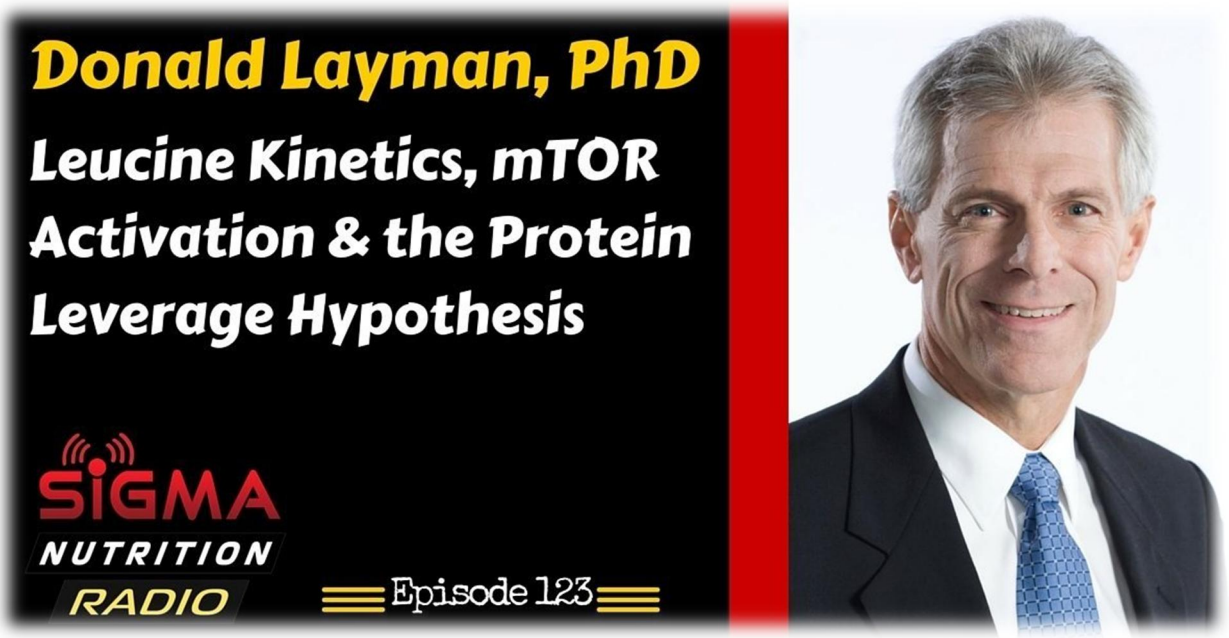

Danny Lennon: Hello and welcome to Sigma Nutrition Radio, the podcast that brings you evidence-based discussions with the world's leading researchers in fields related to nutrition and health. I am your host, Danny Lennon, and you are listening to Episode 123, and today we are going to be joined by Dr. Donald Layman, who is a professor at the University of Illinois. And Dr. Layman's laboratory is working to define protein and amino acid requirements and then the interrelationship between dietary protein and carbohydrates in adult health, and a lot of his research is focused on the impact of diet and exercise on health problems of obesity, type 2 diabetes and metabolic syndrome and all the interrelated issues that crop up with those. Today we're going to discuss all sorts of topics related to protein intakes and their effects, including issues like the leucine threshold and the activation of the mTOR pathway, amino acid oxidation, and things like why muscle protein synthesis drops two to three hours after peaking even when protein remains being fed.

So, you can catch all the show notes to this episode over at SigmaNutrition.com/episode123, and also, if you've not done so already, you can sign up to receive the transcripts to each podcast episode for free and it'll be delivered directly to your inbox, which you will see at the show notes page as well. So let's not waste any more time and let's get…

Dr. Donald Layman, welcome to the show. How are you doing today?

Donald Layman: I'm great! Glad to join you.

Danny Lennon: It's my absolute honor and pleasure to have you on because you are one of the top researchers in this field, and we're going to look a ton into protein metabolism today and how that affects muscle health and metabolic health overall. But maybe before we get into any of your specific work, just to frame this whole thing, can you give people maybe a CliffsNotes version of your background in terms of your area of interest with regard to your research and typically what you guys are looking at in your lab?

Donald Layman: Well, thank you for the comments, and we are interested in overall muscle health, body composition and really protein and amino acids metabolism, and as you get into that you end up also looking at fuels for muscle, sort of protein-carbohydrate balance. We've gotten into a lot of research with the branched-chain amino acids and specifically the branched-chain amino acid leucine, which seems to have a unique role in muscle protein synthesis. So, that sort of whole array of what's the best diet for muscle health both for weight control but also for athletes, healthy aging, and how do we balance protein and carbohydrates in the diet, those are sort of the general areas that we work in.

Danny Lennon: Perfect, and we'll definitely dig into some of the specific stuff that you mentioned there. But maybe to start off, if we talk about some of the science and application of high-protein diets, I think it's maybe important to start and necessary to define what we're talking about when we say that term "high-protein diet" because, depending who you talk to, what is considered high can be different. So what do you define as a high-protein diet when you're trying to address this question in research?

Donald Layman: Yeah, I think that is actually a great question, and exactly, your point is there's a lot of confusion about it. If you look out into the literature, a lot of people consider high as anything above the minimum RDA; anything that's above is high. If you look at the papers in the literature, there's sort of a general philosophy that the average diet's around 15, so twice that, so 30% of the calories coming from protein.

So I frankly think that it's the wrong way to define a protein diet. I think we need to think in terms more of absolute amounts. And so the requirement right now is at 0.8 grams per kg, most of the research is pointing that the healthy adult probably needs somewhere between 1 and 1.5, so I would define high as something above those recommendations. So for me, high becomes something above 1.7, 1.8 grams per kg, and so we're talking intakes of above 150 grams or more start getting into high protein as far as I'm concerned.

Danny Lennon: Perfect, and I think that frames it pretty well because regular listeners to the show will have heard certain recommendations varying all the way from maybe 1.5 grams per kilo up to even above 2 grams per kilo, particularly if we're talking about resistance trainees or athletes, and we've had Caoileann Murphy, who's worked in Stu Phillips' lab, on the forum, and Kevin Tipton. So both of those will be involved in kind of the exercise science realm where we're starting to see more recommendations along that line of above levels which are typically looked at at the RDA and well above them, which are kind of in line with a lot of the research you've looked at.

So if we look at those kind of recommendations for protein intakes, like I mentioned recently, Caoileann Murphy, who has working with Stu Phillips' for the past number of years, was recently on the show, and some of her recent work has been discussing the importance of considering protein recommendations on a per-meal basis as opposed to simply a daily target, and I think this was something I actually first saw coming out in your work a number of years back, highlighting this idea of that we need to start considering protein nutrition around a per-meal strategy as opposed to simply get this much in a day. So what's the deal here when it comes down to protein recommendations in your thinking and how that evolved from your research?

Donald Layman: Yeah, it really is somewhat of a complex story. We got into looking at regulations of muscle protein synthesis in older animals and older adults along with Stu Phillips and Doug Paddon-Jones and a lot of other folks, and what we've all realized is that as we get older our efficiency of protein use goes down. So that's kind of one track of research. The other track is we got into the regulations of muscle protein synthesis and we realized that the process of initiating the protein synthesis required an amino acid that I mentioned before, leucine, to sort of trigger the process. And so as we sort of started putting this question of efficiency together with this leucine signal, we realized that it takes about 2.5 grams of leucine to trigger muscle protein synthesis especially in adults. All of what I'm saying is not nearly as important to individuals under 20. Under 20, you're sort of dominated by hormones, but as we get older we're dominated by diet quality. And so that 2.5 grams of leucine, if you sort of translate that into a mixed meal, what would that amount of protein…does it take to trigger in a mixed meal that translates to about 30 grams of protein? So we developed that kind of a meal concept, and then Doug Paddon-Jones and I two years ago published a paper…journal on nutrition, which sort of was

the report of it, and we showed that if you took 90 grams of protein and distributed it in three balanced meals versus one large meal, sort of a typical American dinner, what we found was the exact same amount of protein gave you more net daily protein synthesis if you had each of the meals meeting that 30-gram threshold. So that's sort of the origin of the meal concept and, as you mentioned, Stu Phillips and some other labs are now beginning to do followup research and sort of showing that same effect.

Danny Lennon: Sure. And so just for people listening, we're talking about leucine triggering this anabolic response or triggering off muscle protein synthesis, and so it seems that there's this threshold of leucine we need to pass and you mentioned that target like 2.5 grams to pass this threshold in order to maximally stimulate that muscle protein synthesis. So how should people think of that relationship between leucine and MPS? So let's say we need to get above that number but, number one, does that mean anything above that number in terms of leucine isn't going to have any additional benefit? And second then, do numbers, say, below that 2.5 grams per kg still stimulate MPS to a certain degree but just not to its maximum amount or are they having any effect?

Donald Layman: Yeah, great question. So let's take the lower threshold first. Most of our methods right now are not so precise that we can differentiate between, say, the 2.5 and 2.2. What we know from the literature though is that if you give a meal that contains 1.7 or less of leucine, you'll get no effect at all on muscle protein synthesis. So the average American breakfast has about 10 grams of protein in it, which translates into less than 1 gram of leucine, so basically the average American is getting absolutely no benefit with their morning protein. What we do know then is if you get something above 2, you'll probably begin to get some effect, 2.5 is beginning to get sort of upper, and some people think that closer to 3 to sort of max it out. So what you've got is a very steep kind of S curve that it goes from nothing up to about 1.7, then it begins to go up, and it probably mostly plateaus at around 3. So that's sort of the triggering process and there is kind of a sharp trigger to it.

The second part is, is there benefit of more? What we need to then think about is protein synthesis has two major stages. One is the initiation stage, which is what I just talked about, which leucine helps trigger these proteins that are called initiation factors, and that's kind of like an on-off switch. Once we get it started, then we have the very expensive elongation phase, and that phase seems to benefit from some additional protein and

certainly additional energy. So most of us I think working in the field now think that it's absolutely important that you get to that 30-gram threshold to get things started and there's probably benefit up to maybe as much as 50 grams of protein at a meal for the rest of the process.

Danny Lennon: Okay, got you. Perfect. One thing in addition to that that I wanted to ask was about then, in relation to that, say, 2.5 grams or 3 grams of leucine, do we have an idea of the ideal blood leucine concentration or the kinetics pattern for maximizing MPS?

Donald Layman: Yeah, great question. What we know is that the leucine effect to trigger protein synthesis definitely requires an increase in the intracellular concentration of leucine and most of the data suggests it has to at least double from sort of a fasting, and maybe triple. So generally, if you look at the blood level of leucine when you wake up in the morning is around 100 micromolar, and most of the data suggests you need to get about to 300 before it's really going to be enough. So that blood leucine is definitely one of the markers we use to see whether the meal was adequate.

Danny Lennon: Perfect, yeah, because it was just actually from a conversation with a friend of mine, Michelle, who's doing a PhD actually and looking at leucine kinetics, and they had mentioned in their lab they had done a study, I think, with 3 grams of free leucine and were finding concentrations of up to like 500 and 600 millimolar in the first 30 minutes. But one thing Michelle had mentioned to me is that when you look at a lot of the current research, there are a lot of mixed reports on leucine kinetics and some studies don’t even mention that, so just looking for a bit of information on that. So, it's interesting…

Donald Layman: And I think that's important. I think it's one of the problems in some of the clinical studies, is that they suggest they're doing leucine kinetics or they're testing, they’ll give a leucine supplement and say, “Well, it didn't work,” but they give you no leucine blood levels before or after. Some places, a lot of the European, especially the Northern European countries, have very large protein breakfasts, and if you put a leucine dose on top of a large protein breakfast you won't get an effect because you've already triggered it. And so people really need to report those levels and ideally they even report the initiation, the mTOR initiation factors.

Danny Lennon: Right, for sure. And just as you mentioned the mTOR pathway, obviously that's what we're going to be…leucine is having its effect on and that’s

triggering off this anabolic response, and we know that leucine's effect on the mTOR pathway and hence on MPS is just one example of a metabolic signal that various different amino acids can play a role in. Could you maybe highlight some of the other metabolic signals triggered off by amino acids that have some role in health?

Donald Layman: So the leucine one is a great one and it's pretty diverse, not only mTOR but it probably has effects on gut hormones or satiety; it probably has effects on glutamate in the brain. So there's a lot of them. Some other obvious ones would be like arginine and nitric oxide, is a major signal; tryptophan and serotonin for a neurotransmitter; let me think – some of the histidines and, some of the amino acid stress responses. So protein amino acids, in general, one of the things that's going on in protein research right now is for years we've thought of protein just as an entity, kind of like carbs are an entity, but now we're beginning to recognize that protein is really just a collection of 20 amino acids and there are about five or six of the essential amino acids that are absolutely critical to how you determine how much protein you need, and we're getting more sophisticated in…I think that's sort of the next wave of nutrition research, is to get more specific about the individual essential amino acids.

Danny Lennon: One thing I did want to pull back onto that I think is particularly important you mentioned was that not only does protein feeding have an effect on this anabolic response, we also know hormones do. So, and particularly when we're talking about mTOR pathway, not only does leucine have that effect but we know insulin plays a role there as well. Is there any way to quantify the impact of each? Or how should we view the effect that leucine and insulin have in triggering muscle growth or muscle repair? In that does the elevation we get in insulin from simply taking in, say, 3 grams of leucine, is that a sufficient rise in insulin to maximize that response or do we get an added benefit from even higher insulin levels?

Donald Layman: Yeah, the balance…mTOR is sensitive to three things in particular and probably some other things, but three really strong signals, one being insulin, one being leucine, and the other being cell energy, ATP. So it's always sensing those three things and the mechanisms of how it's sensing it are pretty clear now. So to your point, that's when I mentioned earlier the difference between younger individuals, sort of people who are under 25 and still growing, they're actually very sensitive to the insulin and hormone part of the signal. And so what we know is that, from a lot of studies of malnutrition, that children with really poor diets will continue growing because they're dominated by the hormone part of that signal. But

once we stop growing and we get into our 30s and beyond, the insulin and the hormones really aren't our friend particularly anymore, and now what we need is we can't be type 1 diabetic, we have to have insulin there, it kind of potentiates the system, but the system now is regulated by the amount of protein. And so now we shift more to that meal concept. The muscle is looking for those boluses of leucine to when it's going to trigger protein synthesis. And so it's really a pretty remarkable evolution how the muscle has kind of learned to sense meals when it has enough nutrients to trigger what really is a very expensive process of building new protein.

Danny Lennon: Yeah, that's actually a really good segue into something that I was meaning to bring up in that I know that a lot of your studies have looked at this concept or this typical pattern we see where, even if you keep leucine levels elevated, you still see this drop-off in muscle protein synthesis that reliably happens all the time like maybe two to three hours after that initial elevation from the leucine bolus dose, and one hypothesis that I've heard mentioned as to why we always get this MPS drop-off at that like two- to three-hour mark after the peak is, back to what you mentioned, around ATP. I think it might have actually been some work that Gabe Wilson was involved in with you as well, in that it's simply due to protein synthesis being such an energy-expensive process and that as ATP gets lower there comes a point where it still has to down-regulate MPS to save energy, if I'm getting that correct. Can you maybe just explain exactly what's going on there?

Donald Layman: Yeah, that's exactly right. It was work by Gabe Wilson and Layne Norton, who were in my lab at the time, and we were trying to look at why, as you said, why is the duration of protein synthesis kind of a set amount? And that seems to be true in humans and animals alike. Once you trigger it, it will run about two hours, two-and-a-half hours, and then it goes back to baseline, and as you pointed out, leucine is still up. Again, I mentioned earlier, protein synthesis has two major parts. One is the initiation part, which is kind of like assembling the machinery, and then the elongation part where the protein synthesis has to run, and that process is extremely energy-dependent and eventually the system just seems to run out of energy.

So the important thing there is that we've got these two parts. One is the initiation part, which is really assembling the machinery, and that's where leucine comes in; we sort of trigger it. But once the triggering has happened and leucine, whether it's up or down, doesn't really make much difference, it just has to be present as an amino acid then. And so then it

really comes into what keeps elongation running, and from our research with Gabe Wilson again, it looks like it's ATP. And so as the cell begins to run out of ATP, it triggers another mechanism called AMP kinase, which shuts down the elongation phase and protects it. And we show that if you give energy in the form of branched-chain amino acids or glucose, you can actually get it to run longer. So it has these two phases and leucine, again, is the triggering step, but then other things come into play as to how long it runs.

Danny Lennon: Sure. So when you talk about using either amino acids or some glucose to potentially elongate or keep that phase going longer and maybe mitigate some of this decline in MPS, are we saying then that we can to some degree stop that response or at least lessen how much it drops off by or is that going to happen regardless?

Donald Layman: I think it's going to happen regardless. The research doesn't really answer that question yet. The two papers that we published show that we can delay it, we can make it run a little longer, but we don't really know how long we could extend it. We know there are papers in the literature where people have used IV feeding of, say, hospitalized people, and we know that if you just continuously feed it's still going to drop off.

Danny Lennon: Right.

Donald Layman: So it looks like the muscle has a need to reset. It runs for a while—one of the things that we always like to talk about is that we can show that ATP will drop by more than 50% just after a protein meal. I mean, that's in the range of what exhaustive exercise will do.

Danny Lennon: Wow.

Donald Layman: So this meal effect on muscle is kind of like, energy-wise, almost like exhaustive exercise, and you can imagine if our ancestors were out in the woods, well, then we would want to become as immobile because we ate too much. [Chuckles]

Danny Lennon: Right.

Donald Layman: And so the body has an automatic defense mechanism to make sure ATP doesn't get too low.

Danny Lennon: Right. So far we don't have any really evidence to suggest that it would be useful for someone, say, to supplement with amino acids in between their main protein meals. Say if they're getting four meals with high amounts of

protein in each throughout the day, is that in theory going to be the maximum MPS response they can get and they're not really going to get much more from maybe taking…?

Donald Layman: Yeah, I think your first statement was correct. We just don't really have any evidence about that. I think we have pretty good evidence to suggest that having all your protein for the day in one meal is not as effective as having it in more than one. And so then we get into the question of, is two better than one? Probably, it looks like it is. Is three better than two? Is four better than…? So we don't really know those answers. At this point, the data's not really there. I personally think that for most people targeting three meals is probably fine. If you're an elite bodybuilder and you're looking for that 110% outcome, I think going to four, even possibly five to just try and max the system, but you're walking a line now of more calories for the protein effect. So I always target three, and again, elite bodybuilders, four or five, and use of amino acids in between. I'm like using branched-chain amino acids after exercise. I think there can be some effect there, but again, really good long-term studies to prove that's effective just aren't out there.

Danny Lennon: For sure. And one thing I did want to bring up because it's something that's commonly kind of discussed but maybe people don't have the correct assumption around it, a lot of people will talk about they may have heard somewhere that if you take in more protein and X amount at a certain time, so at one sitting, it's pointless because you just end up oxidizing a ton of amino acids and they're wasted. Is this presumption that the oxidation of amino acids is always a waste, is that a kind of flawed presumption and can you maybe get into why?

Donald Layman: It's actually one of my biggest pet peeves in the area. [Chuckles] I heard the exact same statement out of one of the experimental biology meetings in San Diego just two weeks ago. And the starting point that people have to recognize is that in an adult, sort of by definition, we're at steady state. We're at balance. We're not gaining or losing protein. So no matter what you eat protein per day is going to be oxidized. So whether you eat 70 grams or 170, you're going to oxidize that same amount or you have to be gaining weight. And so the idea that oxidation is bad I think is totally misleading.

And to go back to the leucine story for another piece of evidence, you talked about the kinetics of the leucine story – well, the KM, the kinetics for activating mTOR, is exactly the same concentration for the kinetics for

activating the branched-chain dehydrogenase which oxidizes leucine. And so what the muscle has is a mechanism where it triggers protein synthesis and then it immediately starts depleting that leucine out of the cell to get ready for the next meal. And so oxidation goes hand in hand with the anabolic response. And one of the things we know is that during exercise—most of it's been done with endurance exercise—is we burn the equivalent of about 10 grams of protein per hour just doing exercise, just burning it, and the majority of that is coming from branched-chain amino acids, which is one of the reasons I like to use a branched-chain amino acid replacement after exercise because we have specifically selectively burned branched-chain amino acids during the exercise.

Danny Lennon: Right. So in a case where we're going to presumably supplement with branched-chain amino acids, are they only useful in a situation where we already have the other amino acids available, so say from previous meals that day, and do we need the rest of those essential amino acids around in order for the branched-chain amino acids to be useful?

Donald Layman: Yeah, I think that's a great question to it. When you trigger protein synthesis, when leucine turns on that initiation process, now you need all 20 amino acids present, and the body can make the nonessential one so you have to have a new supply of the essential amino acids to go with it. And if you don’t put them in, you can watch the blood levels of those go down. The three that go away the quickest are the three branched-chain, and again, that's why I like supplementing those. If you're going to supplement anything, those three are sort of the first targets. But then, as you're pointing out, you need sort of all nine of the essentials to really make the process run. So my comment about using the branched-chain after exercise is as much of replacing the loss of what was burned during the exercise as it is versus thinking about triggering protein synthesis. Sort of does both, but I think it's important to replace the loss also.

Danny Lennon: Perfect. So we're using it as an adjunct to complete proteins throughout the day as well, essentially.

Donald Layman: Right. So, you know, a lot of people right after they get done exercising, the last thing they want to do is a big protein shake. And so with branched-chain amino acids, you can take a small…you can take 5, 6 grams of those in a water solution and it's just part of your rehydration.

Danny Lennon: One thing I really want to ask you about, Dr. Layman, is one thing that because I've seen such wildly conflicting views on this and its potential

viability, is the concept of the protein leverage hypothesis. Maybe you could first explain to people what exactly that hypothesis is and then give your thoughts on how well it is or is not validated in the literature in your opinion.

Donald Layman: Yeah. I am actually a big fan. Steve Simpson is I think a really incredibly intellectual person in this arena. He's actually an anthropology individual in terms of background. And what he has found across all kinds of species including the human is that we tend to eat toward a protein target and that if we have a diet that is very high in carbohydrates, for example, that dilutes out the protein of the diet, then we have to eat more total food to get the protein target, but if you have a diet that's high in protein then you'll eat less calories. And so he has developed that theory and had done a lot of mathematical modeling and quite a few experiments to show that animals of different species and to some extent humans, again, eat toward this protein target around 20% of their calories from protein. But if you, again, like we did in the 1970s, '80s, we developed a food guide pyramid which said "eat a lot of carbohydrates and stop eating animal proteins," what America did is exactly that and we ended up having to eat a lot more calories to get the same amount of protein. And so I think the theory is really quite remarkable. I think that sort of the public health data supports it. As far as really proving it, I think it's a hard theory to prove but people who have tested it, it seems to hold up pretty well. And like I said, I'm a fan of it. I think it does explain a lot of things that we've seen in public health and in obesity and diabetes epidemics of the last 20 years.

Danny Lennon: Sure, and even from a practical perspective I think it probably dovetails in nicely what we do know about high-protein diets and their effect on increasing satiety. One thing that'd be interesting to know, do you know of any data that shows not only the increased satiety levels from eating more protein, because we're fairly clued in on that, but is there anything to show that this increased satiety in turn improves dietary adherence to a hypocaloric diet just by simply making that calorie deficit more bearable and people not feeling as hungry?

Donald Layman: I guess I'll give an opinion here. I think if you go into the literature, it's hard to sort that out. Our ability to do satiety research is not real good where we can give a meal and sort of test how you feel at the next one, but I think these acute tests aren't very useful. What we really need to know is long-term habitual diets and we get into the problem then that we can't follow diets very well.

So, again, back to my opinion, what we've seen in our studies and what I believe from a lot of just work that I've done with people in weight loss is that people who have a higher protein diet are more satisfied meal to meal and they're less prone to snacking. Americans are very habitualized at meals. We eat meals because they're set in front of us and it doesn't…whether it's a big meal or a small meal that tends to be what we eat. I think the real issue is snacking, and people who have higher-protein and lower-carbohydrates meals I think are less addicted to the carbohydrates and therefore snack less. So, again, I have to preface that by saying that's kind of my opinion. If you go in the literature, it's pretty hard to get a really hard support for that. But again, after doing this for 15 years in studies, I have a pretty strong opinion that that is what's going on.

Danny Lennon: Yeah, and I think actually when we talk specifically about fat loss, one thing that has consistently been shown in much of the research including your own is this favorable outcome we see for body composition when carbohydrates are isocalorically substituted for protein. So we take two diets of the same caloric value but one is high in protein, lower carb, and the other is low-protein with more carbohydrate, is the primary benefit here one of just better maintenance of lean body mass during that dieting phase and so allowing the person to lose more of that weight that they lose from body fat itself or do we have other benefits? So, for example, we know that, say, energy expenditure that occurs through the thermic effect of feeding or we already mentioned how energy-expensive it is to synthesize protein. Do they have enough of an effect to actually have a pragmatic real-world effect or is it just a simple case of maintaining more lean mass?

Donald Layman: Yeah, I think all of those factors are in play and to sort of partition which is most important, I don't really know. We've done it in animal experiments where presumably satiety and activity and all those things are being controlled, and we know they will have a different body composition. So we think the thermic effect—and again, I think there are origins of that thermic effect. Sometimes you'll see the difficulty of digesting and absorbing, metabolizing protein. I think it's specifically this muscle protein synthesis, which is so energy-expensive. So I think that is the thermic effect of protein and it's very important that it's meal-based. If you just have a higher-protein diet but you don't distribute it correctly, you won't see those effects, and I think that's one of the controversies. But I think the satiety things are real and I think that the muscle mass increasing, just daily expenditure, I think people probably become

somewhat more active. So I think all of those things go together to make a higher-protein, lower-carbohydrate diet more effective for weight loss, and while there may be controversies about what satiety is really doing or the thermic effect, there's absolutely no controversy that a higher protein/lower carbohydrate is effective at changing body composition. I mean, there are dozens and dozens of studies supporting that.

Danny Lennon: Right, and especially when we think of the real big problem that most of people with a weight issue or facing obesity is not necessarily that initial weight loss, it's that maintenance of that weight loss, and I suppose maybe a piece that isn't addressed as often is, well, if we look at getting a healthy amount of muscle mass, then long-term just that metabolic state that someone's in is going to be a lot more conducive to maintaining that weight loss or having higher energy expenditures as opposed to constantly thinking about losing body fat and trying to keep calories low, etc., etc.

Donald Layman: Yeah. And we did a study similar to that. We did a 12-month-long study and we showed during that initial four months they lost more weight, but when we got out to 12 months what we found was that there were more people in the higher-protein group who were still compliant with the diet and had maintained a higher percentage of weight loss. We sort of targeted a 10% loss of initial weight and we had I don't exactly remember the numbers but nearly twice as many people who had still maintained that threshold after a year in the higher-protein than in the higher-carbohydrate approach.

Danny Lennon: One thing before we start wrapping up here, Donald, that I did want to get onto was protein quality because we've already mentioned the importance of branched-chain amino acid levels and particularly leucine when it comes to a set dose of protein that we're talking about. Now, obviously, some proteins, particularly plant-based proteins, tend to have a poor amino acid profile in terms of those two things and leucine content, for example. Is that going to mean that a much higher dose is needed to elicit that same anabolic response or that maybe someone should consider supplementing those amino acids on top of their normal protein dose to try and get that maximal response if they're not using animal-based protein?

Donald Layman: Yeah, and those two approaches definitely can work. I was actually just, before we called today, preparing a lecture that I'm going to give here at the university. I was actually pulling out some of those exact numbers, so I have some in front of me. One of the examples that we like to use is that, for example, quinoa is sort of everyone's superfood right now and people

talk about it having a complete amino acid mixture, but what people ignore is just how low in protein it is. And so if you take something like beef, so everybody's whipping boy is red meat, so if you take beef, beef has about 8.6% leucine, so to get 2.5 grams of leucine in beef you'd need about 29 grams of protein and that would require about 183 kilocalories to get to it. If you did the same thing with quinoa, quinoa only has about 6% leucine in it, so you need almost 42 grams of protein and quinoa is pretty diluted; you get almost 27 kilocalories per gram of protein. So you need 1100 kilocalories of quinoa to get to 2.5 grams of leucine.

Danny Lennon: Wow.

Donald Layman: So just per meal, you have to eat 11…so three meals a day just in quinoa, you'd have to eat 3300 kilocalories to get to the targets. So one of the things you have to remember in grains is they're perfectly good, healthy carbohydrate foods but they're lousy protein foods. [Chuckles]

Danny Lennon: Right. Before I kind of get to the final couple of questions, where do we have to go in terms of where are the gaps in the current knowledge base right now? What are you hoping to answer in future research and what do you think are the big research questions that hopefully we answer over the next few years in this area?

Donald Layman: Yeah, there's always lots of new research to be done. [Chuckles] I think one thing that we do need more research in is this meal definition. We've got a lot of data showing the leucine effects and the importance of the amount of protein in a meal, but what we don't really have is really long-term body composition data. And that's going to be really hard to get, but when we talk about protein synthesis, sort of the other half of the equation is protein breakdown and it's always a balance of the two, and what we don't really know is how those play out. And so your earlier question about is four meals a day better than two meals or three, I think those are the kinds of questions that we really need to try and get answers to.

The other thing is that there is this sort of discussion about mTOR that's going on on sort of good and bad, and so there are some studies about longevity related to cancer. I mean, mTOR is a nutrient sensor but it is really a growth factor, and so we have to be careful about what's the right target. We know that it's critical to trigger it to start protein synthesis, but there's also some evidence that keeping it chronically elevated is not a good thing. So I think we're going to learn more and more about how to balance meal to meal and try and keep things—there's this sort of

philosophy in nutrition that if a little is good a lot must be better, and that almost is always not true in nutrition. [Chuckles] What we're after is a balance and I think those are the kinds of things.

And I guess the last thing is as we explore that balance, I think we're going to have to get more and more oriented to individual essential amino acids. It's not just a protein number, it's a leucine number and a methionine number and a threonine number and a lysine number, and we have to target each of these correctly.

Danny Lennon: Yeah, yeah, I think for sure those are really important points, particularly when look at that typical thing in nutrition of it's always nearly going to be an inverted U-type curve for how much one needs and you see this point of diminishing returns…

Donald Layman: Exactly.

Danny Lennon: …but a lot of people tend to forget that.

Donald Layman: Yeah. [Chuckles]

Danny Lennon: Before I get to the final question, Dr. Layman, where can people find out more about your work? Can they track you down on, say, a ResearchGate profile or anything on the web they should go?

Donald Layman: I'm on Twitter at @donlayman, so if they want to follow me there, and pretty much you can track me down in Google or Google Scholar in terms of papers. So I don't actually maintain a website for just a lot of information at this point but you're probably right, I should do that. [Chuckles]

Danny Lennon: Perfect. I'll link up to Dr. Layman's Twitter and any of the papers that we mentioned today and some other relevant ones in the show notes for everyone listening. So Dr. Layman, that brings us to the final question we always end the show on and it can be to do with anything even out of today's topic, and it's simply, if you could advise people to do one thing each day that would have some beneficial impact on some aspect of their life, what would that one thing be?

Donald Layman: Exercise. [Laughs]

Danny Lennon: Perfect.

Donald Layman: Yeah, I think that one of the things that is important in nutrition is that if we are physically active, we make everything more efficient and we keep

our daily calorie needs higher, the body is really designed to balance nutrition in the 2000 to 3000 range, and if we're sedentary and only need less than 2000 it's very hard to balance things and get satiety to work right. So I think in terms of muscle health and nutritional health and everything, being more physically active is sort of the one thing we always ought to keep in mind.

Danny Lennon: Perfect, a great answer and something that's definitely been mirrored by a lot of other people before, so it's great to have that validated. And Dr. Layman, I want to say thank you so much for your time. It's been an absolute honor to have you on. I've followed a lot of your research for a long time now, so it's an absolute honor to have you on and chat through it and thank you so much for the great information.

Donald Layman: My pleasure.

Danny Lennon: There we go. That was the University of Illinois' Dr. Donald Layman. In these show notes, I'm going to link up to all the research that was mentioned today as well as where you can find Dr. Layman online, and also in those show notes you'll see the option to get the full transcript to this episode and all the other episodes for absolutely free, and that's at SigmaNutrition.com/episode123. My Instagram handle is dannylennon_sigmanutrition. You can also track me down on Facebook, is probably a pretty good place to go, either the Sigma Nutrition or my own page. If you do go to either of those places, please do put out either a post about this episode if you enjoyed it or any comments you have on it. If you enjoyed it, please share or even tag other people, and all that stuff really helps to keep good-quality information spreading and to bring up some discussion points as well and for everyone to learn. So please do that and I hope to see some of you in the comments on either of those social media channels. And that brings this week's episode to a close. I want to say thank you so much for listening in, and I will talk to you next week.