Introduction to Mast Cell Genetics

Welcome back to our reversing mast cell activation syndrome and histamine intolerance summit. I'm your host, Dr. Meg Mill. And today I'm joined by my esteemed colleague, Dr. Bob Miller.

Dr. Miller is a board certified traditional naturopath as well as an educator and researcher specializing in the field of genetics specific nutrition.

Bob is also the founder and president of Functional Genomic Analysis, an online software program that organizes and analyzes genetic snips for functional health professionals.

I am so excited to talk to Dr. Miller today, because genetics can play such an important role in the way we metabolize histamine, and really understanding that can make a huge difference.

You know, you may have some things going on. We've talked a lot about things that can overload histamine in your body, but you also may have some things going on just genetically that you're not breaking it down very well.

So I'm really excited to dive into this today. Thank you for so much for being here with us today, Bob. Well, my my pleasure. I'm looking forward to it.

And I think we're going to have a lot of fun. But more importantly, give people some clues as to why they might have these mast cells firing so much and so much histamine.

You know, when I, when I teach classes and there's doctors in the audience, I'll say, how many have taught for more than 20 or practiced for more than 20 years.

And then I'll say, how much mast cell activation do you see 20 years ago? And it's like almost none. And then in the functional world, and maybe up to 50% of the people that are seeing functional physicians, so clearly, there's something going on that's triggering all of this.

And I'm hopeful that by the end of this video, people are going understand some of the things that are triggering it. And of course, there's an old adage of genetics, clothes, the gun environment pulls the trigger.

So our genetics haven't really changed a lot over time, but our environment has. But our whole takeaway from today is that those who have genetic predispositions that didn't matter 30 to 40 years ago are now being impacted by it.

Yeah. So that's such an important point. Well, before we dive into all the juicy things that we're going to get in today, can you just give us a little bit about how you got to this place of being this genetic expert?

Sure. Well, as you said, I started out being a just a traditional naturopath. And then we learned about homocysteine. And I was very intrigued when I learned the pathway of methylation that takes the homocysteine, turns it back into methionine.

It's like, well, isn't that fascinating? So it was a, I guess, as we call it, love at first sight. It was like, well, this is very cool. So, that was about 12, 13 years ago and, haven't turned back since and just more excited every day learning more pathways, even as we speak right now, we're looking at some new pathways that can create mass cells and and not break down the histamine.

And, very fascinated by it. And so we, we like to think we're a little bit of a pioneer in functional genomics. You know, there's there's all kinds of genetics.

There's the things you do. Look at your ancestry. You know, you have your professional geneticists who look at disease. But then we're looking at function, in other words, how the body functions.

So very just a little background before we dig into that. You know, what a miracle the body is. We eat fats, carbohydrates, proteins. We drink water, we breathe air exposed to sunlight, and everything somehow gets made.

I mean, when you really step back and think about that for a second, it's like, seriously, that's that's pretty, pretty incredible. Now the way that works is the body makes enzymes that take one substance, turn it into another, then another enzyme comes along and does the same thing.

So right now is we're on this call and people are watching.

How Genetics and Environment Interact

Their enzymes are just going to beat the band to turn one thing into another. What's your DNA? That's the instructions on how to make the enzymes. And when we get a rock called mutations in our DNA, which will have some of those enzymes may not do their job as properly.

So if you get a genetic mutation from one parent, because we all know, you know, we're up. You know, that DNA strand, you know, the tone, the twist. So we get one side from mother, one side from father.

And by the way, at the moment of conception, your DNA pattern is made and it doesn't change. So if we inherit genetic mutations, if it's from one parent, that enzyme, maybe 70 to 80% is effective.

If it's from both parents, it might be 30 to 40% effective. And then on the other hand, there are genetic mutations that call these cause the enzyme to be overactive.

And that's what we'll be looking at today as to why many of the people have mast cells and histamine. They have a combination of genetic issues that they respond more strongly to environmental toxins or they may have less than optimal ability to clear the toxins that would cause it or the histamine.

And in my experience, it's usually some combination of the two overproduction of the mast cells and histamine. Then exposure environmentally to mold or electromagnetic fields or some other trigger, then the ability to calm it down, creating the perfect storm for those people who just can't seem to figure out what's what's going on.

And it's unique for each individual. There isn't just one, you know, somebody says, what's the gene? It's like, well, there isn't one. Either way. I call it the 3D chess game played underwater.

Multiple factors. It's a it's complex. So that's some of the background. I love that. Yes, yes. It's not ever just one thing right now it's a combination.

Yeah. And I know I get we talk about root cause I'm like it's not root cause it's root causes all of the things together. Multiple factors. Yeah. Well you put I know you prepared some slides for today to really give a visual to you on what's going on so we can jump right in.

I'm excited to go. Okay. Well let's do a screen share here. Make sure this works. And you seeing the screen I am. Yes okay. All right I'm calling this a lesser known cause of mast cell activation.

I think people are going to be very intrigued by what we're going to show here today. And we're going to be talking about mast cells from intracellular calcium, and also something from the aryl hydrocarbon receptor, and also upregulation of what's called the NMDA receptor and electromagnetic field.

We call this the 3D chess game played underwater. I had someone actually draw this for me that shows that this is how complex it is. As we just discussed, there isn't one factor involved here.

So I say if somebody is looking for the one thing they likely won't find it. So this will probably be a little bit surprising. We're going to start talking about calcium.

And it's like, what we've been told calcium. It does a body do it. Gut milk. You know all of those things. So calcium plays a key role in of your body functions.

We're not down on calcium. It helps form bones and teeth helps maintain body strength. Your muscles nerve messaging, blood flow, hormones, all of that by calcium.

We need calcium. It plays a very important role in your glands. It triggers actual mitosis. The secretion in nerve cells, release of neurotransmitters in muscles, muscle contraction in cardiac muscle cells, it prolongs heart contraction to ensure adequate ejection of blood.

Key word here. Unless we look at this, it is well known that mast cell activation is critically regulated by intracellular calcium ion concentrations.

And what we're saying here is that calcium is needed for a lot of processes inside the body. But if too much of it gets inside the cell, it can be one of the major contributors to to mast cell activation and histamine.

Now here's another study. If somebody wants to look it up, just, you know, Google the role of calcium in cell injury review. This whole thing will come up.

We're just hitting the highlight here. It says the elevated intracellular calcium concentration is responsible for the medication modifications which alters the cell shape the activation.

And here's the key point results in membrane damage mitochondrial calcification and mast cell activation. So now the question becomes well how does this happen.

So in this little diagram here you'll see you have your cell membrane and you have calcium that you know ideally should be going off to build bones and do all those other things.

But you'll see here we have one little thing called electromagnetic fields from our cell phones. And we're going to dig into something called the NMDA receptor.

Intracellular Calcium and NMDA Activation

And when this gets upregulated too much calcium comes in creating excess intracellular calcium. And look what it leads to. Mast cell activation. And then we're going to talk briefly about arachidonic acid, which I think is a huge problem that everyone should be measuring if they have cell activation.

And then that will create mast cell activation. And then we're going to delve into the arrow hydrocarbon receptor, which probably most people have not heard about.

But for those of us in this field, we I believe we really need to learn about what triggers the arrow hydrocarbon receptor. Now, don't get too scared by this, but this is what happens.

There's something called the NMDA receptor. Okay. And then glutamate. By the way are you seeing my you see my cursor. Does that show up? I can't. See it. Yes. Okay. Good. Yep.

So the the glutamate in glycine which is amino acid will stimulate this NMDA receptor to bring calcium in. Now we need a little bit of that. But when it becomes excess we have a problem.

Look what it does. Excess intracellular calcium and mast cells. And the path we're going down now is that it also creates extra superoxide. Another nasty free radical.

And by the way we are now believing that superoxide that we've known about, you know, we've been talking about superoxide for the last 15 years, maybe the genesis of most inflammation inside the body.

but that's a topic for another time. But remember we said earlier when we first started, there's environmental factors that we weren't exposed to before.

Well, look who the players are. Glyphosate. And there's an enzyme called ton one that helps clear glyphosate. We are finding that when people have genetic mutations on pond one, they don't clear glyphosate very well.

And I don't have a chart of this, but there are companies that do glyphosate testing. And many times when we see this pond, one mutated. The glyphosate is sky high homocysteine.

This is part of your methylation process. we need to methylated our homocysteine back into methionine. And Sammy, that will drive this arsenic, you know, which we're exposed to from rice and some chicken.

And here's one of the bad boys here. High fructose corn sirup. Oh, my goodness. you know, this only came about in the late 70s. And, so one of my favorite jokes is I was born all the way back in 1954.

So one of my favorite jokes is I was born on a completely different planet. We didn't have high fructose corn sirup. We didn't have low phosphate. So all these things are combining to to create this.

Then on top of it, you know, we love our cell phones. they have probably changed humanity more than anything has in in human existence. You know, all the things we can do on our cell phones is incredible.

Everyone has their cell phone with them. No matter where you go, somebody is looking at their phone, they've got Wi-Fi in the house, they've got everything. EMF.

Well, electromagnetic fields will also stimulate the NMDA receptor here. Again, from a genetic standpoint, there's an enzyme called CAC and A1C, which is your calcium voltage channel.

And you can have mutations on here that allows the EMF to be more impactful on the NMDA receptor. And here is one of the the big boys, I do believe, and that is phthalates.

And if anybody's not familiar that comes from plastics, that is one of the things that's in your plastics. And it was just in the mid January of this year, a report came out that said that in plastic water bottles, they've now found there's 10 to 100 times more microplastics than dentists repeated.

They knew it was there before. It's 10 to 100 times worse. And all of our waterways where I'm in Pennsylvania, every waterways found to now have microplastics in it.

It's everywhere. And it's also in our personal care products. If anything has fragrance, it has it. Now look what this bad boy does. There's and we'll look at this a little bit later.

But there's something called the clearing pathway that along the way it makes something called lytic acid. And Quinn clinic acid is neurotoxic and stimulates the NMDA receptor.

Then there's an enzyme called QPR, T that makes something called NAD. And a lot of people have probably heard of NAD and that calms down the mast cells.

We're going to have some slides on that. Look what they leads to. They inhibit the enzyme that turns Quinn Clinic into NAD. Now we also need zinc to hold this back.

We need pickle any acid to properly using the aXD enzyme is what makes pickle any acid. There's genetic mutations you can have on here that limited, but that leads also impacted.

And I don't have it on this chart. We'll show it when we actually look at a on a genetic test. There's actually one of those cytochrome P450 that clears the phthalate.

So genetics lowers the gun environment pulls the trigger. If you have a genetic mutation on AC, MSD and the C wipe that clears the leads and then you're exposed to a lot of phthalates.

Perfect storm. Your NMD was. Doing this showing this because I think like when you're telling people that the glyphosate or the high fructose corn sirup or the Everglades, you're they're seeing not able to see the connection you're giving us, like the exact picture of how the connection is actually playing out in your body.

So it's really great graphic. And there's still a lot of research to be done here. But there's now studies showing that even in autism, there's higher levels of intracellular Celtic.

And it's also related to ADHD. I don't have those slides with me, but when I present on autism and mental health issues, this may be why we're seeing so much anxiety in people.

When I when I talk to folks, I say, are you finding people are getting angrier, more frustrated, less tolerate? It's like, yeah. So I mean, there's there's many factors that go into it, but this could be one of them creating the neuro inflammation.

So to review we're being exposed to all of these things. So why are some people impacted more than others. There's where the genetic piece comes in. you can have, you know, as you know, two people can be living in the same home with mold.

And one person says, this mold is really making me sick. And the other person says, you must be imagining things because I don't feel anything. Same way with electromagnetic fields.

Some people say I feel those electromagnetic fields, they feel horrible. They oftentimes get accused of, you're making this up. There's no I don't feel anything.

So not only are they struggling, but they're made to feel as though they're a hypochondriac. They're doing something which just makes them more stressed and very unfair.

So I hope this would give some solace to people who are maybe impacted by these things. And someone else in the house, or friends or relatives claims they're crazy because it can't be happening, that that just compounds their problem.

Exactly. All right. Yeah. So here are a couple of things that are NMDA antagonist magnesium particularly like magnesium tartrate vitamin K2 because that helps the the calcium go where it belongs.

Cat's claw interestingly is a natural calcium channel blocker. So is resveratrol. Taurine and zinc. So we've actually formulated some products that combine these together to actually try to slow down that NMDA receptor.

now for the porn one enzyme that takes out the glyphosate, as does Zanten, bilberry, pomegranate, quercetin, and just a tiny bit of vitamin C. And we've actually seen when people do a combination of these, when we measure their glyphosate levels in about nine months to a year, the glyphosate goes down considerably when also combined with eating organically.

Now to make that chart just a little bit simpler. Just kidding. We're. you can see on the right here, here's everything that we spoke about.

Glutamate, Glutathione, and Oxidative Stress

Now, there's an interesting, neurotransmitter called glutamate. Glutamate makes you very intelligent, highly motivated, go getter, often seen more so in, in northern Europeans.

so glutamate can also make you anxious. So many of the people who have, high glutamate can't focus. They can't sleep, they're constant anxiety. they don't know what to do. So look what happens here.

There's an arrow is going both directions. Glutamate, stimulates the NMDA receptor, and then the NMDA receptor stimulates glutamate. This is a feedback loop that just keeps going.

Now if that's not bad enough I'm sure most people who are listening this are quite savvy. They've heard about glutathione, the master in oxidant. So glutathione neutralizes free radicals and takes out toxins.

But your body has to make it. And if you look very carefully here, you'll see there's an enzyme called G ss that takes three amino acids cysteine, glutamine and glycine.

And makes glutathione right here. It's as good as I am now. We don't have time to get into this today. But another very important process that's occurring that's harming us.

Something called fair up ptosis. We just don't have time to get into that. But that is where iron combines with hydrogen peroxide and damages the lipids inside the cell.

Now, as you know, your your cells are constantly regenerating themselves and lipids are coming along and rebuilding the cell. Well, if iron and hydrogen peroxide come along and damage them, we're going to have damage to the cell membrane, to the phone.

And the being used by glutathione peroxidase four comes to the rescue. However, for that to happen, cysteine needs to come in to the cell. Glutamate will inhibit the enzyme that allows the cysteine to come in.

So glutamate is more than just making you anxious. It will actually impede this enzyme to bring this in. So what does that mean? Well, that means that you're not going to have enough glutathione in the cell to stop this damage.

And this is where you get leaky gut and just all all the inflammation that's going on because you're not getting the glutathione inside the cell. Now, if that's not bad enough, cysteine, if it's not used to make glutathione can actually become inflammatory.

And we'll show this on the map later because it can turn into a sulfide that further stimulates inflammation throughout the body. So how many people have you ever seen.

They're not doing well. They hear about glutathione and they take lithium and they feel good for about a week, and then they feel worse. Or they learn about NAC and it's like, well, that's going to be my solution.

And they feel worse. How many times have you seen that. Yeah. Regularly. Yeah. So what you've got to do is you've got to take care of the glutamate first.

But that means you may need to take care of this first. But that means you may need to get the daylights out of the body first. or you may need to work on the homocysteine.

And you got to get rid of that high fructose corn sirup. By the way, if you start looking at labels, it is in so many things, even things like crackers and ketchup, it's astonishing.

We're going to look back someday and say, OMG, what did we do here? I know that people played the game like, right, you know, go through your pantry and look at all your labels and like, count how many products that you actually realize had it and that you would never imagine.

That's everywhere. Yeah. So I would say if you go to a like a convenience store, unless you get an apple or a banana or grapes, it's probably as high fructose corn sirup.

Astonishing. All right. I'm going to burn through these quickly. I mean if somebody wants to you know if they're

watching this they want to pause it or something, they can actually read it more carefully.

But here it says glutamate induces calcium influx by the NMDA receptor activation. So you can see how this becomes a feedback loop here. The NMDA stimulates glutamate.

Glutamate stimulates NMDA. And we're in a fun little circus here. Now here we're talking about linolenic acid the inescapable neurotoxin okay. And again I'm not going to read the whole thing, but it acts as an agonist in other words, it it it makes it turn.

Is it on an NMDA receptor and therefore a brain zone, you know, a toxin to the brain, excitatory to the to the brain. It's a neurotoxin glia, toxin pro-inflammatory mediator pro oxidant molecule and can really do a lot of damage.

And the thing leads will impede this bad guy going into the good nad. I'll show that slide a little bit. Now, as we showed you earlier, we need to make that pickle any acid so that we can utilize zinc and pitawanich acid increases the turnover.

Zinc of zinc. In addition to enhancing the absorption and excretion. So if we don't have enough pickle in the acid, our zinc may not be as effective. So here we're talking about here's a again peer reviewed study.

We're not just making things up here. Activation of the NMDA pathway together with the downstream calcium is caused by glyphosate which is roundup. Fructose.

And here they're saying that we propose that the, the effect could be mediated by changes in the Nvda subunit expression and increased activation of the NMDA receptor from Frutos.

Now, here's another simple little chart for us. We're going to move on to what's called the arrow hydrocarbon receptor. and I believe everyone in the functional world needs to be looking at this.

Now, if you remember earlier, I mentioned that, you know, an enzyme that takes one substance, combines with something else and make something new. And depending upon the genetics, it may be sluggish, it may be working properly, or it may be overactive.

Well, the arrow hydrocarbon receptor is a slightly different animal. It depends upon what goes in it as to what it does. So again, most enzymes take something in, they do something and they either do well, not so well, or they overdo it well.

The arrow hydrocarbon receptor can go either direction if we're exposed to smoke. And I'll show you what's underneath is later mold is why mold is so big deal.

High homocysteine over absorb the iron arachidonic acid that we'll touch on briefly hydrocarbons that we'll talk about briefly lead and mercury. It will actually still modulate inflammation and do oxidative damage.

It does that by creating high levels of intracellular calcium that makes mast cells. The high intracellular calcium will actually stimulate what's called superoxide the free radical.

And then I briefly talked about feral ptosis. Remember the previous we talked about how their up ptosis is when the lipids get oxidized. All that can happen.

So that's why some people are really impacted by smoke. You know some people are you know, somebody's smoking a cigaret. One person doesn't notice it. Another person has to run away because they're sick.

They have an overactive arrow. Hydrocarbon receptor.

Aryl Hydrocarbon Receptor and Environmental Triggers

Now, on the other hand, B12 Foley, rosemary, big fan of rosemary, resveratrol, visitin, quercetin, milk thistle, indole three carbon, a whole nitrogen and and luteal.

And when they go into the arrow hydrocarbon receptor, they turn on something called nerve two. And nerve two is an enzyme that turns on all of your antioxidant enzymes.

Now you can actually have genetic mutations on nerve two that it's weak. So think about how this accumulates. Arrow hydrocarbon receptor. They have a genetic predisposition to go towards inflammatory.

You're exposed to these things. You've got weakness on nerve two proverbial perfect storm. And then additionally the arrow hydrocarbon receptor will stimulate an enzyme called interleukin six that stimulates something called nADPh oxidase that stimulates something called kit and kit.

Genes, when they're mutated, make more mass cells. And so if you've got the arrow hydrocarbon receptor upregulated, IL six is out of balance. NOx is out of balance.

It is overactive mast cell activation. So you can see here this can be so many factors that are coming together. So if you're living in a moldy home and perhaps you have some genetic issues that you don't transport B12 into the cells, which is very common, by the way, those people have high B12 in the in the blood, but they might have low B12 in the tissues.

You're just being set up for this to create the mast cells. And we'll talk a little bit later about if tryptophan, which of course people say it's not what's in Turkey. Yep.

It's amino acid has to come down through here and makes concerning again if you're phthalates inhibit this enzyme that concerning will stimulate the arrow hydrocarbon receptor to be pro-inflammatory.

So again you could see 50 people with mast cell activation 50 different ways. They got their. So I believe in the functional world we really need to start looking at this.

And a lot of our research is on this. And towards the end of our presentation, I'll actually show a genetic map that shows someone with extreme mass cell activation in histamine and how they were genetically set up for this.

So this is just a a slide. Again, I'm not going to go through it. If someone wants to pause the video and read it, they can. It's just that there's a ligand on the hydrocarbon receptor where something goes in that, as we discussed, that ligand could be pro-inflammatory or anti-inflammatory.

Okay. Key point the arrow hydrocarbon is critical in controlling Marcell homeostasis. This is one of the things that will stimulate the mast cells. Article title is arrow.

Hydrocarbon receptor controls murine mast cell homeostasis. Someone wants to read the entire article. So it says it. the arrow hydrocarbon receptor ligands result in calcium in reactive oxygen species increase in the reversible oxidation leading to mast cell signaling.

Now the arrow hydrocarbon receptor. This is just a chart of how it can be anti-inflammatory or pro-inflammatory. It can stimulate or inhibit nerve two.

They won't have time to get into these. But these cytochrome P450 is take one substance and make it into something worse than if you're phase two isn't working.

Can really do damage to the body encode one is very helpful. I al ten is anti-inflammatory. Tumor necrosis factor can be painful or it can be inflammatory.

But the arrow hydrocarbon receptor can go both ways on it depending upon what happens. So as you can see this is the two phases of the arrow. Hydrocarbon receptor can be anti-inflammatory or pro-inflammatory.

Now for those who, you know, want to dig just a little bit deeper, here's a representation. Here's the arrow hydrocarbon receptor. And you can see aromatic hydrocarbons, arachidonic acid, mycotoxins, high homocysteine stimulated.

There's other things. But folate and B12 will inhibited. And you can see here on the one side encode one is anti-inflammatory nerve two is helpful. But on the other hand it can stimulate Il6 nux kit mast cells.

Then if we don't have enough NAD because the because the calcium voltage channel was messed up, then we don't have the energy to hold it back. So you see how this is becoming the perfect storm with multiple ball to enter here?

and it. Well, we're finding what we're observing is the people who are struggling the most have multiple things going on, not just one. And then finally, here's your tryptophan.

And that has to go down this pathway here. You see here Kyra nine. And you come down here to make your Quinn clinic acid. And then up to NMDA. You can actually have genetic mutations on the idea to the don't allow the tryptophan come to to come down through here.

And we're still in the research phase of this. But in the gut that tryptophan will stimulate the arrow hydrocarbon receptor to the inflammatory side. So inadvertently, if someone would take some tryptophan because they think that they want to have some serotonin or melatonin, if there's mutations right here, it can actually become pro-inflammatory.

So that's why people get so frustrated. Some well-meaning person says, oh, take this. And then they do. And it's like, oh my gosh, I'm worse. And I'm sure you hear that quite a bit, don't you?

Regularly. And it's really hard because it's so unique. Everyone's different. And so you can't just listen to what the latest influencer saying. So many people are out there saying things and they're just saying things that worked for them, but then everyone goes and buys it and it can have negative effects, and then your you're stuck and you don't understand and it can make things worse.

So it's really important I agree to do the right things for you, which is really unique to everyone. Absolutely. So here they're saying the tryptophan metabolite ten learning promotes mast cell activation through the arrow hydrocarbon receptor.

Again, if anyone wants to read the study there they can find it. Now interestingly, in the gut microbiome you can actually stimulated by the tryptophan metabolite.

And so that's why we're saying we're we're in the early stages of this. But there are some organic acid test that that measure this. And we're now working with a firm that specializes in probiotics.

This probably isn't going to be for a while, but, you know, there may be a, you know, something we need to do in the gut so that we don't have this trip to.

So interestingly, even some of our gut things can stimulate the mast cell activation. Stay tuned for this way. Way too early to comment much on it, but just throwing that out now.

This is just a little information on aromatic hydrocarbons, automobile exhaust, industrial emissions, smoke from burning wood, charcoal and tobacco. They contain the high levels of those polycyclic aromatic hydrocarbons.

That's why some people, even if they're grilling, you know, somebody's having a picnic and somebody is grilling and they get the smoke, it can make them wait, wait, ill. I'm sure you've seen that.

dioxins, they're the result of industrial processes. They're released into the air through different practices, including incineration and trash burning.

Then, high levels of dioxin like potential in cigaret smoke may be one of the reasons. So as you know, some people, you know, cigaret smoke, they don't notice a thing.

Other people have to run away because look what it's doing. It's triggering that arrow. Hydrocarbon receptor, high homocysteine activates the air pathway.

And, we could probably speak for 20 minutes about arachidonic acid, but I measure arachidonic acid in just about everybody who comes through here, who has mast cell activation.

This chart shows the, the omega threes which are anti-inflammatory. And you can see it's low. The, the omega 6 to 3 ratio is high. But this is the one that I put a lot of emphasis on the arachidonic acid to EPA ratio.

I believe this is a very important ratio because that arachidonic acid will stimulate the arrow hydrocarbon receptor. And we don't have time to get into it today.

But we've actually created a formula that supports and I've had 100% success. And I'm not exaggerating because we all try things that we don't, you know, myself included, we try things and it doesn't work.

But so far, we've had 100% success in bringing that arachidonic acid down here. And it, you know, can take nine months to a year, but it can be done. Now, if anybody wants to dig into arachidonic acid, the tumor necrosis factor.

This is when when we do a genetic analysis. This is where we start tumor necrosis factor. Because that is what will begin stimulating the Knox enzyme.

And I don't have that on here. But NOx is what will stimulate the mast cells. And the histamine and mycotoxins virus Clostridium Borrelia lipopolysaccharide.

Stimulate that. And we'll just show this on the map. But there's something called heme oxidase that makes believe and and bilirubin that actually calms this down.

And probably somebody is already thinking is it possible that this is weak. Yep. You can have genetic mutations here that your heme oxygen is weak and you're not able to hold back this cascade.

When I show the actual genetics I'll show that. But for now when Tina Fey gets upregulated, it stimulates an enzyme called play two that pulls arachidonic acid out of the cell membrane.

And then it can make what's called a leukotrienes, which is very inflammatory. Through Cox one, it can make some thrombus in E2 that activates your platelets.

And then it can also stimulate NOx, which stimulates the mast cells. And, so it can do a lot of damage. The adrenal glands have, as we all know, makes the cortisol.

And you know, how many people do that you see. Do you think of, have adrenal fatigue. A lot is high number. You know. Yeah. So what's happening is the adrenal glands have to make the cortical steroids to calm this down.

Arachidonic Acid, Iron, and Detox Pathways

And when you've got this arachidonic acid being pulled out, your adrenals can get very fatigued. So here's that bad boy, that arachidonic acid. So here's a study that shows the the mycotoxins are stimulators of the arrow hydrocarbon receptor pesticides.

They will stimulate the arrow hydrocarbon receptor. Again feel free to search for these if you want to read all the details. persistent hydrocarbon receptor agonists.

That means that stimulates them. Elicit dose dependent hepatic lipid accumulation, oxidative stress, inflammation,

and fibrosis. Ion promotes viral hydrocarbon mediated oxidative stress.

So obviously we need iron that's critical for your red blood cells to carry oxygen. However, excess iron or iron that is not used properly is incredibly inflammatory.

And many people of northern European, particularly the English and the Irish, carry the, the, the, the genetic mutation called HIV, which will decrease their what's called hip sit in so helps it in deficiency, helps it in notices when your iron is too high and lowers it.

There's genetic mutation mutations called EGF e that reduce your helps it in production. Very common in the Irish in the English descent. Interestingly, the reason that occurred is because during the potato famines, the women who had higher levels of iron absorption were the only ones healthy enough to have babies.

So it was an adaptation. But it's not serving us very well right now. So we all know that, LED is bad. So the so the lead intoxication will stimulate the arrow hydrocarbon receptor.

Mercury will stimulate the arrow hydrocarbon receptor. And then as we discussed, NAD suppresses methyl massively granule granulation. Now a lot of people learn about NAD and they think this is what I've been looking for.

And you can supplemented with it or you can get intravenous. And they think this is the answer I've been looking for. And they feel good for a week or two and then things start going south.

I'm sure you've seen that happen correct. Yes. Yeah. It's very individual. Yeah. So what happens is and I'll show this later. There's an enzyme called NOx nADPh oxidase.

And as I often say that's your friend. Unless it isn't used as nADPh to make inflammation. So if that NOx enzyme is upregulated and you start taking NAD, you might be feeding it and making more inflammation.

So that's why in my opinion, we have to calm down NOx first before we do the NAD. Then it can be helpful. Now here's a couple helpful things. Resveratrol has antagonist activation on the arrow hydrocarbon receptor.

The implications for prevention of dioxin toxicity, vitamin B12 and folic acid alleviate the symptoms of nutritional deficiency by antagonizing, pushing against the arrow hydrocarbon receptor.

So here they're saying we propose a model in which B12 and folic acid blunt the effect of natural or agonists at baseline to prevent the symptoms that arise with arrow hydrocarbon receptor over activation.

Now that the problem becomes that the you know, many people learn they have more for and then they think, oh my goodness, I need methyl folate. And they start taking large amounts of methyl folate.

And they feel good for a little bit. And then all of a sudden they feel horrible. And I'm sure you've seen that happen. Correct. It's absolutely. And that's something that is confusing for a lot of people.

Absolutely. so the so what happens is that we need folate. and we all know that when women who want to get pregnant, or are pregnant, they need folate, because if they don't have enough folate, they may have a, you know, they may not get pregnant, a miscarriage or a deformed baby because there's a process called immature mammalian target of rapamycin that stimulates new cell growth.

So if we don't have that, the sperm in the egg doesn't become the baby. However, you know, it's interesting. There's a bell curve for just about everything.

Too little or too much is a problem. So what can happen is there's an enzyme called his to an end methyltransferase. That's the first step of getting rid of your, your histamine and folate can stimulate the.

So interestingly, even though you might have MT4. And by the way I know all about MT4, I teach about it. I've created products for it. I think we've gotten a little bit carried away on that.

you know, up to 44% of the population has one copy of the C6 77. And, you know, for some people it's all about methylation. And clearly it's important.

But I think we've got a little bit carried away. And I think that supporting methylation is the solution for everything. And they're finding that it's not.

So I'm not saying it's not. But I think we've gotten a little bit carried away. I see so many people that we can help them by reducing or stopping their falling despite MT4 now again pregnancy different story.

and just one quick little side note, viruses like Covid use use them to replicate. So if you've got more to upregulated in the opposite of that, which is called autophagy, the cleaning of the cells weakened.

If you're exposed to a virus, you might be more prone for it replicating. So I think we have to be cautious with this that we don't overdo it. Now this is interesting.

Artichoke Laura. Thank can actually calm down the, the arrow hydrocarbon receptor and leading to upregulation of nerve two and encode one that are in oxidants slowly artichoke.

So we've made some formulas that have artichoke in them. Milk thistle prevents the expression of that cip1 a one that's inflammatory and Cox two and also calms down the arrow.

Hydrocarbon receptor indole three carbonyl okay natural ligand of the arrow hydrocarbon receptor. In other words, it goes in there and it diminishes label polysaccharides induce proinflammatory gene expression.

I mean, this is the this is the list of the the bad boys in US interleukin six. and then and then it helps include one heme oxidase and catalase. That's, that's pretty impressive.

Just from indole three carbonyl. One of my favorites Rosemary inhibits aryl hydrocarbon receptor activation that occurs from the dioxins. Rosemary is an incredible, incredible herb.

Now here's a quick review. How do we stop this? Try to limit exposure to dioxins in the pages. Consider high grade air purifiers in the home and workplace.

I mean, I'm sure most of the people listening to this do that. For God's sake, stop smoking. If you are no one, regulate your homocysteine levels. Work with your physician.

But just be careful not to overdo the folate if they're high. look at your omega threes. make sure that your Mega three is adequate. Your academic acid is down stating the obvious.

reduce exposure to lead, arsenic and mercury. Two what? You said we can do a little edit here. Let me just clear my throat. Oh, yeah. Sure. Absolutely.

Let me get a drink. Yeah, we can edit that out. Yep. So let me just mark that down. I'm just going to go. Okay. There we go. We're just going to put a thing up.

I'm not sure if I'm on the. Okay. We ready now. Yep. Okay then eliminate exposure to mold and mycotoxins. for some reason it seems as though mold and mycotoxins becoming more prevalent.

There's discussion though I don't know if it's true or not, but there's discussion that perhaps EMF is worsening that perform meta toxin protocols with qualified health professionals if needed.

there is organic acid testing where you can measure your quality acid and your conditioning levels and, you know,

work with a qualified health professional to normalize if out of balance.

support your phase two detox pathways. That's called a final salvation glucose validation. By the way, glucose rotation is, one of the very important pathways to clear mycotoxins and the threat toxin that we may touch on.

just briefly, make sure you've got enough folate and B12, but be cautious with overdosing. There's a sweet spot. One of my favorite sayings is follow the Goldilocks and Three Bears formula.

Not too hard not to call, not too hard, not too soft and, consider hydrogen water. indole three carbonyl milk. This will resveratrol and the artichoke and, of course, if you want to see where the weaknesses, do your functional genomic testing to see where your weak spots are, because as we've said earlier, what works for one person may not only not work, but may actually even make things worse for an individual.

Case Study: Genetic Drivers of Severe Mast Cell Activation

What I love is you gave very detailed concepts, but the answers are not always easy. But there's like simple there's things these are things people can do.

So I would just like to bring that up of, okay, there are things that you do have control of that it's not just okay, he's showing you the the genetic pathways and that's what you're born with.

But you can make a you can make a difference, which is really empowering. And that's, that's a that's a great message to hear. Absolutely. Now on this little chart here, this is actually the genetics of an individual who has severe mast cell activation.

And his to the the poor gentleman is struggling terribly. I mean, he's beet red, to stressed out all the time. So what we're going to do here is show what's going on with this gentleman.

Here's your TNF enzyme. And by the way this is a map from the functional genomic analysis software. But when I click on one of these it'll actually show what's happening.

And if I click on the HIV you can see there on the right you see that little HIV that came up with a one. Do you see that there. That means he's got a carrier status for hemochromatosis.

So that iron is going to stimulate TFA. Then that stimulates NF Camp a, B. And this is a gain of function. If you look over to the right here you'll see a one.

So the NF kappa he's got a mutation then that stimulates the Knox enzyme and ADP oxidase. And I'll go to another chart. We're able to show how that stimulates the cells.

But for now we're going down the the clearing pathway. There's actually another genetic mutation here on something called ATG or one that actually makes NOx more active.

Interleukin six stimulates NOx. This poor gentleman, he's got a mutation on this enzyme here that creates the potential that Luca try and B4 may stimulate this.

Then we make superoxide. And as I said, I'm beginning to believe superoxide at the root of all of this, that that's where it's beginning. Okay. So then what will happen is we can have difficulty with an enzyme called NQ oh one, though we don't clear the superoxide.

We spoke briefly about Nerf to. And nerve two is what turns everything on. But it's controlled by keep one and keep one suppresses nerve two. And you can actually have an overactive keep one which he does have.

Now to recycle. You're in oxidants. You need to Nadp h. And this gentleman I believe he's some Italian background. The the Italians have many times mutations in G6, PD that causes them not to have enough nADPh to

recycle their glutathione.

so you can see this gentleman has multiple things going on, and he's making progress. Then we make the hydrogen peroxide from the, from the, from the superoxide.

And if we don't clear that it'll combine with iron, which he's got lots of to make water called hydroxyl radicals. And if you remember earlier, I showed you that, that fear of ptosis is when the iron combines with the hydrogen peroxide to damage the lipids.

Now, one of the areas of research that we're really getting intrigued by. And, this might be a topic for another time. There's a substance called BH4 Tetrahydrobipterin, and I believe this is incredibly important.

The reason being is nitric oxide is an important gas that the body makes that dilates your blood vessels. And I would imagine a lot of people listening to this probably have cold hands and feet because they don't have good enough, nitric oxide.

There's an enzyme called NOS2 that responds to the histamine. So when you've got histamine inside the body from the mast cell. So here's mast cells and histamine that'll stimulate the NOS2 to make large amounts of nitric oxide to kill a pathogen.

One of my favorite sayings is that's a good thing. Unless it isn't. Yeah. So if we if we if we got a parasite to kill, that's a good thing. But if there's nobody there, but it's still over stimulated.

We're making excess information. And here you can see the before is needed to make nitric oxide. If we run out of this, we make superoxide free radical.

And then there's more to the story. The NOS2 enzyme will suppress the niacin three enzyme, which is the one that's actually circulatory. And as you know, we're seeing so many blood clots and, you know, thick blood that occurs when NOS2 gets upregulated.

All right. Then SIRT1 supports NOS3 And I don't have it on here. But guess what inhibits SIRT1 High fructose corn syrup Back to that. It's it's everywhere.

Now I'm going to show you another chart later that has a little more detail on histamine. But what we may actually because we're in an hour right now.

So we may need to wrap it up, wrap it up soon. So we're going to finish with this one. Yeah. Oh well perfect. Well I'm just I'm going to quickly go up to the mast cell.

But I'll do it fast okay. I'll do that. Now here's where we make the the histamine from the mast cells. And that will stimulate in us. And then here's where it makes the, the histamine.

And we can have genetic issues that we don't clear the histamine. There's genetic issues that you may not make enough for. And I know we're running short on time.

So we're going to very quickly here go through the. So here's the tryptophan that we spoke about. And here's the arrow hydrocarbon receptor. So here's the block here where he's going to make more arrow hydrocarbon receptor that we spoke about.

That's going to stimulate the NMDA receptor that we spoke about. And that's going to make more glutamate. That inhibits your body's ability to bring the cysteine in.

And in this particular individual he has genetic mutations that he doesn't turn glutamate into energy. So you can see how this can turn into the absolute perfect storm.

And we're hoping to help this gentleman get, get out of this. So if anyone wants to contact us, here's our website, tolhealth.com, our phone number. If there's any, doctors or health professionals watching.

And they would like to learn more about the, the software. there's the software functionalgenomicanalysis.com. Here's how you can contact us. And, we'll be glad to show you how you can use this, in your, in your practice.

So that is a very brief. Although we went an hour, a brief review of, all the things that can go wrong that causes excess cell activation and histamine.

Yeah, I know when you're when you're talking about genetics, I'm sure. I mean, you can go on for hours and hours looking at each. It's so intricate and each that each component like I love your maps because each component is affecting another component.

And it's really getting into looking at all of those connections that are going to play out in the symptomatology. And I do agree with you. I think MTHFR has been so publicized and people like I have are and my life's over, but the it's just one component and it's it's the one everyone's talking about.

But you've done a great job showing us all of that. You know, there's a lot of different components that are at play here. Absolutely, absolutely. Yes. Well, thank you so much for all of the great information you shared with us.

And thank you for joining us. A lot of fun. Thanks for. Having you.