Dr. Greenblatt: So much of our field of psychiatry, mental health, is based on neurotransmitters and receptors, and we now understand that these are all under kind of genetic influences, and genetic differences can have profound effects on our mental health and our risk for mental health and mental illness.

Nathan Morris: So, Kara, as I was thinking about today's episode, and we are talking about neurotransmitters, I kind of started reflecting upon our history together and how I met you and you were in such a great place. You had been running Integrated Connection, an autism remission clinic, and we have just hit it off famously, of course. But as I have gotten to know you over the last five or six years, I have really understood there was a lot more behind the scenes before you were in that great place. And I think as we became friends and we went through your genetics, I think you had a lot of aha moments that helped you have a lot more peace about where you were at before we met, in those years before. And I really would like for you just to give us a little history on that and how genetics maybe helped you understand that this was not some kind of character flaw, the things that you were having going on at that time.

Kara Ware: Nathan, that is really well said. As I looked back upon my journey, when my son regressed into autism 15 years ago, I was carrying around a lot of shame and guilt and embarrassment for years really. Truly, to be honest, up until understanding my genetic vulnerabilities. Because when he regressed into autism, I lost my job. My husband left. I lost my friends. I lost my hobbies. I lost my entire way of life, and we were very isolated. And during that time, depression and anxiety were choking me and suicidal thoughts were a daily battle.

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Kara Ware: And when you and I went over my genetics and I started understanding my COMT and DRD2 and my MTHFR, I started realizing, hey, this was not something wrong with me. This was not something to feel ashamed about. I had honest genetic vulnerabilities, that when interacting with such a traumatic experience, of course, some unhealthy coping mechanisms were being expressed. And as I started learning the nutrients to bypass the common polymorphisms and, of course, I have been living the

functional medicine lifestyle for the last 14 years, I got on board with my son. Thank goodness. I have a lot more self-compassion and can understand how to support my body in times, now, of increased stress.

Kara Ware: And I love this piece as a driver for new patients because I know a lot of your patients that we talk to have depression and anxiety. And left untreated, could lead to suicide. And so, what an important place for us to begin in a functional medicine practice is to help people feel well, like they can make the lifestyle changes, and that they can access some self-compassion for themselves.

Nathan Morris: I think that's so important, Kara, is that we give that access point to patients to have that self-compassion. I thought that was well said, having self-compassion, and I think genetics would open a door. Do you feel like that if you had known that there may be some genetic insight there, that would have helped you approach a provider instead of living in that place you were in?

Kara Ware: Exactly. Instead of suffering in silence, right? You and I have talked a lot about that. And I would have absolutely wanted to know, "Hey, do you mean this isn't a character flaw? This is not something wrong with me? It means I just need higher demands of nutrients?" Okay.

Nathan Morris: Exactly.

Kara Ware: Please, tell me more because I am dying, literally, over here. And what an important step for patients to understand just the nutrient requirements that they need and how that can help tremendously. So, they want to do more changes. They want to be in the functional medicine process and partnership.

Nathan Morris: Kara, those are just such great points on how we can use neurotransmitters to get patients into our practice and discuss things that are very difficult. That is why I'm really excited about our next guest, Dr. Greenblatt, who is a psychiatrist who has been using neurotransmitters and polymorphisms for years, and we'll hear more from him right after this.

Nathan Morris: Dr. Greenblatt, what a pleasure it is to have you today on our podcast. Kara and I are super excited, especially with all your years of experience in psychiatry and genetics. We feel like you are the perfect person for this episode. I have found in my years of using genetics in my clinical practice that the neurotransmitter SNPs are some of the most useful in realizing results and helping the patient feel better right away. Can you explain why these can be so useful in practice or have you seen that?

Dr. Greenblatt: Absolutely. I have been practicing over 30 years and over 10 years looking at these genetic SNPs to help make decisions, decisions around what supplements would be helpful, even decisions around what medications might be helpful. So much of our field of psychiatry, mental health is based on neurotransmitters and receptors, and we now understand that these are all under genetic influences and genetic differences can have profound effects on our mental health and our risk for mental health and mental illness.

Kara Ware: Dr. Greenblatt, I have heard you say in a webinar I was listening to of yours some statistics. I heard you say 44% of adults and less than 2% of kids are getting mental health treatment. In the webinar, you said we know we can do better. So, in this time of this global pandemic specifically of pervasive stress and loss of structure and high rates of unemployment, how can we as functional medicine practices help patients feel comfortable coming to a functional medicine practice specifically for nutritional genomics to take a look at, "Hey, how can we be proactive if we are finding ourselves tipping into some unhealthy coping strategies now with all of these epigenetic influences?"
Dr. Greenblatt: Great question. I think the functional medicine community has a profound ethical and medical responsibility to provide education for our colleagues and our patients about these biological functional vulnerabilities. And so much of the mental illness that we have seen and that is going to escalate over the coming year is going to be related to that kind of genetic environmental dance and the functional medicine model addresses that. It is the only model that addresses it. So, I believe that helping our functional medicine clinicians understand where mental health vulnerabilities will be, genetic and nutritional, can make a huge dent in these growing rates of mental illness.

Kara Ware: The genetic vulnerabilities, I've heard you use that term, and it makes it much more clear for me to understand, hey, this isn't a weakness of mine. This is something that I have in my DNA that makes me more prone to seek out reward-seeking behaviors under stress. So, can you a little further on how we can help patients understand, hey, this is not a weakness. This is genuinely a genetic vulnerability.

Dr. Greenblatt: Sure. Usually, in the sentence where I use the word vulnerability, the next line is always the genes are not our destiny. And I think it is really important that if we have a family history of depression, addiction or suicide, it doesn't mean that's our destiny. Some of these SNPs, these genetic polymorphisms that affect how you metabolize neurotransmitters or nutrients that affect neurotransmitters, it does not mean that we will be depressed. It just makes us more vulnerable. So particularly that environmental factor of stress, whether it is the global kind of stress we're all under or our own individual stresses, so it's that kind of genetic environmental dance, stress being the most powerful variable that will affect these vulnerabilities.

Nathan Morris: Excellent point.

Kara Ware: Yeah, that is great. And your field of psychiatry, you have always said you're working to redefine it and reimagine it. And one of those tools that you have found that has helped to change clinical outcomes dramatically are I heard you mentioned four particularly, which were the SLC6A4, the serotonin transporter, of course, MTHFR-A1298C and the C677T, the TPH2 and the COMT.

Dr. Greenblatt: Those are four of thousands that really affect how we behave and how we feel and how we interact with the world around us. But those are four that are the most important when we assess some of our psychiatric patients.

Nathan Morris: Can you pull out two of those polymorphisms that we could really focus on in the time that we have that most practitioners should be looking at?

Dr. Greenblatt: Sure. I quickly mentioned more around medication. The serotonin transporter SNPs really can determine whether somebody would do poorly on the SSRIs versus some of the other medications. And that is such a powerful mistake in our clinical practice. And so much of these medicines are prescribed by family docs not trained in psychiatry. So that is a helpful tool there. I think the MTHFR SNPs are the simplest to understand and probably have the most profound implications in traditional psychiatry and functional medicine because a vulnerability in the MTHFR SNPs often is the factor in pairing one's ability to recover from depression or addiction or chronic psychiatric illnesses. So, the earlier we can understand these genetic vulnerabilities, the concept of prevention really screams out and has profound implications.

Nathan Morris: Where do you see COMT fitting in? I think in my practice I love COMT because it tells me about somebody almost without seeing them. And I do not like saying that because I always want to look at the patient across from me, but I can almost, with that particular polymorphism, I can tell the person across from me, what they are. I mean, it is such a defining polymorphism for a lot of my patients. Can you speak to that a little bit more, what you have seen with?

Dr. Greenblatt: Sure. I mean, it is similar to the MTHFR in that my world of one foot in traditional psychiatry, one foot in functional medicine, that it guides me when I need to think about medications. And it also guides me when I need to think about nutritional supplements. And hopefully, we can get at the underlying cause and not require medications, but certain the SNPs with the COMT, they do much better with dopaminergic supplements or dopaminergic medications, supplements, or dopaminergic medications, and that has profound implications. Whether it is a school, executive functioning, depression, it is very simple to treat. And that is why like you, it's a very important part of my clinical application.

Nathan Morris: So just to interrupt just a second. So valval is where you get rid of the dopamine, epinephrine, norepinephrine, a lot easier. You are very efficient at getting rid of it. So, these are the people that would have a hard time focusing. So, that is where the dopaminergic would come in.

Dr. Greenblatt: Yes. And some might say too efficiently, so you are always looking for dopamine, and that's why we can support it with some of the amino acid supplements that help support dopamine, like tyrosine, with some of the herbs like Rhodiola, or for those kids that are really struggling in school, those val-val [inaudible 00:11:02] are the ones that have been shown to do much better with these two medications.

Nathan Morris: What about … with the met-met. Of course, I have always heard, and I think you probably agree that stimulant medications, we need to be very cautious. Not do not use them but be cautious. What do you think? Is that true? And, another question is, what do you think these people are going through right now with this time of increased stress, with this particular polymorphism?

Dr. Greenblatt: Yeah, I think the old school was with met-met, you have got to be careful, with any dopaminergic supplement or meds. And I think over the years I have just found what you had said. It is much lower dosages and much more careful monitoring, but there still is a place for supporting dopamine. So that has been very helpful.

Dr. Greenblatt: And I think the COMT, like some of the other SNPs MTHFR we were just talking about. So, our needs for most of the neurotransmitters are going to increase under stress, right? We know that we have higher needs for folate under stress, for the serotonin, dopamine, and all the other catecholamines. And the same with the comp to breaking down our neurotransmitters. So, stress just has such significant implications for kind of revving up the entire neurotransmitter system, which is going to pull for all the nutritional cofactors, and really deplete so many aspects of our physiology, without support.

Kara Ware: In any of your courses, Dr. Greenblatt, are you teaching how to use nutritional genomics in concert with the laboratory eight or nine tests that you use quite often with your patients?

Dr. Greenblatt: Yeah, absolutely. I think in each of the courses we talk about different SNPs. I think the MTHFR comes up very often when we have a psychiatric, educational platform. So, addiction,

depression, ADHD, the COMT SNPs come up a lot in the ADHD courses, the DRD2, and the ADHD courses. So, we have in our educational platform, we have speakers who just talk about genetics and mental health, and in my kind of diagnostic kind of review of the major mental illnesses, we always include what genetic vulnerabilities are important to look at.

Dr. Greenblatt: And it is not just the SNPs, as a psychiatrist taking a good family history, so we might not know your parents and your grandparents what their genes were, but we do know if they struggled with addiction or depression or anxiety or had suicide in the family. That genetic vulnerability is just another layer of this kind of prioritizing and understanding the treatment plan.

Kara Ware: And are those courses on your website?

Dr. Greenblatt: We developed an educational platform called Psychiatry Redefined, where we hope to educate clinicians on the kind of re-imagining psychiatry with this kind of nutrigenomics platform, nutritional, gut, brain connection. And so, it is psychiatryredefined.org.

Kara Ware: And this course would be so relevant for all functional medicine practitioners, we want to help people feel well, because when they feel better, then they are more likely to make more change. Do you find that to be true?

Dr. Greenblatt: Absolutely. I think it is important that our primary care docs, functional medicine docs, really understand it. One, because patients are walking into the offices looking for mental health support. Most of the mental healthcare is with our primary care physicians.

Nathan Morris: That is perfect-

Kara Ware: What course do you recommend them starting with if they go to Psychiatry Redefined? And we will add that as a link in our show notes. But what course would you recommend?

Dr. Greenblatt: I think the simplest would be the depression course. The depression course is a CME approved course, so they will be able to get CMEs. It's geared towards clinicians, and it covers a lot of the nutrients, trace minerals, and the genetics that we've just discussed. So, I think the depression course is the simplest, particularly for a general practitioner or someone beginning to look at functional medicine for mental illness.

Nathan Morris: That's fantastic advice. Actually, I will go look at it. I need some CME myself, so I would love to watch that. Dr. Greenblatt, I think you really pointed out that in times of stress a lot of things are turned on more or they are magnified, especially in the genetic model. With a, let us say someone like myself, with a Val Val, which means a lot of times you will see that as green on reports, it means I get rid of dopamine really well. And you also have a dopamine receptor issue. With the increased stress of what we have right now, is that one of the big drivers you think of addiction and some of the problems that we are going to see with this social isolation?

Dr. Greenblatt: I think it certainly could be very dramatic. I think as we experience this really unique trauma that is not acute, that is prolonged, we're all going to be experiencing the effects of this stress differently. And these genetic vulnerabilities are going to start playing out as you have described. So, somebody looking for that dopaminergic influence might find it from work, from relationships, from other things. And in this time of social isolation and stress, might need to find that through drugs of abuse or alcohol. And it is going to be a vicious cycle of, again, this genetic environmental dance with stress being the music, I guess, that gets louder and louder.

Kara Ware: Dr. Greenblatt, anything else to add to the summary just to leave with practitioners who are looking at how to begin to add nutritional genomics into their practice and make a difference?

Dr. Greenblatt: I think nutritional genomics is an incredibly powerful tool in our toolbox as clinicians. If we only look at a SNP and provide a supplement, we are going to miss the boat. But if we utilize this genetic foundation and integrate it into our treatment plan, particularly in mental health, it has really significant implications for recovery and remission. In psychiatry, we do not use the words of recovery

and remission, we just kind of use band-aids, but looking at the underlying genetics can give us a path towards recovery and remission.

Kara Ware: Okay, Nathan. So, Dr. Greenblatt did a really good job of summarizing why this is such a first important step when we are attracting new patients and re-engaging former patients to start with neurotransmitters. Because as we said, the twin engines of change are self-motivation, I want to do this, and self-efficacy, I believe I can do this, and to have biological access to the dopamine and serotonin is so important for patients to even feel like they can do this. Now, what happens if a patient does not have that variant TT of the MTHFR C677T? Where else can we look at in a report that would be meaningful?

Nathan Morris: I think if we want to keep it really simple, TPH2 is how we make serotonin from tryptophan. If we are not able to go from tryptophan to 5HTP, we need to know that so we can supplement appropriately and help them on that pathway to making serotonin. I think besides the C677T, I found that that one and the 1298, MTHFR 1298 can be additive. You may be heterozygous for both, so you would want to look at the 1298 as well. Of course, another huge thing that we really did not get into as much is the DRD2 receptors. That is the dopamine receptors. There are about three or four variants that are pretty well supported in the literature and knowing the status of, okay, yeah, I'm making dopamine or I'm keeping it around by having a Met/Met COMT. But is that dopamine doing what I think it is doing and knowing DRD2 status can be very, very helpful.

Nathan Morris: So, I think those simple polymorphisms can be a great place. Actually, this is the first place I look on the report when I opened my pure genomics is what's going on with their neurotransmitters because it teaches me or tells me how I may need to be working with this patient even in my teaching style because if they have Val/Val with the COMT and they have DRD2 problems, then I'm going to need to be writing everything down so they can review it after the visit. So, I think it plays a big role.

Kara Ware: Nathan, as you said in our first episode, you could have a 30-minute consult with a patient just to go over these neurotransmitters so that is a nice incremental step into a practice that's affordable and accessible and relatable for most people. So, let us take a moment though to have a practice update about Good Medicine On the *Go* since this is our real-time series. So, we have been working on your patient workflow, each step of your patient experience and what that touchpoint looks like and who are they going to be speaking to and what is the associated technology. Because of course, that will then drive our website creation to communicate that process and the journey they will experience with us.

Kara Ware: We have been talking to some collaborative care team members and having them sign HIPAA waivers and talking about contracts of course, 1099s so that your overhead stays low. So, and we have a lot more to discuss. But where is your head right now in this stage of development?

Nathan Morris: I am a lot less anxious than it was the first time you called me, and I think it's because I've always really bought into your model of creating that collaborative care team. I am going to have someone help me with my genetics quite honestly. That is going to be a big step that I help train and they do a phenomenal job. So, we're going to have it set up where my health coach, which is going to be you, thank goodness, is going to help with that first 15-minute interview, which I think is so important. It will be free. But it kind of weeds, well not weeds out, but it does. It gets the people that are maybe not going to be a great fit for me, and it finds the people that are going to be willing to make changes to their lifestyle, are going to be open to these avenues that we're going to explore with them.

Nathan Morris: Then they are going to from there have a health coaching session. They are going to have a genetic consult that we can start looking at that so they can start understanding before they reach me, and then at that point, I'm going to be able to really apply a lot of my functional medicine knowledge and cost them a lot less money because I'm not spending so much time with them but I'm letting other people help me with that. So, I feel a lot better about it. I think you laid out a nice plan for the patient flow. I think the patient flow was important to understand is we're setting this model up. What is it going to look like for a patient to come into our practice and what are they going to

experience and where are we going to put things in place that are going to help them to succeed and not feel overwhelmed?

Kara Ware: Exactly. This is such good planning of our back and front office systems and how they integrate and harmonize so that we can truly be in a partnership with our patients. I love it. So, let us go ahead and tee up the next episode with Dr. Yanuck.

Nathan Morris: Okay. So, Dr. Yanuck is a dear personal friend of mine, so I'm very biased. So, I'll just put that out there. But he is probably the foremost immunologist I have ever met who could actually teach through his course Cogence immunology. Immunology where I could understand it. I had three books of immunology sitting on my bed stand that just were not doing me a lot of good from osmosis. So, he really understands how inflammation, the role of genetic polymorphisms in inflammation and illness all come together. I am super excited about what he's going to bring to our next episode.

Kara Ware: All right, Nathan, we will be back next week.

Nathan Morris: Looking forward to it, Kara.