DANNY LENNON:

Hello and welcome to Sigma Nutrition Radio. I am your host as always, Danny Lennon on what episode 272 of the podcast. I'm absolutely delighted to be joined by Professor Barbora De Courten on today's show. We are going to be talking about some of her fascinating work, particularly in the area of carnosine supplementation, but also in looking at the mechanisms that may drive chronic disease development, particularly with glucose metabolisms so diabetes and some related comorbidities.

And she was at the forefront of putting out work describing the mechanistic link between increased chronic inflammation and the development of some of these chronic diseases as well as talking about AGEs and how glycation can potentially play a role here too. And over the past number of years, she has looked at the effect of carnosine potentially in improving outcomes in at least the risk of chronic disease development and also improvements in certain markers related to some of these diseases.

So things like instant sensitivity, glucose response and so on. So we're going to dive into some of the work that she's done, look at mechanistically why carnosine may be useful, some of the trials that have been done to date in humans and what questions still need to be answered.

So hopefully this is something a bit new for some of you listening. We will link up to all of the papers that we mentioned throughout this episode in the show notes. So if you go to sigmanutrition.com/episode272, I will link to all the papers we mentioned. And also for those of you who are based in Melbourne, Australia, you can actually get involved in some of these clinical trials.

You will be paid for taking part and there are certain criteria to be involved that I've listed at the show notes page as well. So you will get paid, but you'll also be able to number one, be able to get a number of different assessments done. So diabetes and cardiovascular disease risk, you'll get body fat and muscle measures done, you'll get some other blood tests done. So you'll have all that stuff available to you as well as knowing that you were contributing to science in these areas.

So there are certain requirements based on the studies. So there's two particular studies I'll link to. So if you are in Melbourne, Australia and want to be able to be involved, check that it out. So go to sigmanutrition.com/episode272. I will put all the details to these trials there and you can check those out. And if that is something you're interested of, you can get in contact with the lab. So let's get into the episode with Professor Barbora De Courten.

Barbora, thank you so much for taking the time to join me today. I'm really excited to ask a few questions about your work that you've got going on and it spanned across a number of different areas and we'll probably focus down onto one or two of those in this particular discussion. But just to give people listening some context for your work, can you describe what your work mainly focuses on, what areas and a brief bit about your academic background.

BARBORA DE COURTEN: Maybe I'll just start with my academic background. So I'm a physician, a specialist physician with interest in diabetes, in particular prevention of diabetes, but also diabetes treatment. But most of my life, I spent time researching predictors of diabetes and ran clinical trials to prevent or treat diabetes.

I early on had been focused on in particular inflammation as a predictor of diabetes and how we reduce inflammation and prevent diabetes and also other chronic diseases.

DANNY LENNON: As you said, a lot of your work, looking at diabetes and also maybe some other chronic diseases that are interrelated as well, and when we look at some of these chronic diseases and their development by trying to look at some of the mechanisms by which risk is increased. You mentioned one there is inflammation. Can you maybe touch on one that mechanism by which it may play a role and are there other primary mechanisms that we should be aware of when it comes to chronic disease development?

BARBORA DE COURTEN: So one of the truths, a lot of researchers describe that inflammation means a link to development of inflammation resistance and type II diabetes in human. This was at the time when our first studies were just coming out, linking inflammation to cardiovascular disease, and we looked at this data at the National Institute Health and found that there was a relationship prospectively. So taking baseline data, people who are more inflamed has a greater risk of developing insulin resistance and diabetes.

We then done a series of studies trying to establish if inflammation is actually causal to diabetes. There's many potential mechanisms and a lot of researchers have been researching these and we have also researched this area in humans and found that in particular, two pathways and [indiscernible 00:06:46] J and K are linked to insulin resistance and development of diabetes.

Together with inflammation, there is also oxidative stress which is linked to inflammation and another process which is called advanced glycation which is also linked to inflammation. And all of these three risk factors, if you like, are actually cutting across all chronic diseases. So they're important not only for development of diabetes and its complications, including macrovascular complications such as cardiovascular diseases, as well as microvascular

complications such as a kidney, eye, and nerve disease, but also they are important for all of the other chronic diseases which are all actually interlinked and linked to diabetes.

So it's liver disease, kidney disease, dementia, but also general aging. So they are very same processes and my work has focused on actually harnessing those processes, in particular inflammation and advanced glycation, and the hypothesis that if we can reduce those processes and keep them at bay, we can prevent disease not only diabetes, but potentially all chronic diseases.

DANNY LENNON: Yeah. So when we talk about some of those chronic diseases you've mentioned whether that's diabetes or dementia or cardiovascular disease, for example, a lot of people will be aware that there's typical causes that people discuss whether that's a poor diet, smoking, inactivity, etcetera, etcetera that are related to an increasing risk of these certain chronic diseases. But those causes would have to have some sort of mechanism that's increasing risk. And it seems that regardless of what different causes we're talking about, there's these two or three primary mechanisms that you focused in on of inflammation, oxidative stress, and then advanced glycation end products.

BARBORA DE COURTEN: Correct. And you're very right in saying that poor diet, physical inactivity, smoking, etcetera, all contribute to chronic diseases. In fact, they're all linked between inflammation and advanced glycation, and oxidative stress. So there are many ways how you can reduce inflammation, oxidative stress, and advanced glycation. So improve your diet, do physical activity. They're the most powerful things you can do and there's actually no other medication or supplement which can match the effects of a healthy diet and physical activity.

But then there are other things you can do potentially and that's where some of my work carnosine is coming in.

DANNY LENNON: Yeah, absolutely, and I'm very keen to discuss some of that just, but just whilst we're on advanced

glycation, this is obviously I think a lot more complex of an issue than maybe it seems on the surface when people first hear about it. At least from a dietary perspective, if we look at that, it's kind of well-known that certain foods may have a certain content of AGEs, but that's not really the whole story, I guess, when it comes to advanced glycation within the body itself.

So I'm just interested to hear from your perspective as of right now, what are some fair conclusions that we can come to about from a dietary perspective? How much do people need to focus on the AGE content of their diet?

BARBORA DE COURTEN: So it's a very good question. I think at this stage we don't need to focus specifically on lowering AGE per se because a person eats healthy diet, so diet rich in vegetables, fruits, low in processed foods, and reduced amount of red meat, frying, etcetera. This is the general healthy diet that will reduce both inflammation and advanced glycation in the diet.

So they're the diets which are less inflammatory and there they have less content of AGEs as well. So I think for the public health message, we should eat healthy diet and we don't need to think about so much about if it's high or low in AGEs or high and low in other things. As long as we eat healthy such as Mediterranean style diet or other healthy diets, there are different diets out there. We're going to be okay.

DANNY LENNON: Sure. So let's turn to carnosine and before we discuss some of your papers that you've published specifically, just to kind of get everyone up to speed, what exactly is carnosine?

BARBORA DE COURTEN: Carnosine is actually naturally present in our body. It's a dipeptide, consists of beta-alanine and histidine and it's actually an interesting substance in the sense that it has been shown to improve exercise performance. So athletes who use it, they had better performance physically. So, carnosine has a potential to improve exercise performance and through that improves your metabolic profile, and also it has effects on its own outside of the exercise.

So it's actually, potentially very interesting because you can combine the healthy diet with exercise and potentially carnosine if we find that attractive.

DANNY LENNON: So when it comes to some of those potential benefits for health, and even if we tie this back to some of the chronic disease development we've mentioned earlier, what evidence do we have to date showing that it may potentially play a health benefit role here?

BARBORA DE COURTEN: So it is quite well-established in animal studies that carnosine reduces inflammation, oxidative stress and advanced glycation from the very prophecies we've just been discussing. There is good evidence again from animal studies that each has effect on diabetes, on cardiovascular disease, on dementia, and a lot of other chronic conditions and diabetes complications as well.

In terms of human studies, we have done one of the first human studies which showed that carnosine reduces or improves sensitivity to insulin which is linked then to protective effects, again, diabetes. Now there are several studies confirming our initial findings and we're actually just writing up a paper from a meta-analysis of this trial and you'll hear about the results hopefully in a month or two.

DANNY LENNON: Yeah. That was one of the papers that I really enjoyed reading, the one looking at instant sensitivity and I think it also showed improvements for an oral glucose tolerance test, if I remember correctly. So with that, what is the typical dosage and timing of that supplementation we're seeing in the trials that have shown beneficial impacts?

BARBORA DE COURTEN: So there are several trials they've used anywhere between 500 milligrams per day to two grams per day. There is a heart failure study as well which showed some benefits for heart failure patients, and I believe that was also around 500 milligrams per day.

DANNY LENNON: Okay. Perfect. So for at least diabetes development or pre-diabetics or those instant resistance, you've talked about some of your trials showing

improvements for instant sensitivity, we've mentioned oral glucose tolerance test for some of these other chronic disease that can potentially play a role for. Is there any other mechanisms by which it's reducing risk for those outside of those that we've mentioned or outside of improving, let's say, performance in sports and exercise?

BARBORA DE COURTEN: So they're then the pathway which we need to look at and we're actually running two trials right now and where we're recruiting actively for both trials where we will look at the different pathways. There's little bit of data from studies itself that carnosine impacts on some of the very important pathways for obesity and diabetes such as mTOR pathway and [indiscernible 00:16:08] pathway. And we'll be able to look into this because we're collecting actually some tissues in our trial.

DANNY LENNON: One thing that I did want to ask when you mentioned about carnosine showing this performance in athletic populations for exercise performance, one supplement that I think a lot of people within sports nutrition will be familiar with is beta-alanine and beta-alanine has this effect by increasing muscle carnosine concentration. So, I'm just curious to ask what are some of the key differences, if any, of supplementing between beta-alanine versus directly with carnosine, and have we seen some of the work with beta-alanine also translated into the health sphere?

BARBORA DE COURTEN: Most of the literature from beta-alanine is in exercise physiology as you rightly pointed out. The difference is that carnosine is a dipeptide which consists of beta-alanine and another amino acid called histidine. When you ingest beta-alanine, the synthesis happens in the muscle. So most of the effect would be in particular in the muscle whereas if you ingest carnosine, some of the carnosine cell as a dipeptide will get into the bloodstream and may have other effects in the bloodstream and other tissues that can't produce carnosine.

So that could be potentially one of the effects, but we're doing currently the meta-analysis and there there are some effects of beta-alanine on glucose

metabolism, but you will have to wait for that data to come out and be published.

DANNY LENNON: So for those listening who are either in practice as dieticians or doctors or then even people within the general population who are trying to improve their health, what are the things you feel are safe to conclude right now about carnosine for those that may be considering using it? How well-established you think it is? What type of way should it be used, etcetera, is there anything to be concerned about and so on?

BARBORA DE COURTEN: It's a food supplement. It's over-the-counter available. So there is nothing major as far as we notedly concerned about, however, currently we don't have enough evidence to recommend carnosine for any of the health conditions or diseases. That's why we're doing studies. But if people are interested in carnosine, they should come and participate in our studies. The faster we get done, the faster we have a conclusion. Carnosine definitely has a great potential, but we need to wait for solid trials to confirm the effect.

DANNY LENNON: Sure. So with that said, and I think you've touched on some of this already, what are some of the big research questions that are still to be answered that you are hopeful of getting answers to over the coming years in this area?

BARBORA DE COURTEN: There's lots of them. Currently, as I said, we're doing two studies; one is looking into prevention of diabetes, and the other one is reversal of diabetes. So we had ongoing trial now. Other question is effect of carnosine in diabetes complications, and that's a very interesting one. There is actually quite a bit of supportive evidence even in humans that carnosine may play a role in diabetic nephropathy and animal study, showing positive effects in other diabetes complications such as eye disease, retinopathy, and the nerve disease, neuropathy.

And we don't have major advantage in treatment of the particular conditions. Carnosine could play actually an important role and transform practice. And now the area of peripheral vascular disease, I'm

collaborating with University of Louisville on a project looking into peripheral vascular disease and we're actually just starting a new project which is funded by National Heart Foundation.

Looking at effects of carnosine on peripheral vascular disease, there's very interesting data in animals on stroke and again, a colleague of mine in UK is very keen to do some studies in stroke. And the reason for this is because, well, the animal studies show, and this is across three different organs; one is brain, liver, kidney, and I forget what the fourth one was.

So when they pre-treated animals with carnosine and they tied up a vessel to the particular organ they were studying, they found 30-50% reduction in the infarct or in the area of vent through the organ. And that's very interesting data and exciting data and there's even meta-analysis out there conducted by my colleague and that is very promising.

And the next thing would be to basically take these through stroke patients. The issue is that carnosine is currently not available as intravenous formulation and that is basically limiting in the translation. But that doesn't mean that these couldn't be done.

So there is lots of potential areas. The other area is dementia. There's quite a bit of evidence in both animals and humans that carnosine may improve cognition and, again, a colleague of mine in Slovakia is conducting studies, combining exercise with carnosine looking at a combination in people with early Alzheimer's disease.

So there's a lot of interesting research which is currently happening and I'm collaborating with all of these scientists.

DANNY LENNON: Yeah, certainly it is fascinating and it's going to be interesting to see that play out in these coming years because on one hand whilst there's obviously, if we see more successful trials and more evidence mount in some of these areas that has big implications for quite important issues are these chronic disease

development. This is a very important issue and it also has the benefit of really not having anywhere near the side-effects that someone could be concerned with.

At least from what we can tell so far, it's going to be magnitudes of order safer than maybe some of the drugs that may have a certain effect. So if we can see a discernible and significant change through this, I think that'll be a big breakthrough and it's certainly exciting to see how many different areas it's being looked at.

BARBORA DE COURTEN: And the important part is that the carnosine effects on the mechanisms of these diseases, which are actually important for all chronic diseases, you can actually impact several chronic diseases at once and we don't really have medication like that. So it's not only the side-effects but also the panel of our impact. And the other important thing is because it's a food supplementary, it actually doesn't need the same approval process as a new drug which are being developed. So if we find that it's affecting, because it's an over-the-counter available food supplement, the process to get it in the practice will be much faster.

DANNY LENNON: Yeah, that's an important point that we can essentially streamline that and get that into people's hands much, much sooner which again, could have huge implications depending on how some of these trials work out. So before we wrap up, Barbora, and to get to my final question, for anyone that's kind of interested in reading more of your work or looking at what's going on, is there anywhere you can send them on the Internet? That would be a good place to keep up to date with your work or to find more of your publications,

BARBORA DE COURTEN: The place where you find the publications would be PubMed. That's where all of the studies, not only mine, but also my colleagues are published and searching for carnosine, and I'm very happy if people contact us with different questions and on and off getting emails from patients or practitioners asking me about carnosine.

DANNY LENNON: Great! And for everyone listening, I will link up to much of the papers that we've mentioned throughout today's discussion into the show notes so you can click through and read those, which I highly encourage you do.

And Barbora, with that, we come to the final question that I always end the show on, and it can be completely outside of what we've discussed today, and I apologize that's a big, broad question. So apologies for throwing this at you. But it's simply, if you could advise people to do one thing each day that would have a positive impact on any area of their life, what would that one thing be?

BARBORA DE COURTEN: Yeah, it's something I'm very passionate about; the healthy diet. So eating lots of vegetables, avoiding processed food, anything what is in the packet, essentially because often it's high in sugar and high in salt. Eating like our grandmothers and grandfathers. That would be probably the best thing we can do. We know that healthy diet impacts on old chronic diseases; diabetes, cardiovascular disease, dementia. There are even two beautiful clinical trials showing that impacts our mood even in people who have moderate to severe depression. So I think the best thing we can focus on is eating healthy, wholesome for your processed food.

DANNY LENNON: Thank you so much for taking the time out to talk to me today, but also for the great work you've been doing for a long period of time now and that you continue to do. It's much appreciated. So thank you for that.

BARBORA DE COURTEN: Thank you.