

Kara Ware ([00:04](#)):

It is so freeing for that patient who has struggled their entire life with this for them to suddenly start to gain control over their metabolism. Because these are the people who really get afraid of food. Because even such a small amount of food has such a big impact on them.

Speaker 2 ([00:23](#)):

Good Medicine On the Go with Dr. Nathan Morris and Kara Ware.

Kara Ware ([00:29](#)):

So, we are all used to the advice, eat healthy foods. But what if what is healthy for one person is not healthy for another? How do we discern this for truly personalized nutrition recommendations? How do genetics inform this discussion? Patient's top objectives are mood and weight management, what can be done when eating right and exercise is not working? In episode five, we started a conversation about the relationship between mood and food, these two top patient objectives go hand in hand, feeding on fear or feeding on stress.

Kara Ware ([01:07](#)):

We heard from Morgan Knull about the important connection between the genetic variation, FTO, that plays a role in appetite satiety and the two neurotransmitter SNPs, DRD2, the dopamine receptor and TPH2, the serotonin. If we are not addressing mood and the underlying genetic drivers that influence appetite and diminish satiety, how could patients even expect adhere to the advice, eat right and exercise for weight loss?

Dr. Nathan Morris ([01:36](#)):

Yeah. I love that advice, Kara, eat right and exercise. And what does that really mean? For so long, my own personal journey, I've also struggled with that generic advice, eat right and exercise. And the problem with that advice is that it tends to set us up for failure in my mind. Because we tend to look everywhere for what does eat right mean. Oh, here's this fat here. I'm going to do all fat. I'm going to eat fat so many days a week or I'm going to do this type of fasting or I'm going to do this juice fast or I'm going to do that. So, eat right really is this generic advice that gives no clue to the patient what that means.

Dr. Nathan Morris ([02:25](#)):

And so, it's really sets you up for failure because there's no definition, there's no point where you can say, "Okay. This is what eat right means for me. This is individually how I'm supposed to do it." And I think that was the biggest frustration for me is that I just bounced around depending on the next thing that came along. Even in functional medicine, we had these authorities saying, "This is the right diet. This is what you should be doing."

Dr. Nathan Morris ([02:53](#)):

And that really is frustrating to me because it depended on what I was telling patients to eat and as a practitioner, that was really frustrating because I didn't know. And it wasn't until I really understood

how neurotransmitters associated with our mood such as dopamine and how they connected in with our appetite and satiety genes such as FTO and MC4R until I understood this, I really struggled. And so, I'm really excited about this conversation today because we're going to get some insight into that.

Kara Ware ([03:30](#)):

So, how has that changed when now that you understand the genomics and where to look in a nutritional genomics report, how to personalize this for patients?

Dr. Nathan Morris ([03:40](#)):

Yeah. So, my own FTO and my dopamine issues really helped me understand, hey, you need to avoid sugar like the plague. One, because once I started eating sugar, its own the whole day, there is no stopping to the snacking. And I understood that. That's going to really drive my ghrelin and is going to decrease my leptin. And so, by understanding my own genetics, I really understood the leverage points that I needed to stop that in the snacking, which runs in my family, which of course genetics tend to run in families. And I see that.

Dr. Nathan Morris ([04:15](#)):

And so, that was really important. And so, in my own practice, when I started understanding myself and how important my neurotransmitters, if I could support my dopamine, if I could support with a higher protein diet, stop the snacking in between meals, then I understood that, hey, what's good for one may not be good for the other as you've mentioned earlier. So, the keto diet, it's going to work really well for certain people but people with a certain genetic SNP, which we'll talk about today, [inaudible 00:04:45] too doing a lot of saturated fat is actually going to drive their hunger and they're going to have worse outcomes.

Dr. Nathan Morris ([04:50](#)):

And that's why you have certain patients that we would see that would do really good with certain diets and then the next patient wouldn't then is be very perplexing to me and my practice as I kept cycling through these different diets, trying to figure out which one is the best diet. Well, the answer is none of them are the best diet. It is completely individualized. And you can determine that with a 23andMe test and running it through something like PureGenomics, all of a sudden you've got the power to help these patients understand what is a healthy food for them, why eating right is not good advice for them when they don't know what eating right is, so.

Kara Ware ([05:30](#)):

You mentioned ghrelin, the metabolic hormone, which is basically I'm hungry. So, that's a great place for us to start introducing what we're going to talk about today. We're going to take this appetite and satiety conversation one step further from our episode five with Morgan Knull. And we're going to take a look at really genetic factors account for 40 to 70% of the individual differences in body weight among Americans. And genetics really does reduce our trial and error.

Kara Ware ([05:59](#)):

No need to guess any longer when it comes to appetite and satiety or personalizing nutrition like you said, keto could be really good for one but not for the other. So, Nathan, tell us about these two specific metabolic hormones that we're going to be focusing on today. You mentioned ghrelin and I know the other is a leptin. So, tell us a little bit about how these metabolic hormones play a role in weight loss and how we're going to talk about the genetic variants that influence these metabolic hormones today.

Dr. Nathan Morris ([06:27](#)):

Well, we've already mentioned ghrelin and I mentioned the [inaudible 00:06:30]. That's how I had to remember it. I had to go back and say, "Okay. What is my mnemonic or what is my thing there?" But that hormone is the one that really drives the appetite. That's the thing to remember. And we really are in some way slave to these hormones. It's almost irrational what they can make you want to do and eat more. And ghrelin's that way and especially when it's not balanced by things like leptin. Leptin is that I am full hormone that's telling us that, "Hey, you don't need any more." And there's things that help with that, the type of diet we're eating, whether we're exercising, exercise is really helpful for leptin. That's why exercise not only burns calories but it also helps control these hormones. So, there's some connection there.

Dr. Nathan Morris ([07:14](#)):

So, these two are the ones that we're really going to focus on because I think along with the dopamine and the serotonin, which we've discussed in the past, these actually work in concert with these neurotransmitters to really almost... It's a not conscious desire in our patients to eat. And if we can start helping them understand that this lack of control, they see is an emotional or spiritual weakness is not really that, it's really being driven by these hormones, which is telling us what to do every day. And if we can give them that empowerment, then we're really going to have success in our dietary advice.

Kara Ware ([07:54](#)):

Absolutely. Genetics really helps us. I know as me as a patient, I understand my predisposed vulnerability and it offers patients solace and a lifelong journey of answering the questions, why can't I stop snacking and why don't diets work for me? So, Nathan, why don't you go ahead and introduce really the three genetic variants that we're going to speak about today that play a role in regulating these two metabolic hormones, leptin and ghrelin?

Dr. Nathan Morris ([08:20](#)):

So, we're going to go back to the alphabet soup of genetics. So, bear with us, we'll have these things explained in our show notes. But FTO, we talked about in our previous episode and it's connection with dopamine. But this time we're going to talk about FTO and its relation to ghrelin and leptin and also probably one of the more important genetic determinants of weight and childhood obesity, MC4R. This one's a little harder to treat. And so, this one really helps patients realize that exercise and the way they're eating and are probably going to be a lifelong thing.

Dr. Nathan Morris ([08:53](#)):

It's not going to be a six week thing. They're going to get the weight off and everything's going to be a hunky-dory. And then the other one I mentioned previously was APOA2, really has to do with our saturated fat intake. And the fact that when we get above 22 grams per day, we really see a large amount of weight gain compared to keeping it below that number of 22 grams. So, it's a really helpful SNP because there's a great intervention there by decreasing saturated fats.

Kara Ware ([09:22](#)):

Yeah. Dr. Penny Kendall-Reed, our guest today is going to talk about that, how the APOA2, the saturated fats is going to trigger FTO and MC4R that you just gave us a brief explanation of what we're going to talk about today. So, Dr. Penny, she tells us that food sets up a patient's hormonal distribution, energy levels, quality of sleep, inflammatory pathways, et cetera. And she talks about the role of the metabolic hormones play in appetite and satiety. And why learning these polymorphisms that Nathan just mentioned regulate leptin and ghrelin is another first step in transforming food as an obsession to food as a gift and a pleasure.

Kara Ware ([10:04](#)):

And so, making it reasonable for a patient to eat right. In addition to being a dear friend, Dr. Penny is on PureGenomic scientific advisory board and she is the creator of her own genetic interpretation platform, GeneRX. And she is the author of the recently published book, Fix Your Genes To Fit Your Jeans. Her book is a metabolic manual that provides specific nutrition recommendations for fats and proteins and carbohydrates and intermittent fasting and more to address the larger picture of the hormonal influence that prevents weight loss right after this.

Speaker 2 ([10:41](#)):

This podcast is sponsored by the Atrium Innovations, family of professional brands, offering evidence-based supplements, advancing scientific research and providing clinical protocols and technology to empower practitioners globally. Our brands include Pure Encapsulations, number one trusted and recommended brand by practitioners, Douglas Laboratories, Genestra Brands and LivingMatrix, the fastest growing digital patient management system for functional medicine.

Kara Ware ([11:15](#)):

There are a lot of variables when one talks about weight loss. Today as is our nature, we're taking a complex concept and distilling it down to identify what SNPs a practitioner can reference in a nutritional genomics report to continue addressing the appetite and satiety concern. It's important to listen to episode number two with Dr. Greenblatt and episode number five with Morgan Knoll, because these podcasts there were building on one another.

Dr. Nathan Morris ([11:45](#)):

Yeah, Kara. There are many steps to look at when personalizing nutrition like TCF7L2 and that's how we respond to sugars and carbohydrates and a gene AIPOQ, A-D-I-P-O-Q, that regulates a third metabolic hormone, adiponectin, that is our fat burning and thermogenesis hormone. We can't cover them all because it gets a little overwhelming but these are really important. And Dr. Penny does a great job in

her book of covering these. And hopefully we can get to these in subsequent episodes. But I think if we understand the things we're talking about today, that's a real good foundation for where we're going and personalizing diet and nutrition advice.

Kara Ware ([12:28](#)):

Dr. Penny, you have been researching this for a long time. Please give us a quick introduction to the metabolic hormones.

Dr. Penny Kendall Reed ([12:35](#)):

Really there's three main hormones that control our metabolism from a point of view of fat burning or the rate of the metabolism, if you will, to food cravings, to hunger. And those are those three hormones that you mentioned, the adiponectin, leptin and ghrelin. And there's all sorts of different genes that will code for how much of these hormones do we make and that's individual. And that will certainly impact why one person can easily have a tiny square of chocolate and say, "I don't need anymore," whereas the other person is consistently thinking about the rest of the chocolate bar that is in the room next to them.

Dr. Penny Kendall Reed ([13:12](#)):

Ghrelin means I'm hungry, leptin means I'm satisfied, I have enough fuel sources. So, how the body normally regulates those two is prior to a meal when our blood sugars are low, the stomach stimulates the production of ghrelin and that sends a message to the brain saying, "Okay. Let's go find that food." And normally, under normal metabolic control, those two hormones literally will feed off of our blood sugar levels in what we're eating but not so much with genetics.

Dr. Nathan Morris ([13:44](#)):

Penny, why don't you start off by telling us about the genes and polymorphisms that are influencing ghrelin and leptin?

Dr. Penny Kendall Reed ([13:51](#)):

FTO plays a role in the production of all three of those hormones. So, has a big impact on our metabolism and when you're variant, it'll do so in a negative way. So, the allele there, which is the variant allele will have more ghrelin production for a lower stimulus. So, they're more hungry thinking about food so much more, they'll have a lower leptin production. So, they don't get that satisfaction. They need a really large meal in order to get that satisfied I'm done feeling. And then when they do get any fat burning, it's at a much slower rate. FTO does not like simple sugars or saturated fats and that will augment the adverse ghrelin, adiponectin and leptin ratios there.

Kara Ware ([14:35](#)):

Okay. So, FTO influences all three metabolic hormones. And when you are a variant, you're more likely to be obsessed with food. And of course have an increased appetite and diminish satiety plus you burn fat slower. This is why a patient is always thinking about when they will eat again and struggles with losing weight. Even the sight of food can be enough to move someone to eat even if they just ate a full

meal. It sounds like too much sugar and too many saturated fats ignite this variant to drive patients back to the fridge endlessly.

Dr. Nathan Morris ([15:09](#)):

Yeah. Recommending paleo or keto without understanding the patient's FTO and the APOA2, how well they respond to saturated fats and the next SNP we're going to talk about, MC4R, how fats really trigger all three of these polymorphisms that play a role in appetite and satiety. Penny, can you tell us a little bit more about MC4R and how it affects leptin and ghrelin and the patient's behavior?

Dr. Penny Kendall Reed ([15:36](#)):

Absolutely. MC4R seems to kick in at a much younger age than FTO and certainly a lot more sensitive to saturated fats than FTO is as well. And that's why with the MC4R variance, there's actually a 43% increase in weight and obesity entirely independent of diet and exercise. They produce so much more ghrelin and so little leptin. FTO does as well but just not quite to the extreme that MC4R does. And MC4R has a big role in leptin and ghrelin. So, ghrelin, it is our hunger hormone. It's the hormone that says, "I don't have enough fuel sources in my body. So, go seek out food, fill up my fuel stores." And so, they're part of it is actual physical hunger but it's also food-seeking behavior. And this is where you're exactly right, it ties in with DRD2 because ghrelin will stimulate all of the dopaminergic pathways in the VTA.

Dr. Nathan Morris ([16:40](#)):

We learned from Morgan that dopamine and DRD2 dopamine receptor in particular plays a big role in appetite and satiety. Now, we've heard that ghrelin and leptin are also major effectors of dopamine that can drive food-seeking behaviors.

Dr. Penny Kendall Reed ([16:54](#)):

If you left me on my own device, I'd be in the fridge all the time. But so, because a high ghrelin will stimulate dopaminergic pathways, meaning it'll ask dopamine to be filled up when you don't produce a lot of dopamine already through your DRD2 gene or your ANC1 gene, then you already have less dopamine there to begin with and if you ask those pathways to be stimulated and they don't have the neurotransmitter to stimulate it from a genetic point of view, we're going to do it through a lifestyle variable point of view, which means your brain is just going to say, "The only way I'm going to get my dopamine up is if I start eating again."

Kara Ware ([17:34](#)):

Okay. What I'm hearing Penny is when a provider looks to a genetic report, it's not enough to just look at FTO or MC4R to understand eating behaviors, it's also important to look at their DRD2 to make sure their dopamine is also responding appropriately. If a patient is carrying multiple variants, their actions and demand for dopamine may need a multifaceted approach once again reiterating eat right is not good advice. There are potentially more steps we must take to help our patients.

Dr. Penny Kendall Reed ([18:05](#)):

When it comes to the body as you know, we can't separate out different systems of the body. We can't separate out metabolic from neurotransmitters, they're all going to interact.

Kara Ware ([18:16](#)):

So, let's talk about the practical advice for providers to help regulate patients ghrelin, their appetite hunger hormone and leptin, the satiety hormone. So, to change the obsession to food as a gift and a pleasure, how can we help our patients with the FTO variant regulate their ghrelin and leptin? We know these are constant snackers, who may also be seeking dopamine hits if they're a variant and their DRD2 SNPs, how do we give these patients hope for controlling their hunger?

Dr. Penny Kendall Reed ([18:47](#)):

FTO will also dictate how much protein we need per meal. And that's also really important. Because the variants, the alleles, they need a lot more protein than the people who are the [inaudible 00:18:59] that actually have the faster metabolism. So, using the dietary and the metabolic genes there again, really is that perfect winning combination for our patients. With the FTO, the variant position actually needs the highest amount of protein. And if they don't, they need about a one to 1.2 grams, mostly towards the 1.2 grams of protein for every kilogram of body weight or a 2.2 balance. And then, that gets divided into three. And that gives you your meals worth of protein. If you feed a variant FTO less protein than that, their ghrelin won't go down, their leptin won't go up. They're still going to be like, "Where's my fridge?"

Dr. Nathan Morris ([19:43](#)):

On a higher protein diet, those with the allele had greater reductions in food cravings at six months compared to those who do not have the allele. This means that those that have a one copy of the variant or both copy of the variants have a predisposition to responding well to a high protein diet, which I found to be very true for myself and managing weight. It takes a little while but it works. They also may experience weight regain if they go off the diet and lifestyle changes.

Kara Ware ([20:12](#)):

Yeah. I found that to be true for myself too, being FTO variant. So, let's talk about hope for the hopeless. MC4R, this SNP, if a patient carries this variant, they're constantly trying to find balance and they've more than likely tried everything without success. These are the patients who are constantly dieting and exercising with little weight loss. So, we learned that their ghrelin is increased and their leptin is diminished.

Dr. Penny Kendall Reed ([20:39](#)):

If somebody's a heterozygote for MC4R, it's an 8% increase in obesity independent of diet and exercise. So, the MC4R people, this is the childhood obesity. They were the kids that were really, really overweight. And then the patients who come through our office and they say that they're not eating very much and they truly are not eating very much but their MC4R's heterozygote or variant. And these guys, we have to use that Piper betle Dolichos biflorus acetyl-L-carnitine combination because we have to treat this from a supplemental point of view to alter those hormones. They will not do it with lifestyle

and diet alone. Leptin is a really difficult one to bring up from a lifestyle point of view. We really need to use some natural supplements there.

Dr. Penny Kendall Reed ([21:26](#)):

And some three really good ones that help to balance those metabolic hormones are Piper betle, Dolichos biflorus and acetyl-L-carnitine. Particularly the acetyl-L-carnitine, that is one that really starts to balance out leptin. So, leptin is like insulin, too much is not good, too little is not good. It's that Goldilocks position and the acetyl-L-carnitine will help to balance out the production of leptin and stop leptin resistance. Leptin really does not like snacking. So, the more snacking... Because every time we eat, leptin is released. So, if we eat four, five, six times through the day, we're releasing leptin four or five, six times a day, just as if we were to do that with continual release of insulin and we become insulin resistant, the same thing will happen with leptin.

Dr. Penny Kendall Reed ([22:17](#)):

So, leptin does not like snacking and it does like fasting. So, and that's, again we'll look at other genes like TCF7L2 and APOA2 to determine exactly how low that will trigger, certainly intermittent fasting, increasing exercises as well. But the big caveat there really outside of those lifestyle variables is altering those hormone production with a supplement. And it is so freeing for that patient who has struggled their entire life with this for them to suddenly start to gain control over their metabolism. Because these are the people who really got afraid of food. Because seeing such a small amount of food has such a big impact on them.

Kara Ware ([22:57](#)):

Okay. In addition to FTO and MC4R, APOA2, which has been mentioned earlier, also affects these metabolic hormones. So, what can we recommend for patients who have an APOA2 variant?

Dr. Penny Kendall Reed ([23:12](#)):

So, the variant for APOA2, they will actually increase their production of ghrelin, increase the amount of fat that is absorbed through the intestines and increase the production of LDL cholesterol as well as inflammation when they consume over 22 grams of saturated fat per day. Under 22 grams of saturated fat, that gene isn't triggered. It just stays quiet and they'll absorb the normal amount of saturated fat. 22 grams is really easy to reach. So, if we look at those ketogenic diets or bulletproof diets, they start their day with a coffee and they stick in an ounce of bulletproof or MCT oil or coconut oil, right there, there's 16 grams of saturated fat in that one ounce.

Dr. Penny Kendall Reed ([24:00](#)):

Then they'll stick in some butter or ghee. That's either seven and a half or eight grams of saturated fat right there. That one single coffee has tipped off the gene for the entire day. So, anything that they eat for the rest of the day, they're going to absorb that as fat and increase their ghrelin, increase their hunger, increase their food seeking behavior. And then don't forget, that's also going to tip off FTO, MC4R and now we start to see how all of those interact again together. And then below 22 grams of saturated fat for that gene, not a problem.

Kara Ware ([24:36](#)):

And if a patient does not have the risk variant for APOA2 Penny but they do have the FTO variant and our MC4R, would you still recommend reducing saturated fats?

Dr. Penny Kendall Reed ([24:47](#)):

I was still pulling the [reins 00:24:48]. So, for a heterozygote with APOA2 alone, I go up to 28 grams of saturated fat but then I'll pull them back down to about a 24 if they're a variant for an FTO or an MC4R. Absolutely.

Kara Ware ([25:00](#)):

This is exactly why genetics is so empowering. Again, it helps us understand what eating right is correct for the personalized nutrition recommendations for each individual. It really shows us that we can nurture our nature. It isn't one or the other. We have our DNA, which is our nature but we can nurture it to be able to express optimal function. I really love that what genomics brings to patients, that it's no longer just us beating up on ourselves.

Dr. Nathan Morris ([25:34](#)):

Yeah. That is such a gift to the practitioner because we can now really help that patient stop that terrible cycle of weight loss, weight gain, weight loss, weight gain. And actually, every time they lose weight and gain it back, they gain a little bit more. And patients see it as a flaw, Kara, within their own self wheel, their own emotional... And it becomes a part of them. And this really takes away that guilt that so many people feel because they can't lose weight. And so, I just love it as a practitioner being able to take this, what I think as the first place I usually go in my genetic report is I look at neurotransmitters and weight. Because as you said, that's really what a lot of patients are seeking right now. So, so excited about what we've talked about and the tools we've been given.

Speaker 2 ([26:26](#)):

And the beauty of it is that when you reset those three metabolic hormones, sticking to a diet is so much easier. Because all of a sudden, ghrelin starts to come down and you're not thinking about your fridge 24/7, your leptin starts to rise. So, you're like, "Hey, I'm good. I know I had that small meal and I'm good to go now."

Kara Ware ([26:49](#)):

So, today we explored the larger picture of the SNPs that influence the metabolic hormones, ghrelin and leptin. And the eat right on this certain diet is difficult without understanding the neurotransmitter and the genetic variations, FTO and MC4R that play a role in appetite and satiety.

Dr. Nathan Morris ([27:11](#)):

So, that leads us perfectly into what we're going to be talking about next, which is really interesting. Because just as the diet, because we never hear just eat right alone, we always hear eat right and exercise. And exercise is just like diet. If we don't give people the right type of exercise, which is huge, I mentioned that at the first of the show, that leptin, which is a really important hormone to tell us that

we're full or we don't have to eat as much is really influenced by a moderate amount of exercise. So, what is the right exercise that are going to help support these neurotransmitters and these hunger hormones that we just discussed? What exercise is going to help us gain muscle mass versus what exercise is actually going to inflame us and make us less healthy and start this inflammatory cascade?

Dr. Nathan Morris ([28:01](#)):

And I think that is just as important as the eat right advices. How do we exercise? So, we can do not just a dietary advice but we can also give exercise advice by looking at genetics, which I think is really empowering and really helped me understand that I didn't have to feel guilty about the fact that I hated running, that I hated long distances and then I'm more of a high intensity interval training guy. And guess what? My genetics really approve that out. And I lost weight and I felt better. So, really excited about our next episode when we'll be exploring this more fully,

Kara Ware ([28:37](#)):

And that will connect back to episode number three, immune insights when Dr. Yanuck shared the genetic variant IL-6 role and the inflammatory cascade. So, once again, find our show notes and educational resource links on karawarecoaching.com/podcast. While you are there, drop us a note and tell us what do you like? What topics would you like us to discuss next? And if you're ready to integrate PureGenomics into your practice, you can find a scheduling link on our show notes to schedule a free business integration consult with me. And so, you'll find all of that at karawarecoaching.com/podcast and we will be back in a few weeks.

Dr. Nathan Morris ([29:18](#)):

Looking forward to it, Kara.

Speaker 2 ([29:20](#)):

This is Good Medicine On The Go with Dr. Nathan Morris and Kara Ware. For more information on this podcast and to schedule a free business integration or nutritional genomics consult, visit karawarecoaching.com. That's K-A-R-A-W-A-R-Ecoaching.com.