Welcome to the Cutting Edge Health Podcast with Jane Rogers, where we discuss science to help prevent cognitive decline.

**Jane Rogers:** I have the Alzheimer's gene, APOE4, and I'd always thought that increased my chance of getting the disease. Today's guest has found a way to negate the disease-causing effect of this allele. He even suggested to me in an analysis of my blood work, that APOE4 was not my family's problem. He thinks we have a mitochondrial insufficiency that has most likely led to our family history of Alzheimer's.

In his book, published in 2021, Dr. Dayan Goodenowe lays out an entirely new theory to me as to what causes Alzheimer's, especially in those with APOE4. He says his real skill is looking for connections in large data sets. What he found as the cause for Alzheimer's is simply groundbreaking. They're called plasmalogens. Dr. Goodenowe is founder and CEO of Prodrome Sciences. It's a fascinating interview. First of all, Dr. Goodenowe welcome to the broadcast.

**Dr. Dayan Goodenowe:** Thank you very much for having me, Jane. I'm looking forward to our conversation.

**Jane:** We have about 40 minutes and we're going to dive in. There's a lot of territory I know you want to cover. I think people, first of all, have never heard this term "plasmalogens". What's a plasmalogen? How does it affect people when you're looking at cognitive decline?

**Dr. Dayan Goodenowe:** Plasmalogen is a type of fat, it's a lipid, and it's part of the biological membranes of the human body. It's one of the core building blocks of who we are. One of the things when we talk about Alzheimer's in aging, we have certain pathologies that accumulate in the brain like neurofibrillary tangles, and amyloid plaques, but also the brain also shrinks. It shrinks like a grape shrinks into a raisin if you will. When you think about dehydrating a grape into a raisin, you have this nice plump grape, and it's full mostly of water. When it shrinks, when it dehydrates, it shrinks into a raisin. It does that cause it loses water.

Now the brain is fundamentally made of fat. When the brain shrinks, it doesn't lose water, it loses fat, it loses lipids. One of the critical lipids, it loses is plasmalogens. It's not just in your brain, it's all parts of your body. The human body fundamentally is comprised of cells, and cells are these three-dimensional spheres, cubes, rectangles, if you will, comes in various shapes and sizes, but they're all defined by membranes, and membranes are what compartmentalize the human body.

Those membranes are like walls in your house, so how you can separate your kitchen from your bathroom, from your bedroom so you can do certain activities in certain areas that don't affect others, same thing that your house is separated from your business, which is separated from downtown and one city is separated from another city. This compartmentalization that occurs on a large scale in our geography happens in the human body as well. Instead of using walls made of wooden plaster, these biological walls that your body has, that gives this compartmentalization are made of lipids or fat. They're made of a class of lipids called phospholipids.

What these phospholipids do, one part of the molecule is polar, likes to be in the water, like a soap, and one part is a fatty acid side chain that likes to be in oil. You have this water and oil mixture. What they do is they mix together to create what's called a lipid bilayer. Two of these molecules connect so that the polar group standing outside and the non-polar group stay in the center, and the body creates an impervious wall by doing that.

All of the membranes of the body are made of these walls and the cells themselves and how they're packed because you have trillion of these cells or more, so you have lots of them. That's what's packed up, and when they're full and plum with the bright lipids, you have full and plum skin and brain and tissue and heart and lungs and kidneys. That's what the body is fundamentally made of. It's one of the core physiological structures, and plasmalogens are one of those critical building blocks of those membranes.

You have multiple types of phospholipids. People will hear about phosphocholine and hear about sphingomyelins. You'll hear these technical terms. Plasmalogens are one of those and they're a critical one because most of the building material your body can get from your diet. You eat an animal product, you eat an egg, you eat plants. All these plants and animals, they're made up of cells as well. There are cell walls, like when you eat a plant cell wall, you're getting the fat, lipids from the plant cell wall. You eat them, we take those, and we incorporate them into our walls, and that's how we live.

There are certain classes that you don't get from our environment, and plasmalogens are one of those. They're very special because during their manufacture, your body makes them completely from scratch, but the last step in their manufacture creates a very sensitive bond. It's called a vinyl-ether bond and it's technical. It's designed like a fuse in your house or your breaker box. If you have a pulse or you have something bad that happens, the breaker switches and your house doesn't burn on fire.

Plasmalogens are like that. They're biological fuses and their last step in their manufacture makes them very, very sensitive to oxidative stress and damage, and so your body makes these to be sacrificed. It throws them out there to say, "You know what? Break the plasmalogen first before you break essential fatty acids like a DHA fish oil or your flavanoids or your CoQ10s," or some other molecules that are much more critical in our environment we don't want to use up and become depleted in. Plasmalogens are your first line of defense. That's what makes them very potent antiinflammatories and antioxidants, probably the most important antioxidant in the human body.

Your body multitasks. It takes one molecule and it'll use it for many different functions. Plasmalogens are like that. That's why it's a critical component of your brain. We're talking 20% to 30% of your brain are these plasmalogens. I tell people it's like you're baking your Thanksgiving cake, for example, and you have your favorite brownie or lemon-orange recipe, it doesn't matter what it is, but the recipe calls for certain amounts of all materials.

Say, your recipe has 10 ingredients. You have excess of nine of them, but one ingredient, say flour, you only have half of what the recipe calls for. It doesn't matter if you have excess of the other nine, you have half flour, you make half a meringue pie. The amount that you make is dependent upon the entire recipe filled up. These plasmalogens are one of those molecules where you can have excess of other things but if they become deficient, your body down-regulates to that minimum component. This is where the concept of biochemical reserve comes in.

You need to understand, biochemically, what the body needs. Some of it, we get ourselves, and then as we age or get a disease, sometimes we become deficient in certain things. These deficiencies have longer broad-based effects. Plasmalogens are one of those type of molecules.

When we're talking about plasmalogens in cardiovascular health, lung function, there's rare diseases where children are born with a mutation that prevents them from making plasmalogens at all. These children are born with dwarfism. It's called rhizomelic chondrodysplasia punctata, RCDP. It's a very high mortality disease. Children very rarely live to their 10th birthday. They typically die in early childhood because your body requires these plasmalogens. They mostly die of pulmonary disease, lung function.

Premature babies that are born too premature, they'll quite often get a disease called bronchial dysplasia. That happens when they're born, because they're getting all their plasmalogens from their mother and then if they're born too early, before they are able to make their own plasmalogens, their lung function is severely impaired and they get bronchial dysplasia.

We have these issues. We know how serious a plasmalogen deficiency is early in life, but it's a very robust system. We normally make enough of them for most of our life. Later on in life, now all of a sudden, for any number of reasons, toxicity, a hundred different reasons why, but for an individually, their ability to make their plasmalogens become impaired or the balance gets disrupted, in that they are consuming so many or they're being broken down faster than they can make them.

The problem with plasmalogens is that you can't get them from your diet or you can't get very many of them from your diet. That's where the plasmalogen supplementation comes in so that we can actually restore them in a targeted way.

Back to structure and function, so your lungs, your heart, your kidneys, all these membrane structures, so cholesterol regulation and cholesterol transport, is critically dependent upon plasmalogen levels. People with high plasmalogens in their blood, typically, will have good levels of HDL. Their HDL levels are high, their triglycerides are low, because they're made in a certain organelle that also contributes to that, so your body is always in balance.

Now, when it comes to brain function and cognitive impairment and cognitive functioning, that's dealings with the neurological systems now. Neurological systems are your signaling pathways. They're the light switches that-- you have your wires in your wall that go across long distances and nothing's happening while that wire's going on. They're protected by that protective coating, but then at the light switch, there's a connection plate. That's where the wires get bared, you can see the copper inside the wire and then you have the switching part.

Your neurological system has a very similar way. Whereas in a light switch you're physically moving the metal switch, the body is biological. We're not made of wires. We're made of biochemical molecules. All of the stuff that we see in our physical world, the body has to do using biochemicals. That fusion process that occurs how one neuron communicates to the next neuron, it actually opens up little vesicles, and little molecules called neurotransmitters move from one neuron to the next neuron. They hit the next neuron, and the next neuron says, "Wow," wakes up, and it continues on the process.

That's process of signal transduction. It's called a synapse. The physical process of releasing neurotransmitters into that synaptic cleft requires these vesicles, these little spheres that contain the neurotransmitters. They come to the membrane and then they release their neurotransmitters. That fusion and release process is dependent upon plasmalogens. They're the critical molecule in the membrane that allows vesicles to fuse and release their neurotransmitters.

When membranes become deficient in plasmalogens from the neurological perspective, you get an impairment of synaptic function, and that, of course, is reducing neurological function.

Those are what plasmalogens do. They do a number of things. They are part of your membrane structure, neurological signaling, and then that protective coat that protects that copper wire in your wall, well, that copper wire in the human body is called an axon. That's the long neurological system that connects your brain to your fingertips, for example. It's a very, very long axon. It's like the copper wire, but like a copper wire in your wall, your body protects it. It protects it with what's called myelin sheath. In the brain, the cells that do that are called oligodendrocytes, but in the periphery it's called Schwann cells.

People talk about multiple sclerosis or Lou Gehrig's disease. Those are diseases in where that protective coat is like a mouse chewing on your wires in the wall. Sometimes lights flicker, sometimes they work for a little while and then you don't know what's going on. That's what happens when the white matter gets degraded. That white matter, which is that protective coating, is comprised of high levels of plasmalogens, but a different type, your omega-9s, your oleic acid types. In the brain, in your neuro-muscular junction that your neurons connect to your muscles to make your muscles move, that's also driven by plasmalogen levels.

It's a really critical core component of human physiology. It's not just some little serotonin receptor complex in the brain, which is important for certain things. We're dealing with really something that's core to human physiology. This is why the epidemiology data is so scary, you can look at it, scary in the negative sense, positive in the other sense, that people with high plasmalogens live a lot longer than people with low plasmalogens, 30 years longer. It's not a small thing. Plasmalogens levels are more important than your age in terms of your longevity and your functionality.

**Jane:** You're finding this from your study in Chicago?

**Dr. Dayan Goodenowe:** Correct. Very large longitudinal study, looking at people over 20 years of **[unintelligible 00:12:56]** blood samples, looking at their cognitive status. There's a decline in cognition, but you also want to see you have high cognition, and then obviously we'd have mortality data. We can look backward and say, "What are the biochemical markers that are predictive of longevity in which are predictive of early mortality, and plasmalogens are one of those molecules. It's important.

That's actually above and beyond the correlation and the association of plasmalogen with cognition. Having Alzheimer's disease or not even Alzheimer's disease, having any type of cognitive impairment reduces your lifespan dramatically. It makes sense that you're not healthy. If you're not thinking properly, if you have cognitive impairment, dementia, clearly that's an indicator that there is a deficit, that your health is impaired in that area. You've reduced functionality. You'd expect something of a general nature to have a negative impact on your lifespan.

Dementia itself, independent of its cause, whether it's Parkinson's-related or Alzheimer's, pathology-related, is not a good thing. Even after we correct for the negative impact of cognitive impairment on lifespan, plasmalogens also affect your mortality even in people that don't have cognitive impairment. It's important above and beyond that. That's why we're talking about plasmalogens and neurological function.

**Jane:** What you wrote in your book was that if you have APOE4 allele, heterozygous or homozygous, you can build up your level of plasmalogens in your body and be able to negate the detrimental factors that come with that genetic allele if I can always keep my plasmalogens levels up.

**Dr. Dayan Goodenowe:** Correct. It's understanding genes aren't magic. They're not some mysterious lightning strike out there. The genes of your body, they are logical. They're your genes. They're there to keep you alive. They're not working against you. If anyone's working against the genes, it's you working against your own genes. People think they give genes is deterministic quality and they don't. Genes are passive and reactionary.

The APOE4 genotype or any other genetic risk factor have to mediate their association through a biochemical mechanism. There has to be a question why. Why does the APOE4 genotype biochemically translate into an increased risk for Alzheimer's disease? The risk association is absolutely clear. An E4 genotype dramatically increases your risk for Alzheimer's.

In a random naive population of people who do not know that they have an E4 genotype, as soon as you know something, then the statistical work loses its value because then people start changing their behavior.

APOE4 is all related to cholesterol regulation and cholesterol transport, so people who get cognitive impairment when they're old. There's usually three things associated with that, the three most common things. One is this accumulation of amyloid plaques in the brain. The brain starts accumulating these peptides called amyloid. It's not causative. It just happens. You see it. You shouldn't have it. It's not a good thing to have extra amyloid in the brain, but it's not a direct causative. It's a biomarker.

If you have amyloid accumulation in the brain, it means something is not working right, the regular regulation of the amyloid protein is no longer, properly forming. You didn't have the amyloid when you're 30 years old, and now, you have it when you're 80 years old. Something that was working when you're 30 is no longer working when you're 80. APOE4, something related to the APOE4 genotype, is involved in that amyloid regulation process. Something about the APOE4 makes it more difficult to regulate amyloid as you get older because people with an APOE4 genotype, on average, will have higher levels of amyloid in their brain, but not all of then do.

The other pathology that's common with Alzheimer's or age-related cognitive impairment is the formation of neurofibrillary tangles. These are little protein fragments of phosphorylated tau, is the actual peptide. The third one was shrinkage. We talked a little bit about shrinkage.

APOE stands for apolipoprotein type E. Your body has several types of apolipoproteins. People hear about cholesterol. You have your LDL cholesterol and your HDL cholesterol. The reason the body creates these peptides is that these lipids, especially cholesterol-type lipids and triglycerides, are fat. They don't dissolve in water. The body is mostly water.

When your veins are pumping through your body, it's not oil, you're not a hydraulic car. Your biological water, going through your veins here, is pumping through there. Just like you don't pour oil down your sink without plugging your pipes, the same thing happens in the body. The body's trying to transport triglyceride, which is basically fat. It's like pouring bacon fat down the sink. It's not a good thing.

Same thing with cholesterol, cholesterol's like that as well. The body says, "Well, how do I move these really fatty molecules in an aqueous environment or water-type environment?" How the body does it is with these APOE proteins. What they do is these peptides or proteins are very large and they're very, very water-soluble. They're basically transport trucks. The fats will stick to these proteins and then these proteins are water-soluble. These proteins will then transport fat across the body. You have many different types because you have different reasons for different things.

When people talk about LDL cholesterol, for example, LDL, which is called low-density lipoprotein is APO lipoprotein type B, it's the B type. These different proteins have different functions, so LDLs transport cholesterol, all the cells of your body peripherally. You don't have any LDL in your brain then the cells say, "Hey, I need cholesterol. I'm starving," it'll take the LDL cholesterol and bring it into the cell. That's how cells get cholesterol from your liver and from your circulatory system.

The other cholesterol that's most common is called HDL cholesterol or high-density lipoprotein. That uses a protein called apolipoprotein A2 specifically. That is your reverse cholesterol transport where LDL goes into your cells and you use LDL to feed cells cholesterol because cholesterol is really, really important, one of the most important lipids of human body. You do not want to be cholesterol-deficient. We get obsessed with high levels of cholesterol, but low levels is far, far more dangerous than high levels.

Your body needs cholesterol. All your cells need cholesterol, but it needs to regulate it. It's like the thermostat on your wall. You don't want to be freezing and you don't want to be boiling. You want to be able to say, "When it gets above a certain temperature, I want to turn the air on. When it gets below a certain temperature, I want to turn the heat on. I want to be able to regulate the temperature by keeping it within range.

You have to have something that controls both ends of that spectrum. LDL feeds cholesterol, HDL pulls it away. It's called reverse cholesterol transport. LDL goes into your cells, but HDL does not go into your cell. It stays on the outside of the cell. When your cell has too much cholesterol, it pumps out cholesterol, and HDL picks it up and takes it back. By using those two systems, your body can keep cholesterol in the membranes where it wants.

If you're running low on cholesterol, you'll bring in more LDL. If you're running too high in cholesterol, it'll send more out with HDL. Those two systems keep your cholesterol where you want them. Different cells in your body in different parts of your body will have different optimal levels of cholesterol. These two systems become hand in hand.

**Jane:** Where do you want to see cholesterol level? You said you don't want it too low, but you don't need it too high.

**Dr. Dayan Goodenowe:** Optimal cholesterol levels for humans are between 220 and 260. As soon as the total cholesterol goes under 200, all-cause mortality doubles. If you're an E2 carrier, they're not cholesterol savers. They export a lot of cholesterol. Their natural levels are a bit lower, so they should be around low 200s. In E3 carriers, it should be in the 220 to 230 range and E4 carrier, their natural healthy levels should be in the 250,260 range.

**Jane:** You're talking APOE2, APOE3, APOE4?

**Dr. Dayan Goodenowe:** Right. I'll tell you why that affects us as we get older, but not so much when we are younger, and is related to the plasmalogens concept of this. You have this regulation in and out. Now, it's a long story, but the periphery of your body is like the Interstate Highway System. I'm moving cholesterol from my liver to my fingertips, long distances. The body uses this interstate highway system of your veins and arteries, and it uses these LDL and HDL particles to send cholesterol and triglycerides long distances.

Your brain doesn't operate that way. Your brain is like Chinatown. It's a bunch of little streets. No straight ways. It's a bunch of really localized environment. These big semi trucks just don't work in the brain. They can't maneuver. They are not adaptive. The brain uses a protein called apolipoprotein E. Now E is interesting because E is ambidextrous. apolipoprotein E has both LDL functions and HDL. It works equally well. It can go into your cells. Your body can use apolipoprotein E to feed cells and it can also use apolipoprotein E to remove cholesterol from cells. Your body use it for both purposes in the brain. People that are born, say, with an apolipoprotein B, APOE B, deficiency, they're born with a genetic mutation, your body will up-regulate APOE, and you'll use APOE for the rest of your periphery.

In the periphery, you normally only have about 5% or so. It's a very small amount of APOE. In the brain, it's firstly 100%. There's a little bit of APOA. The brain uses apolipoprotein E, and this is where becomes famous now because the brain uses APOE as its cholesterol transport. It uses it for both purposes, both feeding cells cholesterol and removing it. It's the removal process.

Now, how the cells do that is that they have different proteins that recognize the APO protein. There's the LDL that basically says, "Oh, you're food, I'm going to pull you in." Then there's proteins that pull cholesterol out, and there's different ones. For APOE variants, the E2, E3, E4 those three variants affect the function of basically one single protein in the brain, one of these HDL-type proteins. It's one of the proteins that exports cholesterol out of cells, and is related to a disulfide bridge. Proteins or peptides will have sulfur.

A disulfide bridge is like a magnetic screen door. You have a magnet on one side and a magnet on the other side, and it hits together and that's a disulfide link. If you have that, the screen door closes. If you have a magnet on one side and no magnet on the other side, the screen door doesn't pull. You need on both sides. What happens is, E2 has two of these things and it works. E3 has one. E4 is missing them, so it doesn't form these disulfide bridges. It reduces the function of this cholesterol export.

Like everything in the human body, nothing is absolute. E4 carriers are cholesterol savers. Your cholesterol system, as a general rule, you can think of it like a power plant, where you have a main power plant like your liver, that's delivering energy to all the cells of the body or the houses. Every single house has their own solar panels. They're capable of generating their own electricity, and there's a balance. Your cells make their own cholesterol. They're not reliant upon the liver for cholesterol. Every single cell of your body makes its own cholesterol, and it makes its own hormones and other things from that cholesterol. It's a critical biochemical pathway.

There's a certain amount being made inside the cell like your solar panels. If you're making lots of energy, enough cholesterol in yourself, you don't need anything from the power plant. In fact, you'll donate energy back into the circulatory system. The circulatory system is your total cholesterol levels. If you are energy-efficient, if your cells are healthy and making their own cholesterol, your cholesterol levels are actually good and high. They're regulated normally.

E2 carrier, they export cholesterol a lot. They're like a teenager with an allowance. They just can't save money. They make cholesterol and it's gone. They're always exporting cholesterol, so they're always needing cholesterol to replenish what they're exporting. They always have a naturally low level of total cholesterol because they're always taking cholesterol into the blood supply. E3 carriers are like the middle bear in *Goldilocks* and it needs a little bit, but not a lot.

E4 carriers are cholesterol savers. They make cholesterol but they don't send out very much. They have naturally high levels because they're very energy-efficient in their cells. This is totally normal and healthy for 50, 60 years of our life because the E4 genotype doesn't become a risk factor until 60s. It basically just shifts the Alzheimer's curve to a lower age group.

The reason for that is that the other component of exporting cholesterol is plasmalogens, called cholesterol acyltransferase or these ACAT enzymes. These enzymes esterify cholesterol, and allow it to get exported and that process is under plasmalogen control.

When you're young, you have good plasmalogens. Your APOE4 is actually protective against certain bacterial and viral infections because it creates a more stable cellular structure, but as we get older, and when you start losing the plasmalogens, all of a sudden, the two people in the three-legged race are no longer balanced anymore. You have the plasmalogens as they become deficient, specifically, the omega-3 plasmalogens. Those are the ones that regulate cholesterol transport. They're no longer carrying their share of the cholesterol export. Since the APOE4 carriers are more dependent on the plasmalogen-mediated cholesterol export than an E2 or E2 carrier, they become more susceptible, or they're more affected by a plasmalogen deficiency in their membranes.

Long story short, if you have high levels of DHA plasmalogens, it doesn't matter what your E4 carrier status is because it balances out and it neutralizes that risk factor because the risk factor for APOE4 is that if other cholesterol clearance doesn't happen. What happens in the cellular membranes, then in the brain is, if you're not exporting cholesterol properly, all of a sudden, your temperature gauge is supposed to say, "Hey, I want my room set at 75 degrees, and when it gets to 77, turn the air on. When it gets to 73 turn the heat on." It's regulating it. The plasmalogens are doing that for people.

Obviously, if you're an E4 carrier, what happens is when it gets to 77, the plasmalogens aren't triggering. Now it has to get at 79 or 78, or 80, and then finally at 80, it says, "Okay, now I'm going to turn it on." All of a sudden, your regulation of temperature, instead of being tightly regulated, becomes very loosely regulated and you end up with high levels of cholesterol in the membranes, and then that affects the amyloid pathway. It also affects your membrane synapse function and everything else, so the amyloid process no longer works properly, and amyloid accumulates. That's the APOE4 story.

**Jane:** How does someone tell what their plasmalogen levels are, and then how can they remedy that? Do they go to the grocery store and get some omega-3s? What do you do about that?

**Dr. Dayan Goodenowe:** Obviously, we can measure them. We have blood tests that measure the plasmalogens. It's the type of plasmalogens and the plasmalogens in relationship to your other molecules. Remember, the concentration, it's like a bottle of vinegar. It can be 5% acetic acid, or 10% acetic acid. It can be very strong. You want to look at your blood work and it's a relative level.

The plasmalogen level in your blood, you want to be higher than your non-plasmalogen levels because that means the quality of your phospholipids is good. That means that your body is making as much, if not more, of the plasmalogen so that the cells are maintained. It's the type of plasmalogens, these DHA plasmalogens that you want elevated. There's several ways.

Obviously supplementation; we can directly supplement them and provide precursors that go into cells of the body, and allow the cells to make them in situ, which is actually more important than your circulating levels. Your circulating levels give you a sense of how your body is functioning. Is your body healthy? It doesn't tell us what's going on in any direct sense.

A plasmalogen precursor goes right into each of the cells and allow the cells to make their own plasmalogen. That's one. Naturally, mechanisms is your intermittent fasting, because plasmalogens are made in an organelle called a peroxisome. This is what gets turned on during fat metabolism. Your intermittent fasting is very important, getting your body into lipid metabolism because plasmalogens are actually made from lipids, from the fatty acids. You want that intermittent fasting, moderate resistance training, building muscle material, because muscles are also peroxisomally mediated for high proximal active cells. Those are the two big ones.

Your overall diet is helpful. You want to make sure that you're not copper-deficient or other types of mitochondrial function.

Those are the core components of plasmalogens. You can go to ketogenic diet, but I'm a more intermittent fasting person. I think people should have balanced diets, get good fat, animal fat. We can get our **[unintelligible 00:30:20]** and things from some plant sources, but some of the plant-based fat is not the most digestible by humans. There's certain animal fossils that are better like in your eggs and livers type of thing, from proper sources, of course.

**Jane:** Now you have a blood test, don't you? that really sorts this all out for folks?

**Dr. Dayan Goodenowe:** Yes. We can measure all this. You know the guessing, and then you can intervene and fix it. The other part, plasmalogens are made in an organelle called peroxisome and that's anabolic or it builds things. It's where we make things for your membranes. The other core organelle is called the mitochondria that many people talk about. The mitochondria is catabolic where it's a energy-generating cell. It's our little nuclear plant in all of our cells. These things work hand in hand. Often what we find in young people is that when they have mitochondrial deficiencies, it'll actually cause excess peroxisomal function from an inflammatory perspective.

As we get older, sometimes we get these mitochondrial weaknesses that can play just as an important role. Your body's designed to work. There are several core systems. I talked about the plasmalogen system and the brain shrinkage process and the amyloid process.

The other one is this neurofibrillary tangles. That's your methyl transfer system. People talk about homocysteine, phosphocholine, and creatine. We measure all that stuff. When you looking at your body's health, you want to look at these core operating systems because they give you the biggest bang for your buck, if you will, understanding basic human physiology because your body's designed to work and you want to make the big things working first.

It's like, if you're a gardener, if you don't give your plants nitrogen and water, it doesn't matter what fungicide you're using or what insecticide you're using because the plant's not going to grow. You're not going to get the benefit from fancy stuff until you get the core stuff working. There's certain core human physiological systems that need to be working. Your B vitamins, these are essential vitamins for reasons. We've known about them for a long time.

The blood test looks at these core physiological functions: plasmalogens, phospholipids, your methyl transfer system, it looks at your cholesterol regulation, double-checks muscle like your creatinine and your uric acid for oxidative distress and mitochondrial function. You look at those things in context, then you can target each one because there's basically very simple supplements. If they're using the right way and the right proportions, it can fix especially all of these things.

**Jane:** Where can someone find this blood test?

**Dr. Dayan Goodenowe:** Prodrome.com is where the blood test is, and we're constantly expanding. I always recommend having a good functional med doctor on your side because everyone's personal situation is slightly different and should never take any blood test in its pure sense. It should always be interpreted in the context of your personal life and your personal issues and goals because it's designed to help you understand yourself.

If you have a sleep disorder, "Is there anything in here that tells me why I can't sleep at night?" and then we can work on that, or a brain fog. You should look at yourself as a system. When you're looking at blood work, the body is actually very, very smart, but it's very simple in its smartness. It's adapting to the environment. Your genes is an adaptation to the environment that you're exposing yourself to.

Your cells and your nucleus and your genes, they have no idea what you're going to do in the next 30 minutes. Are you going to have a salad or are you going to have a point of ice cream? Because they don't know. They're going to have sensors out there to say, "What is this crazy person doing to me today? How am I going to react to it? Your genes have a go-to list of things. They start learning who you are and say, "Okay, ah, I've seen this before. This is what she's done to me," and they'll react to it. Your genetic structure is an adaptation, and it's choosing the best scenario under its circumstances.

If you're a type 2 diabetic, if you have fatty liver disease, that's actually the best circumstance for you versus all the other worse options that your body has for you. When you want to change your type 2 diabetes or your fatty liver or sarcopenia, you have to say, "First of all, why is my body doing this? Why, of all the options, has it chosen this as the least damaging to me?" You need to change the environment internally and externally, so the body can then readapt to the right environment, and then it will readapt to that.

When we exercise, we're training the body, the body's saying, "Holy crap, this person is doing X. I better make more mitochondria because I need to adapt to this circumstance." What you do is you create these reserve capacity by training the body to be in reserve capacity so the days that you're not working out, you have excess capacity. If I'm moving my mouse around, I'm not lifting weights I'm way under my functionality. That, biochemically, works the same way.

You're in control and all your genes have windows and your body has a window in which it wants to live in. You just need to find that window and then stick to it. The blood test helps you to do that. It helps you say, "Why is my mitochondria function totally out of whack? Then I got to work on giving it some more support." Give it some N-acetylcysteine, give it some carnitine, make sure your B vitamins are up, and then you can say, "Now it's operating properly."

The whole point of this kind of work is to put your mind at ease. It's the randomness of our world that is frightening. It's our lack of knowledge that's frightening. Obviously, you can't control everything in this world. You get a bad enough insult, even the healthiest person is going to get affected by it, but you can control a lot of these factors. That's what the new institute's all about. We're getting more and more of our mass spectrometry systems up in place because it's measuring this and being able to, in an objective manner, put things where they're supposed to be.

The good thing about humans is that we have decades and decades of health, typically. We don't have to create life from scratch. We just need to understand good optimal function, If we deviate from that optimal function, we need to know how and why, and then we need to move it back to where it's supposed to be. I keep a very simplistic approach to that.

**Jane:** Dr. Goodenowe, your book is *Breaking Alzheimer's*. I've read the whole thing and I highly recommend folks get it. It's technical, but yet you have a very gifted way of talking to the layperson.

**Dr. Dayan Goodenowe:** You're welcome. Well, people should realize don't throw away all the logic in your life. Human body and your biochemistry is logical. Everything that you've done to be successful in your life, you apply it to this. Just the words are different. Don't be intimidated by the jargon that all of us scientists used.

**Jane:** Before we go, you've started to tell the story about a 95-year-old. You can almost predict whether that 95-year-old is going to make it to a hundred, and that's with testing his or her plasmalogen levels. If they're high, you're going to bet on the side of "That person's going to make it to be a centenarian."

**Dr. Dayan Goodenowe:** Absolutely. That's just one core system. We are really going to be looking at longevity in a very different way. Our personal presumptions and our assumptions, these are what define the outer boundaries of our thought and exploration beyond which we will not think. This presumption of death has really defined medicine forever. Essentially, all medicine today is palliative care. All we're doing really is easing your pain till the inevitability of death. Maybe in the best case scenario, I'm going to prevent you prematurely meeting that inevitability.

When we're dealing with health today, we're dealing with fixing symptoms, but we're not talking about perpetual function. The human body's made of immortal materials. The very first law of thermodynamics is matter cannot be created or destroyed, it gets transformed. We're actually made of immortal stuff. Biochemistry, the molecules in it, the carbons and the nitrogens and the biochemical transformations that they perform, these are immortal. They don't have a timeline associated with them.

Now, they're confined to our biochemical systems, but there really is no physical or chemical reason why that functionality cannot continue indefinitely, just a matter of understanding it. We can't use our ignorance or lack of knowledge as a crutch and say, "Well, it's just too complicated. We can't figure this out. It's just not possible." We've done that with airplanes. We've done that with everything else. The four-minute mile, for crying out loud, not humanly possible to run a mile more than four minutes, but soon as you break these barriers, you start thinking about the world in a very different way.

These presumptions of mortality of this human lifespan inevitability has really prevented us from really thinking beyond that box. You get a lot of people that think in crazy portrait of Dorian Gray-type thoughts. You're going to be the same picture you were when you're 20. That's crazy talk. That's not what we're talking about here. We're talking about just functionality. A car should last forever if you want it to. It's not magic. It's just function. The brakes of a 30-year-old car should work the same as it brakes of a brand new car. It's brakes. It's designed to squeeze a disc and stop a car from moving. It's not rocket science. It has to work. There's a purpose for it. Fix it. Start thinking about it.

We're building more and more tools and technology and getting the community involved in it so they can actually start interacting in their own life and start really breaking down these mental barriers of health and functionality and try to destroy this mysterious black box, scariness part that really stops people before they even start on their journeys. That's what excites me.

**Jane:** If I'm celebrating my 120th birthday, I'm going to come looking for you and say, thank you. [chuckles]

**Dr. Dayan Goodenowe:** Absolutely.

**Jane:** You made me think further than 80, 90, 100.

**Dr. Dayan Goodenowe:** Ideally, I'd like you to forget the year you were born. To really think immortally, we have to stop counting the years. The years are irrelevant. It shouldn't be a contest of how long you can live. The real test of longevity is being blind to your age. It's not relevant, how old you are. Whether you're 50 or 150, you should forget how old you are.

Your age should become irrelevant to your world and your life. It shouldn't have any impact on your decision making, should have no impact on your quality of life. You should live independent of your age because we still fall in that same category. "Ooh, am I the nicest looking 120-year-old?" It's like humans are so competitive, "What's my age match? What's my biological age?" These things, really to get past that, you have to get to a point where you don't even see age, you don't think age, it's irrelevant how old you are, and you make no decisions based upon your age.

**Jane:** We'll have to get over our age discrimination that we seem to have in this world, which is still one of the discriminations that's a problem.

**Dr. Dayan Goodenowe:** It's terrible. It's the worst discrimination on the planet. Absolutely. There's no discrimination worse than ageism. It really is. I guess you could argue with people. There's there's definitely other serious issues, but it's one of my pet peeves.

**Jane:** It's a big one. Dr. Goodenowe, thank you-

**Dr. Dayan Goodenowe:** You're very welcome.

**Jane:** -for your time.

**Dr. Dayan Goodenowe:** Thank you for letting me ramble on about topics.

**Jane:** I've loved it.

**Dr. Dayan Goodenowe:** This is what we live for.

**Jane:** Thank you very much. You have a great day now, okay?

**Dr. Dayan Goodenowe:** You too. Cheers.

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