransferase activity in the brain.

And that's where tau comes in. So so tau and tau is another chemistry. We can go into that details. But Count Tau is tau acts like a peristaltic pump to accelerate your organelle transport down axons and back and forth from the synapse from the cell body.

And so you have microtubules. So, so tau is called a microtubule associated protein map. And your body all your cells have these rails if you will, microtubules.

And they're basically transport rails. So you can move things from the cell body down to the synapse and back and forth. So when a mitochondria gets damaged, you need to send it back to the cell body.

And when you get new mitochondrial created, you get sent from the cell body down to the at do to the the synapse. And so neurons can be quite long. Right.

And so you have a very long distance between the cell body and the synapse. And so you have normal transport. And then you have what's called accelerated transport of the organelles.

And the the tau protein is involved in accelerated organelle transport. It's how the body moves organelles quickly down the axons and how it does that is like a peristaltic pump okay.

So when targets phosphorylated it it expands. And basically it's like a negative squeeze. So it squeezes and it basically it's like pushing the the organelles down.

So and it acts like a peristaltic pump. So it squeezes and then releases. So as it, as it, as it moves down the, the axon, it, it squeezes and releases and then and it creates this, this process.

So the squeezing part is called force is the phosphorylation part uses kinase is it's the De phosphorylation that relaxes it. That is the problem. And so if you have folate deficiencies or CRH elevations, the ability for tau to become De phosphorylated, the relaxation phase goes away.

And so you can turn tau neurofibrillary tangles. Density goes up and down based upon your methyltransferase activity in the brain. So methyltransferase in the brain is really critical not just for calling maintenance, but for tau formation and for, amyloid processing.

So I go through all those things in great detail. People don't realize that we actually know a lot about this stuff. We've known about it for many years, so really good research has been done on it.

And then we get focused on this idea of trying to remove the amyloid plaques, which is really quite irrelevant. The amyloid plaques are, first of all, you shouldn't have amyloid, right?

So if you have elevated amyloid, that's the biomarker that you have something wrong like there is there's a system not working properly. Right. It means what I can your arteries.

That's right. That's something going wrong. Right. So so your question is not remove the plaque. The question is where's it coming from. Like what? Why why why is it happening.

And and then as you move up there's very a lot of the work has been really, really done very well. Like your atherosclerotic plaques, like a cat, like your, cholesterol acetal transferase system.

Okay. Highly modulates plaque formation and your macrophage levels. And so that's all driven by plasma allicin levels like your plasma drive your your cholesterol is tariffication and cholesterol efflux capacity rates.

And so these are things that have been very well studied. But they're done in isolation. And that's the very frustrating part. Is it. You got a whole group of tau scientists.

They've been studying Tao their whole life. And all they do is talk to other cow scientists. They talk to each other about their own little esoteric thing, and you get a whole bunch of amyloid people talking about amyloid, and you got all these people doing imaging, all this amazing imaging of human brain imaging and and also the biochemistry of brain shrinkage.

And they talk they don't actually integrate their data almost never. And so each of these sectors have been actually quite well studied. But most people don't get a chance to actually experience the simple biochemical mechanisms that drive these common features.

And so that's what the definitive lecture series goes through, goes through each of those systems in detail. You talk about calling the cognition. The biochemistry of cognition is is well established.

I guess it's not controversial. We've we've we've studied this backwards, forwards, sideways. We can turn it on off like, we know. Seriously, we have studied this thing to death like we've known about it for 40 years with a 50 some years of research on this stuff.

So it's not it's not a mystery. Okay. The mystery is, is where, you know, in a functional medicine perspective is understanding the causation cascades, okay.

And getting into those causation cascades and we run up against issues of monetization, to be honest with, you know, to say that when it's a lot of drugs to fix one problem that's patentable, if you went down the same pathway and then you found, well, the best drug is actually a natural supplement, same as to science is done away with.

There's one more activator. That said, this works is generally regarded as safe. Let's do the studies which I credit you with. And a supplement company.

Lots of companies don't do that. Let's do the studies and show that this is the right molecule. And then you've developed a blood test, which I encourage our our listeners to take to look at your website for the Prodrome Sciences, blood test, which looks at these systems, the methyltransferase system, the plasma management system, the bruxism system, mitochondrial assessment.

Pretty fascinating. We've gone over, I don't know, a couple of dozen now. I was yeah, I'm still still learning. And, only one of them, so, you know, so the the list was interesting, your whole different take on cholesterol and cardiovascular disease.

But we can't we don't have time to go into that today. Maybe we'll have you back at some point, but, I think, it's we're, it's 211. I know you had a little bit of heart stopped at, running late, but that's okay. But.

So what did you say? What? You are a your website is, you know, program. So, doctor. Good. Now.

## Closing Thoughts and Resources

com is where all the educational material is, you know, it's, people have a Dr. G the Ian owi, dot com. That's where all the educational seminars and get the book and so on and so forth.

And then program science is so prodrome.com/pro dromey.com is where you can get supplements. And also blood testing from there. So that's kind of where it's all about.

Yeah. So it's been as always fascinating talking to you. The, the biochemical pathways the lipids everything is, is really amazing. Do you have any parting words?

Well, the fun part is that this is all fixable. Okay? People think that biochemistry is some strange world, and it follows basic principles of our everyday life and just uses fancy words.

And we get stuck in the jargon of things. But the the organizational structure and the logic of biochemistry in life is the logic that we observe in our everyday lives and so many other areas.

And so people shouldn't be intimidated by it, and it should be fun. And the biochemistry, metabolomics is not like your genes, which you can't change.

What you were born with. Biochemistry is yours. You can modify this at your own will. There are so many ways that we can tweak one system or another. And so I tell people I'm I'm in human biochemical engineering.

That's what we do. We engineer humans based on basically. Take a look at what you got. We can add a little bit here, add a little bit there, get the right fertilizer mix.

And so we can get things done. And then you should see ultimately effects from that. And, and that's that's kind of

where my biggest passion really is, is on the educational side and getting into the community side and, and breaking some of that.

Just the fear. People are so intimidated by it. And as soon as they realize that these are simple protocols and they're simple concepts, the words might be hard to learn, but the underlying principles are are common to everyday life stuff. So.

Well, yeah, I mean, you definitely helped, to sort of break it down into more, understandable kind of subject area and, encourage, people to go out and get your book Breaking Alzheimer's because that, you know, you do a great job there, too.

Great. Thank you again, Dan. Thank you so much, Joseph. Okay. Have a great one.