

## March 2012 Issue | Deanna Minich, PhD, CN, RYT

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Welcome to *Functional Medicine Update* for March 2012. This month we're very privileged to have as our clinician/researcher of the month an individual who I think will speak to this long-standing discussion we've had within *Functional Medicine Update* that I call the food/supplement conundrum: How important is the composition of the overall diet in modulating metabolic function in such a way as to increase or decrease the relative risk of age-related chronic illness in comparison to the benefit or value of nutritional supplements that would augment specific nutrients? This is a very interesting dialectic to engage in because it's not an easy question. There are so many different variables at play that to try to make this overly simplistic and say food versus supplements would be to do a *reductio ad absurdum*—to really try to reduce things to first principles and lose the meaning.

### **Food versus Supplements: A *Reductio Ad Absurdum* Oversimplification**

The reason I say that is we now recognize within the field that as we are examining these associations and trying to demonstrate causality between a substance or an intervention and an outcome, or a principle and a causation of disease, then we have to take into account things like genotropic and genetic variability. We have to take into account the variety of environmental modifying factors that can serve as triggers. We have to look at specific temporal effects within circadian rhythms that can influence outcome that may, if we take a snapshot of data at the wrong time of the day or at a different time of day we might end up having a different picture of the physiological status of the patient. A simple example would be this: What happens if we were measuring random blood glucose levels in populations and we just happened to choose populations right after they had eaten (within two hours after eating a big meal) and we made that our assumption as it relates to the average blood glucose level in the population rather than taking fasted samples? I think questions like these become a very important part of how we piece together this complex puzzle, which ultimately leads us into decision-making in the chronic disease area. That is part of the broad topic that we're going to be discussing with Dr. Deanna Minich today--this interrelationship of personalized lifestyle medicine and nutritional intervention to both the prevention and management of chronic illness. Before we get into this discussion and the specifics, let's look at some general principles.

### **Defining Biological Response Modifiers**

Does our food contain substances that are beyond that which we would call protein, carbohydrate, fat, vitamins, minerals, essential amino acids, essential fatty acids, water, that serve as biological response modifiers? Now, what do I mean by a biological response modifier? The term really refers to substances that have molecular interactions with specific characteristics of our metabolic web in such a way as to modulate function and to create different phenotypic outcome. That's a long-winded sentence. What does it really mean? It means: Do we have biologically active substances within our foods, beyond that of the traditional "fabulous 50" essential nutrients, that regulate in some way the expression of our genes (i.e., nutrigenomics) to then alter metabolic function in response to environmental stresses? That's what's known as a biological response modifier.

Since the dawn of the science of nutrition, I believe we have recognized that food has multiple effects on human function at the whole-organism level. But for many years we didn't have the tools to be able to really evaluate specific components of the food, when broken down and isolated into their component parts, on how they mechanistically influence various aspects of function on the whole organism. Over the last 10 to 20 years the tools of molecular biology and molecular genetics, cell biology, and biochemistry have become more sophisticated, more refined, and more available for general applications outside of the specialized research labs of a few major academic centers. We are starting to really see an opportunity to evaluate some of these characteristics of foods from a different perspective: What are the natures of various substances within the food that may serve as biological response modifiers, and do different foods have different personalities as it relates to their biological response-modifying capability?

### **Food is Your Best Medicine, and Now We Have the Tools to Explain Why**

This obviously traces its lineage way back to Hippocrates, if you think about it—food is your medicine, and medicine is your food. Also Dr. Bieler's book, *Food is Your Best Medicine*.<sup>[1]</sup> What was not understood during those periods of time was exactly how substances within foods would regulate function and serve "medicines." That's, I think, a part of what is emerging now in this more recent age of nutritional research (nutrigenomics research), the mechanisms by which these particular substances that reside within various foods that we now call biological response modifiers and how they influence specific cellular function and specific tissue types to create specific cellular outcomes or functions.

#### *Red Yeast Rice as an Example of a Biological Response Modifier*

Let's look at a traditional Chinese medicine (TCM) as an example. It's a culinary nutritional substance used in traditional Chinese medicaments and cooking called red yeast rice. This is an interesting concept if you start looking at it from a whole-organism level. This is rice that has become moldy, basically, with a specific type of fungus that produces a red-colored metabolite, and so it colors the surface of the rice a moldy red. It's a specific strain of fungus, and it has a specific set of genes that encode a specific metabolic biosynthetic pathway that results in this series of compounds that are within red yeast rice (within the actual fungus itself), which have been found by phytochemists and medicinal chemists to be a member of a class of compounds called monocolins. So, monocolins are an interesting class of bioactive substances that have been synthesized specifically by this form of fungus that grows on rice and produces this red color.

What do we know historically about red yeast rice from a TCM perspective? First of all we know that in TCM the view of anatomy and physiology of the human organism differs from that of western medicine, and so the circulatory system, the vascular system, has kind of a different configuration, or at least let's call it a different symbology or representation, than it does in the western medicine. It doesn't mean that the heart and blood vessels are in different places; it means that they play different roles.

With that said, what we can say is that within the scope of a western analogy to Chinese medicine, red yeast rice historically has been found to be useful for conditions on a whole-organism level (functional conditions) that would tie to what we call (in the west) cardiovascular-related issues. For thousands of years, this empirical observational connection was known between red rice yeast and the nature of outcome of health in individuals, so it became part of this empirical pharmacopeia. Only recently, as I've indicated, have the constituents—the chemical constituents within red yeast rice—started to be understood as being these monocolins. And as individuals have studied monocolins in much greater detail, they found that they have unique biological response modifying characteristics.

In the west, one of the individuals who has taken this on as a focus of study is a colleague, and that's Dr. David Heber, Professor of Medicine, Chief of the Division of Clinical Nutrition and Director of the

Center for Human Nutrition at the University of California, Los Angeles. Dr. Heber has done work with his group on trying to understand the nature of the monocolins that are present in red yeast rice and their influence on human health and function. If you go back and look at his publications, what you'll find is back in the 1990s he started publishing a series of papers that started to evaluate the role of red yeast rice as a blood cholesterol-lowering substance in humans. He's done very detailed work correlating the monocolin content and the various constituents within the monocolin family (in other words, the specific chemical principles, like monocolin , for instance) and their relationship in consumption to the effects on blood cholesterol in humans.

One of the interesting papers in this series was published in the *American Journal of Clinical Nutrition* in 1999 and titled "Cholesterol Lowering Effects of a Proprietary Chinese Red Yeast Rice Dietary Supplement."<sup>[2]</sup> In this particular paper—it's a clinical intervention trial in humans—Dr. Heber demonstrates that when an individual consumes a set amount of red yeast rice that contains a certain percentage of these monocolins, it significantly reduced total cholesterol and LDL cholesterol and triglycerides as contrasted to placebo, and actually did so in a way that was comparable to some of the first generation statin drugs, which--as we know--were themselves first derived as fungal metabolites and were found to be cholesterol lowering as a consequence of what was proposed to be the ability of these statin molecules to block 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA-reductase), the rate-limiting enzyme step in cholesterol de novo biosynthesis.

So we were told that the cholesterol-lowering effects of statins (like, Mevacor/Lovastatin—the first statin that Merck brought to market), was a consequence of inhibition of cholesterol biosynthesis at the hepatic level. And it turns out, as Heber and others now have defined, that the red yeast rice monocolins have a similar effect on lowering the biosynthesis of cholesterol, and in fact these monocolins are chemically identical (some of them) to the first generation statins (the Mevacor/Lovastatin-type molecule).<sup>[3]</sup> And that led, as you may know, to a very, very big point in law, where Merck took exception to nutrition supplement companies that were selling red yeast rice as a cholesterol-lowering nutritional substance because they said that some of these bioactive molecules were identical in chemical structure to the patented structure of the statin drug (Mevacor). The history of this is quite interesting because you probably recognize that at first this was upheld (the Merck contention) and therefore there was going to be a prohibition of the availability of red yeast rice to be sold as a nutritional agent. And then that was contested in federal court by a manufacturer of a red yeast rice dietary supplement and the Merck judgment was overturned, and that was kind of a vindication for nutritional substances being able to be used as bioactives derived from food and spice sources. And then, to make the story even more confusing, there was subsequently another intervention at the court level, which once again went back and reconfirmed Merck's supremacy in this area. So this became a very cloudy area: When is something a drug and when is something a food? That was back in the early 2000s.

Since then, what has come to be recognized is that the Chinese red yeast rice story (the bioactives of monocolins) is really just the tip of the iceberg. There may be thousands of molecules that are biosynthesized by plants and proteus that are biological active and have been used historically as foods or spices or condiments, and have tissue-specific effects, just as we saw with the monocolins in red yeast rice. A whole array of papers have been published, such as "Anti-inflammatory Properties of Culinary Herbs and Spices that Ameliorate the Effects of Metabolic Syndrome."<sup>[4]</sup> This was a recently published paper in the journal *Maturitas* that demonstrated that there are many, many different types of foods and spices and herbs that modulate inflammatory mediators, such as nuclear factor kappa B (NF-kB) and

peroxisome proliferator activated receptor gamma (PPAR $\gamma$ ), ultimately signal to the genes inflammatory signals and up-regulate the expression of cyclooxygenase genes and all those kinds of factors we're well aware of in the arachidonic acid cascade. They serve as anti-inflammatory modulators of the gene expression of these inflammatory downstream mediators.

#### *From Single Ingredients to Whole Diets*

We also recognize that there is a whole array of papers and studies that have been done looking at diets rich in fruits and vegetables, and how these diets are known to suppress blood biomarkers of metabolic stress in relationship to insulin resistance, metabolic syndrome, and Type 2 diabetes. An interesting paper on this was recently published in *Preventive Medicine* in 2011, about outcome of biomarkers as it relates to the consumption of diets that are rich in fruits and vegetables and have these bioactive components.<sup>[5]</sup> An extraordinary review paper appeared in *Nutrition Research Reviews* in 2012 titled "Health Protective Mechanisms of Whole Grain Cereals: What is Beyond Fibre?"<sup>[6]</sup> This paper looked at not just the vitamins and minerals that are in whole grains, but also the different bioactive compounds that are able to modulate cell signaling and gene regulation, including things like sulfuric compounds such as glucosinolates, lignan, phytic acid, polyphenols, the whole family of what you might call the lignan-related or hydroxylated flavone families that all serve as very important regulators of function of how genes are expressed.

Then we can look at things like chronic kidney disease. If you look at fruit and vegetable diets it is an alkalinizing diet, it contains very high levels of various nutrients, including essential fatty acids, minerals, and vitamins that help to improve kidney function, and it contains a whole array of these bioactive phytochemicals that are in certain plants that help to reduce inflammatory conditions and improve function at the kidney level. If you want to look at a good review of this, *Kidney International* in 2012 published a nice review of this work.<sup>[7]</sup> This article is about how the key to halting progression of chronic kidney disease might not be in the pharmacy but rather in the way that we eat in the marketplace (foods).

So there is something very dramatically valuable about foods and the array of these bioactive ingredients they have which may differ from that of just single vitamins, single minerals, or single ingredient nutritional supplements. It certainly doesn't mean that nutritional supplements are without value. What it means, however, is that they play a role within the context of the full diet and the genetic uniqueness of that individual, and how that expresses itself, then, into function.

We're now going to move to a discussion with Dr. Deanna Minich, who I think is an expert in this whole area, to kind of explore this in greater detail, and look at this personalized lifestyle medicine/bioactive ingredient in food relationship—this symphonic relationship that people share with their food that orchestrates the function and ultimately their health and disease patterns.

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### INTERVIEW TRANSCRIPT

Clinician/Researcher of the Month

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This discussion is with someone I would consider to be one of the world's experts in the application of personalized lifestyle medicine through the lens of nutritional therapeutics and diet therapy. I'm speaking of my colleague and friend Dr. Deanna Minich. Dr. Minich, for those of you not familiar with her background, is a trained nutritional scientist. She has an undergraduate degree, a Master's, and a PhD all in the area of nutritional science. She then worked in one of the major food companies as a nutrition professional. She went on to become certified as a Fellow of the American College of Nutrition and a Certified Nutrition Specialist. She brings, then, a body of knowledge both practical, from the commercial side, but probably most importantly, practical from the food nutrition side into the development of successful programs to implement personalized lifestyle medicine. She is really a world's leader in the whole area of phytonutrients and how they are applied, and the role that they have in therapeutic nutrition intervention. She has been an author of reviews as well as research articles on the development of food plans, and is really one of the architects, along with Dr. Kristi Hughes and Lyra Heller, in the FirstLine Therapy food management program at Metagenics.

Deanna it is wonderful to have you as an expert on Functional Medicine Update. I've looked forward to this for years. I think it is the perfect time to bring your expertise into this field because lifestyle medicine is getting, finally, the marquee publication visibility I think it deserves in attempts to combat this rising tide of chronic disease.

Maybe you could start by telling us a little bit about how your personal journey took you into the area of nutritional therapeutics and food plan management and development.

DM: I'd be glad to do so. And I just want to say, Jeff, it's such an honor to be on Functional Medicine Update. I follow you very closely, as you know, listening in my car on the way to work, and it's just amazing to have this opportunity at this time, so thanks for having me on the program.

My personal journey with food and eating I would say started when I was very young. I often tell people that I became a nutritionist at the age of nine. That was partly because of my mother and my upbringing. When my mother was pregnant with my brother, her third child, she really became invested in what the whole family was eating. She really started to read labels. She started to make her own food from scratch, everything from yogurt to bread to just really unique dishes. I remember this was a very traumatic thing for me growing up because I would be bringing strange lunches into school. I remember being on Girl Scout trips where I had to bring my own food all packaged up. I couldn't partake in kind of the campfire s'mores and all of the other fun activities there. Food and eating was a little bit of a jolting experience for me when I was very young. I wasn't able to see outside of the bubble that my mother was doing something really good for us. So as I evolved into my teenage years kind of continuing on this track of really healthful eating and getting into my own issues, I would say, as it relates to more emotional eating and really struggling with eating certain foods and having lots of guilt.

As I went into college, what I noticed was that I was really gravitating towards the area of medicine and science, so really thinking about the body from a physiological perspective and really dismissing the food aspects that my mother had brought us all up with. By the time I was in my junior year of undergrad I was

ready to take the MCAT. I had taken all my pre-med courses and I was working every single summer during my breaks at different medical offices. I was a candy striper in a hospital when I was a teenager, so I really had more than just a theoretical perspective as to what medicine might be about, because I had experienced it in every opportunity I could take. And also, in our family we had lots of different health issues. At the age of twelve I watched my mother and father really nursing my grandmother to health in the best way that they could; she was dying of cancer, of breast and bone cancer. So I was all set to go to medical school, but after this one summer working for a cardiologist in Chicago, I had this revelation: "I can't do it. I can't go to medical school." Because what I was seeing is that it is really an all-or-nothing path, and it was really a path that was directed down this trajectory of writing prescriptions. I remember being in there with the doctor, with the cardiologist, and him not even really looking at the patient, writing a script within probably about five minutes of the conversation, and I just felt: "That's not me. I can't do it." I'm an all-or-nothing person and I felt: "I can't go down this path of doing this kind of cookbook way of working with people and treating them."

#### Medical School was Not the Right Path

So, at this point, I really had to make a decision: Is it medical school or is it graduate school? I started exploring a little bit more and I realized I wanted to do something more preventative rather than treatment-oriented, so I decided to go to graduate school, and I went to the University of Illinois at Chicago.

#### Postgraduate Work and Research in The Netherlands

I signed up for a program in human nutrition and metabolism, working with Dr. Phyllis Bowen, who is, in my opinion, really a leader in the whole area of carotenoids. I was not only a teaching assistant, but I was also a research assistant and I got to do some fun studies with lycopene and beta carotene. That was very stimulating. At that point it wasn't as much clinical as it was research-oriented. After three years, I finished my Master's degree and it was really a revelation for me and I decided I needed to go on. I was thirsty, I was hungry for more of this information. I decided to embark upon a PhD program, and went to The Netherlands for this. I went to the University of Groningen, which is up in the north of Holland, a small town. What many people don't realize about The Netherlands is that really their science is impeccable, so they've got many different universities, one of which is Wageningen. It's very well known in their agricultural sciences.

I joined a group that was focused on human nutrition and metabolism specific to pediatrics and also specific to fat metabolism in the body. My PhD mentor was HenkJan Verkade. He's a medical doctor (a pediatrician) and also a PhD. He's brilliant. He's just like you, Jeff. He's really an integrative thinker. He synthesizes the literature. He's always asking the tough questions. I had the privilege of working with him for four years between 1995 and 1999, working on animal models up into really full-fledged clinical trials with babies with cholestatic-type of conditions, and also children with cystic fibrosis. We were trying to find optimal nutritional regimens for these children because their absorption of fat was impaired. So this is where I started to see the phytonutrient aspect during my Master's degree training and then I started to see this whole evolution of essential fatty acids and what that could do for the body on many levels.

#### Work in the Food Industry

As you mentioned, after that I went into the food industry—first the medical food industry working with Dr. John Cooke, who is a cardiologist. He had a wonderful product called the HeartBar(R) for peripheral vascular disease. As many people may or may not realize, a medical food is a specific nutritional product that is designated for a particular clinical condition. So in this case it was really looking at peripheral vascular disease and we had a number of different nutritional agents in that product.

From there I thought: "Well, wouldn't it be interesting to move my way into a larger food industry to see what I can do to change eating on not just my own community level because I was really starting to get

into this, but also from an industry perspective?" I joined a large food manufacturer in April of 2000, and I have to say it was pretty tough. It was enjoyable because I really got into the guts of the food industry to see what they are about, and as I always tell patients, food companies are going to make what you buy, so really the power is in your hands if you want to make a change. So that was a great experience. I was a nutritional expert for many of the different brand groups and I got to work on organic food brands as well as mainstream brands, and I even was active in doing clinical work.

From there, I really started to get into the clinical aspects. I was also working in private practice at that point, and I had started to use a number of Metagenics products, actually, and really found that they were intriguing, that they were working in patients, and this opened my perception into a whole new view of nutritional medicine, and I was really looking at nutraceuticals and medical foods much more closely.

JB: I think that is a model for the perfect background of a professional qualified to deal with the broad-based issues that surround personalized lifestyle medicine—everything from the genomic side, the biochemical side, metabolic side, and human behavior side, because that is, in the end, where the tire meets the road: what people will do and whether they'll comply and adhere with certain programs. Your role now is the Vice President of Scientific Affairs for Metagenics and you are really one of the key people in developing the clinical applications of much of what we're working on in discovery and interfacing that with the FirstLine Therapy (FLT) personalized lifestyle medicine program. It sounds like you couldn't have found a better match to your background, talents, and expertise with your present professional challenges, which leads me then to the question of what you have learned and now kind of taking many of these things gained through your training, your background, your experience and taking them out into the field with patients and practitioners who have different backgrounds, different expertise, and different needs, and different responses. What have you seen through the multiple clinical trials and the interactions you've had with people over the last nearly 10 years?

Teaching Personalized Lifestyle Medicine Around the World

DM: Yes, it's been a fabulous experience. As you alluded to, in my role what I am able to do is to talk with doctors and practitioners worldwide. Just this year I was in South Africa, Mexico, Australia, Taiwan, and London talking with thousands of practitioners and really getting to not only educate them on clinical protocols, but also to hear about their challenges and their different approaches, because with functional medicine the way I see it there are really many paths up the mountain. Every patient that comes in is very unique, and you can have as many unique approaches as there are practitioners probably. So I've really learned a lot, and what I'm also able to do is not just speak from clinical experience from working at the Functional Medicine Research Center, but also from doing clinical trials and being involved with the research aspects, which really brings me back to my graduate school days of looking at nutritional medicine in a very structured way, and then having publications so that we can create more credibility as it relates to these nutritional medicine protocols. I think that's really important to get the word out.

So I've learned a lot, and what I can say from working with Metagenics over these last ten years is I'm starting to see a percolation of interest in many different circles, and I do think the paradigm is changing under our feet. I'm excited, because as we have seen in the *New England Journal of Medicine*, we're starting to see in *JAMA* now, there is discussion about lifestyle medicine: What is lifestyle medicine? How do we educate physicians on lifestyle medicine approaches?[8],[9] So I feel like we are really in the sweet spot of really catapulting forward into this change.

Word Choice is Important: Diet versus Food Plan

JB: One of the many things that I think is of note that you have accomplished over the last years is the incredible development of this low glycemic load modified Mediterranean food plan. Through your education of me I've learned not to talk about this as a diet but as a food plan. I think it is important for you to help us understand the distinction between a diet, which is a four-letter word, and a food plan, and

also, what is this low glycemic load modified Mediterranean diet that you and Barb Schiltz have developed and have published ?[10]

DM: The “D” word—diet, the four-letter word—and I’m glad that you’ve been consistent about using the food plan language rather than diet. I think much of how we effect change in patients comes through how we language things. We could say to a patient: “You have metabolic syndrome” or “you have a precursor condition that will lead you in the direction of type 2 diabetes (something like ‘pre-diabetes’).” So I think language is really important, and I think when we think “diet,” as Brian Wansink has said in his book *Mindless Eating*, it’s like “die with a ‘t’ on the end.”[11] People think of deprivation, they think of something temporary, and so they can’t wait to get off the diet. And when they are off the diet, their way of eating can be radically different than when they were on the diet. So then you have these huge extremes that happen, and that can really change us not just physiologically but also psychologically. I think it is good to go into a lifestyle change program with the idea that this is really for your lifespan, and we’re making small incremental changes, whether we’re moving like a snail or we’re moving like a grasshopper (kind of jumping forward), these are changes that are meant to stay. So, yes, whenever we’re working with patients, what we like to say is “food plan” rather than the diet word.

#### Making the Mediterranean Diet Even Better

Actually I really give lots of credit to my mentor, Barb Schiltz, who worked in the clinic for 10-plus years and together with Dr. Dan Lukaczer came up with the FirstLine Therapy food plan. And the FirstLine Therapy food plan really has lots of different elements. At the heart of it, it is really based on a low glycemic way of eating, which is really important for many different chronic conditions. We focus a lot on cardiometabolic syndrome within FirstLine Therapy, but really it’s so good for whether it is cardiovascular disease, cancer, or developing signs of insulin resistance, so it really fits a whole spectrum of different conditions. And then as an adjunct to that, as we went on in our research we started to look at all of the publications coming out on the Mediterranean diet. In my review of the literature, I would say that the Mediterranean diet is probably the most studied diet. If you go PubMed and you just type in “Mediterranean diet” with quotes, you’ll come up with thousands of articles. In fact, there was a study—I think it was published in the *Journal of the American College of Cardiology*—looking at a meta-analysis of all of these studies in thousands of different individuals following this way of eating and showing that it is very compelling for metabolic syndrome, cardiovascular disease, and even mortality.[12]

As Barb and I were going through the creation and evolution of this FLT food plan, what we noticed was that the Mediterranean diet really, in our eyes, wasn’t perfect because it was too high in carbohydrate and in a lot of the grain-containing carbohydrate. What we decided to do was to modify the program to incorporate a lot of the phytonutrient density aspects of the Mediterranean diet, but then to take out a lot of the high gluten/high carbohydrate aspects. So really the FLT food plan is more of a Mediterranean diet “style” rather than being a pure Mediterranean diet. We’d like to think that we made the Mediterranean diet even better. And also there have been publications talking about how certain foods on the classic Mediterranean diet—things like pizza and other carbohydrates—may be higher glycemic, so we had that concern as well. The modified diet is really low glycemic, it’s Mediterranean-style, high in phytonutrients, and what Barb would tell you if you were talking with her right now is that it is very low in sugar. She feels very strongly about the sugar aspect—that we get too much sugar in our foods—and so it is really about having the patient become aware of all of the hidden sources of sugar in the food supply, and teaching them to read labels, and really to become aware of that.

JB: I think that’s a magnificent description, but there might still be—in the minds of our listeners—some confusion as to how they differentiate a diet from a food plan. I know you’ve done some studies on weight loss and calorie control and so forth that maybe would help our listeners to understand the

difference between a food plan and a diet.

#### Mixing Art with Science

DM: Yes. I would say, in my experience, the way that we use a food plan in the clinic if we are not doing a clinical trial but we are doing more of a case study, where it is more of an individualized approach to working with a patient, is they are really not on this program for any set duration of time. What we really want to do is change their eating. Maybe a patient is not ready to make the leap into working with the full-on FLT food plan as we have it, so we will kind of inch into working with them. I remember many times just working on this: How do we get more vegetables? And then finding creative clever ways to do that and we would also look at food diaries. What I think is really important is food color. We are really moving away from the “analysis paralysis” aspects of eating and looking at calories, looking at grams of protein, carbohydrate, and fat, really moving them into this line of thinking: How do they feel when they eat certain foods? What are the colors they’re getting? And instead of taking their diet diaries and analyzing them, looking at the grams of all of the macronutrients and all of the vitamins and minerals, what I think is one of the best ways to promote patient compliance is to take a package of colored markers and to circle all the different colors in their foods, in what they are eating (and that would be natural colors—that wouldn’t be things like M & Ms or other things that are artificially colored). We can see from the get-go what they are getting. Are they getting the rainbow variety? One of my other favorite tools when doing a food log is to fold the page in half, and on the left, be writing the foods they are eating, and then on the right, how they’re feeling—what types of things are going on for them throughout the day, are there certain stressors, and if there are certain stressors, how does that change their eating? That really gives me a great palette to work with as we have the therapeutic encounter because really then it is not just about the dietary aspects, right? It’s really more about how do they feel, what do they notice in their bodies, what’s changing, how’s their energy level? They start to develop an awareness of how their mood and food work together.

JB: It sounds to me like you use a lot of terms that interrelate to the concept of the art of living. It is very interesting—knowing you—that you are this interesting bicameral mind that’s really got the reductionism on one side of science and the synthesis of art on the other. You are an artist. I’ve seen your art and it’s beautiful and you bring that into your work and into how you language things (the use of a word like “palette” for instance, and use of marker pens with colors to indicate the diversity of the rainbow of food). When you distill it down, how does that all relate to communicating change in ways that people understand, so you’re an effective guide/counsel in personalized lifestyle medicine transitions, and secondly how does that relate to ingredients, or let’s call it density, of phytochemicals in food to ultimately what a person is eating?

DM: That’s a great question. Yes, I think it’s important to bring art into the science and to really create this hybrid. When you see patients, you’ve got lots of different personalities and certain people will resonate with certain things. Some patients are clearly more structured than others. For those who aren’t as structured, what I think is really fun is to go down the path that’s a little bit more artistic and to talk more about the relationship with food and eating rather than get bogged down in the details of all the different nutrients that they may not be getting because they may not be hearing that information. In my opinion, I don’t think the patient needs to know all the intricacy of what all those color compounds do, but I do think it’s important for practitioners to be aware. It’s really interesting because there have been lots of different reports on what colors people are getting too little of, or how much we are consuming in the way of produce, things like fruits and vegetable. Many, many people are not meeting their requirements for the different colors, especially for green, and blue, and purple. How does that translate into the body in terms of the effects that these colors are associated with? I think if you were to ask me this question 15 years ago, probably the simplistic answer would be something along the lines of just

talking about antioxidants, and how we need these colored compounds because they work like antioxidants in the body, and we've got all this oxidative stress and we have to somehow quell these free radicals. That is what we knew at that time and that is what I knew this during my graduate days working with carotenoids--that these were very potent antioxidants, so I might have given you that answer then. But really in the past 5 to 7 years, we've been seeing a whole flurry of articles coming out talking about the pleiotropic effects of these different phytochemicals and what they are doing in the body. What I often say to patients is that these colored compounds are not just antioxidants, but they are physiologically being routed to certain parts of the body for certain functions. What we know from Dr. James Joseph's work at Tufts is that—as an example—blueberry compounds find their way into certain parts of the brain that are responsible for learning and memory.[13] We also know that things like curcumin can also be very protective in the brain, preventing the build-up of things like beta-amyloid.[14] I think that's pretty interesting, because why does the body shuffle these different phytochemicals to certain parts of the body? What are the functions they are serving, and what are their roles on a cellular level? And what we see, if you start to scratch the surface of this research, is that these nutrients, or really these phytochemicals, are having very specific effects at the level of the cellular communication. This would be things like protein kinase transmission, and really conducting a signal throughout the cell.

Jeff, I really like it, because for many years you've been talking about how food is information and it is really true because if you look at the literature, and even in our own research at Metagenics, we're seeing that a lot of these compounds within food—these colored compounds—are changing the cellular communication, and they are changing it in a beneficial way, so almost getting that cell back into balance so that this becomes more like a system-wide effect: we move from the cell into kind of a ripple effect of restoring function throughout the body.

JB: When we look at the interesting epidemiological evidence around fruits and vegetables, what you're saying really starts to have some fundamental “a-ha” understanding at a mechanistic level because we have known for years, without a really good explanation, that cultures or groups of people who eat higher levels of fruits and vegetables in their diets have a much lower incidence of virtually every chronic disease, even down to the Seventh Day Adventists living in Loma Linda, California. They are neighbors of people in the Los Angeles area—they all share the same water and air and freeways--but yet they have a much lower incidence of all sorts of chronic diseases, including diabetes and heart disease. People have associated that with that group's increased consumption of fruits and vegetables, like we see in other studies (epidemiological studies) around the world, but no one has ever really been able to provide an effective mechanistic link between cellular physiology and those epidemiological observations. I think the article you authored in Nutrition Reviews, which was “Beyond Macronutrients,” talking about the nature of phytochemicals as it relates to insulin sensitivity, that model—to me—is a remarkable opening up of a new paradigm in nutritional science taking us beyond the age of vitamins.[15] That's how I abstract what you've said. Can you take us down that road a little bit?

#### Phytonutrients and Insulin Pathways

DM: Sure. Especially even within my nutritional research training there was so much emphasis placed upon the macronutrients, and I think it is really starting to emerge that the phytonutrients—even though we really only get such a small amount—are really having a huge impact. In that article, which was in Nutrition Reviews in 2008, what we did was essentially look into a number of the different phytochemicals and how they impact insulin pathway targets. We looked at everything from resveratrol, to quercetin, cinnamon, and green tea. These are a lot of the things that are already used in traditional medicine, but we wanted to understand the molecular biology as to how they work at the level of the cell. In this review article, we essentially put together a lot of the research that showed that many of these different actives tickled and modulated in some way the insulin targets, things like insulin receptor

substrate 1, PI3-kinase, PKC, glycogen synthase kinase—all of these aspects of communication within the cell that are all related to the effect of insulin coming into the cell receptor. If we look at how these agents can beneficially impact things like metabolic syndrome and insulin resistance, it seems to be a likely link. And even in our own research at Metagenics, we have tested a number of these different plant compounds, and there have been a couple of stars that have risen to the top. What is really interesting is that we were able to show, in a kinase model in addition to a cellular model, that these plant actives can change up the cellular physiology, and then we took that knowledge and moved that into a clinical trial in which we saw dramatic effects in the group that was given the targeted phytonutrients. We looked specifically at individuals with metabolic syndrome. We leveraged the research from our cell animal work, and we put those actives into a medical food, and essentially saw a 43 to 44{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} reduction in markers related to metabolic syndrome, which is really phenomenal. You don't typically see that in the literature with different dietary approaches.

JB: So when I look at this, what I'm starting to recognize is when you marry the food plan concept together with specific foods that are low glycemic load with a variety of colors, meaning rich in vegetable and fruit products, and then you start to tie that with the emergence of our understanding of nutrigenomics, molecular-based nutrition, and ultimately even nutriepigenetics, that what we're really starting to see is a whole new paradigm that's emerging in how to personalize food plans for individual needs, which then takes us into functional nutrition and its application to functional medicine. Have you ever thought of yourself as the inventor of this concept, because it's a pretty powerful evolving model?

DM: It is a very powerful model, functional nutrition is. And it's not that one food plan fits all, by any means. My experience has been specifically in the area of cardiometabolic syndrome, but we're starting to extend our research into other patient groups as well, so looking specifically at groups that are relatively healthy—maybe have some metabolic disturbance—but they are overweight, and what kind of program would be suited for them? I do think that looking at the whole lifestyle and really starting with the bedrock of food...the way I think about it is really food first, and correcting of signals on a very large level. If you think about what the average American eats in a year, it is something in the neighborhood of 2000 to 2500 lbs of food, so that's a lot of information running through us. It is really important, I think, to focus on the food first and to correct the signals at the level of the cell, which you'll start to see in the physiology and in the expression of the patient's symptoms. With the FLT food plan, which is what we've worked a lot with in the clinic over these past years, we've seen incredible effects, and in fact the effects have been so dramatic and so pronounced that as we went further into studying our different targeted phytonutrients, we didn't really think we could do much better than the FLT food plan for individuals with the metabolic syndrome. But to our surprise, adding in these targeted phytonutrients, things like hops, rho iso alpha acids, things like proanthocyanidins from a tree that grows in Africa and Asia by the name of *Acacia nilotica*, what we've found is that we can really get those signals corrected. Of course, we did have exercise built into one of these studies as well because that's going to help to improve insulin sensitivity. So it is really a lifestyle—a programmatic—approach to chronic disease and, in this case, metabolic syndrome.

Functional nutrition is really like a kaleidoscope: we're not just focused on one aspect, one condition, although one condition like metabolic syndrome really does radiate out into many other chronic disease conditions. In our clinic, we've just completed a study over the course of 12 weeks in which we were looking at overweight individuals. We tried out a different food plan program, and we're right now in the midst of looking at the results, but preliminarily they look just fabulous. Can we keep these effects alive in the patient over a longer term? I think that is really a point of interest as well, because in a lot of these different studies, we see in everything from the Atkins program to Weight Watchers to Jenny Craig, all of

these different types of diets, which are—again—short term, patients can lose weight, but then the questions are: 1) Do they keep the weight off?; and 2) Do we see an improvement in these biomarkers over the long term? Many times we get so focused on numbers like weight and weight loss that we really need to look at the shifting sands of the different physiological biomarkers within the body.

JB: I think you have led us to a really great place to kind finish our conversation because for many individuals it is not just the treatment of a disease (that's the negative, fear-based model), but rather it's the promotion of successful aging, and that's more of your positive, outcome-based expectation. What we're looking for is how do we achieve, in an individual, the rectangularization of their survival curve, compression of morbidity, and letting them live with good health out to the limits of their biologically determined lifespan? When we start asking that question it leads us to others: Do these types of dietary or lifestyle changes do things that epigenetically, or at the molecular level, modulate the aging process? Is there something that goes on that really can help promote successful aging? Are we protecting the most valuable legacy we own, which is our book of life in our genome? I know you've been engaged in some work in those areas as well, as it relates to genomic stability and to successful aging. How does this concept lap over from a disease focus into a successful aging focus?

First Wellness, then Graceful Aging

DM: I'm so glad you asked that question because that's definitely something I feel really passionate about. As a practitioner, I think we definitely do look at biomarkers and we're trying to move patients from chronic disease back into a state of wellness. What I also think is interesting along that spectrum is to move the patient into optimal health and then ask the question: How do we help them to age gracefully? It's not that we can anti-age or prevent aging from happening, but how can we get them a better quality of life? This conversation actually brings to mind a patient I recently had in the clinic. Dr. Lamb and I had been seeing this patient for I think about a year. When he first came in I remember he was a little bit worried. He had just been diagnosed with type 2 diabetes, and at the time he was 61. He was feeling kind of depressed about it, and, just kind of thought this was the end. I clearly remember saying to him: "You know, you've got 30-plus years of your life. We really need to embark upon a whole new lifestyle medicine way for you." And he said: "Deanna, 30 years? That's a long time." He said: "I've never thought of myself living so long. Once I knew that I had type 2 diabetes there was no way that I would ever think that I could live another three decades." And I said: "Absolutely. We're going to work on this. We're going to work on how you feel and really get you back." Just recently we had a visit with him—I think about a month ago—and he said to me: "Deanna, I think I got my 10 years back." He feels much more vital. He feels energized. I think it's exciting because even though I don't talk about things like genomic stability, or heart rate variability, or a lot of these different aspects of aging, what we clearly see is that his body is changing. His mind is changing. His attitude is changing. And this is just so uplifting for me because within one year's time for him to say that he got 10 years on his life, that he really feels like he's made an impact, his body composition has changed, his way of eating—he's been so motivated and now even his wife, his family, has seen the change in him and is wanting to adopt more of what he's doing. And they were all very reticent in the beginning. You know, things like this, I'm sure your listeners see many times when they start to follow this type of program, but when I think of aging on a more scientific level, as I've been working with patients and reviewing the literature, at the end of the day what I really have seen is that it is all about flow and fluidity. If we're talking more in the artistic realm and more metaphorically, then it's about keeping the body moving and fluid and flexible. There are common things in the literature, things like neuronal plasticity (the flexibility of neurons). How do we keep things moving in the brain and have complexity of the synapses all communicating?

And then there's heart rate variability. The more your heart can be variable in its heart rate pattern, the better the chances are for things like reducing cardiovascular disease risk and also reducing mortality. And then also the gut and thinking of the whole aspect of metabolic inflexibility, which is what metabolic syndrome and all of these metabolic disturbances are. How do we create more metabolic flexibility? These three things—just thinking of brain, heart, and gut—and weaving them together, creating more flow, and I think we can do that with lifestyle changes. I think we can do that with food, with activity patterns, with stress management. I've seen it with patients, and with this one particular patient just recently really brightening my day. Hearing him say that he got his 10 years back was a testament to everything we've been doing.

JB: I think that's a beautiful way of bringing this discussion to a close. I want to give you one other attribution. We had the fortune, just recently last week, of having one of these spontaneous moments of "a-ha-ism" that really comes out of your work and the work that you've been doing at the Functional Medicine Research Center and the advocacy that you and Barb Schiltz and others have had in the food plan (the low glycemic load modified Mediterranean food plan). It turns out that at a meeting the audio technology group was taping, there was an individual who had taped this meeting a year previously and had heard you speaking and this had motivated him in his own life. Unbeknownst to me he had gone back home, sought out some care from a functional medicine practitioner, had gone onto the food plan that you have pioneered and described, and this year at the meeting he was willing to stand up in front of an audience of several hundred and talk about the flexibility that it gave back to him. As a type 2 diabetic who was the father of a 1-year-old at the time, he was 39-years-old and was very worried about his future. He couldn't bend down to really play with his daughter on the ground because he had so much musculoskeletal pain, and this year all of his parameters have normalized. He's off all of his medications. He lost, I think it was, 62 lbs on the food plan and through lifestyle changes. And then his wife brings his now 2-year-old up to the podium and he bends down comfortably and picks her up off the floor as a testament to his range of motion and his function.

This is better than real, right? This is what we're all here to do. I think what you've said is actually the aspiration we're all trying to work toward. These signals really do create the outcome that we call our lives, our phenotype, and our function. Thank you for sharing this. It's been a very powerful journey with you over the last 45 minutes in the milieu of the changing architecture of food and its relationship to function.

DM: Thanks for having me, Jeff.

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