Danny Lennon: Caoileann, welcome to the show. It's great to have you on. Maybe to get us started, could you maybe talk us through a bit about your academic background and the work and the research you've been up to over the past number of years at McMaster and what you've kind of been looking at.

Caoileann Murphy: So the last four years I ran Stu's lab and my research is focused on how we can use nutrition and exercise strategies to maximize rates of muscle protein synthesis in older adults, because we know that by the fifth decade of life muscle mass and function tends to decline, so we are looking at ways to either prevent or to slow the loss of that muscle mass. So my studies specifically have focused on the pattern of protein intake throughout the day. So we know that how people typically consume their protein is in a skewed manner, so small amounts of protein at breakfast and lunch, let's say you have a bowl of cereal for breakfast and cheese sandwich for lunch, not a whole lot of protein, and then they usually have about 50% of their daily protein at dinnertime if they have a steak or a chicken breast or whatever. And we compared the skewed pattern of protein intake to a more even or balanced pattern of protein intake throughout the day with a slightly larger serving of protein at breakfast, lunch, and then a slightly smaller serving of protein at dinner, and we looked at those in conditions of energy balance and energy restriction and also in conditions of energy restriction plus resistance training in overweight and obese older men. And then my last bit of work over in

Stu’s lab looked at leucine supplementation and whether we could use that to enhance rates of muscle protein synthesis in older men again.

Danny Lennon: Awesome. And we'll definitely dive into some of that and, maybe before we do, it might be worth getting everyone up to speed and on the same page, so before we discuss some of those specifics, could you maybe just briefly explain for maybe those who aren't familiar what the process is or what we mean by things like muscle protein synthesis, muscle protein breakdown, maybe how that relates to things like nitrogen balance and actual muscle mass?

Caoileann Murphy: So the muscle is constantly being turned over, meaning that the protein in the muscle is constantly being built up and broken down. So if you get up in the morning and consume a meal that contains protein, there'll be a rise in amino acids in your bloodstream and that will stimulate muscle protein synthesis. And at the same time, the insulin response to that meal will mildly suppress muscle protein breakdown, so as a result the rate of synthesis will exceed that of breakdown and that muscle protein balance will be positive. If you then go for a period of time without food, so let's say in between breakfast and lunch, then the rate of breakdown will begin to exceed the rate of synthesis, so you would have a time of net negative muscle protein balance. And then that balance will swing into a positive situation again following lunch, for example, and then a negative and so on throughout the day. So those fluctuations in net balance are roughly “equivalent.” So the time you spend in net negative balance tends to be roughly equivalent to the time you spend in net positive balance if you are a weight-stable younger adult who's maybe not doing resistance training. And then, over days, the net balance adds up over time to influence your muscle mass, so if you spend more time in a state of net negative muscle protein balance, then that would translate over time to the loss of muscle mass, whereas if you spend more time in positive net muscle protein balance, then that would result in muscle hypertrophy over time.

Danny Lennon: The other thing you mentioned was about leucine. I suppose that ties into when we're thinking about these various different stimuli that can trigger off muscle protein synthesis. What would be the main ones that we know from research actually trigger off MPS or what kind of factors are required for that?

Caoileann Murphy: So it's the essential amino acids in protein that are responsible for the increase in muscle protein synthesis in response to protein intake or food intake. In particular, the amino acid leucine appears to have an important

role as a trigger. It appears to be the most important amino acid; however, all of the essential amino acids are required to serve as building blocks for the building of new muscle protein.

Danny Lennon: And so I think if we turn to maybe the first thing would be to look at things in the context of a calorie deficit because, as you said there, when we're looking at the either accrual of muscle mass over a long period of time or the loss of muscle, it's going to come down to this tradeoff between protein balance. So then if we take a situation where someone is in a calorie deficit because they're dieting for whatever reason, if we first take…let's take a typical general-population, normal-weight person. When they enter that period of calorie restriction or negative energy balance, what does that potentially do to muscle protein synthesis rates and does that have any risk then for this increased loss of muscle mass potentially over a long dieting period?

Caoileann Murphy: Yeah. So a number of studies have looked at how muscle protein synthesis is affected by calorie restriction. These studies, at least for short-term energy restriction anywhere between about five days to three weeks, have pretty much consistently shown that it results in a decrease or downregulation in muscle protein synthesis both in the fasted state and in response to a protein-containing meal. So the downregulation appears to be about 15 to 30% and that's been shown in young adults, middle-aged and older adults. Two studies to date have looked at the influence of longer-term energy restriction on muscle protein synthesis. Those results are a bit more equivocal so we definitely more studies to look at the longer-term effects, but certainly at the beginning of a period of dieting there does appear to be this downregulation in muscle protein synthesis. And we know from previous work that when someone goes on a weight loss diet, if they don’t perform exercise, they typically lose about 25% of their weight as lean body mass, a major component of which is muscle. Now, if someone incorporates exercise, they can reduce that amount to, a meta-analysis suggested, about 12%, so about 12% of the total amount of weight they lose would be lean mass. And some recent work has suggested that by including higher protein intake along with resistance exercise, which is the most anabolic form of exercise, that there is potential to actually completely preserve lean mass or even to potentially gain lean mass during a period of dieting or energy restriction.

Danny Lennon: Yeah, sure, and I think I definitely want to double back at some point to that particular study that you guys at McMaster did with that big calorie deficit.

Caoileann Murphy: Oh yeah.

Danny Lennon: But first, when we talk about the reasons for why MPS is downregulated, do we have any understanding of the underlying mechanism? Like is it simply because it's just like energy-expensive to do so the body wants to save some energy by having less synthesis or is it because someone is decreasing their protein intake and so therefore the body's used to a higher level of that?

Caoileann Murphy: Yeah, so we don't really know the mechanism and the hypothesis is that because muscle protein synthesis is an energy-requiring process, just like you said, that there is this kind of downregulation to conserve energy, and there is some evidence from animal studies that it could involve AMPK but we don't really know the cellular mechanisms. And in terms of habitual protein intake effects, the muscle protein synthetic response during energy restriction, one study compared young adults who are consuming either their recommended daily allowance for protein of 0.8 grams per kilogram per day or else two times the RDA or three times the RDA, and they found out when all the participants consumed a 20-gram serving of protein that those that consumed two or three times the RDA were able to respond to that amount of protein and increase muscle protein synthesis whereas those that would consume the RDA for protein were not able to increase their rate of muscle protein synthesis in response to the 20-gram protein meal. So it's been hypothesized that by having a slightly higher protein intake you may preserve some of that sensitivity to food intake and that isn't the case with a lower-protein diet.

Danny Lennon: Okay, so I think that actually dovetails nicely in with that study like I mentioned that recently came out of McMaster lab with the 40% calorie deficit and it seems that things like the high-protein diet and resistance training were able to like not only mitigate that lean body mass loss but also maybe allow some to increase that even in a hypocaloric state. Can you maybe just lay out for people who haven't come across that study what went on there and the kind of results found from it?

Caoileann Murphy: Sure. So that was Tom Longland's study and it was a four-week fairly severe energy restriction and 40% energy restriction. And they were not athletes. They were young guys that were recreationally active and they consumed either a lower-protein diet, which I believe was 1.2 grams of protein per kilogram per day, or a higher-protein diet of 2.4 grams of protein per kilogram per day, and they all undertook a high-intensity exercise program for the duration of the four weeks of the diet. And that

program involved resistance training as well as high-intensity interval training and they found that the lower-protein group preserved lean mass whereas the higher-protein group were actually able to gain lean mass.

Danny Lennon: Awesome, and I think that was a really cool study because it just shows that not only is it important for…like we always think that, "Oh, if someone's going to be under this massive calorie-restricted diet, they're going to have to lose a lot of lean muscle," but now we're starting to see the importance of not only the daily protein intake but I suppose putting that in conjunction with resistance training, which I think is a theme we'll probably come back to.

One thing I wanted to touch on in particular was protein distribution because I think like you mentioned at the outset that has been a lot of focus of your own work, and in one of your recent papers I remember reading I think you stated, you were talking about the growing need for more people to look at the protein intake on a per-meal basis rather than simply a total protein intake for the day.

Caoileann Murphy: Mm-hmm.

Danny Lennon: So when we look at, say, protein distribution, based on your research, I mean you can bring up some of that, do you think it's fair to say that bolus doses of protein with hours in between those feedings is likely more anabolic over the course of the day than, say, if we were to either have a huge bolus just in one go or on the other extreme maybe hook someone up with an IV drip constantly infusing amino acids into the bloodstream? Is there something about those bolus doses of certain amounts with this almost refractory period in between for distribution?

Caoileann Murphy: So the kind of rationale for a balance or an even pattern of protein intake throughout the day comes from the dose response relationship between the amount of protein consumed in the meal and the subsequent muscle protein synthetic response. So we know that in young adults, both at resting and post exercise, about 20 grams of protein appears to be sufficient to maximally stimulate muscle protein synthesis. That dose has actually been refined to about 0.24 grams per kilogram body mass per meal. So if someone consumes less than that quantity of protein in a meal the muscle protein synthetic response is going to be submaximal, whereas if they consume over that quantity of protein the muscle protein synthetic response isn't going to be any greater and those amino acids will just be oxidized. And we know that the muscle protein synthetic response is

transient, so if you haven't done exercise and you just consume a protein-containing meal, the rate of muscle protein synthesis will increase and be back down to baseline in about three hours.

So then if you were to consume let's say about 0.24 grams of protein per kilogram body mass at each meal of the day, then the idea is that you would maximize your rate of muscle protein synthesis on each of those occasions. Whereas if you consume that typical skewed protein intake when you consume just a small amount of protein at breakfast, let's say you have 12 grams in your bowl of porridge or whatever, then you're going to have a suboptimal muscle protein synthetic response at breakfast. If you consume another suboptimal dose at lunch, let's say 15 grams, then you'll again have a suboptimal muscle protein synthetic response. And then at dinnertime, let's say you consume 50 grams of protein. If you're a young adult, then you're only going to use about half of that to stimulate muscle protein synthesis and the rest will be, at least from the standpoint of muscle protein synthesis, wasted. So over the course of the day then, your cumulative rate of muscle protein synthesis would be less compared to if you had a more balanced even pattern of protein intake with an optimal serving of protein for stimulating muscle protein synthesis at each meal.

Danny Lennon: And that kind of skewed pattern is actually something we kind of typically see, right? I mean, I think in most observational data, I think even like NHANES said something on people's protein intakes. We see that like pretty low-protein breakfasts, a bit better at lunch and typically the vast majority of people in the general population are getting most of it from the dinner meal.

Caoileann Murphy: Yup, yeah, about 50% of protein at dinnertime.

Danny Lennon: Okay. Can you maybe just then talk specifically about the paper that I think it was published like last year that you were the lead author on that examined the protein distribution, so this balanced distribution versus a skewed one, I think it was in older adults as well in looking at like the energy-restricted state as well.

Caoileann Murphy: Yeah.

Danny Lennon: Can you maybe walk us through how you set up that in terms of the methodology and then the kind of results you got at the back of that?

Caoileann Murphy: Sure. So I guess before I get into that, it was kind of following a study comparing a balance and a skewed pattern of protein intake in younger adults, and in that study it was shown that having 30 grams of protein at breakfast, lunch and dinner resulted in a rate of muscle protein synthesis over a 24-hour period that was about 25% greater than the same amount of protein consumed in a skewed pattern. So we thought it'd be really interesting to look at that in older adults particularly as they're the ones that would stand to perhaps benefit most from a strategy to enhance rates of muscle protein synthesis compared to younger adults who typically tend to have a stable muscle mass.

So in the study that we performed, we got a group of 20 overweight and obese older men and we randomized to receive either a balanced pattern of protein intake or a skewed pattern, and we brought them into the lab and we measured muscle protein synthesis over a 13-hour period, so an acute period, using a prime-constant infusion, which is the method often used to measure muscle protein synthesis. We gave them 75 grams of protein and in the balanced group that was provided in an even pattern, so they consumed 25 grams of whey at breakfast, lunch and dinner, and in the skewed group they consumed 10 grams at breakfast, 15 at lunch and 50 grams at dinner, and we measured muscle protein synthesis over the course of the day. And we did that on three occasions, firstly under conditions of energy balance, secondly after two weeks of energy restriction, and then finally after two weeks of energy restriction combined with resistance training.

And what we found was that in the energy balance condition, there was no difference between the balanced and the skewed group. Now, one of the reasons that could account for that at is the time that we designed the study the available evidence suggested that about 25 to 30 grams of protein was required per meal to maximally stimulate muscle protein synthesis in older adults, and since that time a retrospective breakpoint analysis has been performed and refined that dose to 0.4 grams of protein per kilogram per meal. Because of the high body mass of the participants in our study, it meant that the quantity of protein they were consuming per meal in the balanced group was likely insufficient to maximally stimulate muscle protein synthesis. But anyway, after the two weeks of energy restriction, we found that the balanced pattern of protein intake actually stimulated muscle protein synthesis to a greater extent than the skewed protein intake. However, in both groups, the rate of muscle protein synthesis was lower than the energy balance condition. After two weeks of energy restriction

plus resistance training, there was no improvement compared to energy restriction alone in both the balanced and the skewed group such that in the balanced group the rates of muscle protein synthesis were actually restored to the higher levels we observed during energy balance, whereas in the skewed group the rates remained below the energy balance level and they were also lower than the balanced group.

Danny Lennon: So essentially by even going into that energy-restricted state by combining the resistance training and this balanced pattern of protein distribution, people were able to keep their MPS response the same as if when they were back in that energy balance.

Caoileann Murphy: Exactly.

Danny Lennon: Wow, that's pretty impress…I think that's a really important factor then as well when people are considering even the practicalities. Just one thing before I forget, when we're talking about these figures of protein and these recommendations either per meal or per day, are these in talking about a particular type of protein source? Because presumably the amino acid profiles can be different between all these different sources and we have higher-quality or better-quality ones that will have I suppose higher levels of, say, the branched-chain amino acids, etc., particularly say something like whey protein. So are they in reference to any particular type of protein or is it kind of just a general recommendation that would do in most cases?

Caoileann Murphy: So most of the dose response studies have been conducted with a high-quality source of protein and it's typically then a liquid source as well, so something like whey, and in that breakpoint analysis that I mentioned by More, et al. 2015 that was relevant to whey. So our available evidence is, well, based on the amount of protein that stimulates maximal muscle protein synthesis when the source of protein is high-quality and it's not consumed along with any other macronutrients. So I think that there's a real need for further work examining the dose response relationship between protein and muscle protein synthesis when the protein is provided in context of normal foods and within mixed macronutrient meals because that's how people typically consume their protein.

So the reason that that might be important is because if you consume a mixed meal, there is typically carbohydrate and fat and fiber, all of which would slow down the digestion and absorption kinetics, and it's hypothesized that a rapid and pronounced peak in plasma essential amino acids and in particular leucine is important for stimulating muscle protein

synthesis. So if you were to consume a mixed meal, it's possible that the plasma amino acid response might be a bit more blunted, which could affect the muscle protein synthetic response. In addition, if we consider that if you were to consume a meal that contains, let's say, 20 grams of protein, some of that protein will be coming from plant-based sources which are typically lower in protein quality and lower in essential amino acids and lower in leucine, so we don't necessarily know that that would have the same muscle protein synthetic response as a 20-gram bolus of high-quality why protein, which is very rich in essential amino acids and rich in leucine.

Danny Lennon: For sure. I think that's an important one because that's typically where I've had people questioning stuff around particularly, say, if they have a client that is a vegan client and he's using some sort of vegan protein, is it going to be this…can they go in those same dosage recommendations or should they be adding in a bit extra as a kind of buffer or should they be maybe using some leucine supplementation on top of it, etc., etc.? And like you said, we just don't know a lot of those answers yet.

Caoileann Murphy: Mm-hmm.

Danny Lennon: And I suppose the other consideration when we talk about the absorption rates as you mentioned, because we know, for example if you compare whey and casein are the two that people typically think of with different absorption rates, so they may have varying degrees of effects on muscle protein synthesis but on the flipside then, how does that affect muscle protein breakdown because I suppose that's what we really care about, right? That net balance of the two.

Caoileann Murphy: Mm-hmm.

Danny Lennon: So maybe if casein has this prolonged elevation over time but isn't as absorbed as quickly, it might have just less muscle protein breakdown. But I suppose these are just questions that still need to be looked at, right?

Caoileann Murphy: Yeah, and also when we talk about these studies that I've just looked at on isolated source of protein consumed in the fasted state, we can't necessarily translate directly to the real-life situation. So if someone consumes a protein-containing meal, then the…or sorry, like a complete meal which contains carbohydrate and protein and everything, this will result in an increase in plasma insulin levels and we know that plasma insulin doesn't have to get that high in order to maximally suppress muscle protein breakdown at least in young adults, so we may be kind of

splitting hairs and it may be more about focusing on a high-quality source of protein or even a larger serving of plant-based sources of protein. And I think when we talk about plant-based sources of protein, another interesting avenue for research would be to look at protein combining. So we know we need all the essential amino acids to serve as the building blocks for muscle protein synthesis and grains are lower in lysine, whereas pulses are lower in methionine. So by combining them together, can we induce a greater muscle protein synthetic response or an equivalent muscle protein synthetic response compared to an animal-based source, for example?

Danny Lennon: If we turn back to looking at this discussion around older adults and protein needs because I think it's just a really fascinating area, and obviously I've talked with Brendan Egan a bit about this, and particularly when it comes to not only trying to preserve muscle mass and muscle function with age but also this conflict we have when it comes to those who are overweight and obese getting into older age because when you look at, say, mortality risk and health issues, it's clear that excess body fat is not a good thing, right? And reducing fat mass alone will lead to an improvement in several health markers. But on this flipside, we see this conflict that, as we mentioned with the calorie deficit that can potentially put people at risk of losing more muscle mass, now we have people who are even more susceptible to that. And so then I think one of the big things Brendan talks about is this how big of a deal muscle mass and muscle function is in terms of like mortality and chronic disease risk in the long-term for people. So, I mean, there are all these areas that we're trying to look at. So how should we think about…like what are your current thoughts on this delicate tradeoff between trying to get overweight and obese older folks to decrease body fat mass but this risk that we have with, say, even like sarcopenia for example?

Caoileann Murphy: So yes, certainly there are the health benefits associated with weight loss even in obese older adults, are certainly very significant, then I think it should be a goal for obese older adults to reduce their fat mass. However, I think it would be particularly important for those older adults to receive advice on how best to do so so they can achieve what we call high-quality weight loss, which is a higher fat-to-lean mass loss ratio, and the strategies that appear to be effective as we kind of mentioned earlier which were some form of resistance exercise during the weight loss period as well as consuming higher protein intakes. So I think it'll probably be an area for future research, and a recent study has examined the influence of a more

balanced protein intake during weight loss in obese older adults and they found improvements in physical function in older adults that consumed closer to an optimal serving of protein at breakfast, lunch and dinner compared to those who have the more skewed pattern of protein intake.

Danny Lennon: With that then, obviously that's been one of the areas you've been looking at. With your career from this point and what you're kind of looking at in the future, where is your research mainly going to be focused around and what are you…what kind of I suppose research questions are you particularly interested in addressing?

Caoileann Murphy: So I am starting a postdoc in UCD soon working with Dr. Brendan Egan and Dr. Helen Roche and my work there will mainly focus on malnourished older adults, and I'll be hopefully looking at muscle protein synthesis but also looking at…it'll be a longer-term intervention study and we're looking at different nutritional supplements and how they ultimately influence muscle mass and function when consumed repeatedly over time.

Danny Lennon: Yeah. No, that is really interesting and I think because it was one of the things that Brendan mentioned around…we have obviously this whole area of sarcopenia and this anabolic resistance that older adults can exhibit and essentially this blunting of the anabolic response to things like protein or resistance training and trying to decrease that resistance through things, I think he'd mentioned things like fish oil, which there are some studies on lately, I think even Kevin Tipton's group published something on recently.

Caoileann Murphy: Yeah.

Danny Lennon: And then leucine was another one that you mentioned. Do you see any of those playing out or have you seen anything that suggests that you hold much faith in those being used in conjunction with all the other things we already know?

Caoileann Murphy: Yeah, I think that the omega-3's are a really interesting one. A recent study showed improvements in function in older adults supplemented with omega-3's without even doing any exercise or there was no exercise intervention, and then some previous work has shown that supplementation can improve rates of muscle protein synthesis and response to food intake in older adults as well. So I think that's a really interesting one and an area that will receive quite a lot of research.

And in terms of leucine, so the acute studies to date have shown that if you add leucine to a suboptimal dose of protein for an older adult that there

will be an increase in the rate of muscle protein synthesis compared to the suboptimal dose without the extra leucine, and a number of studies have shown that but since that time several longer-term intervention studies with the leucine supplementation have been conducted in older adults and those have failed to show any influence on muscle mass or strength. So the hypothesis has been or it has been speculated that perhaps it's because the older adults in those studies were consuming optimal amount of protein already, so the extra leucine couldn't have any further benefit, and those older adults were consuming about 1 to 1.1 grams of protein per kilogram per kilogram per day.

And another thought is that maybe the…when we look at rates of muscle protein synthesis in response to the isolated protein doses with leucine, we're not getting the full picture compared to if they were to consume the leucine along with their normal mixed meals, which is what they did in the longer-term studies. And so my last study actually in McMaster focused on measuring the rate of muscle protein synthesis over a longer time period, so over a three-day time period with leucine supplementation of normal mixed meals in older adults. And I guess I don't want to give it away yet, but I think that leucine potentially does hold some promise as a method for overcoming anabolic resistance, but it will be important for, again, further work to be done and it's possible that those longer-term intervention studies just weren't, even though they were long-term, they just weren't long enough to show changes in muscle mass using the methods that they use. We know that the changes in muscle mass occur very gradually in older adults, so we might need years to see an influence on muscle mass and strength and function.

Danny Lennon: Yeah, a hundred percent, and I think even people who train regularly will know that the changes in gaining muscle mass tend to be a lot, lot slower than changes in body composition going the other way in terms of decreasing body weight, and that's even in people who are training and young and healthy, never mind in older populations where it becomes more of an issue to overcome this inability to gain muscle mass.

Caoileann Murphy: Mm-hmm. Yeah.

Danny Lennon: So I think that's a really worthy point. And I think the other thing is maybe we'll get to a point where all these different interventions have the potential to be a piece of the puzzle and that it's essentially using them all together as opposed to one thing being enough to overcome all the obstacles for an older person to hold on to muscle mass, right?

Caoileann Murphy: Yeah. Exactly, because all these things likely have just a very small effect, but maybe when you add them all together, then it can result in something significant.

Danny Lennon: If we talk then finally before we start to wrap up, obviously having had the opportunity to work with Stu Phillips and the others over in the lab in McMaster, which is obviously extremely well-regarded within the scientific community, it's obviously a pretty big deal for this area of research as well, considering the breadth of the work that Stu has done and the other people there, I'm sure there are endless things that you've probably learned from him and from the others but are there like maybe one to two things that particularly stand out as a learning experience in terms of just how to approach things or anything that will stick with you as something particularly impactful that you learn?

Caoileann Murphy: Hmm. Something that if I ever go on to have my own lab—I love the way Stu runs his lab. There's a very strong ethos of teamwork and we all kind of give each other a hand out and I think docs really kind of…we tend to run a lot of studies and things tend to be a bit haywire, but everyone helps each other out and it all gets done and the...it's just such a lovely environment to work in. And the participants all really enjoy it, which I think is really important for subject retention. So I'd say that would be an important thing that I learned over there, among many other things. I barely knew what muscle protein synthesis was when I went to Stu's lab, so I hopefully learned one or two things since then.

Danny Lennon: Awesome. And before I get to the final question, where can people track you down online if anywhere, things like Twitter or can they find your profile on ResearchGate or anything like that?

Caoileann Murphy: Yeah, my profile is on ResearchGate. I do have a Twitter account. I think it's just @CaoileannMurphy.

Danny Lennon: And I'll link to that in the show notes for people. If you do want to go and check out more of Dr. Murphy's papers, they'll be all linked up there. And I'll put some links directly to some of them on PubMed as well in the show notes to this episode.

So that brings us to the final question that we always end the show on and as always it's a big, open broad one, simply, if you could advise people to do one thing each day that would have a positive impact on some area of their life, what would that one thing be?

Caoileann Murphy: I think it would be just to be physically active. We know that being inactive, even reducing your step count to less than 1500 steps per day, which is not unusual for someone that stays in the house all day, can result in a downregulation in muscle protein synthesis after just two weeks. It can also result in a loss of muscle mass in older adults, and for older adults it's very difficult then to get that muscle mass back once it's lost. So I think for everyone, everyone can benefit from being physically active every day, but particularly for older adults, to just move around as much as possible can have a huge benefit in terms of your health.

Danny Lennon: Perfect. Caoileann, this has been great. This has been really, really informative, lots of really good information, and I really want to say thank you for your time as well.

Caoileann Murphy: Great. Thanks for having me, Danny.