Danny Lennon: Hello, and welcome to another episode of Sigma Nutrition Radio. My name is Danny Lennon. I am here with Dr. Alan Flanagan. We're at episode 454 of the podcast. And today we're lucky to be sitting beside. One and only Dr. Eric Helms, Eric, how are you?

Eric Helms: It's a pleasure to be here and even more pleasurable now that there's one other doctor in the room. Dr. Flanagan, thank you. Mr. Lennon, it's great to be here with both of you.

Danny Lennon: Yeah. Thank you. I love being reminded of my inferiority, that I certainly don't have a complex over. We're lucky enough to be right now in Brisbane, Australia, where we've been at the sports nutrition association annual conference. And today we actually wanted to talk about something that's came up both during the conference and then some of our conversation afterwards relating to some issues around protein and assessment of protein quality, and even many questions that we have a lot of assumptions over. And I think Alan, of course, this is related to some of what you presented on, but I think to frame this initially, I think an interesting way in one of the things you had mentioned is when people have this conversation around animal versus plant proteins, which is better or how should we even compare those? That can be the wrong question to ask for a multiple or a multitude of reasons. Yeah. And we're gonna work through

some of those. Can you maybe just give an opening to that idea and some ground where we can explore?

Alan Flanagan: Yeah, so I think framing a lot of the, a lot of the conversation that we have about protein, particularly when it comes to exercise, adaptive responses and otherwise not necessarily population health where this conversation has tended to be more fraught, but it is relevant for population health.

If, for example, we're going to be, seeing more of a trend or in the population towards more plant-based sources of protein or reducing meat consumption, or even relying more on things like Mycoprotein sources. So it's irrelevant. It does have a relevant population component to it.

But part of the problem is it frames the question in a way that one over emphasizes these what we would call protein quality scores. And then secondly it opens up the debate to get bogged down along the ideological plant versus animal plant versus omnivore lines, rather than actually recognizing that we commonly have foods that may have differential effects even within a class.

So within the class of animal proteins, we would have foods that might have differential effects. And then when I even mentioned the word differential effects, then that becomes itself important because what effect are we talking about? A lot of the time when we're talking certain sources of protein plant animal, or within a class of plant or animal having differential effects, it's often in relation to outcomes like muscle protein synthesis. So it's something that, we'll get to discussing what's that signifying as an actual outcome. And the difference between say kind of proxy outcomes, the difference between, obviously with hard outcomes and then also other methodological factors that our listeners tend to enjoy us delving into, but really important to consider things like how long has this been measured for?

And if we're citing a particular study in support of saying "A is better than B" or" A is the same as B", is it appropriate to take the methods used in that study and then extrapolate them out to either a whole day or even an entire diet? So I think an initial point of departure is this concept of scoring systems.

We discussed yesterday that there was two that have historically been used. One is being replaced. Now the older one is the protein digestibility corrected amino acid score. And that relied on measuring amino acids in the colon, in the large intestine. And the problem with that is it took the level of protein in the food being measured, the crude amount of protein.

So let's say you've got a hundred grams of Greek yogurt, and you've got around 10 grams of protein in that a hundred grams. It would use that crude protein total rather than considering the amino acid composition of it. And then because it was measuring in the large intestine at that point, amino acids undergoing bacterial metabolism.

It's not a reflection of true amino acid absorption in the small intestine. So that was replaced by the digestible, indispensable amino acid score. And that did make the improvement of starting to treat each individual amino acid as an individual nutrient. And then. Also measuring that amino acids digestibility at the end of the small intestine in the terminal ileum.

And that was more of a reflection by measuring at that point before transit into the large bell, it was providing a reasonably more accurate estimate of how much had been digested in the small intestine. And it adds up essentially the digestibility of each individual amino acids to, to provide an overall "quality score".

And the difficulty with this is that sure, if you stack up say a, a plant source of protein versus an animal source of protein based on amino acid composition of an individual food. And I should caveat that often with plant foods, they're based on the raw amino acid composition of the, of a Lago, for example, which is not gonna reflect what happens after it's actually being processed or cooked or heated.

But when you stack that up, you can see this per and it's very easy for someone to point and say haha, animal proteins are lower quality that doesn't actually speak to the effect of any given protein source on some of these outcomes we're talking about. And it also doesn't speak to the effect of a total dietary pattern with multiple different sources of food.

So although they might be useful to some degree in terms of the conversation we're interested in, which is how do these food sources and in

this context from a macronutrient perspective, specifically dietary protein composition of these food sources, influence health, and obviously then as well, performance and adaptive responses to training.

It's probably too simplistic just to focus on something like. The indispensable amino acid score, because in a sense it can miss the forest for the individual amino acid composition of a food for the trees of a total dietary pattern.

Danny Lennon: So before we dig through each part of those, I think maybe if we open a few more tabs and that we can come back to throughout that, cause I know this is also an area that you've looked quite extensively, that Eric, when you see these conversations around either the plant versus animal issue or just more dietary protein in general, based on maybe some of the stuff Alan has put there or other issues that came up in our conversations yesterday, what are maybe a few tabs you might like to open that we should revisit throughout this conversation?

Eric Helms: Yeah, absolutely. We can plant some seeds. When I was initially writing my literature review for my masters, this is when I first had to grapple with. inconsistencies in data, where I would look at applied outcomes and they did not make sense when I was looking at mechanistic studies.

And when you're being taught to do a literature review and understand a new topic, you go through the fundamental literature. Like I was learning about things. I never ended up even doing amino acid kinetics, phenylalanine tracing studies. I never did that.

Nitrogen balance to go even further back. I wish I was considering doing, but ultimately I decided that I didn't want to correct collect urine for my masters. And not collect feces. They used to have through that. You can estimate it. So don't worry folks. I didn't collect feces. I was gonna estimate it. And you also estimate sweat and saliva. Would've been a lot of fun. But I decided not to do that. I also looked at other things that have of fallen out of favor: three methyl histidine excretion which is something that doesn't capture they only capture a certain animal or plant-based protein, so it makes it's a useful metric, but it doesn't actually give you something you can use in most free living populations.

So there's all these different mechanistic ways to try to assess protein requirements. And then you run up against do I even care about protein requirements as someone who is a sports science researcher. And that's when I first started thinking about, okay so I'm after outcomes, right?

So I'm after optimizing performance or changes in body composition that go beyond what might be sufficient for health in different contexts. When you first start grappling with this like the meme where the guy like starts to have his brain, grow, go grow and then the final one is this like epic explosion of the brain where he understands all things like it starts as, oh, the RDA is about requirements, but not about, enhancing performance. And the next level is going, oh, proxies aren't the same as like the actual the outcome measurement. And it keeps going from there when you start to dig, and peel back more and more layers about the way that these studies are conducted.

And I think the place I got to, which I quickly abandoned fortunately, was let's just throw 'em out. Like I don't, these mechanisms are pointless, which of course they're not , they're actually how we set up and hypothesize things, but it helped me construct what I call; when I teach students about translational research in its role is that it's the final step in the quote unquote chain of research, and the error that you don't wanna make is to jump steps, to be doing your, what I would describe as mechanistic or bench research and then to immediately in your discussion, talk about how it could be applied. Yeah. Or conversely all you collected was a pre-post one RM test, and you fed people two different types of protein, and you spend three quarters of your discussion hypothesizing, why one got better instead of just dropping a couple hints at what it could possibly be, but then talking more about your findings and how they fit with the other applied research.

So those are unfortunately still very common Cardinal sins. And I think the only way to avoid them is to have a better understanding of the limitations of the various metrics you're looking at and the testing methods, which is not fun work, but it's honest work, to learn about some of these things.

Yeah. So anyway, when I was writing this literature review, I, probably the most obvious one that I think your listeners would be very aware of, especially if they pay attention to sports. Nutrition is the papers by, a and Aragon first wrote a narrative review about some of the issues with protein timing, because there were, we were at a point in the mid two thousands,

late nineties where this was like the thing like it was creatine and it's making sure you have your protein right after your workout.

And I think that one is like a really like we, that the myth has been busted. It probably went too far. Now it's come back to something more reasonable and we simply understand that protein timing there's limits to when it matters and when it doesn't. But if you understand the issues with the protein timing overreach that occurred in the mid two thousands, you actually, if you think about it, you understand the issues with the overreach of pre-bed protein intake, of protein quality, of the refractory period and protein distribution, all of these various threads of protein research often come back to some of those same issues with the the methods of investigating these. And it's almost somewhat of a throwaway just to say we just need more longitudinal research cause I am actually interested in why can't we connect very well between these proxies and these outcomes and understanding that I think will be a really big step forward because ideally we do wanna be able to model and predict things, so it's not always retrospective. We're not there yet, but I think we can be, and we won't get there just by simply going well, screw all the mechanistic research.

Danny Lennon: Yeah. Yeah, I guess so there's a number of different ways we can look at this issue of comparing, say different proteins or which is better or different sources and so on. And the whole health conversation is something we might revisit and we can come back to, but if we look at the outcome related to let's say athletic performance slash recovery, muscle hypertrophy, muscle repair and look at it through this. Lens we have then the actual end outcome of changes in muscle.

And then we have these various proxy measures, which we're gonna look at. So that's one issue that we can delve into. And then we have actually what are we gonna look at in terms of the protein as the intervention. And there's some issues here around different sources, supplemental versus whole foods, et cetera.

So I don't know if you have any preference for which way round we do that. But if we look at the issue of assessing what is best, let's say for hypertrophy, I might start with you here, Eric. think it's so common now that everyone is gonna presume. Okay, we're gonna talk about what is the impact of protein on muscle protein synthesis.

And again, we can look at an acute period versus more a chronic period. There might be a difference there. And then there might be a difference in well, is MPS telling us what we actually think it is. Can you maybe just highlight some of the issues that come up when we, I suppose default back to thinking if a certain protein has a better MPS response over whatever timeframe is therefore "better" or "superior" in some way,

Eric Helms: Man, there are so many takes on this and there's a few different, like it basically highlights that we simply don't have the oomph behind sports nutrition research that we need to not to basically only at any single time with any type of study design, can we address some but not all of the limitations and not the same limitations at the same time I'm recalling right now, a conversation I had with Ian McCarthy who some people might be familiar with, if not, an online thinker and pretty smart guy, but not directly involved in research.

And one of the things that he was frustrated with is just the variability in human research. Like the common sports nutrition study, when you've only got a couple hundred dollars to fund it is you tell people to eat a certain thing. Don't even provide it to 'em check some dietary food logs, make sure that they said, and they thought they did eat it.

And then you have, 'em follow a training protocol. Maybe you train 'em through it. Ideally, at least you're of clamping and controlling in a lab, setting the training, and then you measure some anthropometry, body comp and performance afterwards. And that's an extremely variable outcome you're going to get.

And the compliance with the nutrition as you both know and the listeners know as well is hit or miss. And it's not until we have meta analytic data where we can. The statistical power to overcome that variability, that we can actually say anything definitively about an outcome. So for example, everyone, and I love it that this has been cited so many times like the Morton meta-analysis on protein.

And there's been a couple by some Japanese groups as well that have found the same thing that as you increase total daily protein intake up, up and around say 1.6, 1.5 grams per kg. You start to get diminishing returns after that for impacts on strength and hypertrophy. And so people will cite that

meta-analysis but what they don't realize is that probably two thirds to 70% of the studies that are actually being meta analyzed have non significant findings and a debate I had with me back in the day; I made a claim that I've never seen a a study where a higher protein got a worse body composition or performance outcome than a lower protein group. And and I was like but look, these are all small sample sizes, but that should tell you something like high protein is important. And he found one study where that was the case, but I still have not found another.

So what we're looking at is basically like 30% that show higher protein outperforms lower protein, one crazy, probably statistical outlier showing the opposite and then a whole crap ton of null, which really just tells you, this is a small this, the area is fraught with small sample size research, but higher proteins in general are better than lower protein intakes.

And then with the meta analysis, it becomes clear. You take, 2000 people across 30 studies and in 24 of those studies, there was non significant differences and you have a clear, significant difference favoring this higher protein intake. So that's the issue with human research. So when Ian McCarthy to close that circle said, I prefer looking at MPS.

Because at least I know that data is real it's controlled. They came to the lab, they're in a fasted state, they were given this type of protein or that type of protein or waited this long. Or we waited that long, or we gave it in this dosing pattern or that dosing pattern. And I'd rather just go with that.

But the problem is that if you just go right I, if I'm gonna pick and choose which limitation I wanna deal with, I hate the limitation of humans being humans. I'm just gonna go with this mechanistic data. Then you're forced to accept conclusions that don't comport with those meta analyses, where we've overcome that variability with statistical power.

Like just to give the reader an example, if you ignored all outcome based data on hypertrophy, and you said, all right, so what do I need to do with protein to optimize it? It would be that I need to take a universal dose for everyone of 20 grams of way every three to four hours while you're awake with one dose of casein before bed.

And it gets you to about 120 grams of protein. Maybe a hundred and yeah, probably about 120, even for someone who weighs like a hundred kilos for everybody and you must eat at least four meals a day to accomplish this for it to be optimal. And that's less than the meta-analysis sites of 1.6, and after that, maybe some potentially beneficial, but diminishing returns and you can't find studies where you see that a higher meal frequency of protein actually seems to matter. So here's one, there's the classic study by Areta and colleagues. It came out in 2013 where they showed that the pulse strategy was better than the bolus or like the inter basically here's what they did.

They gave people 80 grams of whe protein after they come in for overnight fast and watch them for 14 hours. And literally all they had was 80 grams of whe protein. One group got eight doses of. One group got two doses of 40 and then one group got four doses of 20. And the total area under the curve of muscle protein synthesis was highest for four set to 20.

So you combine this with some other mechanistic research, looking at the leucine trigger and the refractory period. And you get this idea that you gotta wait long enough and you need to give just enough to ally stimulate, but not more, or as quote unquote wasted. And that's the way you eat. Boom. However, then you have higher quality levels of human data.

So the kind of the equivalent of the Morton meta-analysis, that seems to disprove this from a total daily protein intake on distribution, is this systematic review; I believe it is by, I can't remember the name of the author off the top of my head, but it is no, I got it. It's Hudson and colleagues, the effects of protein supplements consumed with meals versus between meals on resistance training, induced body composition changes in adults to systematic review and that's 2018.

So they systematically reviewed all these studies, where they either gave people with their meals a protein supplement or between their meals effectively creating those two different dosing strategies where the with meals is your you're wasting protein. It's too much. It's only three bolus a day.

And the, between meals, you've got these six evenly spaced, roughly 15 to 30, 30 gram doses. When you look at the individual studies yet the systematic review really didn't find any discernible difference in terms of body

composition outcomes. . So again, like when you look at these large scale analyses of metadata, where you've overcome that limitation that Ian was rightfully criticizing.

That is an indeed a problem. It sucks. You gotta wait five years before your study can be used, until someone else does a meta-analysis on it. And hopefully they do it. But that's ultimately the closest thing we have to truth and it doesn't comport. With some of these fundamental studies that are seen as groundbreaking mechanistic, understanding of the way protein kinetics operate.

And it's not that I think that those mechanistic studies are wrong. It's just that they're highly controlled studies that are very internally valid, maybe minus one or two things, which we'll eventually talk about, but their external validity, their application in the real world, they're miles away from what's actually occurring in the actual kitchens of people's homes.

Alan Flanagan: Yeah, I think so. There's a couple, one is that we've talked about this before, cause you made the point that part of the problem with a lot of this research is the individual studies themselves are null, small sample sizes and meta analysis becomes generally the tool to try and overcome that.

And, but then the question is it's a big thing we've talked about nutrition, meta analysis before is whether it does or does not accomplish that depends on the primary included studies and their quality and how uniform they are. My, and correct me if I'm wrong here, my general sense of this specific area is that meta-analysis probably does accomplish that because we're typically comparing doses that are largely and sources of protein that are largely, like they compare 25 grams a away versus 25 grams of soy, or sometimes the dose isn't matched exactly like that.

But there isn't necessarily the background variability in population that you would get in a lot of other meta analyses. So actually I think this is one area where meta analysis works. Because typically the population group studied is relatively similar. There's often a if resistance exercise or if there's an exercise component, you can know what that exercise intervention was and make sure that you're not matching studies that had RT (resistance training) with studies that had triathletes.

So I, I do think that probably does accomplish that, but it still doesn't correct for those other issues that you're raising these methodological issues of: okay, if we synthesize these evidence, we can come to some big picture conclusions, certainly in relation to total protein intake. And then the question that becomes reconciling that with obviously it, it gives you a tool to reconcile discrepancies in individual studies.

But it doesn't necessarily cover all of the gaps, I think for the methodological issues that arise that are still used in the primary studies. So at best what it probably gives us is an ability to synthesize some big picture conclusions in a very general sense, probably mostly in relation to total protein intake, but they don't resolve any of the other questions that arise from that research.

And I don't think they necessarily answer some of the questions that the mechanistic research leaves open in relation to the yeah, like MPS, how important that is, across the day and these kind of variables, that're still you're still left with individual studies that kind of form, the linchpin of claims that are made in support of that.

Danny Lennon: So let's say we've take an example of someone cares about muscle hypertrophy and they're saying, "okay, everyone will accept that MPS is just a proxy measure for actual muscle hypertrophy. In a research setting that is very useful in terms of the type of studies we're gonna do." And that's uncontroversial in terms of people in the field, how much, or what is the span of disagreement, do you think in terms of how good of proxy that is?

Because there's some people who might say it's actually good enough that it's actually a really good marker that it's very valid. There's some people who are more concerned about relying on it too much. And then second, how much do you see that as even an issue? Is it like, does that concern of how good proxy it is disappear once we marry that research up with actual muscle hypertrophy research, and then try and come to a conclusion? If that makes any sense?

Eric Helms: It does make sense. And I think this has bounced around in my head and in people I've talked to and how they appraise it over time, because we're actually still learning some of the methodological issues.

And what is a threat to external validity over time? It was only 2017 I think when Damas did their research, which it like in the evidence based community, it got taken up as "oh, muscle damage doesn't matter." And I think I find that's an interesting thing that they didn't find any relationship between muscle damage and hypertrophy.

And that it actually seemed as though the body had to repair muscle damage before it started giving "resources"towards building muscle. That's really cool. And it's interesting from a mechanisms hypertrophy perspective, but the most important finding in that study for anyone who's interested in protein is that the initial scores for MPS were 0.1 R-score related to hypertrophy, like explaining nearly nothing of the variance of hypertrophy and that they had to correct for the damage. Meaning that the initial one to two days of MPS that you're looking at, maybe not two days, but at least the most of the studies are two hours long, right?

The long ones, like are more like 14 hours. But when you're looking at the initial scores of MPS, which are occurring in 80-90% of these studies, which we look at as MPS, if there's a high component of damage, it's completely confounding the results. That's what we learned from Damas. So how many, so it's basically, anytime you look at a study on MPS where it's untrained individuals, you're looking at MPS, that's explaining the variability in muscle damage.

Anytime you look at a study where they're doing an unaccustomed exercise, even though they're trained, you're looking at the muscle damage variability. Anytime they use an exercise, which might be at a long muscle length or has a strong eccentric component, you're looking at that muscle damage variability, and even in people who are reasonably well trained, there's still a much more robust muscle damage response than people with a really, long training history, with a multitude of exercises training at a high intensity, with high volumes who have a really robust repeated about effect.

That's gonna be present in all types of protocols. Now the interesting thing about Damas to give some credit to MPS was that once you corrected, I think for the first 24 hours or 48 hours, and you have to excuse me for not remember the exact methods of this study. Then there was actually a pretty strong relationship between muscle protein synthesis and longitudinal outcomes and hypertrophy.

So we know there's potential for MPS to represent actual outcomes. And that's why it hasn't been abandoned. And I don't think it will be nor should it be. I think most people would've assumed before that study: "oh muscle protein breakdown that contains all of that". And that's a small part of it.

We didn't even look at that, so that would've been damaged, but apparently that's not the case. There is the formulation of new proteins that's occurs as a part of the muscle damage process. And that's like a duh, when you think about it. But that just wasn't the perspective. So that's one example of a more recent understanding of these mechanistic shortcomings.

But even before that, if we go back to Areta, they came in a fasted state and only had whey . So now we've taken literally the fastest protein on the planet. And we've put the person in a fasted state. So gastric emptying is at its fastest. And then what do they eat throughout the rest of the day? Anything else? Any lipids? Any fiber? Nothing. So we've created this, hyper speed version of digestion. Which of course is gonna have an impact on amino acid kinetics, absolutely. And absorption.

Alan Flanagan: And there could be a number of ways that we could actually like start to parse this in terms of duration and potentially then the relationship between MPS and outcomes.

And whether it's even relevant for us to consider those outcomes. And I think we could think about studies that look at the kind of two hour post-prandial period, that real short duration of MPS. And I think it's very easy in those studies to compare whey to virtually anything, including other animal source proteins and say, whey is superior because you get this immediate response, and again, that you know this, oh, that kind of flood of amino acids into circulation circulating leucine. If you measure it as well as MPS bang through the roof, that's great. The leucine trigger that's why quote unquote whey is superior. And then you extrapolate out over say five hours or even further than that.

And a lot of this tends to fall away as far as a "superiority" to whey in particular. And then you think about beyond MPS. Then if we're looking not just at a postprandial, acute responsiveness, where we're looking at circulating substrates or MPS itself, if we're looking at actual lean mass accretion, for example, fat free mass accretion or changes in actual

performance parameters what are the outcomes then over eight weeks, 12 weeks.

And I think thinking about it that way gives us slightly more of a picture of how to maybe have these related to each. And so yeah, in the short term period whey is probably superior to everything else for these responses, for these outcomes for MPS and for circulating leucine whey will jack it up over four to five hours?

No, there was that one of the studies referenced yesterday was this study that used a wheat protein isolate and over two hours, not a, but four hours later, there was more muscle protein synthesis from the wheat protein than the whey again, probably to do with more durable amino acid circulation versus the whey.

And then extrapolate then out over the course of a whole day, if we're thinking about some of this stuff and some of the differences in these proxy outcomes, amino acids in the circulation, muscle protein synthesis. And we think about all of the various different protein. Types that have been used in these interventions pea, rice, whey, casein, wheat isolate forms.

Otherwise you start to be able to possibly at least form a hypothesis that in the context of a mixed diet, most of this is possibly irrelevant at a really micromanaged level. And then if we think about, okay, then let's just think about outcomes over the long term then it seems to really just start to become less relevant as far as some of the micromanaged aspects, because with the strength and outcome data, it seems once these kind of big picture aspects are in place, that then, improvements in bench press or squat one rep max, or improvements in other performance or body composition parameters. So I think a lot of this probably comes down to taking a particular outcome and focusing on it possibly out of context or too much or not giving it the wider context that outcome should. And then not doing due diligence then to relate that particular outcome to quote unquote hard endpoint, so to speak.

Danny Lennon: Yeah so I wanna build on that, but maybe first as a recap for people where we've of got to so far is saying, okay, if we have an interest in either muscle hypertrophy, muscle recovery, and we're talking about protein

rather than only having to rely on an outcome of actual muscle hypertrophy, because there's some difficulties there that we can certainly address.

A lot of the research is gonna look at muscle protein synthesis as a proxy measure. And that is on the assumption that if we theoretically maximize muscle protein synthesis over the course of a day, and we stack multiple days on top of each other, over long enough period of time. That should give us an indication; you're more likely to build muscle than not, let's say, or more likely to promote recovery than not. And then if we shorten that down, we know that there's probably a benefit to more than one protein feeding per day. So that's where we look at this per meal muscle protein synthesis. But then now we've also got people to a point of saying, if you solely focus in on what is the immediate MPS response of feeding, particularly an isolated protein source, as we see in lot of these studies and you look at which one gives the biggest muscle protein synthesis response in that immediate period, that's probably not the best question to ask when you're thinking of superiority or even more than that, just how should I eat for this particular goal?

So with that in mind, people might be now thinking what are better questions to ask if this is my goal? And there's probably a multitude of these where would you start trying to give people some hints of what questions they should be asking as opposed to which protein source has the best MPS response?

Eric Helms: Yeah it's a tough one. And, I've sometimes I've thought and, to be honest, it would, I'm surely not the perfect person to think about this, but I do think that the proximity and the participation in doing some of this mechanistic research creates a certain focus on it. That I have seen a disconnect in some of the ways that I would say, like applied sports nutrition researchers like myself and mechanistic researchers view things like Jorn Trommelen or Stu Phillips, they would be great to talk to about this because they've done these things that I've just had to wrap my head around and scratch my head and think, why does this comport with the stuff I do? But, for example, when you do see correlations that explain at least a reasonable amount of the variance in hypertrophy with these proxy measures, they do things like looking after the acute period, looking at, after the 48 hour period and they do things like like looking at area under the curve, which is not always done in some of this MPS data, which anytime you don't look like area

under the curve, you look at the peak whey is always gonna kick everything's ass. Cause it gets dumped into your bloodstream immediately and creates this, hyperaminoacidemia and boom, you're you get a strong, immediate response, but when you start to look at like AUC data area under the curve, over multiple hours, all the other proteins start to catch up , and when you think about it what's actually gonna be the closest proxy to me growing muscle over months and years? Is it gonna be the peak point that occurred in the first hour of that training session I did six months ago? Or even yesterday? Like on a repeated effect? Or is it gonna be the total area of the curve that, that overall cumulative muscle protein synthesis and like logically you'd think the latter.

So those are a couple things that I would definitely encourage people to do or to look for whether they're either involved in research or they're reading it from a methodological perspective, those types of things. I don't know how to do them, but I know that they make a lot more sense and they get around some of these issues.

And I also think that doing research in an actual post-prandial state would be like you're introducing like confounders. And that's the reason why you come into things fasted. But you're also matching what is happening in the real world. Some people work out first thing in the morning before they go to work, and that this data might be reasonably representative of that situation, even though it's not representative muscle, they'll grow long term. But most people are doing that, working out in the lunch break or working out in the evening. I work out most of the time after two meals and I think a lot of lifters do, and I would love to know what does it look like when you're stacking digestive curves on top of each other? Cause I think that's the reason why we don't see that marrying of this idea that you have to eat every three hours and, refractory period's over sweet jacket up again.

It doesn't really make sense because in that, those artificial conditions that I described as hyper speed, digestion like in Areta, you've essentially removed so many aspects and you've created this peaks and valleys perspective of what human digestion is like. When, in reality, like when you look at some of these other lines of research, like how long does it take to digest an omelet? How long does it take to digest 20 grams of protein from lean meat? Yeah. We're talking like six to 12 hours, yeah. So the only time when you're truly in a place where you're not digesting anything is if you had an early dinner and

went to bed and then woke up late and you hadn't had breakfast yet, or if you're purposely doing time, restricted feeding, but outside of that the laboratory conditions are quite different.

And another thing that I would say is that we probably need to be doing studies where there's a mechanistic component and a longitudinal component, and they're built to inform one another. because a lot of the times right now, like the easiest thing to do is you get a supplement company to give you a couple grand. They give you a bunch of protein powder and you do an acute study head to head comparing the protein powders and it creates this false comparison where we have so much research comparing whey to soy, to casein. And because of that, everyone thinks as an example, casein is a slow protein. I got news for you. It's literally the second fastest protein out there. It's behind whey. Everything else digests slower than it. Almost every whole food protein that I can think of. There's a great review by Bilsborough and Mann that I read early on, it's a 2006 review, a review of issues of dietary protein intake in humans. And it has like proteins speed to various proteins and casein is second, it's. When I remember I used to go to GNC when I was like 2004 and they'd be like, oh, you need casein, because it'll last you throughout the night. And I'm like, okay, I won't have chicken breast instead at dinner, I'll have casein.

And I'm like, that's actually, I was you're wrong. Like that's casein is a relatively fast protein. It's just compared to way, which is lightning speed. So it's the way we do research influences our perceptions about these proteins in ways that are often not ecologically valid. So I think if we start to go okay, when is internal validity important it's and like your data won't be bad if it's confounded quote unquote by the fact that someone has eaten or trained yesterday, it'll have the noise, but that noise will be repeatable and it will be representative of what we're actually interested in measuring.

Alan Flanagan: Part of the problem is we're hemmed into this paradigm where the assumption is the only way to proceed is with the classic randomized trial. There are so many different ways of doing even randomized trials that are potentially more valid designs from an ecological standpoint; n-of-one trials, for example, and otherwise.

And I think that idea of combining the mechanistic data with longitudinal data, it can be done. But if groups just keep repeating the same thing, then

we don't get these open questions answered, but also we don't build on methodology and nothing improves. And so the same types of studies will be repeated for a few more years and then someone will churn out a new meta analysis.

So I think that those problems are a kind of meta level issue that a lot of different domains of science have where, the assumption is well, the classic, longitudinal randomize them to whey and randomize them to soy. And off we go and we will get them to do 3x 24 hour recalls of baseline and follow up. And that's our kind of control of diet. You can certainly design studies to be more ecologically valid. You can certainly try to at least have a consistency with say when they train during the day. And then you can adjust for that. You can adjust for how many meals they had or whatever.

There's the way there's always ways around these kind of issues. I think what it ultimately leaves us with is this body of evidence that probably has a lot of gaps filled even then in review papers. And otherwise gaps will be filled based on the mechanistic data. Rather than the big picture data.

And I think that's where we get a lot of these recommendations for quite micromanaged strategies. Like you mentioned, like how long did were bros; me included in my early twenties. I wouldn't leave the house unless I had a shaker with some protein powder in it that I could mix with water if I was stuck in traffic, because heaven forbid I go across two and a half hours without a dose, so these things do die hard. But I think a lot of those practices that translate into the real world and become the basis of advice are often coming from extrapolating more from the mechanistic data rather than the big picture data.

Because I mean with this particular area, if we were just to, if we were just to leave people with the big picture data, we'd probably at this point only end up saying it's your total daily protein and don't worry about anything. And that may not be valid either.

Danny Lennon: Yeah. And I was gonna ask about that because yeah, if you take the two extremes, which I don't think really any competent practitioner tends to lean towards, but if we took those two extremes, it would be on one end of saying, look, we know from, for example, the systematic review that

the Morton one and others that just get 1.6 grams per kilo and above, and don't worry about any other protein related questions at all.

The other end would be let's solely look at muscle protein synthesis, and just four times a day. Can you surpass this amount of losing? Yeah. And then as an added bonus, maybe from a, an intact protein. And so then in between we're left to, okay, how do we merge these together? And I think one of the interesting things that kind of speaks to this gray zone where you were saying we have to fill in the gaps is yesterday, someone asked the question about.

Generally a lot of people, I would say in, in evidence based space would say, look, probably total daily. Protein is most important for this goal but also distribution matters a bit like one meal per day is probably less than optimal. And then the dosing in that meal. And then also the types of proteins you're consuming in terms of like their amino acid profile is also important.

But how much each of these contribute, right? This is impossible for us to give any real answers to, but it speaks to this interesting thing at what point does it matter? Yeah. And this kind raise the idea of, if you're on a really low protein intake, would distribution matter much more the per meal feeding matter much more then if you're getting two grams per kilo maybe it's less relevant.

So from a very sort of pragmatic perspective, if you had sports, nutritionists coaches, or just athletes coming to you, and they said, okay what do we actually know from the literature. How would you start piecing together some of the question on like protein intakes and what degree of confidence would you have on each one of those recommendations?

Eric Helms: That's a great question. That is basically just you phrasing the same question you asked earlier that I went off into internal validity, external validity, mechanistic, nonsense, but I'll actually answer it this time. I promise. So I mentioned that this is, this has changed even in my own brain and others in that conversation.

And this is actually something that (Eric) Trexler and I have gone back and forth with. We've had for us epic peer review battles. So it's, a couple of polite comments that we resolve in five minutes. And I, because I tend to come from the school of like neutral, positive, let's do it, bro. I'm trying to get super

jacked and Trexler has reformed from that. And now he's more reasonable and I refuse to because I still wanna look amazing in posing trunks. He generally lies on the side of being open to there being an applied study that will confirm the MPS data, but he'll make recommendations purely based upon the applied stuff.

And I tend to lean on I use different wording. I'll say, definitely do at least this. And it's possible that you might get an additional benefit from doing these things. And now I've changed it a little bit, so that I'm, I tailor my recommendation to who I'm speaking to. And I think because you always don't wanna do harm, right?

So for certain people asking them to eat a fourth or fifth meal or to weigh and track their actual grams of protein or do those things is not a big deal at all. They're possibly already doing it. They like to do it. They want more data, they wanna do these things, your typical bodybuilder for other people.

You're asking them to devote brain space, time, and energy, and to do something that's annoying, or potentially make them unhealthily focused on their nutrition. So I often gauge what are the potential downsides to adding a variable that they need to track in their life? What are the potential upsides or even just making them feel like they might be doing something a little more proactively.

So it's a, so I tailor my message to who's listening. So often, so I would say what we do know from the applied research is you probably want to have at least three bolus of protein per day to reach those meta analytic targets of say at least 1.6 gram per kg of protein. And if you do those two things, everything else becomes far less important.

And we don't have long term high sample size studies to confirm that maybe over 24 weeks, it wouldn't make a difference, but it's probably not a bad idea to do other certain things to encourage optimization. If that's for you I would say, if you put a gun to my head and you said, Hey, if I studied body builders for a year and one group was on 1.6 grams per kg, vegan proteins, only three meals a day in eight hour window.

And the other group was on two grams per kg, a day, omnivorous diet. They got it also postworkout within two hours every time. And they had four meals

at least would they grow more? I'd say, I think they would, I think they might like, it would be a very small difference. Yeah. But they might, and I'm not confident enough to say it won't make a difference just based upon the applied studies we have.

Yeah. And that's because of the mechanistic data. Now, the thing about the MPS data is you can find conflicting studies and this is something that I could be wrong about, but I mentioned it to you as a little casual side, holy shit moment. I was like, I'd never seen someone report reliability statistics in an MPS study and it's not that. And like you said, you see where the amino acid goes. So it's not that it lacks face validity, but I don't know what the normal biological variation within participant is. Because between participant it's like threefold, I'm looking at a study right now and you've got, FSR rates as low as 0.02, percentage per hour up to 0.075. So there's a lot of between participant variability

Alan Flanagan: And you can't find any research that's actually done repeated measures to determine intra individual variation. Exactly. And then to be able to at least have that to correct for potential measurement error.

Eric Helms: So there's some false potential false positives in the MPS data. Cause you can look at some of these studies and you presented some of it where you can create different hierarchies of protein. If you cherry pick studies where you can show that milk is worse, the way is better than peaweigh is worse than peacasein better than way is worse than casein.

Alan Flanagan: You know and also one of the, one of the, with MPS in particular, in this general kind of framework, we discussed a little bit yesterday of, flood, flood the circulation with the amino. Get a nice leucine, curve hit that leucine trigger threshold for the actual intake of the amino acid and then this big spike in the blood levels.

But then you look at some of the studies and they don't connect. And I don't think it's a limitation. I think it's challenging us to think about some of these assumptions, even within the mechanistic data. So you have the mycoprotein study where with, versus the milk, you get this like big milk spike of circulating leucine, but the muscle protein synthesis was substantially higher in the mycoprotein group.

It's not to say that what we're looking at is wrong. It's just saying that some of the assumptions that we hold from the mechanistic data require continual challenge, I think.

Danny Lennon: Yeah. One of the pragmatic things that you've just touched on Eric is that the magnitude of change we would even see. So even that theoretical situation where we do everything mechanistically correct. And even if we were to say, yeah, you would get a benefit. This is very much in the realm of optimization for someone whose sole goal is to put on as much muscle as possible, let's say, but then pragmatically when we think about it, for someone who generally wants to let's say, maintain muscle mass, recover from the training sessions, is a health focused person; would it really make a difference if they generally aim to know what good source of protein were consume them when they were having their main meals and without tracking anything end up at 1.4, 1.5 grams per day of total protein. And didn't really think much beyond that? Like what is the magnitude of change in muscle mass that they would actually see?

And would it be meaningful to what their goals are? These are just practically questions that may be irrelevant to most people, unless their goal is to optimize, which I guess is where most of this stuff is focused.

Eric Helms: And that is ultimately the difference between people who operate in a sports science place and people who operate in... and the studies are very similar. When you do sports science, you manipulate a nutrition, variable you manipulate a training variable or both and you look at these outcomes, but when you think about the difference at an elite level sport of what dictates success, compared to someone who is untrained versus trained two years, huge difference, comparing someone who placed 10 at nationals to the national champion, who then went on to compete at, the international level of sport, very small difference in terms of the actual magnitude of numbers, but we know like a 9.8s hundred meter sprint compared to a 10.1 are light years apart, even though they're yards apart, right? Yeah. So the you, if you don't do the due diligence of communicating these things in the right way to the right audience, you can really get people, get their nuts in a loop about stuff that they will never be able to actually notice the difference in themselves.

And I, so I will say if we look at total daily protein intake, comparing less than 1.6 to 1.6 or higher, that's a graded dose response. You have to go all the way down to the RDA and to compare it to double the RDA before you get a moderate effect size. Yeah. So once you and, okay and that's, and when you look at the, like the, these meta analyses on total daily protein intake, they're encapsulating all the other things related to because the protein was consumed at a time in relation at some point to training.

So all that variability is contained within it. So it can't be more than a moderate effect size so if we look at the, for example, the the Schoenfeld meta that first started questioning the the relevance of protein timing. They found a small effect size from having things in the post-workout window.

And then when they controlled for studies that match protein intake, it went down to a trivial effect size. So if the individual effect of the timing of when you eat protein in relation to your training is a less than 0.2 standardized mean difference or a trivial effect. And we're operating within the potential total possible at the group population level of a moderate effect, you would expect all those other little factors are at most gonna be trivial , but far and away the biggest thing is it has to be just the total overall protein dose. And maybe you could do some things to really mess it up, but you'd need a long time to see it. So for example, there was a I wanna say it was Mor. They did a eight week TRF. And then they came back and did a year long TRF, which was an extension of the first one. And in the eight week TRF there was no significant difference in body composition. But when you looked at the year long one, you started to see some body comp stuff that favored the non intermittent fasting quote, unquote eight hour fasting window group.

And I reviewed that in mass and I was like, oh, this is cool. A year long study. And you do start to see these differences from. Small like this, basically, the classic question when Martin Berkhan was like the the Jesus come to tell us all that the three hour, eat every three hours, get your Tupperware, like you said, all the bros, if I didn't have a protein shake within 20 seconds of finishing my drop set, I shouldn't have done any drop sets. It was a waste of time. And you only trained with drop sets, right? So like he came and just turned everything on its head, not only is it unnecessary, it's actually worse, it didn't do it that far, but it was this complete overturning of the, of, it was a zeitgeist of "Hey, we can eat an eight hour window and it's just as good." And now we're starting to see that. Okay. If I study people for a year, I can see

small, but significant differences between groups from only restricting myself to an eight hour feeding window. And again, that's not a study on protein timing. It's a study on a eating window, which tells us something about it by implication.

Alan Flanagan: Yes. Because even the, even if you look at the 12 week study that they did first, you saw some, although overall kind of differences, weren't significant between the two groups.

In some particular measures, there was a little bit of a signal in the noise that was like hold on a minute, something's happening here, particularly for lean body mass and body fat. So the eTRF group ended up putting on a little bit more lean mass, losing more fat. And of course, Martin Berkhan that study came out was like "I've validated".

But I guess the point was by, by implication. And this is something I've told about a lot, just in relation to the time restricted feeding research, because a lot of there's a lot of overlap between what we're discussing here is, are we talking about the duration of a feeding window itself, having some importance?

Are we talking about the relationship between that duration of a window and the energy intake within that window. So for that Moro study, the TRF group were consuming the guts of two thirds of their energy intake in a really tight timeframe around their training session. Whereas the 12 hour group weren't.

So is there some sort of temporal relationship between exercise and just, and this wasn't even a protein study, right? This was just a mixed diet. So is there a relationship with the temporal aspect and then, O other questions, even more kind of nitty gritty is, does the actual then timing of that intake related to the temporal window matter as well?

And like you said, okay. So with a lot of those meta analyses with the protein intake on total intake, That those issues will themselves be brought into the actual ultimate effect size and precision of effect estimate in a meta analysis. But that in and of itself is a problem of meta analysis.

If those factors are important because the meta analysis won't give us that it will obscure whatever those factors are that are important. And that's an

issue. We see play out with a lot of nutrition studies where, you know, issues like the actual magnitude of the comparison and intake, cause all nutrients exist, macronutrients included, on a bell curve of action. So you mentioned there that you have to go to get double the RDA versus the RDA to start to get moderate effect sizes. That's totally unsurprising for the nature of nutrients. So when you are comparing within a narrower range of intake you don't get large effect sizes.

So it's the same with, if we're comparing saturated fat, you're not gonna see much comparing someone consuming 14% to 11%, but consuming 19% versus 8%, you're gonna see a big difference in, in blood lipids and risks. So I think these questions, I think that those syntheses of evidence that exist to date are helpful to bring us back to, the first principles that you just, put to Eric in terms of overall level of intake.

And secondarily you probably do want that maybe in three meals, let's just say without going further and micromanaging it. But that's not to say that some of those other issues that we've touched on are not relevant. We just don't have enough right now to be able to. What their relevance is, if any. And I guess that's the fun of science.

Eric Helms: And another angle you could take would be to try to create like that year long, eight hour window which turned the initial 12 week study on its head more went from looking like it's favorable for time restricted feeding to then a year later, oh, actually it's slightly worse. From that aspect, the body composition outcome, you can start to do things that stretches the limits of what we think is true from the mechanistic research in reasonable applied settings, to test it, to try to disconfirm that hypothesis.

So for example there's some four hour time restricted feeding studies which look a little worse on, on net. When you look compared to the longer one. Or if you look at associations in plant-based eaters of just having lower total daily protein intake, lower lean body mass scores at the population level.

However, when you look at like comparing head to head of vegan diet when they hit that protein intake. So I think if you constructed some things where you're like, instead of just comparing these, like you said, things that are along a spectrum that are just an inch away from each other, all right.

Have one protein feeding in a four hour window, but still hit the total daily intake. Then we might get an idea of, how important are these other things? If you meet one of the criteria and not the others. And I think what we'd see is you can construct scenarios where these things are important , which I think speaks to the fact that look the MPS data. If you get around some of the noisiness and some of the issues with the methodology behind it, and you look at consistent trends, That probably is telling you something that is true. And then the question of how much does it matter and in what context that interacts with all these other things.

So if you're someone who without really thinking about it, you eat three meals a day and a snack, and, you train any time besides first thing in the morning and you're an omnivore. You don't have to tell that person shit except eat 1.6 grams per kg or protein or higher, and just distribute it between your four, four meals and make sure not any single meal is just like a massive proportion of it.

But if you approach someone who is finding that, they have a time restricted eating window, and that works well for them. It helps them with their sleep. For example they're not an omnivore, let's say they're on a vegan diet. And they train first thing in the morning in a fasted state. And, but they're already eating, a high protein diet of 1.6 grams per kg, I reckon you could see a reasonably large difference for them. By doing certain things, like getting them to wake up and have a peaprotein shake and go, okay, so we're gonna extend your fasting window. You can still be fasted, but now we've actually got you to the point where you're training after protein.

You, you have more feedings throughout the day. We've figured out ways to improve the quality of your vegan diet. We've taken a vegan diet. That's actually low quality. And now we've supplemented it with peaprotein to get a vegan diet with high protein quality. And they might go from 1.6 to 1.6 or 1.6 to 1.8. And you wouldn't think there'd be a major difference, but they might actually see at an individual level large differences because they were doing things that actually hindered these things that we would might think from a bodybuilder perspective. They're oh, you wouldn't do that. Those are Cardinal sins that are really minor, but if you stack 'em all up they could matter.

So anyway, like the way I end up communicating this to finally answer your damn question, Danny is I tell people, look big picture, big rocks and. Only think about anything beyond this. Once you've gotten these down and they're incorporated into habits of your life is to have a serving of protein.

With each meal, have at least three meals a day, reasonably spread out train at some point between the two beyond that, don't even worry about it. If you need a protein supplement to hit 1.6 grams per kg. Great. If you're already there, let's just maybe take a little out of dinner and put it into to breakfast, have an additional egg, and then don't have quite as large of a steak or whatever.

But I try to get them to hit the, like the big rocks I've hit the total daily amount, eat at least three meals and don't have a massively imbalanced amount of protein between meals. Cause we have seen in a few like comparative studies, like the typical Western eating pattern is, this increase in protein, across meals.

And when you look at least associational data, you tend to see people who. That pattern, even at similar protein intake, not carry as much muscle mass. There's one study that has a, non-significant finding leading in that favor and some associational data. So like when we look at actual outcomes, you can make an argument for those aspects.

Then you have to reach to say, you should have, a slow protein before bed. You should have at least four meals per day. You could cite, the MPS data. So if the person comes back to me and they're like, sweet, I've sorted it, I've got three servings of 40 grams of protein spread out throughout the day.

And I eat between, meal two and I train between meal two and three. Anything else I can do? And then I'll go, sure. Like now that you've that's not non-issue and it's not like you came back to me with an eating disorder as well, then sweet. What do you think about getting one more protein bolus, at night?

Cool. We can do that. Great. And then we can figure out what makes sense for them. So long as it doesn't displace something else or create a burden that is not worth the potential, squeeze is not worth the juice .

Danny Lennon: I think we can apply this as another example to the original point that we were talking about if this comparison of plant versus animal protein, and we alluded to at the very start way, this may be the wrong question.

And we've spent some time here discussing the differences between looking at mechanistic, work on MPS versus these kind of harder outcomes. And this really plays out in these online debates of plant versus animal protein, depending on which side of the discourse someone is. So you'll have people say, "look, it's completely irrelevant what type of protein you pick. Because once you get enough, then it doesn't matter". And on the other side, you'll have people that will typically have looked, and this was the way it was for the longest period of time, this isolated whey versus something else: you can look at that amino acid profile, and so one is clearly "better" than the other and again, these are both two ends of an extreme that is represented in this discourse. Hence why, again, this may be a problematic way of looking at it. Yeah. So to revisit that question you, that we said right at the start of why, after your investigation into this plant versus animal protein question, you ended up coming around to do you know what I think this is the wrong question, despite this being a head to head that we've seen in all this research, right?

You and Eric have both talked to.... There's loads of papers we can look at whey versus soy. But this is ultimately maybe not the best question at least people pragmatically to be thinking about in the way that they currently are.

Alan Flanagan: Yeah. And I think one of the, one of the big, just, unescapable realizations, if you look at any of this literature and we discussed this yesterday is, and we're talking about ecological validity today, Is just the sheer lack of food based intervention.

Like we don't know how foods influence these outcomes. We're so obsessed with, for the most part, we, there are a number of studies that have looked at food. So we mentioned there's study for example, that compared whole eggs to egg whites, and yes, when it comes to that over, again, and this is over 300 minutes, so it's over about, five hours odd, whole eggs, have a greater effect on muscle protein synthesis.

Okay. What does that mean over a longer period of time? What does that mean over the course of the day? There's some interesting research that has souped up not both, mycoprotein and then souped up milk proteins with additional amino acids and found not just no effect, but that the food in its intact original form had a greater effect.

So this kind of obsession with amino acid composition, this obsession with, get this hyper aminoacidemia response in the blood get circulating leucine spike through the roof, hit that MPS threshold. Like again, that, that is where the focus of the plant animal debate tends to be. It's largely based on comparing isolate versions of plant animal proteins.

And I think it's the wrong question because it's moving us away from the ecological validity question of, is there an effect of a whole food matrix? No, no study. One example is yet where is the study comparing in a normal say vegetarian or vegan diet versus a normal omnivrous diet, tofu, which you could hit your leucine threshold with about 160 grams of tofu versus say 150 grams of non fat Greek yogurts. So macro wise, they're fairly equivalent you're not getting a massive calorie or carbohydrate difference between the two foods. But they're whole foods. And I don't think we can answer those questions based on any of the supplement studies. We can't. So it's not that it's just this plant or animal question.

It's that within the construct of say, quote unquote, plant proteins, there's clearly going to be different food sources. Of plant protein that probably have different effects. If I feed someone tofu versus lentils, what's their response going to be. And the adaptive response over time. And again, we can see the same in studies that have compared, beef to milk, egg, whites, to egg yolks or whole eggs.

So I think the question comes back actually more forget the plant animal binary. There's probably just differences of individual foods and the food matrix and the food matrix is going to be relevant based on everything we know already from the amino, that's at least where we can take the mechanistic stuff that we know and say, at least our hypothesis would be that the compositional differences in the whole foods would have an, and if you do see differential effects, then you know that there's some sort of food matrix, food, synergy stuff going on.

You might not just be able to explain it at that point in time, but part. Part of the brilliant, we've talked about this before. Part of the benefit of a top down approach and a whole food approach is you don't actually need to keep hammering away to figure out you don't need that reductionism.

Because the exposure of interest is food itself and all of those questions are actually open and unanswered right now. And it'd be great to see, people as Eric, you said, unfortunately the easy out is you get a supplement company to give you a shit on a protein powder.

It's just we need to get a, I dunno, tofu company to start, we need corn to start giving people yeah. A food companies. So I think the question is probably more that there are differences between foods. And I think that is worthy of study, but I also think that any such foray into the study of the difference between foods, irrespective of whether they're plant or animal origin, Is actually to take that finding and have it be contextualized against total dietary pattern.

And because let's say we do this let's say I, we get funding tomorrow and we do our tofu versus Greek yogurt study. You're not just gonna eat tofu and Greek yogurt. So I, I think that, there's two ways of then approaching that one is the slightly more ecologically valid, but we don't really control for the rest of people's diets.

We try and get them to keep habitual. We do a good analysis of their diet as an assessment to then know what we're adding this tofu and Greek yogurt to fine that's one way. And then the other way is actually we're taking two dietary patterns and we're going to control the other aspects of that diet to then have more this food comparison, but then you would know that comparison is relative to whatever that background diet was.

And both of those have strengths are limitations. Yeah. So yeah, I just, I think this whole plant animal debate that playing out online and game changers obviously really kicked it off with a lot of this stuff. I think it feeds into the big ideological battle that we have in nutrition right now.

I think it's a pointless debate in most instances because it leads us to these absurdly reductionist kind of positions overall but certainly as it relates to protein I think it's the wrong question. And I think there's a lot of more open

questions that relate to actually foods per se, and a total diet beyond whether it's a plant sourced or animal source protein.

Danny Lennon: Two things that spring to mind there. One is obviously if you say, which is a better protein animal or plant, even if we focus in just on muscle, it's it almost doesn't mean anything. It's yeah. So it is way better than wheat protein. We could probably make a case yet probably if you're gonna just consume that maybe over two hours, but maybe not over four hours but then, but maybe not over a day.

Yeah. But then is soy better than collagen protein? Yeah. Yeah. And then, but again, these are just reductionist on isolated types of protein and you could have, again, it's on a food basis, right? Some plants are probably gonna be better than some animal products and vice versa. And then the second thing, and you bring up The Game Changers: I think that largely gets into a whole other conversation around health, but that again comes and it comes back to why you said that we have to think of it in the context of an overall dietary pattern, right? Yeah. It's not just the protein, if you compare two diets that predominantly are, let's say a vegan diet and an omnivorous diet that have lots of animal protein and just plant protein, then changing that changes a number of other nutrients, which have important aspects on health.

But yeah, even for muscle, just the idea of plant:bad, animal:good is probably just the wrong conclusion to come to. Yeah.

Eric Helms: I agree. And it was funny. You were bringing up the whole egg versus egg white. We don't know why. Yeah. Cause it actually doesn't make sense when you think about it from the leucine content comparison, for example. I thought there was even more in the egg white or they match for leucine...

Alan Flanagan: Sorry. I think you're right. Actually I think, sorry. No what it was, what I remember from that, what I had yesterday was the actual postprandial leucine response yes. In the blood was like 9% higher from egg whites than it was for whole eggs. There was a 34% increase in circulating leucine in the egg white group versus 25% in the egg yo group. So again you're seeing this dis and we saw that with the mycoprotein, with Benjamin Wall's mycoprotein studies, oh, the milk; big spike in leucine, but actual muscle protein synthesis and otherwise favors the mycoprotein.

So we're seeing effects. That are not explained by a lot of the simple heuristics that people have come to internalize about this question.

Eric Helms: Yeah. And I wanted to, it made me when you brought up that egg study, it reminded me of a very recent egg study that came out where it's like a Rocky study where they compared five boiled eggs versus five raw eggs. And there was a difference in the appearance rate of amino acids, but no difference in muscle protein and synthesis. So it's yeah, like you have at the top level, you've got people's diet, then you have the food matrix, which can be different even within the same food based on preparation or removal of part of it.

And then lower than that, you have, okay. Just the isolated protein source and then lower than that, you have just the isolated amino acids, or at least the non combined amino acids. And I think we have to just make sure that these different levels of analysis at each one of these steps. Are aware of their limitations and try to connect with one another, which is, I think where we've lacked recently, we've had these just two very separate worlds.

Not always. I think like Damas is a great example or oh, there's another one that I can't remember then there's a few times where they've combined these proxy and outcome measures the acute and the chronic, the short term and the applied and those are great. Because then they're actually in the study trying to figure out how they connect and those, I think those individual studies have been worth more from a like an epistemic understanding of how this all works than hundreds of other studies combined that even though they answered their research question, they're just not useful.

And sometimes they even serve to confused. Like when you get okay, one study way was better than soy. Next study casein was better than way the casein was worse than soy, but hold a wheat was better than like it doesn't, like these studies. they answer the research question, but when they're thrown into the big melting pot of trying to understand the MPS picture, it makes it murkier.

But these individual studies where they really do try to make those connections, they give us these kind of monumental leaps forward, where we go, oh shit, we're measuring damage, and we can start to have these more productive conversations. So I think really it just, we just need to have

research where we identify the level of fidelity we're examining the diet at, and then we acknowledge those limitations.

So when we're looking at the entire diet, we acknowledge that we're looking at this crazy multiple regression of everything in life that might go into, why did you grow, two centimeters of bicep thickness over a year. And when we look at okay, in a lab for two hours, here's what happened to MPS.

How much of that does that explain in that multiple aggression? A very small amount. Yeah. So having that whole full spectrum of connection, then you can start to do better things as a practitioner. You can take a look at this study and you can go, I'm not just gonna throw it out of just a heuristic of going "ah, MPS doesn't matter, I wanna wait for the applied studies", which if you're gonna have a heuristic, that's not bad, but you don't have to like, like you can go, all right, I've looked and surveyed at some of these broad, systematic reviews or looks at, multiple MPS studies. And I see these trends, those trends are real, but they only matter in certain contexts and for certain clients that those, my differences might be meaningful, just a subjective term, determination.

Based upon the context, I can then tailor my recommendations to that. So sure. My default can be eat more than two meals. Eat more than one than 1.5 grams per kg. And eat a mixed diet and spread it out and make sure you lift weights and maybe take creatine if you have, the time energy proclivity and wanna spend $10 on it and that's it for 90% of my clients.

But then if someone comes to me who wants to, compete in track and field or shot put or body building or whatever, then I can go, okay. And for you, let's where are you at? Let me meet you there. And we can have additional steps that might make worthwhile outcomes for these small changes that could matter for you.

Danny Lennon: Fantastic. Before we, we close this out, are there any open loops or any of threads of thought that either of you would want to bring up that we haven't got to yet, or certainly haven't finished off concluding on?

Eric Helms: One thing I would say is I would just wanna recommend anyone who wants to do a deeper dive on this to read a great open access paper: "making sense of muscle protein synthesis, a focus on muscle growth during

resistance training" by Witard, Bannock and Tipton, that's a pretty damn good review that kind of connects this to the actual practice. So that's a pretty good review. And I, it covers a lot of these issues. So if you wanna do some deeper reading, check it out, and it's got some interesting points between connecting some of the acute data with long-term data. So that would be just recommended reading for people who want to do a deeper dive into this.

Danny Lennon: Tremendous. And that would be linked up in the show notes for people. Alan, anything you wanted to add before we close out?

Alan Flanagan: I think I, I guess the part I'm always bad at , what's the kind of practical, application, I think for, what the evidence showed for people that are following, pretty much plant exclusive diets.

Like the, I think it would be remiss us to say that there's nothing that they need to consider. And that there are ways. You know of improving if as those diets can tend to be just habitually by virtue of food choice, lower in total protein. So it can be worth it for people that are either making that transition or already there that are interested in strengths, hypertrophy performance, to do a little audit on their total protein intake and to make.

And, you it is clear that leucine obviously is important in that context now whether the exact amount in distribution across the day. But it certainly does appear that, making sure that total doses is reached of daily protein intake leucine, rich sources of protein, like peaprotein, for example, and mixing different plant sources of protein as well is probably all a good idea in the context of a plant exclusive diet.