Dr Lee Hamilton podcast transcript

RM: Welcome to the human performance and health podcasts. Today we're going to talking about protein synthesis with a particular view of dietary intake, exercise and inactivity. To help us today, we're joined by an expert in the field, doctor Lee Hamilton who joins us from Stirling University. Could you give us an introduction to your research area and a background to yourself, please.

LH: I started in this field doing a degree in sport science in Dundee University. Then I got a PhD where the topic was trying to understand some of the signals that regulate muscle growth in response to loading and, in particular, how resistance exercise converts the signal of loading in adaptative response like growth. From my PhD I then transitioned into a post doctoral work at the medical school in Dundee and I worked on some of the molecular links between diabetes and dementia in a neuroscience lab. After two and a half years there, I managed to transition my way back to muscle in Stirling, where I am currently. Predominantly, my research is try to understand the molecular signals and how exercise and nutrition regulate adaptation and maladaptation in muscle.

RM: Thank you, Lee. Why is important for the scientific community to investigate the processes involved in muscle mass growth and breakdown?

LH: Who is funding this kind of research knows the potential benefits involved. Talking about muscle mass regulation, you reach your peak around 30 then you start to lose muscle mass. When you are still above the disability threshold it is fine, but for a lot of people losing muscle mass will take them across the disability threshold where they're no longer able to get up out of a chair, or doing some steps, or cross a road safely, etc. So understanding why we lose muscle mass with age is important, as well as how muscle mass is improved with exercise. So far we know few interventions in humans to improve muscle mass, such as the use of testosterone, but it is not widely prescribed due to potential side effects. But exercise, fortunately, has not negative side effects, so understanding how exercise improves muscle loss may reveal some novel pharmacological therapies that might allow us to target those that are unable to exercise or they are losing muscle mass because of other diseases, and prevent muscle mass loss.

RM: This is really good material. I am interested in how we can help people, longevity and quality of life goes in maintain and increase muscle mass while we become older. Your quality of life as an individual will improve is you can maintain muscle mass, so we of the scientific community are interested in understanding which proteins to target to improve or increase muscle mass, for example. May you give us a brief introduction about some terms, so people don't get lost when we speak about these topics, such us protein synthesis and protein breakdown, net protein balance and amino acids.

LH: From a muscle function perspective, the proteins we are most interested in would be the block of a protein, namely amino acids. So protein synthesis simply is joining of the amino acids on a particular sequence do create a protein. Proteins that do the work of contraction allowing us to move, those are the results of amino acids joining together in the right sequence in the synthesis process. Amino acids come from a number of sources, you have endogenous amino acids, but most come from what you eat, so proteins in your diet that are broken down into amino acids by your body and adsorbed. Net muscle protein balance is the balance between breakdown and synthesis of proteins, so the breakdown is breaking down of proteins into their constituents, the amino acids, then using them for oxidation or recycling. Hopefully most of us young and healthy at the end of the day have the balance between breakdown and synthesis remaining the same. But if you do resistance exercise you push the equation in favour of synthesis and getting some proteins in your muscles, gaining muscle mass. But as we get older, the equation tend to shift to breakdown of proteins and we lose muscle mass.

RM: So among the things you mentioned, we have endogenous amino acids that we can manufacture within our body and use to build new proteins. We are also particularly interested in those proteins within the muscles that contract and allow the movement. This is why they are related to life and longevity. Then we have the exogenous amino acids that we get from our diet. However, we haven't still touched the MAIN (Domain?) protein in protein synthesis, but I think it is important since it's a key to protein synthesis. would do your level best to sort of explain that particular protein and why it's so important?

LH: Protein synthesis is really a complex process. Part of the reason why protein synthesis is so complex is because each step in the pathway acts like a lock and key in the system to sort whether or not protein synthesis should occur or not. We can think of it like a series of logic steps in computing system, which tick two divergent inputs to create a single output, and they're basically a lawyer for computers to make decisions and filter signal noise. And really this is a very complex series of logic steps built within all our tissues, which terminates whether or not to bind to mRNA transcripts to make more proteins. A protein complex, the rapamycin complex, is so called because it was discovered as being a target of the drug rapamycin, which is a immunosuppressant that has been used for preventing an immune cell growth on stents. So to prevent the growth of tissue on stents in people's arteries, for instance, I use rapamycin. The way mTORC1 acts to control protein synthesis involves a series of signal associated with the environmental conditions of cells, the amino acids concentration, the energy status of the cell, the oxygen status, the mechanical loading status of the cell. And when all these things are aligned in the right way, mTORC facilitates protein synthesis to increase. In response to a stimulus, such as feeding, protein synthesis can elevate. And we know that that complex mTORC1 is absolutely required for stimulus induced increases in protein synthesis. Lift some weights or eat some protein, therefore, leads to the activation of protein synthesis in response to stimuli dependent on the activity of complex mTORC1.

RM: I would like now to ask a question, which our students and the general population may be really interested in. In your opinion, does someone who is trying to increase, or whishing to increase muscle mass, require the addition of synthetic proteins or amino acids, or can they get enough from their diet?

LH: Nutritionists and Dietitians in sport and exercise usually food as a first approach. So I always try to encourage food first wherever possible. Most people should be able to get everything that they need from eating whole food sources, and they shouldn't have to resort to supplements. I think then that synthetic amino acids are not necessary. But there are several reasons why people want use supplements, for instance they are incredibly convenient and also very cheap. For example, if you want to get your post exercise nutrition and quickly after the gym, maybe you're doing three sessions a day and a busy day, then something like whey protein or whey protein carbohydrate, makes quite convenient. But it's certainly not necessary to maximize adaptive processes. Branched amino acids are certainly very effective in activating mTOR, but they're not necessarily as effective on activating the protein synthesis element as say a whole protein source would be. So from that point of view, like a senior sport and exercise, nutrition register, I would definitely encourage food as first approach.

RM: What was the source of the sport and exercise science and nutrition?

LH: It will tend to refer to the senior SENR, sports and exercise nutrition register. A lot of people that do a sport sciences or nutrition degree will be able to get graduate registration and then become fully registered. Then you can put together a portfolio of nutrition dietician, work in a sports setting or performance setting and you can then sort your request for membership by submitting a portfolio. A lot of industry bodies will like to see SENR registration to get full jobs as sport nutritionist or dietician.

RM: Thank you Lee, that's really informative. I think there are a few other little questions that maybe relate to that is that, and you mentioned actually most people can get much of what they need from their diet, but there are a few cases in which, you might want to tap into protein supplementations for speed, am up delivery and convenience really more than most. By a chemical and molecular perspective, if you look at mTOR and look at branched chain amino acids, you put two and two together and come up with five. However, in reality, the practical element of it doesn't seem to work, but in terms of optimal time, is there an optimal timeframe that someone should be looking to consume?

LH: I guess it depends on what your goals are. For glycogen re-synthesis, it seems to be kind of a window of opportunity in terms of getting your fast source of carbohydrates as quickly as possible after glycogen depleting exercise, to ensure that your recovery, synthesize your glycogen as quick as possible. So, from that point of view, there's perhaps an optimal window to get food into recover from exercise if recovery and not context is considered as glycogen re-synthesis. A lot of people want to hear me talk about protein synthesis and growing muscle and hear my point of view on the most optimal way for recovering and growing muscle. From that perspective, there was a study about 10 years ago. In this study, they give to one group of older adults their protein immediately after exercise or it was within 30 minutes. The other group got their proteins delayed, and in the delayed group was not observed muscle mass growth. This study was a 12 weeks training program. The group that got the protein immediately they significantly increased their muscle mass, more than the control group. The first thing this study is saying is that there was a 30 minute window of opportunity to get your feeding in to substantially improve muscle mass. Otherwise your gym session would be worthless, or not as effective. Your colleague Nick Hurren showed that after resistance exercise your muscle is sensitized to the effects of feeding, and the period of opportunity is by 24 hours. So the anabolic window could be as wide as 24 hours, potentially 14. Every meal you eat after an exercise session, you're likely to get an improved protein synthesis response to feeding. I guess what would be optimal to do then is looking to try and maximize the number of feedings you can fit in after an exercise session to obtain the most benefits from it. in another really good study, they looked at the distribution pattern of proteins after an exercise session, where the question was if it is better to get your protein for the next 12 hours in two boluses of 40 grams or four boluses of 20 grams or 8 boluses of 10 grams. The results suggested that 20 grams times four feeding occasions is probably the optimal window. Resistance exercise synthetises your muscle for at least 24 hours. Some people suggests 14 hours, but every feeding is an opportunity to improve your muscle mass, rather than optimising timing per se.

RM: That's a really interesting. Thanks Lee. I think that's a really important point. you can get an amino acid availability more frequently with smaller doses. But does that matter on the population? I'm just going to talk about different populations at the moment and we often focus on those gym beasts who go to the gym even on Friday night before discotheques to make sure their body will fill their t-shirts. This because these guys are a good target since they supply many of the subjects or they volunteer for some of the studies we do. About the research you just mentioned, where they use different timings, was that done in a similar population or in a different population?

LH: The majority of the work has been done comparing young healthy men, some other work with older, usually healthy individuals and in some other cases very old. I have done some work on an 80 year old plus. But overall, a lot of the work was on homogeneous population of young healthy, active man that usually weigh around about 80 kilos in their mid twenties and they're usually students. The studies done comparing young to old would certainly suggest that older adults have this impaired sensitivity to feeding. They present anabolic resistance, a term that means that, when you give an infusion of amino acids to a young man, he might maximize muscle protein synthesis, whereas an older man would need a much bigger infusion or feed of amino acids to achieve the same maximization of the protein synthetic response. And the breakpoint analysis suggested that older individuals need potentially as much as double the amount of protein per feed to maximize their muscle protein synthesis response compared to young ones. So, If young men needs 20 grams of whey protein to maximize protein synthesis, an older man, perhaps over sixties, will need as much as 40 grams of protein to maximize protein synthesis response.

RM: And we don't really know what are the differences between populations, as well as what are the potential differences between someone who is insulin resistance or diabetic or pre-diabetic and those that aren't. There's still a lot that we don't know. And I I've got other few important questions, that seemed to come up quite a lot and that is this negative or potentially negative effect. I'm curious about how pathways might be interfering with one another in different populations, diabetic versus healthy control, and this, we call it concurrent exercise. From your perspective and your knowledge, cardiovascular jogging type exercise response would interfere with any benefits or positive goals of resistance exercise?

LH: It seems that there is a pathway, which, during concurrent exercise could potentially inhibit muscle growth. As we mentioned before, mTOR is really the key controller of the protein synthesis response and to both feeding and resistance exercise, and we know that you need to have a functional mTOR in order to be able to grow muscle in response to loading, certainly in rodent models and that pathway can be inhibited by energy stress. So it was really nice series of studies that show energy stress, as glucose deprivation, or oxygen deprivation, or pharmacological activation of that energy sensing pathway can interfere with the ability of the tissue to increase protein synthesis. So activating a pathway we often refer to it as AMPK, it is a protein that senses the concentration or the ratio of amp to ATP, which is kind of considered the cell fuel gauge. So when the fuel gauge gets too low, that protein AMPK becomes activated. This causes a series of events which inhibit mTOR and inhibit protein synthesis. And even if you do very high intense endurance training and even if you can activate the energy stress pathway, it doesn't seem to interfere in vivo in humans with the activation of mTOR. It has been done some stuff with unilateral exercises, training, one leg with resistance training for instance, and then training the other leg with the concurrent model, so endurance training and resistance training. And he was able to show that even though AMPK can be activated with the endurance training, it doesn't seem to inhibit the muscle growth. But they never actually measured muscle mass and these studies are just showing that there was an inhibition on strength. So the individuals that cycled at the same time as resistance training, their strength gains were significantly impaired compared to lose individuals. You just lifted weights alone and the interference effects seemed to take weeks before that interference effect was evident. The issue of these studies however, is that they don’t really go long enough, they don’t train people beyond eight weeks period so they can’t figure out what’s really going on. Personally, I think it is not a molecular interference effect. And when you look at the amount of analysis that have been done on concurrent training, the effect on muscle growth is quite modest, but it often doesn't come at a significant. The effect is most significant is on power. The ability to improve your power output with resistance training is very much impaired with concurrently doing endurance training. And to me that suggests, you know, one of two things, either it's a neuromuscular effect or it's an effect on the non-contract tissue. Perhaps endurance training is interfering, somehow in neuro muscular adaptations that prevent you from expressing your power as well as if you hadn't done the endurance training or perhaps there's endurance training interference effect at the level of the connective tissue. The tendons perhaps prevent effective transmission of force that allows you to generate high power outputs. My personal take on as unlikely to be driven by a muscle growth effect, which is therefore unlikely to be related to the molecular interference and it's probably more likely a neuromuscular interference effect.

RM: You and I will be interested in the molecular side, but actually from an applied side, it seems to be getting or interfering with your ability to produce power. I think we've covered quite a lot of the material and I just wanted to get your view and a couple of other things before we finish. We know that the majority of individuals that engage resistance training sit in two camps. There's those want to increase muscle mass and that's a key goal from a visual perspective, and there are those who are perhaps slightly overweight or obese, and want to lose weight for health reasons but also increase muscle mass which will have a visual improvement on how they look as well. The first group would be different from the second, for example, the individuals that want to engage in low repetition but high or very high workloads to maximally increase their muscle mass gains potentially will be very different from those that perhaps would engage in lower intensity training. So my question is, for that type of population where they're really interested in massive muscle protein and muscle mass growth from a visual perspective, can you see any long-term health implications for those individuals that are developing the fast twitch muscle fibers? The atrophy, the decrease in muscle size comes a lot quicker with those types of muscles as we get older and become progressively inactive. And I think for me that's a research field that we haven't really looked at, I see negative implications of muscle breakdown as we become more inactive for any reason. An age is a good model for that. What is your prospective about it? A great example of someone who developed a huge amount of muscle mass over time is Arnold Schwarzenegger. And now you look at his pictures and you can see that he is displaying signs of muscle atrophies, so a lots of proteins breakdown. He also got a huge amount of amino acid pool. But as you become more inactive, all the amino acids and the components that hold muscles deteriorate quite quickly and progressively over time as he ages and becomes more inactive. I think that at some point there will be some health implication.

LH: Perhaps older professional bodybuilders could have some health implications, especially in the modern era where there's a lot more drugs around. I think Arnold has been quite open about his drug usage, now. But when you look at Arnold as someone in his seventies, he looks like a shadow of his former self. He is still in great shape for a 70 year old. I'm not saying that everyone has to use the same strategies that professional bodybuilders would use, but certainly think there's an argument to be made for trying to hit your peak bone and peak muscle mass, and get as much muscle mass as you can while you can, because the more you can do that, hopefully the further away will be from that disability threshold as you age. From your muscle as an amino acid reserve perspective, there was a case of a bodybuilder who basically got stuck in the mountains for a couple of weeks. The doctors suggested that if he had not been a bodybuilder, he probably would have died a lot sooner, but since he had this big reserve of muscle mass, which of course provided the amino acids which are gluconeogenic substrates that essentially keep them alive. So I think there's certainly a case for trying to gain as much muscle mass as physically possible for you. I certainly wouldn't advocate taking a lot of drugs to achieve that. I think we can get there naturally, with, consistent training and consistent good nutrition, so we can certainly keep ourselves well above the disability threshold. But I certainly don't think having a large muscle mass would necessarily have negative health implications. The negative health implication would come with the bulking strategies through a lot of these guys would use where they really often don't seem to mind too much, where their calories come from. Of course there's going to be highly impossible to eat 10,000 calories and hold on processed food. I think that may become a problem for people when the 10,000 calories come predominantly from quite unhealthy sources. There is maybe a health implication with some of the bulking strategies. But again, you don’t necessarily need to go on a ‘bulk fears’ to effectively grow muscle and to keep yourself healthy and above the disability threshold.

RM: And you don't think that perhaps muscle type, rather than just muscle mass could be more beneficial as we get older. You rightly said you don't necessarily need to go on a boat just to remain healthy and fit. I guess there's a difference in what the goals of the individual are.

LH: There's a really good review that really beautifully summarizes all of the changes that occur in older muscle. One of the things that the review highlights is that our muscles tend to lose type two fibers as we age. You tend to get this clustering of type ones and of course type two are those that provide power - type one to provide power as well, but type two is a much more powerful than type one fibers. You think about trying to prevent yourself from having a fall, so if you trip and fall, its muscle power, not necessarily strength that you need to prevent the fall. If you become unstable, you need that power in your quads and in your plantar flexors to prevent yourself from falling. I think that's partly why the increased risk of falling increases a lot as we age - is because we lose the ability to produce high amounts of power because we lose type two fibers and there's probably some neuromuscular changes as well, which contribute to that rather than just the loss of muscle mass. If I have to pick one training strategy to try to keep myself above disability threshold, I'd probably focus on developing power and maintain my power as much as possible, maintaining type two fibers. We know there is quite a big disconnect between muscle mass and muscle strength and big muscles not always equip strong muscles.

RM: Thank you for that. There is still anything you want to add that you feel is important to the field before we finish the discussion of today?

LH: From the metabolic health perspective, I guess if you look at insulin sensitivity is one of the key metrics of healthy metabolism. Among the exercises or nutrition strategies that will enhance all aspect of your health, resistance training is certainly a very good way to do that. A lot of the work has been done on endurance training and higher endurance training improves or modifies insulin sensitivity over time. Endurance training can enhance insulin sensitivity for circa 72 hours and similar studies have shown that resistance training can have a similar effect. But I think there's no one perfect exercise regime for all outcomes, but certainly resistance training can be a good strategy to also improve your metabolism alongside with endurance training. But I certainly wouldn't say that one exercise protocol is a panacea for all. What’s important is finding what works for the individual.

RM: I think we can agree certainly from a metabolic point of view that resistance exercise would be beneficial for your glucose metabolism because there's no doubt that increasing muscle mass is a really good way of giving yourself an extra storage capacity for any extra glucose or sugars that might be in your system. I was thinking, from my perspective, that we can all say that fat metabolism as we get older is probably a key goal. Thank you Lee for your time, it was great to talk to you again.

LH: Thank you, see you soon.