Introduction and guest credentials

Hi everyone, and welcome back to this episode of the Reversing Methyl Activation Syndrome and Histamine Intolerance Summit. And I'm your co-host, doctor Tom Moorcroft.

And today we're all in for a really amazing treat. I have the great honor to speak with the Marcel master himself. Doctor Theo theory is. And he's one of the top Marcel researchers in the entire world.

He's a professor of immunology, and his research is really focused on the kidneys of selected secretion of cytokines and other pro-inflammatory molecules from mast cells.

He's, has a broad background in immunology and has been studying the regulation of mast cells and their role in allergic and inflammatory diseases for over 30 years.

He is one of the most widely published people I've ever met. He's published over 400 peer reviewed medical journals, and is cited as one of the top 5% of authors in the immunologic research field.

He discovered that mast cells are inhibited by certain, natural flavonoids, including and especially luteal and, and tetra hydroxy luteal and subsequently developed a well known mast cell blocking supplement.

Neuroprotective. So, I am just so honored to, have an opportunity to talk with you, Doctor Theo. And welcome to the summit. Well, thank you very much for the invite.

Delighted. Especially since I'll be talking, hopefully about a subject that I'm absolutely passionate about. Yeah, I'm very interested. I, I was remarking with you as we were, you know, getting started, before we hit record that, you know, I just remember back in an Islands conference, you know, we're all studying Lyme.

And it was like the first time I'd really gotten exposed to your work. And it really changed the way I looked at my patients with chronic illness. So I'm really excited to be able to share some of that with our listeners today as we talk about mast cells and neuroinflammation.

So what what got you interested in in mast cells of all things and what's the structure? It's a very interesting story. Back in 19, 72, a long time ago in the summer, I had just graduated from Yale and, I had spent a few weeks at Albert Einstein College of Medicine, where a very well known duel was going on between two professors.

That was evidently an annual event. And in that particular time, the duel were, between Professor Baruch, who was a history pathologist. Jackpot were Canadian, and, Sam Zeichner, who was a biochemist.

And they chose to hash out a topic which was mast cells. And I was like, wow.

How mast cell research began

And the biochemist comes after I felt that it was an incredible cell because it either contains and or can make as many as 100 different biologically active mediators.

And, Jack powder felt that it was actually a useless cell because he had done a very important experiment. He had injected in the peritoneal cavity a rat's gold particles and the mast cells notorious about taking things from the outside and storing them in their granules.

So the mast cells took up the gold, and then he sacrificed the animals over time until old age, and the gold was still there. So therefore, he said, under laboratory normal circumstances, the mast cells don't to granulated, because if they had, the gold would have been released, the macrophages would have removed it.

So these were the two extremes at that time. I was starting my PhD, thesis at Yale. I was undergraduate doctorate in pharmacology, and my medical school was at Yale.

And, I was working between two very strong minded but very good French professors. So one was Bill Douglas, who was a neuron anatomist and Paul Green Cart, who was mostly, sort of a biochemist.

And Paul Gregor had gotten the Nobel Prize, actually, in Physiology and medicine a few years into my PhD, and we were looking for a good secretory cell to study.

So Bill Douglas was very interested in the pituitary gland, while Gregor was interested in neurons specifically in general. And they told me, go find a good cell.

And I recalled the discussion at Albert Einstein. And I said, how about the mast cell? Here's a cell that has a thousand secretory granules. Each secretory granules stores about 50 or so molecules that we know, and that when it's triggered, it makes another 50 or so.

And it is not only triggered by allergens. So I said, what better secretory cell to study than the mast cell? And I did all my PhD thesis on the mast cell, between 72 and 78, so to speak.

And I've been hooked ever since. Ever since. Wow. That's kind of cool. Like, so the mast cell seems like it's interesting because I was thinking, as you're talking about that in medical school, it's sort of like, the mast cell lets out histamine and it's a white cell, and that's kind of like all you need to know. And that's, unfortunately, this is pretty much what it is still being taught, even at the National Institute of Health, where they ought to know better than that.

And here's a little, story as well. The mast cell were discovered by, Paul Erlich in 1887. He was part of his doctoral thesis. But at about the same time, in 1901, there was an experiment that was being conducted out of the Oceanographic Museum at the Principality of Monaco by two French scientists, Paul Kerry share.

And the experiment was they took jellyfish tentacles because jellyfish men of war were rampant at that time. The ground them up, they gave them to dogs, injected the dogs and they were pretty sure the dogs would be protected from subsequent stinks.

So they had a term ready for it. They were going to call it prophylaxis. However, and they immunize the dogs and they re-exposed them to the jellyfish.

They drop the blood pressure, the bronchi constricted, they went into acute. Anything like that. They died. So they called it anaphylaxis. So determine if l'acces and mast cells were discovered at about the same time two years apart.

But they were never connected until 1947 when histamine was discovered in mast cells. So hundreds of years went by. My God. But we realized, and now, since 1947, we're still kicking the same idea that histamine is the main, problem in all of these conditions, which is not.

It's just like, so remarkable because it's like literally it's like I'm like, everything I've been taught is just that's really what it is. So what else is in and, you know, anaphylaxis is obviously a thing that all all of us learned in medical school and a lot of people know about bee stings or shrimp.

And it's a scary thing. But so what else is going on with the mast cell and in, in our health. Like what are the things that we need to know about it to start to learn to kind of set the record straight, if you will, about what they're doing.

So first of all, we've got to realize that one does not have to be allergic in order for the mast cells to fire. So they're individuals. And as you know, in medicine, if we don't know something, we call it diabetic.

So there's idiopathic anaphylaxis out of the blue someone response. And what are the key molecules in wasp

venom. It's called mustard baron. And you're not allergic to mast apparent much.

The part will trigger the mast cells in its own right. So we have to stop thinking of the mast cells responding only to allergens, which is a big deal. I'm not trying to minimize that.

Mast cells beyond histamine

All right. I think I respond to molecules released under stress, molecules released from, you know, viruses from, bacteria, fungi, mycotoxins can trigger the mast cells.

And probably the most important message for today, as far as I'm concerned, is that the mast cell is very dynamic. It's not just a static cell. You trigger it, it will really something. And that's the end of it.

It changes as you go along. So mast cells are very different in the skin. In the gut your mouth. And we have time to talk about in the brain. And when the mast cells are triggered, they're reactivity to other stimuli changes enormously.

And I'm sure you and other colleagues, certainly I have had numerous patients who had a little kind of allergic diabetes. I prefer sometimes a topic diet, such as because that's a little broader, the just strict allergy, and then they undergo major surgery trauma.

God forbid someone dies in the family and now they're exposed to everything under the sun, so the mast cells can change their reactivity. And we have to be very cognizant of that, because if we think we're going to stop the mast cell at one point in time, we're just missing the dynamics of what is happening not only with a muscle, but in the whole body.

So what's leading to that? I mean, it's like because I mean, you know, we talk a lot about the hyper responsiveness, almost like the mast cell being a sentinel to protect us, but then it gets it's on guard all the time, rather than only certain times that like what is leading to this and what is that pathway that we need to be looking at?

Well, that's easier said than done. Let me let me start. Historically, the mast cell has been identified in species over 400 million years. So all the way from mollusks to octopi to a zebra fish has tons of mast cells, to invertebrate vertebrates.

And, of course, you know, humans. So obviously the mast cell played a role at some point. And and I'm sure it's still pleasurable. Now, that is not necessarily detrimental, but maybe go go back to millions of years ago.

So those invertebrates or, you know, small vertebrates etcetera do not necessarily have developed immune nervous hormonal systems. So the mast cell boasts other colleagues and I believe played a role because it makes, synthesizes and releases all such molecules.

It makes and it responds to endorphins. It makes in response to catecholamines, it makes in response to sex hormones, so forth, so on. And as we developed, other systems took over and the mast cell sort of maybe remain a sentinel shell for maybe poisons, maybe toxins, maybe parasites going up, you know, behind, etc..

And as we've evolved even more and then we had antibiotics, you know, we were purified by being inside homes with, you know, air conditioning and vacuum cleaners and whatever.

The muscle probably didn't have that much to do with protecting us, but it would still there is the canary in the mind for things that might still be dangerous, and it probably does that in some individuals more than others for genetic reasons as well.

However, when it comes to stimulation, we know that even stimulation with an allergen, which is through immunoglobulin E, can actually talk to other receptors in the surface and a good example of that jumping way ahead is the drug zona.

The neutralizes circulating IgG E, but it has been shown with publications that it is helpful in vibration or dark area in pressure or DIC area. There's no IgG involved there, so that by definition means that when you strip the IGF from the surface, this is what John does.

Or other similar drugs that the body doesn't sig anymore. And what do the cells normally do? The interior eyes, the receptors. I don't need that many receptors anymore.

The dry ground. Right. That is the cell does that. Other receptors that might be linked gallantly might also be drawn and internalized and destroyed and vice versa.

If you stimulate something too much, maybe other receptors get expressed. And then now you have, you know, core reactivity. So I just submitted two weeks ago and invite you to review and my cell activation and one of the table shows is that the mast cell expresses about 50 different receptors on the surface other than the receptor for IGI.

So obviously the receptors are there. They're there for some reason. And even though there are also some inhibitory receptors, no one has ever found net chiral or synthetic molecules to stimulate the inhibitory receptors to shut the mast cell down.

So we're still basically in the dark. Interesting. So ensuring more precisely your question, I don't think there's just one pathway that we might address to inhibit the mast cells.

But I tend to think how can we actually block the last steps of the mast cell activation. So yeah 50 receptors I you know different stimuli. They'll go through various pathways eventually they have to release something.

So if we can block that final release step, that might be our best bet to shut the mast cell down. Right. And it's kind of like the Holy Grail, it seems like, because I mean, you know, it's almost I'm thinking as you're talking, this is one of the things a lot of us are just like, let's block histamine.

And it doesn't it doesn't always seem to work that easily. Not at all. Besides, now, you might have put your finger to something very important. We always say histamine is in the secretory granules.

There are about a thousand of them. Partial, presumably in those granules. We also have enzymes like triptans and chi base and carboxy peptides. Just to give you some, we always thought that all of these are released together, and that doesn't seem to be true at all.

We have many cases in mast cell activation. Histamines released by triptans are not released. And very recently over the last few months, there are three publications independent publications that in individual cells that suffered from Covid 19 times, was elevated in the blood, but not histamine and our treat case.

So how a nurse is then is being released from the same granules without trepidation. Histamine. Since we always said this is the granulation and a paper that was just published this week, and maybe we'll return to this if we talk about Covid was quite fascinating because it showed convincingly that the spike protein binds to Chi base, and the two together can damage the blood brain barrier.

Okay, this was just published, so the whole idea of what the mast cells do in certain conditions, including Covid 19, is really changing rapidly. Man. This is like this is like, opening Pandora's box, right?

I mean, because one of the points I want to highlight is like testing for folks like, and Covid is so critical, we need to talk about it as well as neuroinflammation.

And with testing, a lot of times, like I just remember as you're speaking, I'm like, oh, yeah, you know, it's like a lot of us will run like a trip tase and stopped to verify it's anaphylaxis or whatever, or, or earlier, you know, phase of anaphylaxis.

So but a lot of people, I think, get frustrated that they say I have mast cell activation syndrome in our testing is kind of miserable for it, but it's almost sounding like the symptoms that you can get from mast cell activation may not just always be histamine related.

Not at all. Back in 2000, 15, two colleagues of mine, Gemma King and Peter Valeant and I wrote a review in the New England Journal of Medicine. And I was grateful to the journal.

I still am, because the title was Mast Cells Buster Psychosis and Related Disorders. So it opened up the door to the possibility other molecules are being released.

And in fact, one of the diagrams that we have having that, journal shows the muscle in the middle and depending what the trigger, the outcome is different and it can affect every organ of the body.

And I want to stress that paper, because many colleagues might not know there was a supplemental file to that paper. Okay. So if you visit Google Journal of Medicine, I was the first author, so you can easily pick it up.

Testing and biomarkers for mast cell activation

There was a supplemental file that has never existed before and has not existed since, showing a human mast cell de granularity in real time. So I have a mast cell in three dimensions between two coverage clips, perfusion gated with a neuropeptide, and within five seconds you got boop boop boop boop boop boop boop.

And it granulated sugar. So once you see that, you know how dynamic and powerful the shell is. And we're not talking about histamine. So I would urge you go back to the journal and go to the supplemental file.

And, and you will be really, impressed. And I'm not saying this because I took the video. It just it's so powerful to see how dynamic you see thousands of granules speeding their content out.

That's what happens in anaphylaxis, but not necessarily during infections, etc. when the cell releases molecules without undergoing the granulation, without tryptophan, without histamine.

So in this last review that I submitted, hopefully will be accepted, I have a list of what I propose should be potential markers of mast cell activation beyond histamine.

Entry is right. I'm sure all of us are going to be so interested in seeing this and checking it. I mean, are there particular things that are we should be kind of maybe considering clinically to start looking at or what we should.

So first of all, I mean, it's obviously important to measure treat case because if case is high it's telling us something. So either you've got to, you know, must decide doses or you've got this genetic condition, you know, alpha hyper trip to simian, which is also very confusing because these patients have a lot of symptoms in many organs.

And yet in alpha hypertrophy. Samia, it is the alpha three days monomers that are released and they're inactive. While in the granules it is the beta treat case head trauma that becomes active when it's released.

So beyond me how in inactive monomer can still cause symptoms in about five different organs. You know so so we still don't know what it means. And of course we don't have any drug to block trip cage period anyhow.

Okay, so having said that, to the extent possible it is important to measure at least a prostate gland in leukotrienes and in histamine metabolite in the urine, because that is telling us that the mast cells are spitting out other mediators than just triptans.

And it used to be that we need only a 24 hour urine to measure that. Now it suffices, at least at the Mayo Clinic, to give them first morning for it, but it has to be called if it comes up to room temperature, they're gun.

So you're going to get negative results. And then finally there were four papers. One was published from my group,

the other from Doctor Metcalf at NIH, the other from Doctor Scribner in Spain, showing that interleukin six levels reflect disease activity better than picture histamine.

And of course, my colleagues say, you know, we can't really measure al shakes because all six can be released in other inflammatory diseases, of course, but if there's no other comorbidity, why not measure it?

You know, if someone has inflammatory bowel disease, well, it might be coming from the bowel, etc.. And a paper was published recently confirming what we had also published extensively, that vascular endothelial growth factor is actually increased both in master cytokines and cell activation patients.

And I always measure that because it tells me whether the vasculature is actually leaking, in which case you will promote inflammation, etc.. Finally, and I'm trying very hard, to come up with a way to measure platelet activating factor puff.

Puff has been known for many years, but it is impossibly difficult to measure in a clinical laboratory. However, there have been very good papers, including a paper in the New England Journal of Medicine, doctor Vedas or Vedas in Kannada that showed that levels of puff in the blood were more reflective of severity of prophylaxis and in the histamine retrieved case.

But because we cannot measure it, we ignore it. However, even if we cannot measure it, there are ways to block puff, and that should be actually a regular component of treatment of mast cell activation diseases.

Moving forward. Again, if we have time, I'll get back to this. Yeah. I think that, maybe the way we can kind of structure flowing through the rest is because I think that blocking path is like that.

I mean, these are the things that we need to know because as you mentioned earlier, there's different triggers, stress, viruses. And I'd love for you to touch on things because a lot of our patients that we're talking with are exposed to mycotoxins, other Candida, maybe even a lot of people have tick borne illness or even community acquired pneumonia bugs that are persistent.

And then obviously, as you mentioned, we should maybe talk a little stress and dovetail right in the Covid. If you want to kind of like play with that a little bit, because I think that this is what our audience is, these are some of the things our audience is experiencing.

And certainly, obviously knowing what to do after Covid and how Covid impacts, mast cells and then how to block some of this is certainly totally high yield stuff here.

Sure. And super exciting. This is like I feel like kid on Christmas right now. I mean, such great information. Let me before we get into, you know, Covid and the like, let me just first say that the terminology used is very confusing.

Still very confusing. So let me just start out by saying generally separate mast cell diseases into the primary. And as an example would be either systemic mashed potatoes cutaneous mashed potatoes.

So by definition you have a lot more mast cells. Then you have the second. And in most cases of the primary, the mast cells are also activated. So we should really reserve the word activation for many different settings, not just mast cell activation syndrome, which I will return.

So whether you have systemic Munster psychosis in probably 100% of the people, the muscles are activated by a change in cutaneous master say dosage. The muscles are not as activated as in systemic but they're more activated if you rub you know, the lesions ET etcetera etc.

you know heat. So that takes us to the secondary which might be allergic rhinitis. Allergic rhinitis. It might be what do we call pressure to carry our physical or to carry us.

And then the third category is idiopathic. So if you got Oedipus and if he lacks angioedema, idiopathic IC,

whatever. And now you have a category mast cell activation syndrome, which according to my colleagues, it has to have a potential invasion within 48 hours of an episode, which is almost impossible to measure unless you have an indwelling catheter, and most laboratories will not even measure it.

Most emergency rooms don't know what it is, let alone measure it. And then you have the category of muscle activation, comma unspecified. And that has its own diagnostic code.

So we don't have to necessarily be going crazy. Is this really mast cell activation syndrome. Because if it doesn't have triptans let's just call it muscle activation and specify it.

Treatment basics and antihistamines

It still has a diagnostic code. You can still do a whole bunch of testing on it, etc.. So but most everybody talks about the M-class, the syndrome. And I think that just derails sets from thinking that muscle.

Can it be activated in many, many other conditions. Give you an example unrelated to all of this, in solid tumors, whether it's breast, pancreatic, ovarian cancer, prostate cancer, we have accumulation of muscle.

Nor knows why we always thought that there were being accumulated to kill the tumor. And yet the tumor cells are smarter than us. They prevent the mast cell from the granulation.

I've never seen too granular much cells around tumors, yet they stimulate the muscles, at least BGF and other until proteins that allows near vascularization growth of the cancer metastasis.

So the cancer cell can do what I have not been able to do in 40 years can tell the muscle what to do to each advantage. If I could tell the muscle what to do, I can tell the muscle don't release until a genic factors release tumor necrosis factor.

I kill the tumor cells and I don't know how to do it. So that's why the muscle cell is fascinating. I mean, my mind is like a microcosm of pharmacology circulating in the body.

If I can put a microchip in the muscle and tell it what to release in, what part of the body are the best, best treatment ever for many conditions, for maybe 100 years from now, that's exactly what we'll be having.

So coming back now, what is the original approach for treatment and I will leave the good stuff for the end. Once once you identify that there is activation of my cells, you have a clinical history.

You, you know, you give them some antihistamines, a little, a little better, you know, something is brewing. And if you actually scratch their underarm, and you get your monograph here, then, you know, the muscles are activated by pressure, which means that they're ready to fire, no allergens. You.

So I always do this. The scratch test. Yeah. Because if they're positive, that is telling me that antihistamines probably are not going to be enough, to take care of this patient because the muscle responded to pressure.

And not necessarily the analogy. So what do we do? We try some antihistamines. Three things to know about antihistamines that we usually don't think about.

Number one, they're not all the same. Number two, about 15% of the people get wired, even though we're supposed to be sedating to some extent. So a lot of people just don't tolerate that.

There you go. Yeah. So so it's it's very hard to tell a patient no take you know X it's good for you and the patients you know pulling their hair because they're not wired.

Number three there are many histamines that have additional properties. Give you an example. Hydroxide in or anthrax. It's slightly sedating and it's slightly anti-anxiety.

Many times you give them to children who have increases at night. That might have had a very difficult day. I find it very useful to give it at night, for instance, it puts you in a deep sleep so people, you know, before they go to Ambien or, you know, whatever, you know, not being able to sleep.

I'll give them a little ladder. So then you have antihistamines, one of which I'll mention that I'll, I'll return to it, which is robot agent Robot. It has existed in Europe for 20 years, in Canada for three years, still not in the United States, but it's as good an antihistamine as any.

It partially blocks mast cells, and it was designed to be a puffy orbiter to get three birds with one stone. And by the way, anybody can get a robot from Canada with a U. S.

prescription through a Canadian online pharmacy. You don't have to compound it. A lot of patients, you know, physicians get it from Canada. I'll return to this when it comes to Covid, as well.

So then what do you do after that? Well, you try to block the mast cells, and, you know, most everybody reads about Crumlin Block in the mast cells. I published on Crumlin as an undergraduate at Yale in 1971.

It worked perfectly in rats. It was very bad in mice. And it really doesn't block human muscles, okay? It just doesn't interest me. It became word of mouth that it's a good blocker because they called it muscle blocker.

It gets absorbed less than 5% from the gut. Does it inhibit anything? Yes, it inhibits histamine release, maybe about 20%, mostly in the gut. It doesn't do anything else and the body gets used to it very quickly.

We call that passive relaxes. So we start with 100mg. You know a file a day that it becomes, you know, about three months itch 400mg four times a day.

And by that time you have about 15% of explosive diarrhea. So it's not an easy drug. And it's very expensive as well. So don't get me wrong. If someone has GI symptoms that they take and do well or part of their elbow and I find nasal crumb quite useful.

So nasal chromes nasal spray. So I find you for allergic rhinitis quite useful but not the oral crumley. But anyhow some colleagues will try crumley because it's available.

Then what do you do? Well, do you think maybe leukotrienes are involved? We know leukotrienes are extremely broncho constrictive. That's why we have Cingular.

But because we don't know what to do, we might say, okay, nothing else is helping. Let's put you on ten milligrams regular and hope for the best. Sometimes it works, sometimes it doesn't.

It really doesn't have that many side effects. I'm leaving the polyphenols out. I'm talking about the sort of the straightforward, you know, colleague who doesn't think outside the box.

If someone has tremendous itching. They're my thing about Jola, okay? And that's about it in terms of what they will do. Some will go crazy and they'll show.

I'll put some on a plaque and they'll God forbid, okay, so but they do. Okay. They do. You might also put someone on more exotic tyrosine kinase inhibitors.

Those are work well for to psychosis, but they do not block mast cell activation. So you know for some of the doesn't have much to say does is they're not going to work.

So that takes me back now to almost 40 years ago when I was studying Crumley. And if you think of Crumley, it's a butterfly with two wings. And I did one of the first searches on molecular mimicry back that.

And what do you know? The basic structure of a polyphenol compound is almost identical to one of the wings of

the butterfly. She was very similar to Crumlin, and that's what got me interested in flavonoids to begin with.

In addition to the fact that probably look good on flavonoids was Doctor Middleton, but unfortunately died many years ago, and his colleague had called me up about 1998 or so, and he said that he had left in his will that I actually take his work on flavonoids and write a review.

And I was I was really taken and honored. Wow. We published a review in Pharmacological Reviews in 2000 about flavonoids and has become classic, basically, in terms of citations.

So the flavonoids are very antioxidant. They're anti-inflammatory and they can block mast cells. But there are 3000 of them in nature and all of them are not the same.

And all of them don't do the same. And some are bad actually. So when we talk later about polyphenols compounds, I have to actually differentiate and say why?

We have to be very careful about what we choose and how we give it. Taking me back, we were amazed over the years that many patients with mast cell or allergic like problems, we get worse when they were stressed and that was well known.

And of course, what did we used to hear each other in your head, right.

Flavonoids, stress, and brain involvement

Separate. We were the first that published that the main hormone released under stress cortical throbbing releasing hormonal CRH. It released outside the brain and it stimulates the mast cells to release molecules without histamine entry proteins and changes the reactivity of the mast cells to allergens as well.

So there's no question that stress via CRH can actually do a job on the mast cells. Therefore, in treating or attempting to treat any of the patients, we're talking about reducing stress in any way possible is very important in my mind.

If, if they continue to scream and stress no matter what do we do, they'll continue to have problems. So I had one patient from Brussels who used to trade diamonds in, in, in the upper parts of Russia.

And she would come back and you will be covered with, with eczema and all kinds of other problems. And I said, well, what what do you do? When do you go up there?

Well, you know, I've got some bags with diamonds and, you know, bags with dollars and a couple people Kalashnikovs. And I don't know if I'll come back alive.

I said, you're crazy. I mean, you're screaming and stress. So I said, look, he was also Greek American. I mean, that Belgian American. So, Belgian Greek.

So I said, you just go to a Greek island, you know, for a couple of years and forget to chill out. Chill out. Okay. And and he did phenomenally well. I mean, you know, it's obviously anecdotal, but it was true.

And I had received actually five U. S. patents on how to block shear rates as it relates to matter related diseases. But now I was interested in bringing them, as the lawyer say, reducing it to practice.

So 70 years have gone by and the patents are gone, and we still don't have any way of blocking this or CRH receptor antagonists or such kind of diseases.

So to finish this part, from the very beginning, I was amazed by the fact that the DNA eminence, the little stroke that connects the hypothalamus to the pituitary, has as many mast cells per unit volume as our skin, the mast, the brain doesn't get allergic reactions.

So what do they do? Immunoglobulin E cannot cross the blood brain barrier unless it becomes, you know, leaky compromised because it must be doing something.

And of course, she arranged right there hypothalamus make CRH in addition to other molecules. So it became apparent that the mast cells may be contributing to certain neuropsychiatric symptoms, both indirectly by releasing things outside the brain that might cross the blood brain barrier, as well as by being activated inside the brain.

But to this day, no one really has focused on mast cells in the brain in spite of, you know, Norse publications by myself and other, colleagues. So let me stop and let you ask.

Yeah. Well, I mean, I just think it's phenomenal. I could listen to this all day because there's so many pieces that are kind of bringing together some of the questions we have, and, and I know that we don't have maybe all the answers like you just alluded to, but I feel like it.

It gives me comfort that and hopefully to our, the any of the patients who are experiencing these symptoms watching that, we're starting to understand why you're reacting the way you're reacting.

And we may not have all the answers yet, but we've got scientists leading us in that direction. And I love the fact that stress, like we keep saying, everybody's all de-stress, de-stress.

And that's all nice, right? But for us to be able to understand there's a scientific basis and we know that de-stressing will for sure help balance out our Marcel, you know, response.

That's a lot of hope because you have so much control. You have more control over stress. It sounds like then our supplements or our medications have over your mast cells.

Correct. We published two separate papers and another colleague published a third paper in one instance where a patient with cutaneous master psychosis said, after a very stressful when she was covered, she she, you know, she went from a few lesions to hundreds of lesions and we measured CRH in the blood and it was off the roof.

We had another patient that we published. We had systemic much to Scientology notoriously, we'll get worse under stress. And in that instance, not only we measured and we showed she was high in the blood, but we took her biopsies.

There were done in Michigan, and we restrained the biopsies where there were clusters of mast cells with a fluorescent antibody to a receptor and the muscles lit up like light bulbs.

So we know what is happening. It's just that we don't have a way of blocking the release of CRH or the action of CRH as of yet. So but there are ways to reduce stress that might not necessarily require, you know, benzodiazepines and other things.

And again, if we have time, we can get into that. Yeah. I think there's so much and we've you know, we definitely have some. It's great to hear this because a lot some of the other speakers in the summit are do talk about like limbic stuff and stress reduction too.

So but we now we have we're seeing the science of it. One of the things that I really would love to hear about too, is you had mentioned Covid, and I'm sure we've talked about it several times here as one of the things that might have a unique relationship with mast cells.

And I would want to make sure we we put that in and then give you a chance to talk about polyphenols and how to properly utilize them. Well, just as Covid started, you know, I published a couple of papers two and a half years ago, immediately saying that most of the action, at least at that time, appeared to be in the lungs.

We know mast cells are in the lungs. We know mast cells contain lots of cytokines and pretty much patients were dying because what was called cytokine storm.

Yet the ability of the virus to bind to each key receptor, which is angiotensin converting enzyme two Ace2 receptor, had nothing to do with cytokines.

The Ace2 receptor is important for the virus to get in, get into the nucleus and multiply. So where were the cytokines coming from? So that was question number one.

Question number two was can we actually block the mast cells in the lung. And of course if one could actually squeeze something in the nose or have them inhale it, that would be tremendous.

But no one ever did that and they still haven't done it. Number three, can we measure anything that comes out of the mast cells in the blood to see if, in fact there is some outcome or through syncope in, you know, alveoli fluid.

So when I was writing this reviews and there were published in different journals, one paper came out from France showing that in the alveolar receptor of patients that had died and they did pathology, the mast cells were activated.

They didn't measure what, but it was the first paper. And the second paper came out showing that chi base was high but not treated case. Then a third paper came out a few months ago showing that when they infected mice with Covid well the SARS-CoV-2 protein not Covid, the muscles in the lungs got activated, but they only release chi mace.

And when they went to patients and they looked at asymptomatic, symptomatic and severe patients, Chi major was actually tracking with the severity of the disease.

Again, no triptans, no histamine. So there was clear evidence that the muscles were being activated, although it threw us for a loop as to why molecules that are in the same granules are not released together, we still don't know the answer to that.

At the same time, a paper was published the very few people paid attention to, and that was actually published in proceedings Academy of Sciences, where they looked at 81 countries and they looked at the level of pollen and the incidence of Covid, and they tracked together the more pollen, the more Covid.

And they said that maybe because you breathe the virus and if you have an allergic response in the nose because of the allergen, etcetera, the type of immunity shifts and doesn't protect against the virus.

To me, it was an obvious indication that if the muscles are activated, they're maybe they're were making things more likely to occur because of the Covid infection, since it goes through the nose.

Right. And finally, we did some experiments which since only one paper recently actually published because we didn't have time to publish because the shot our lab down.

But we showed that the spike protein, recombinant spike protein can stimulate the mast cells. So you didn't need the whole virus, just the spike protein.

And at the same time, because we were very interested about what happens in the brain, brain fog, long Covid, etc., we also took human cultured microglia, which as you know, are the defenders of the brain.

And the spike protein recombinant also stimulated the microglia. And two papers now have been published showing the same thing. So you don't necessarily need the whole virus, which to some extent worried me because if the spike protein can cross the blood brain barrier or damage the blood brain barrier, then it can get in and set up sort of a local perivascular inflammation.

And that's exactly what had been shown in pathology of patients who died. There's perivascular inflammation. And I wrote a paper in molecular neurobiology about a year ago, less than a year ago.

And the question was, could the spike protein be responsible for Covid 19 neurologic symptoms? And we actually showed in a diagram whether you have microglia or muscle cells how basically the spike protein can do that.

COVID, long COVID, and mast cell activation

And we proposed that it might be through toll like receptors that respond to viruses fungi and bacteria. And since then three papers should be published, one in nature showing that the spike protein can stimulate receptors unrelated to each main receptor for invasion, which is Ace2.

So for about two years we were missing the boat, basically focusing on Ace2. While the the muscle expresses all tau like receptors one through nine. You know, for is for LPs, two is for fungi, etc..

So with that in mind, immediately I said, can we block the mast cells by using at least whatever we have available. And what was available was literally a question in the luteal.

It in terms of inhibiting the mast cells, both we and others published on that immediately. A Canadian group did a clinical study on quercetin and it showed that you could actually reduce symptoms.

Another study was done in India with very few patients showing the question could again inhibit the symptoms to some extent that we're not focusing on mast cells necessarily, but the difficulty is the question is absorb less than 10% from the gut.

And so is luteal. And that's why we focused on how do we increase absorption of both question and luteal. So we put both quercetin and luteal in together in two preparations.

One is called neuroprotective. It's a smaller capsule because some individuals cannot swallow bigger capsules. And the other is called fibro protech. That is almost double the amount of both.

Quercetin luteal again in olive oil triggers absorption. Since then we have two clinical studies ongoing. One is actually about to start in the Miami VA long Covid clinic, and one is going on in Greece, and we published one paper which was literally, changed our thinking.

This was a lady well known from the big city in Florida two years ago. When done with Covid, she had all the symptoms you can imagine. She was given everything that was available at the time, including her convalescent serum, and she realized it's remission and dexamethasone, you know, the works, everything.

Yeah. And her lungs basically were showed damaged that she was put on a double lung transplant list and she was living on ten liters oxygen. Okay. Holy cow.

So what we decided I was asked to consult through a friend. And your primary physicians went along. God bless them. So we put them actually on fiber protec.

You know, four of those a day. We'll put her on another supplement called Brain Gain. That is much more helpful if you have brain fog, not necessarily symptoms all over the place.

We put your on route pal from Canada because as I said earlier, it blocks above and they're independent papers that is involved in Covid, including two papers we wrote.

And then we put her also on a null drug that we don't think about anymore, cited tech society to take a suppressor gland in a, you know, agonist we used to give it to protect the stomach for all time is taking nonsteroidal anti-inflammatory drugs, but it's anti fibrotic.

And in this patient the lungs were actually fibrotic. 100 micrograms per day, not milligrams. Don't make a mistake. And then because she was not exchanging enough oxygen, we put her actually I use her poison injections subcu three times a week in three months.

Her lungs looked so perfect. She was taken off the transplant list, and she's. She's back to a little practice. Now, that doesn't mean to say that every patient you know, will will have such amazing, you know, turnaround.

But it points to the fact that we have ways to address aspects of Covid and what is really most important for the brain, the polyphenol compound charcoal, phenolic, because they had hydroxyl groups attached to the benzene rings.

And that's called a phenology. Green. The more hydroxyl groups you have, the more phenolic you are, the more antioxidant you are, but the less inflammatory you are and the more phenolic groups, the less likely you'll get into the brain.

That's why we focused on luteal, because unlike quercetin, which has five hydroxyl groups, Ludhiana has four and slightly to get into the brain. So the quercetin part of the neuroprotective, the fiber attack catches the mast cells outside the brain and it acts like a decoy because it gets metabolized to allow luteal into escape and get into the brain.

I love it because like, you know, it's so funny. It's it's so many of the folks speaking with us here, and obviously yourself and myself are our scientists, and yet we're still looking at sort of functional medicine and quote unquote alternative.

And, and I think that this is like for me, like so much hope because we're, we're using real science to get real results. And we understand that maybe we need, you know, side, you know, one of these medications or maybe we need a supplement and to do that.

So one of the things that we had talked about that I think is really important is when you talk about the the polyphenols, I mean, give particular tips for the public to kind of navigate, because like what you just said is there's certain ones we shouldn't we shouldn't use.

And then there's also dosing considerations. So number one please try to find out the source, the purity and the amount. No one mandates that the FDA does not mandate that so many supplements will say proprietary blend.

And they will not tell you what that right. In fact, many of them do that. That's number one. Number two, the polyphenols compounds, all of them are yellow.

The more hydroxy groups you have, the more color you have. So if you open up, whether it's a capsule or a pill and it's not yellow, there's no there's no quercetin there.

There's no luteal in there. Okay. So that's kind of a quick way to find out if someone is pulling your leg. Then the source is very important. And again supplements don't tell you the source.

As you will see in the supplements I helped develop, they'll say in parentheses with Latin because that's how it's supposed to be by the FDA. What it is, right?

The reason is because the cheapest source, of course, in some of the flavonoids is actually peanut shells, but no one is telling you it's from peanuts.

So if you are allergic to peanuts and you taking it, the next cheaper source is fava beans, but about 20% a mediterranean extraction. People like myself, you know, Greeks, Italians, you know, Jewish North Africans, they lack dish Expedia if you like dish Expedia and you had fava beans, you get hemolytic anemia.

Go chase your kale. Now you know you're going to be running to a hematologist. Why not fish out of your shell? Sure are going to fish. And the third, which is also very important, is the most polyphenol.

Something is the more likely about 20% of the people to get hyper on it. These are people that have phenol intolerance. And we know why. Because the enzymes that break down phenols, the mutations.

So I always ask for, you know, ginger patients for about six different enzymes because that will direct me not only about supplements but about drugs.

What to give them, how much to give them. Because, you know, we separate people in fast metabolism and slow metabolism. So if someone is slow, metabolize metabolism one gram of quercetin might be five grams for them.

And you know it might cause problems. So try to find out source purity and amount okay. The second is that too much of something is not necessarily good.

So I'll give you the example that I gave you before we started. Some of my colleagues will say, well, you know, your your absorb less than 10%. Let's give them two grams.

That means it will absorb 200mg, 1800 milligrams will stay in the gut. They will shut down your bile flora and it will cause dysbiosis. They you start chasing your tail. It's true.

How do I fix dysbiosis? That's why we mix them up with olive palmar soil. And what is olive oil? If you take the olive oil, you're left with a bit and a little bit of the shell of the of the olive.

If you squeeze that, you get a thicker aureole. And in in Greece we use it as a salad dressing, but it is cheaper than olive oil. In trying to keep actually the cost down.

And it's not like you can take any oil because as you know, the old lake acid content of the olive oil or the olive oil is what causes you to have heartburn.

You know, which if your lake acid is too much, you kind of get heartburn. So the typical olive oil that you buy, you know, anywhere is actually 1 to 2% or like acid.

The olive oil we use is 0.1% or ten times less to make sure that we don't run into that problem. And the third problem to watch out, which maybe I should have said earlier, is that soy flavonoid.

Many times you see soy by flavonoids. So flavonoids soy flavonoids are estrogenic. So if God forbid, a lady has, you know, ovarian cancer, you know, breast cancer, those would be a no no.

Absolutely not. No. Yeah. So again, not not everything is is the same, unfortunately. And at the end of the day, duration of time is more important.

Polyphenol selection, dosing, and quality

The amount I always especially when we don't know where the patients are, sometimes they'll just order something and then you don't have the chance to talk to them.

I always say start with one and slowly increase to the extent tolerated. And then of course, you know, if someone were to come to you, it would be important.

Do they have any endocrine problems to have thyroid disease? Because a two grams a day of course will shut down thyroxine production. But if you have someone who is hypothyroid then it would be good because you want to shut down thyroid production in hypothyroidism.

So there's so many things that enter you really need to know. And unfortunately, so many patients just buy over-the-counter or the internet and it's just impossible to be able to help them all and help them navigate through.

Yeah. You know, it's interesting. I mean, I think of a couple things. And one is that, so much of what I do like, and I kind of learned about like sort of the conversation, we're having a mast cell activation syndrome in the summit.

And today with you is comes through the world of Lyme and tick borne illness. And I hear myself saying all the time,

it's low and slow and long is often better.

If I had a choice between really high dose and really long course at a low dose, I'd take the second one 100% with you on that. And that's what we see with mold. That's what we see with mast cells.

And so I'm really glad to hear you say that. Mycotoxins are very high on my list. I've got numerous patients who were just horribly affected by exposure to mold and or mycotoxins.

And just to be clear, for the audience that might not be aware of it, mold types of mold make different types of mycotoxins, and mycotoxins stick to everything.

I wrote a little editorial about mycotoxins and inflammation, and I quoted actually from the Old Testament. So the rabbi, the rabbi said, we're talking about 3000 years ago.

If you find a house that is infected, my ball you carried down, that's exactly called by God. And if someone has been wearing clothes that were exposed to mold, you burn the clothes.

There could not have been more, right? Wow. You don't pay attention to tobacco toxins. You know. Of course, if you have musty smell and you see, you know, water stain on the walls, you know, you got you got a problem.

But the mycotoxins are very difficult to measure in the air, and they stick to carpet, rugs, etc.. So a number of occasions I had people just leave their homes for 2 or 3 months if they could, and feel much better.

And we don't have good ways to measure mycotoxins. We tend to measure mycotoxins in the urine. But, you know, I've sent urine in four different labs, and I get, you know, four different results back. Yeah.

And someone would argue some mycotoxins, like a toxin, is found also in food. You know, sources, so I always say, you know, wash, if you don't want to peel the fruit, wash it with a little bit of soap.

First you've got to get the micro toxins, out, no matter where they come from. But you, you have to address them. It's it's so important because. And it's like this taking out the a little bit of toxin over time, doing the duration and kind of getting the understanding that we don't need to do everything all at once, I think to I mean, except maybe the the long haul Covid lady who's going to get a lung transplant, you kind of have to sometimes some people throw the kitchen sink.

One of the things I did want to highlight, though, that that I kind of heard you sort of saying, is there, there's maybe directly saying there's a there is a quality of product in, you know, medication and supplement and the sourcing.

So I know that a lot of us have spent a lot of time getting different supplements, different places. The protocols get bigger, they get costly. But please remember to work with your practitioners to make sure that you're when you're spending money on something that maybe your insurance isn't covering, get the good stuff rather than because otherwise you're going to be doing this for a little while.

And if you're using lower quality stuff, you can actually be making your symptoms worse, not better. Correct. We're actually show, you know, the company algo not has made, you know, a number of the supplements that we've been talking about and it is actually on the health store as well.

So where many physicians have their own kind of, you know, store and I'm writing actually an article with, one of the functional medicine physicians was responsible I and the Mayo Clinic.

So we're trying to get out there, and it doesn't matter whether someone in my mind uses the term injury integrated medicine or functional medicine, as long as they look for the reasons why.

So functional medicine should not be necessarily that we should not be using medicine. We should not be actually looking for the science. You know, functional medicine in my mind, or integrative medicine is to look at the whole

puzzle and not necessarily just a piece of the puzzle, but if for each piece or as many pieces of the puzzle, we can find a reason, that's how we should be making our selections, you know, moving forward.

And in fact, I wrote, a little editorial called Luteal in Supplements. All the glitters is not gold type of thing. And I compared all the luteal in supplements in the United States that were available, you know, two years ago when I wrote it.

And you'll be surprised they'll be, for instance, one particular component says 100mg luteal. But then when you read down only 10% of that during the rest routine, and I'll say a word about routine, there's another one that says 25mg luteal, which is, you know, a drop in the bucket.

And then you read that it's actually two capsules for to the 25mg. But the word luteal, it shows up with with big letters. You've got to read small letters to see that it's not enough, luteal in there.

So the important thing is that quercetin in life, in nature exists with a sugar attached to it. And that's your routine. Serotonin is quercetin glycosides.

So when someone bites quercetin, they removed the sugar. Now why is that important? I use routine two whenever I have GI problems because routine will be cleaved by GI by flora in liberate quercetin in the gut.

So it's liberated slower. So for instance in Europe protech there's 100mg luteal, but 80mg of quercetin or 70mg and 30mg routine because I'm trying to catch the gut.

The rest of the body and the brain brain. So but if you're going to have a 100mg routine, it's not going to help. You will all stay in the gut. So that's why I'm not saying routine is bad.

Sometimes I use the word inactive because if you take human cells and culture and you add routine, you will not repeat them because the cells don't have the way to clear the sugar.

So, you know, sometimes when the words are used, you know, the mind is faster than, than, than your mouth in terms of what you're trying to explain. The bottom line is, I really believe we have good substances out there, and if they can be put into better formulations, we can be doing wonders.

I've been trying for three years to create an intranasal luteal. I haven't been able to find funding whether it generated for corporate America, because they're not patents on it.

That's so interesting. Yeah, it's one of those things I think it's so, just everything you've shared with us today is just so inspiring because there is hope.

And I think that so many of us feel that there may not be hope, but, you know, and this is another reason to like I really recommend people find a practitioner if you're having symptoms like this, don't go it alone.

There are people who know what they're doing and like even like I mean, I know that like many of the guests, including you on our summit as well as our, you know, our host, Beth O'Hare, I love she wanted to bring this whole group of people together because, like you just said so eloquently, functional medicine is bringing science to all of this.

It's not it's.

Hope, research funding, and closing remarks

And the way the body functions, not so much like no Western medicine or an all herbs and supplements or just meditate in a cave and you'll be better. But it's the bringing together of all these things.

So highlighting all that, I would you know, I'm just so thankful for the time to talk. And as we kind of land and bring

all this together, are there any kind of closing words of hope you want to share?

I mean, I feel like the whole thing's just been this amazing, like masterclass. And then also I feel so as a provider, sometimes I do feel like my patients are losing hope and I might so thank you for bringing that back.

Three three parting comment of your wish. Number one, there's absolute hope. There's always hope. And if we don't have hope, then we're stressed out and then we're spinning our wheels.

Number two, as you said, find the right person. And if that person is not the best person, at least open the door. That that person might talk to someone else who might not know more.

And I tend to think that functional integrative medicine colleagues are a little more open to talking to other colleagues than than not. The third, probably the most important thing is in 40 years in research, I've never been funded by NIH to study the mast cell.

I've always been funded through, you know, eczema, through psoriasis, through autism. There's got to be a request for applications for just studying the mast cell at this point is way, way overdue.

And in that vein, I've been fascinated, not necessarily pleasantly, by the fact that patients who did very well, who before they got well, we're saying, my God, I'll, I'll give you anything to make me feel better.

And I've never asked for money other than give some money for research. They just disappear. There's got to be some money to help. I'm not necessarily me.

Whoever is out there struggling to find answers, without money, there cannot be any research. So I'm begging people that are on the way to recovery, or those who are begging for recovery who might be independently wealthy.

We need donations, tax deductible donations to the universities to help out with this research. I mean, we're lacking we used to be many more in the area of mast cells.

I could have counted 20 maybe colleagues. Now we're down to about seven who know about mast cells, and three of them are retiring. So and we don't have younger people coming into this because there isn't money into this.

These are complicated patients. They require a lot of time. You know, insurance companies don't cover many of these things. So we've got to find a better way to address the patients and do the research that eventually will help everybody.

So, well, a great call to action for everyone. And and if maybe you don't fit into that, you know, into the ability to personally find anything, one of the other things we've seen in the Lyme world is that public talking to their, you know, to the representatives and to the, their local governments and those folks who are representing them in Washington does make a change.

And there are some changes that have gone on in the last couple of years that have really made a difference. And so if we can dovetail on to the new work that's been going on with Lyme and all these other parts, let's I mean, the Marcel seems like something that should be studied.

So if you happen to think about it, just write to your congressperson or representative as well. And if you know anyone. So doctor theory it's I mean my goodness, thank you so much.

You're so generous with your time and your knowledge. Thank you all you've done over the past like four plus decades to help all our patients get what I'd like to you and all of you listening are there.

Thank you so much. So everyone, thank you again for joining us for this episode of the Reversing Marcel Activation Syndrome. And Histamine intolerance syndrome, and our summit, I should say.

And my name is doctor Tom Moorcroft, and we'll see you in our next episode.