DANNY LENNON: Stephan, welcome to the show. Thank you so much for joining me on the podcast today.

STEPHAN VLIET: Yeah. Thank you for having me Danny. It's a pleasure.

DANNY LENNON: I am looking forward to having a good discussion over a number of different topics, particularly related to some of the work that you have published in the field that I have really enjoyed reading, and it's been a number of papers that are quite insightful and as well as some of that throw up some really interesting questions that we can maybe dig into later in the show. But maybe just to start off would you be able to give people listening just an idea of your academic backgrounds and leading up to where you are currently working from and conducting research?

STEPHAN VLIET: Yes, so that sounds good. So, it really started for me when I was in my early 20s. I was in my last year I think of business school, so I was doing something completely different than what I am doing right now. But yeah I was really interested in, sort of from a hobby perspective, I started to get involved in weightlifting and actually started to research it myself just using my university account and not read economic journals but predominantly physiology journals. So, after my Bachelor's I did my Masters in Exercise and Nutrition Science, but I had very little research exposure there, so shortly after that I joined Dr. Luc van Loon's Lab in the Netherlands and it's

really there where I first got involved in research, and after working there for a year I started my Ph.D. at the University of Illinois with Dr. Nicholas Burd who I actually met in the Netherlands because he was a Post-Doc Luc van Loon's Lab. Last summer I finished my Ph.D. at the University of Illinois and currently I am at Washington University at St. Louis working under the guidance of Dr. Mittendorfer.

DANNY LENNON: Perfect, and I think for anyone listening who keeps up-to-date on research in this field will certainly know a number of those names that you just mentioned when you talked about Luc van Loon and Nicholas Burd for example, and the work that's coming out of both of their research labs at the moment in this area is quite phenomenal and obviously you've been contributing to that. So, maybe to start I'll probably jump around here because there's a number of different areas I would like to ask you about, but seen as only recently I think it was February when a review paper I think you were an author was published titled "Achieving Optimal Post-Exercise Muscle Protein Remodeling in Physically Active Adults through Whole Food Consumption." I thought it was a really nice paper and certainly was addressing an area of the research that maybe isn't taken care of quite that often when we look at effects of protein on say MPS, and muscle protein balance, and so on. Can you maybe give just people an overview of that particular review and what you were trying to I suppose get out with that paper and what questions you were trying to examine within the review?

STEPHAN VLIET: Sure. Yeah, so it all started off when the paper to be published a few months before where we compared the consumption of whole eggs versus egg whites and we found a higher muscle anabolic response after whole egg consumption versus egg whites in young trained individuals after a bout of resistance exercise. So, at that point the results initially were maybe a little bit surprising to me at least, because some of the previous work out of Dr. van Loon's Lab suggested that if you eat protein you add fat to it, for instance casein or whey protein shake adds fat to it that does not change the muscle's anabolic response compared to just eating protein. But this is not obviously a whole food source, so more we made these findings I started

to dig into the literature and actually found out that there was quite a bit of literature actually coming up specifically about lipids and how they can actually act as messenger molecules to the mTOR pathway and also play a role in potentially driving that muscle anabolic response. So, in that review paper reviewed with the literature on some of the nutrients that are in whole food sources and come to find out is that – actually a lot of work was already done years ago which showed that if you – and this was done in animals, if you have rats for instance and they are vitamin A deficient then the rate of muscle protein synthesis decreases. The same with vitamin B6, with B12, with Zinc so there was actually already quite a large body of literature suggesting that the role of micronutrients which I think has been somewhat underappreciated in our field. So, we reviewed with that literature, and then more recently a lot of work has been done specially Omega 3 fatty acids which Dr. Mittendorfer has done, my current advisor. So yeah I was really interested in some of these nutrients that are contained in whole food sources that could potentially explain our results.

DANNY LENNON: And we'll maybe dig into some of those in a bit more detail and I think it's particularly interesting, because many people who are listening will have heard us talk on the show before about muscle protein synthesis and just in general now within people who have an appreciation of evidence based practice when we talk about for example, nutrient intakes to try and maximize that MPS response a lot of the conversation tends to center around say the protein dose per meal, and then more specifically the leucine dose. But as you've kind of pointed out not only in the review but the previous paper comparing the whole eggs and the egg whites there is something else that maybe part of this puzzle when it comes to the overall anabolic response there. So, maybe a good place to get to would be to back up to that previous study that you mentioned on the protein from or the whole egg consumption versus egg white consumption. Can you give people just an idea of the methodology for that paper and how that study was laid out, and then maybe leading into some of the findings and implications from that?

STEPHAN VLIET: We recruited healthy young men. They were quite trained. We mostly recruited them from power lifting club, so they were trained individuals which made the study really interesting if we could even find something in them because the idea is that the more trained you are the slower your or at least the response of muscle protein synthesis is not as long lasting, for instance when you're very novel when you just get into weightlifting. So, we studied these young men. They came in on one day during the week. They would do a bout of resistance exercise, leg press, and leg extension 4 sets each. Afterwards they received either 3 whole eggs or – which equates to roughly 5.5 egg whites so they were matched for protein, both providing 18 grams of protein. We would take blood and muscle biopsies, and then calculate their rate of muscle protein synthesis. So, a week later they would come in again perform the exact same bout of resistance exercise, go through exactly the same protocol but only this time the individuals that received whole eggs on the first day received egg whites now and vice versa, so this is randomized crossover design which is really strong because you control for a lot of individual variability that way. So, what we found was is that despite the fact that the egg whites were digested and absorbed at a higher rates or at least quicker, I should say, than the whole eggs initially. And we know from some of this work done predominantly by Eve Barrie [00:15:44] also by Dr. van Loon is that – and it's predominantly for whey for the casein work if you have bigger surge of amino acids in the early stage you have a stronger muscle protein synthetic response. But we actually found that the egg whites were digested and absorbed quicker and amino acids became available in the plasma and thus subsequently for the muscle at a faster rate. We still found that the whole eggs gave a higher response actually when it comes to muscle protein synthesis, which means that maybe just the amount you know like the leucinemia or the rate at which leucine becomes available in the amino acid – or at least in the plasma is not per se purely dictating the muscle protein synthetic response at least when it comes to whole eggs, other factors come into play and of course the main thing with the whole eggs is that you need to have the amino acids become available and over a 5-hour phase the amount of amino acids that became

available were similar between whole eggs and the egg whites, so you can measure it over a prolonged phase there were no longer differences but what stood out was the fact that we found a higher response in muscle protein synthesis which we attribute to some of the factors found in the yolk because if you compare an egg white versus a whole egg you'll notice that all the micronutrients, vitamins, minerals maybe growth factors, microorganisms they are all contained in the yolk. So, if you take all the yolk out of the egg and you end up with a source of protein, the egg white is predominantly protein and doesn't provide a whole lot of other nutrients. So, we studied some signaling proteins and most of your listeners are probably familiar with the mTOR pathway. We studied the phosphorylation state, which is really an indicator of the activity and we found not differences. But we also registered a fact that we just put them through a heavy bar resistance exercise and this is a real big stimulus to mTOR but even if you have a big stimulus to mTOR it doesn't per se mean that this will translate into a – one-on-one translates to your rate of muscle protein synthesis.

DANNY LENNON: One thing that I did want to ask there you'd obviously mentioned that when you were hypothesizing at the end of the study some reasons that may explain the results that you've found was obviously looking at the components in the egg yolk that weren't going to be in the egg white and the potential effects of certain micronutrients, some of the lipids, growth factors and so on. Just based on at that time point in terms of the hypothesis you had that might explain the differences in that study at the time that you were completing that has that changed versus now after you kind of done this further review look maybe at more areas of the literature had a chance to think about and digest more of those studies again. Is there anything else outside of those components or any other ideas that you've been discussing with colleagues that may kind of contribute to these differences between whole food consumption versus say isolated protein and the responses?

STEPHAN VLIET: Yeah I mean going into the study we hypothesized there wouldn't be any differences, so that the amino acids composition which is very similar was going to

drive the response and we expected no difference between whole eggs and egg whites. So, I got a little more of an appreciation for it afterwards and I did knew about the study by Kevin Tipton that was done I think now almost 2 decades ago or at least now one-and-a-half decades ago where he found that the whole milk gave high muscle protein synthetic response or at least a net balance across the muscle which is an indicator of muscle protein synthesis with whole milk consumption versus the same amount of protein from skimmed milk. Now, these findings were really yeah sort of, even if you read the paper unexplained, and then later Dr. van Loon's Lab in the Netherlands did some work where it gave people casein and that milk fat and then there was no difference in the response. So, I guess also with time different paper maybe was a little bit – yeah sought to go to the background, but then when I read that paper again and it's been combined with our findings it all of a sudden made a lot of sense, and then looking into the literature I mean it's still very much interesting and always interesting as if you're writing a paper a lot of work came out and this is only from the last year or 2 years or so, for instance a recent paper that came out also showing, for instance oleic acid can actually help in the muscle signaling response and muscle anabolic signaling through the mTOR pathway. It's can also improve rates of muscle protein synthesis in old rats that were deficient, and then looking back at even older literature some of the vitamins and minerals were already clearly acts as co-factors in muscle protein synthetic response and it should become efficient in them mostly done on animal study we would limit muscle protein synthetic response.

We did do some follow up analysis and this work has not been published yet, but this is done in Canada with some of the authors that were also on the paper with Dan Moore in his group. And what we actually found was is that if you look at for instance, mTOR phosphorylation which is a very true measurement of the activation but it doesn't really tell you where in the muscle mTOR is. So, what we found was with OX it is closer to the lysosome and perhaps in a better position to stimulate muscle protein synthesis. And this is at least some recent work that suggested that this maybe, for instance modulated through phosphatidic

acid which stabilizes mTOR and if you look at for instance DX it's very rich in phosphatidylcholine which can be easily converted to phosphatidic acid and also other fatty acids such as oleic acids can actually be converted to phosphatidic acid. So, we think that at least a good starting point for future research would be to look at, especially when it comes to OX, look at the lipid composition and see if that's a next – and this is predominantly also if you look at the strong literature on Omega 3 fatty acids for instance, they act as signaling molecules to the mTOR pathway and subsequently can improve muscle protein synthesis. So, these are some of the things that I think we should look at in the future.

DANNY LENNON: Yeah I am glad you mentioned that. I was actually going to ask for your thoughts on kind of next few sets of research questions in this area that might be worth looking at, so I am glad you brought that up. To maybe change tracks likely from those areas of study and that just general area that we've examined, I wanted to ask about something else that I've seen in this kind of general area of looking at muscles response to both feeding but also really to resistance training. And there's one thing that I've seen kind of touted in a number of papers at this point that regular resistance training leads to increased nitrogen retention when compared to people who are not doing resistance training habitually. Can you maybe first confirm it if that is indeed the case because I could be incorrect on that, and then secondly if it is clarify for people the implications of higher nitrogen retention and what this may mean in a practical level?

STEPHAN VLIET: Yeah. Nitrogen retention is actually – the research methodology that we use currently is we use stable isotopes and actually labeled amino acids, but years before we did that – before the advancement of mass spectrometry which is really the tools or methodology that we use, people were doing a lot of work on nitrogen retention which could be the indicator of – basically the more nitrogen you would retain you would be in an anabolic state and if you were losing nitrogen you would be in a catabolic state. So, just to go back to your question obviously if you're in a positive nitrogen balance you're presumably restoring protein. If you do a resistance exercise then the idea is

that you would be storing this in the muscle of course because you just gave an anabolic stimulus to the muscle. But I would personally argue that actually measuring direct incorporation of amino acids into muscle protein it will give an actual better indication because you're not looking at it at a whole body level you're looking at it on a muscle specific level which is ultimately what you're interested in.

DANNY LENNON: For sure and I suppose that leads to a question that I've definitely seen people have conflicting information on some kind of misconceptions around as well and that comes down to when you're comparing those who are highly trained or at least have been training with resistance training for quite some period of time versus people who don't do any resistance training at all and how that translates to recommendations for protein intake for maximizing that muscle protein synthetic response. Is there any clear differences between those two groups in terms of what should be recommended and if so where does the current literature stand on it?

STEPHAN VLIET: Yeah, so what we know is that when you get more trained the muscle protein synthetic response is probably not as long lasting as when you're untrained, when you're untrained to sensitivity might resist 24-48 hours. When you're trained the muscle protein synthetic response will be as long lasting and initially I think it mostly has to do with the fact is that when you're not used to it, so when you're quite novice to stimulus to resistance exercise there also appears to be a lot of muscle damage initially that also needs to be repaired really. And so, in terms of differences in the amount of protein that you would recommend to someone I am not per se sure if – there are some – I mean some people argue that some researchers would argue and some researchers would argue that you actually become more efficient as you become more trained, but on the other hand if you've been eating a high protein diet for very long time your amino acid oxidative pathways are up-regulated, so in that case if you were to lower your amino acid intake again your body would have to adapt. But when it comes to protein intake generally athletes if you have a lot of calories to spare then maybe opting for a little bit more on the higher sides of protein versus the lower

sides I would say is beneficial if you want to maximize the response. In that case if you would ask me I would not per se – if you become trained give someone the recommendation to maybe lower their protein intake from like let's say 30 or 40 grams per meal to 20 or 30 grams per meal.

DANNY LENNON: Yeah, thanks. I think even from a practical level when people start considering this the people whose protein intake is likely to be high anyway is going to be those that are lifting weights and typically if someone sedentary and doing none of that just getting them to eat a baseline good intake of protein can be quite a challenge, never mind having them eat more than someone training anyway, so it might almost be a moot point?

STEPHAN VLIET: Yeah, exactly. Probably the best thing they could do is actually, especially if you look at older individuals and sedentary individuals is that they actually start training to begin with, because that is a very open stimulus obviously to the muscle much more so then, and then obviously foods, protein, as we follow now also whole foods can actually help with sort of maximizing that potential. Make sure you get stimulus during resistance exercise and subsequently you sort of fulfill that potential that you just created.

DANNY LENNON: Exactly. It's a great point and I think one that kind of echoed when Stu Phillips was recently on the show essentially making that point that when people are looking at like how you'll maximize this MPS response if you're only looking at feeding and you're not actually going and doing some form of resistance training you're to a large degree missing the boat there because that's the thing that's going to have more direct or at least strong influence over at least muscle initially, so definitely that point has been echoed. Something that kind of just relates to these differences in maybe different sub-groups of people in terms of protein response and therefore intakes one that I think people may have heard previously is the dampened anabolic response to protein feedings that can occur in elderly populations and this whole area of anabolic resistance. But I am wondering is there a kind of literature on other sub-groups that may exhibit this kind of decreased anabolic response,

maybe not in the same way or review the same mechanisms but at least might have a decreased anabolic response. I'm kind of thinking of – I believe there may have been some work looking at this in maybe overweight or obese groups and a difference in anabolic response. Can you kind of shed any light on this and do we know if there are clear differences between healthy weight versus obese folks for example, in terms of their anabolic response to protein?

STEPHAN VLIET: Yeah, absolutely. We did some work on this in our lab and this is done by a fellow Ph.D. student Joseph Bills who actually would be joining me soon here in Washington as well, so it'll be fun. But what he actually found was is that in obese and overweight individuals he found a dampened response to muscle protein synthesis, at least dampened muscle protein synthetic response for feeding. This was done after feeding 36 grams of protein coming from a pork patty, so really probably definitely high amount of protein but in obese individuals they had a dampened response. What this has to do with again probably a multitude of things. Also they have chronic activation of mTOR, so it might be what you'd refer to maybe as a ceiling effect. So, when you then give another anabolic response by feeding you're not responsive to this anymore because mTOR is already up-regulated to a high degree, so there's not much room for stimulus anymore and this might be due to the fact that maybe there's some inflammation going on, chronic low-grade inflammation, there's increased muscle proteolysis or there's a release of amino acids from the muscle into the muscle peripheral this will activate mTOR and you get this chronic activation, you come in this vicious circle where this is activated all the time, and then when you feed someone there's actually no more stimulus and these types of differences in the obese individuals. And recently my final study that I did more of a in a very clinical population, the disease population, patients that undergo hemodialysis and they also seems to have this elevated proteolysis, and then when you actually give them a protein meal they don't respond as much and similar this is also well documented in burn patients and probably at least one of the things that

this has to do with is indeed, for instance chronic low-grade inflammation.

DANNY LENNON: Yeah, super interesting and I look forward to seeing more kind of work in that area that sounds fascinating. I do want to get onto another topic that I'm keen to hear your thoughts on and it's in relation to those kind of upper limits of protein intakes that we've seen emerge from I suppose most – I suppose the consensus now in various different review papers on total daily protein intake. Most recently I think the Morton paper talked about for people that calorie balance somewhere around 1.6 grams per kilo should be enough to kind of theoretically maximize the MPS response of the course of the day depending on how that's distributed, for example other groups have varying different numbers in and around that and I think on a practical level most people might say okay on average if we say 2 grams per kilo is probably close to that. A upper limit where you're probably going to get that benefit going far, far beyond that number probably isn't going to have anymore inherent benefit at least for muscle building. But one hypothesis I have seen that relates with different area is the potential for a much higher intake maybe something close to 3 grams per kilo having a benefit for athletes immune function, particularly those who have maybe very high workloads or very intense training. Have you seen anything in that area that might indicate this kind of roller of high protein in diets for immune function in that area at all?

STEPHAN VLIET: I guess yes. I think this is mostly the direction work done by Kevin Tipton's group and where the authors found that – this was done in cyclists, with very heavy workloads or very heavy trainings bouts and the way it was done is cycling multiple hours a day. So, maybe if you look at it like a Tour de France, for instance when you are on the bike 6-7 hours a day you really put a lot store on a I could guess your immune system. So, from that perspective higher protein intakes may be helpful, but my concern would be, well not so much for maybe Tour de France like I'd say probably spending 10,000 kilo calories a day, so they have the room to eat that much protein but from a general perspective obviously if you go so high on protein there will be a limited return, and also maybe like

carbohydrates are important for performance and you really start to turn into dough. So, my concern would be that you really start to become low in some of the other macronutrients plus it'll also be a very expensive way to make glucose by eating so much protein, whereas you're probably better off eating it as carbohydrates and obviously also eating enough fats to support endocrine function and meeting your essential fatty acids needs. But I think if you were to eat 2 grams per kilogram per day yeah you would probably make some nice the muscle protein synthetic response, and also if you look at it from maybe resistance exercise standpoint you're generally not training 4-5 hours a day either.

DANNY LENNON: Right. Yeah, I think you make a really, really good point there in relation to – for someone practically trying to evaluate this idea of how far do I increase my protein intake. If you look at this in an isolated setting and say well there's research here indicating that I go my protein up to 3 grams per kilo it might not impart his immune function benefit, but as you expertly pointed out you have to balance that off with what tradeoffs do you have to make to get there. So, one example you gave is well a set level of calories that's going to start eating into say your carbohydrate intake which may have this net negative effect on immune function. If you're trying to get the super high protein intakes through supplementation or a lot of supplementation that could be taking away from calories you could have put towards whole foods, which again kind of micronutrients could have a role here in immune function. So, I just want to reiterate that point you made of not looking at any one thing in isolation and evaluating the bigger picture of a certain nutritional choice because I think it's important for people to consider.

STEPHAN VLIET: No, yeah. I was also going to add. Yeah, I would absolutely agree with that that the nutrient density of your diet is very important and if you look at it, for instance like a caloric standpoint let's say you're eating 3,000 calories a day you can eat those calories from nutrient dense whole foods or you can eat those from same amount of micronutrients from maybe more nutrient depleted process foods and you're going to have probably a different response or

different phenotype or different performance. So, there's definitely something to be said to also when you look at your macronutrients or breakdown of percentages also making those actually count by the food choices that you make.

DANNY LENNON: Yeah, absolutely especially when you're considering this in the long-term as opposed to just a immediate recovery response to one training session. The longer term is probably where some of this would start showing up. Before I start wrapping up on the final couple of questions Stephan I am really interested to hear from your own personal perspective and the area of research you're looking at what are kind of the next few research questions that you are most interested in trying to answer yourself in your own work and what do you see going on with your research over say the next 2, 3, 4, 5 years perhaps?

STEPHAN VLIET: At the moment I'm doing a little bit more working into glucose uptake, studying glucose metabolism and how that is altered in human obesity. But also still interested in looking at some of these probiotic different nutrients that are contained in whole foods and how does it alters the muscle anabolic response. For instance, one hot topic at the moment is vitamin D. Definitely some work coming out from Eve Barrie's group I think last year showing that actually vitamin D deficiency reduces the rate of muscle protein synthesis, and then restoring this amount of vitamin D can increase it again. So, at the moment I'm doing some work on vitamin D supplementation in elderly individuals and studying the muscle protein synthetic response, so I'm very excited about that. Yeah, I would like to do some more research on whole foods obviously I've got an interest in it and I think the nutrient density of the diet is very important not just looking at it because obviously maybe for the listeners of the show and also for me I'm being into lifting weights myself I was interested in how can we optimize muscle protein synthetic response, but also from a broader health perspective arguably looking at some of the nutrient components in whole foods and how they modulate the health because arguably a healthy athlete also a well performing athlete.

DANNY LENNON: Yeah, absolutely. I think we're starting to see more and more that kind of crossover from traditional sports science literature, and health and nutrition kind of literature and this kind of cross between the two in both directions in more recent times and like you say a couple of examples with the role of vitamin D now we're starting to see in lots of sports nutrition literature and role of probiotics and all this type of stuff that were traditionally cornered into health research perhaps. So, I think like you said there is a lot to be said for those and looking at the health of the athlete in general as opposed to just acutely the recovery from training and performance, so that all sounds super interesting and I'm definitely looking forward to see more work that's produced by you and your colleagues in this area. So before we get to the very final question Stephan, if people listening want to track you down online or on social media or look for more of your research on ResearchGate or anywhere where is the best place for them on the Internet to find more of your work or a bit about you if there is?

STEPHAN VLIET: Yeah. Surely, my Twitter handle is vanvliet Ph.D. and I'll spell it out it's V-A-N-V-L-I-E-T and then P-H-D. And then my work could be found probably on PubMed or also Google Scholar account again if you just type in my name you could find some more of the work that I do.

DANNY LENNON: Perfect. And for everyone listening I will link up too that stuff in the show notes as well as the research papers we've mentioned throughout today's episode. And so, that brings us to the final question that we always end the show on and this has to do with pretty much anything even outside of today's topic and it's a big broad question, so forgive me for springing this on you right at the end, it's simply if you could advice people to do one thing each day that would have a positive benefit on any area of their life what would that one thing be?

STEPHAN VLIET: That's a good question. There are a lot of things you can do to improve our health, but I think with most things in life it's just sticking to the basics I think is really helpful. Go to bed when it gets dark, get up when it gets light, eat mostly foods that are raw and wholesome nature, try to limit your stress a little bit. I

know these are very broad things, but I always try to think of myself is that I'm trying to live an ancestral lifestyle in a modern day era.

DANNY LENNON: No, I like that a lot and like you say there are quite broad, big things that maybe most of us are kind of aware of, but the thing is that most of the time we're not doing them or at least things that we should be. So, I think yeah remember that the big picture stuff.

STEPHAN VLIET: Yeah. Certainly we're doing lot of things maybe that we're not so much adapted to from an evolutionary perspective and I think that's – to put it on a broader scale I think where most of like the cities these raising rates of obesity and diabetes and situation of our health because of those reasons.

DANNY LENNON: Absolutely and you've mentioned just a few of those whether that's to do with nutrition or whether it's to do with circadian rhythm and mismatch with our sleep timing and all that type of stuff. It's huge and I think like you say those basics where things that we put more focus on as opposed to little details I think we'd be in a much better position. Stephan this has been great I really, really enjoyed this discussion. I've really enjoyed hearing your insider thoughts on some of the research you've mentioned and I look forward to reading more of it in the future. I want to say thank you for taking the time out to do this today my man.

STEPHAN VLIET: Absolutely. Thanks so much Danny it was my pleasure.