DANNY LENNON: Kyle, welcome to the podcast thank you so much for taking the time up to join me today.

KYLE MAMOUNIS: Thanks for having me.

DANNY LENNON: So there are plenty that I've been wanting to ask you and particularly reading some of your work has thrown up I think a lot of hypotheses that could be useful to explore when we're considering human health and just maybe before we get into some of the specific issues maybe just to give people a general bit of context about your background can you maybe explain your background in academia and how that's led you to your focus on your current research.

KYLE MAMOUNIS: Well I knew that I wanted to do nutrition research when I first got into experimenting with diets in my twenty's so I just got a bachelor's in Biology and then I got kind of discouraged because I was on the Internet and it seemed like everything had been done in research so I didn't go to grad school right away, got a couple of odd jobs and then finally I decided, okay I want to do that so I went to Rutgers to start a PhD in nutritional biochemistry and I was having trouble

finding in an advisor because funding just every year kind of gets worse and worse for graduate students and there's not always a slot in in the labs that you can go into in the department and then towards the end of my first semester I saw a talk by a new faculty member that was just hired on to the animal science and the chronology Department which can share graduate students with nutrition and exercise science. There's a couple of different departments that can share graduate students among them. And he was talking about estrogen and the hypothalamus and energy balance really nothing to do with nutrition but. I didn't really have any other, anywhere else to go so I walked up as if I could hang out in his lab and we got along okay together. So from there I just tried to cobble together a nutritional experimental project with the tools that he had in the lab to study the hypothalamus.

DANNY LENNON: Awesome and so I think that's a probably a good place to segue into some of the topics I wanted to bring up and some of that is going to center around this kind of connection between obesity, hypothermic inflammation and then as we'll probably get into more specifically looking at the different proportions of fatty acids within the diet as well. But maybe just to again to lay some context for the rest of the conversation when we're talking about hypothermic inflammation as a potential mechanism in driving obesity can you maybe explain for people just what the kind of mechanisms are there that might explain that or what kind of things we've been investigating looking at the highest hypothalamus particularly in obesity development.

KYLE MAMOUNIS: Yeah the history starts a while ago maybe in the fifty's or sixty's. Experimenters have found out that if they go into the hypothalamus and ancient certain parts of it they can get obesity, they can even get for animals to sort of waste away and not eat at all they get different behaviors like that and over time they figured out which clusters of neurons in the hypothalamus seems

to drive feeding behavior even metabolism like body temperature and so that was the basis for the hypothalamus being important in energy balance in general and then later on in the eighty's and ninety's and then into the twenty first century.

People are finding that in situations like insulin resistance or when the whole left in question started these same areas of the hypothalamus that if you injure them can affect energy balance also have are ritually express in some receptors and left interceptors and are very reactive to glucose and even amino acids getting into that area the brain which is very porous compared to the rest of the brain, the rest of the brain is much more selective in what it lets in but the hypothalamus sits right on top of the pituitary and is more fully bathed in circulatory blood it's sort of right on the edge of the blood brain barrier so it keeps a pretty good look on the systemic circulation unlike the rest of the brain.

So all of those things together led people to start look at looking at how lifestyle effects and diet could be mimicking in some way the lesion experiments that were causing obesity so that was the basis of the hypothalamic inflammation hypothesis which is that if you could develop inflammation in these areas of the brain and inflammation blocks insulin signaling and interferes with lepton signaling and the other metabolic things that that would be involved with. We know what it does that in a rest of the body so presumably these cells would behave the same so if you get localized inflammation there it could reduce the hypothalamic ability to sense energy balance and you know turn up the metabolism or turn down energy intake when there's enough.

DANNY LENNON: Yeah thanks I think kind of turning to some of your work and I read the paper that you published I think came out just earlier this year that among other things kind of looked at this question of not only hypothalamus information and obesity development

but looking at it from the context of a high fat diet driving that but looking at the specific fatty acid profiles and as I'm sure we'll probably dive into that study a bit more in detail in a few moments but from the outset to maybe get a flavor of why this was something you want to explore. Obviously we have high fat diets implicated in in being one way to induce both hypothermic information and therefore obesity particularly in these rodent models that you're looking at and a lot of the time at least conventionally saturated fats tend to be implicated as one of the kind of key driver here or at least to some degree but as I think your work was at least hypothesizing it as definitely been intriguing to me to see to point out there. Number one could be a lot of sources of potential error in how high fat diets have been typically evaluated or at least described in literature and then also maybe we need to reframe how we look at the high fat diet driving these things at least a bit more detail. Can you maybe just touch on how you came up with this hypothesis that you want to look at and why it was something that was I think jumping out at you that needed to be explored.

KYLE MAMOUNIS: So there's a few different areas that I notice when I get into. You know when I was in grad school I was really interested in asking questions other people weren't asking and most of the other students you know it's not really a super inquisitive environment so it doesn't always encourage that but I did notice I was sort of coming from the paleo sphere and especially six or whatever years ago. The whole demonization of saturated fat, people were really pushing back against that and I found just a few pieces of information that made no sense which is of course that over the time that supposedly the obesity epidemic happened, saturated fat consumption went down.

Especially in relation to Omega 6. And then when I got into the actual animal literature I noticed that the titles of the papers sometimes or the abstracts or the introductions by the way they report the results if you

really dig into the methods you can see that sometimes they misspeak about what their own experimental diets contain. In some cases it's a pretty gross oversight they'll just literally miswrite it as I found that a couple times but what usually happens is the most popular fat to use for rodent models is large and sort of as a historical error be the way that the Fatty acid profile of lard as reported is based on a U.S.D.A. database for the most part.

That is from the mid twentieth century and pigs had a very different fatty acid profile than so, like the company that we used to research diets they're probably the biggest supplier of these diets for experiments on animals in the world and they did internal testing and found that the saturated fat and the monounsaturated we're quite a bit lower in their actual supply and that this was all made up by linoleic acid. That was double digits percent higher than they and everybody else has been reporting so at the epidemiological level of what humans have been consuming it doesn't really make sense to pin obesity on saturated fat since the consumption has gone down and then at the experimental level it seems like people mistakenly assume that the saturated fat causes a problem so say if the saturated fat takes up twenty percent of the fatty acids and then the rest are moderate saturated and polyunsaturated. They will just report that the saturated fats causes obesity and they won't compare it with a diet is different they just assume that twenty percent or whatever it is it's really interesting almost sociologically.

DANNY LENNON: Yeah for sure and that's something that definitely jumped out to be especially as I started reading some of your explanations on this and I think it was in one of your posts you touched on that kind of statistic of over time we've seen a decrease in taken saturated fat over. However many the last number of decades but during that time that reduction in saturated fat has been kind of offset by an enormous increase in calories contribute. For those listening is a

polyunsaturated fatty acid or a buffers and that was kind of really intriguing to me again as to why particularly in this question because it may be coming from a lot of the cardiovascular disease research that is being conventionally thing to do right reduce saturated fat increase buffers in their place and that's going to offset cardiovascular disease and obviously we can get into a whole debate around that as a separate question but it's certainly interesting in trying to understand obesity and that's what I liked about these questions you were asking with your research so maybe if we turn to that paper specifically that we've been talking about. Can you maybe start by outlawing really the objective or the question you wanted to set out to answer with that particular study and then how you went about setting up to try and answer them.

KYLE MAMOUNIS: So I hold this position and the papers that the first two chapters are published in the third one's coming out but the two main questions were, is hypothermic inflammation involved in at least in the rodent models when you see the obesity happen from the high fat diets that people use can that be measured as sort of causal? And then looking at the specific types of fat and I see a difference in both the obesity and other things like insulin resistance and body composition. As well as that hypothermic inflammation, the genes that I'd be measuring to try and find their gene expression can I get a difference in that by keeping the amount of fat the same but changing the composition from pretty much all saturated to very high unsaturated with a lot of acid sort of like the modern human diet.

DANNY LENNON: Perfect and so for some of that work one I particularly remember was when you looked at I think was that instant tolerance test after consuming oils of differing amounts of the linoleic acid that I cannot remember the exact proportions. Can you maybe touch on some of that work?

KYLE MAMOUNIS: Yeah the proportions are easy to remember if you just so throughout the papers I abbreviate them the diet as their percentage of linoleic acid so one percent is the one that's mostly coconut oil so it's mostly saturated and only one percent of the calories are from linoleic acid and then there's fifteen percent in twenty two point five percent. Twenty two point five percent represents basically like a soybean oil or safflower oil. That a little bit more than half of the fatty acids so a little bit less than half of the calories or from fat and then of that a little bit more than fifty percent from linoleic acid that gets you twenty two point five percent number and then fifteen percent is in the middle and I just raised mice normal see fifty seven black mice the ones that most people use in the lab when they're not trying to do anything too specific.

They do have a tendency to get fat from a high fat diet. And I fed them these diets for I believe three months and then gave them just regular glucose tolerance test and insulin tolerance test and that's really where I saw the biggest difference was in the glucose handling because they all got fat unfortunately. Although the coconut oil mice were a little bit less fat but when you look at it they were still fatter than the low fat controls that I had so you know maybe like some guy that's two hundred fifty pounds to one hundred eighty pounds I don't know. But in terms of glucose tolerance the high fat diet mice all seem to dispose of glucose kind of slowly compared to the low fat mice but when we gave them insulin the glucose disposal was the same in all of the mice except the highest except the linoleic acid, the 22.5% group. So even though there glycaemia might not have showed it compared to the other high fat groups it seems like they were resistant to insulin more than the other high fat groups.

DANNY LENNON: Interesting and just kind of to clarify just so I have a Ryan also for those this thing we have these four groups you obviously got the control of the most fat then you have three high fat diets comprising different amounts of linoleic acid versus saturated fat acids and

that's one percent, fifteen percent and twenty two and a half percent of linoleic acid contributing to those calories and seeing these changes in market for in some resistance in that high a linoleic acid group and essentially indicating that that diet probably induces or has potential to induce in sort of assistance and maybe therefore obesity more than the other diets with lower levels of linoleic acid. Are we right up to that point?

KYLE MAMOUNIS: Yeah it would be interesting to see if I took those animals out to longer dietary manipulation if eventually they're glycaemia would get higher because I didn't take their blood insulin at the time of the insulin tolerance test before it or during the glucose tolerance so I can't know for sure but I suspect that the way they were able to keep their glucose disposal the same as the other high fat groups is by secreting more insulin and that's usually the step towards pre diabetes. So eventually it hit a wall where if you keep increasing your insulin resistance you can only secrete so much insulin and then it starts getting reflected in glycaemia and causing overt symptoms like urination and then a lot of the co-morbidity problems with obesity.

DANNY LENNON: Perfect and obviously with a road model like this it's going to be probably most useful at least in some sense for generating further hypotheses of where we go next and things that throws up so for you once this stuff it came through what were the main things that number one you took for or that you are probably most excited to see where we can go from this or what you'd like to build on the back of that.

KYLE MAMOUNIS: Well. You know the biggest thing that I got out of doing all these experiments well as what I learned when I was looking up the rest of the literature because in the same way that I found this problem of misreporting fatty acids and other problems with obesity research and sort of picking on saturated fat unjustifiably I found a lot of research that had either

been relatively ignored or things that I was able to find that weren't in the field of obesity but we're studying fatty acids in a different body system but I was able to get ideas for future experiments that made sense based on some things that I was learning using fatty acids and manipulation of obesity.

DANNY LENNON: Sure I'm sure there's some people listening thinking about these percentages of linoleic acid that we are using these diets and how that might in some way correlate to what a similar intake could be in humans. Is that a useful question to ask and is there any way to look at that or how do those numbers match up to what might be possible or even likely in the human diet.

KYLE MAMOUNIS: Yeah these numbers are physiological. The twenty two point five percent is high but I based my recipe off of another research group. Joe Hibblen and he works with omega 3 and omega 6 fatty acids and he published something about endo canal Benoit's which is one of the downstream metabolites of omega 6 fatty acids and his diets were one percent and I believe eight percent of calories from linoleic acids. And then maybe one that was higher than that and so I tweaked his numbers a little bit and then I added a twenty two point five percent as just a maximum to see if I could get kind of an extreme phenotype difference from that but the fifteen percent is if you're a person that eats a normal diet you know has fried foods that are all fried in vegetable oil and salad dressings they're also having no oil it's definitely not inconceivable to get fifteen percent of your calories from linoleic acid. And I believe the national average is between eight and ten.

DANNY LENNON: Now that makes sense and that's really interesting to me for sure especially number one like you mentioned there, just how common buffers are in various different foods within a standard that someone's going to consume never mind someone who is actually trying to reduce saturated fat as much as possible and typically at least within dietary guidelines may be told

that polyunsaturated fats are one way to replace that with it does throw up some more of these interesting questions. So when it comes to trying to pull these into some more practical conclusions and again there might be quite consume a lot of work still to do when it comes for people listening to try in think about the healthfulness and that's a generic term I devised of these different saturated or these different fatty acids that are within the diet, what way do you currently align your thinking in terms of how to think about not only saturated fats but polyunsaturated fats, predict the omega 6 for example or I'm just really kind of thinking about some questions we should probably ask ourselves before we make some definite conclusions.

KYLE MAMOUNIS: Well it's a big question. Well I have a practical just a simple practical goal for myself but I try to avoid polyunsaturated fats mostly omega 6 but I'm not really too convinced by the omega 3 literature at this point either I don't know how closely you've been following that but a lot of those early studies maybe twenty or thirty years ago that showed real big increases in cardiovascular outcomes with fish oil or a lot of fatty acids they have been replicated very well. So I think in general I just try to stay away from it and I basically just try to consume saturated fat and a little bit of modern saturated fat but on a really deeply philosophical level I consider these plant fats as plant fats and if you look at plants that are grown in cold areas versus hot areas like coconuts are grown in tropics and they have saturated fat they have mostly saturated fat and then the plants that we press for these polyunsaturated oils are grown in cold climates and it's the same thing with the fish the deep cold water fish have a lot of and warm water fish and lakes in the Amazon are much more saturated and as a human, a warm blooded you know mammal that walks around at fairly high temperature.

It seems like and also humans produce saturated fat when they're given sugars and I don't think they

would do that if it was bad for them so in that context really just think of saturated fat as sort of a mammalian fat that seems to work well with our metabolism and our enzyme systems and with the heat of our bodies and that polyunsaturated fat is a plant fat and it may be necessary in very small amounts. But you can get those eating meat in fact the ruminant animals that get a lot of polyunsaturated fats from consuming grasses they have very specialized stomachs with all kinds of bacteria that saturate those fats for them. And that's what produces some of the Trans fats in dairy fat that you know people say oh they're okay because they're natural. That's a fat that's caught halfway in between being saturated by these bacteria from the buffer state that cow consumes it in. So from that perspective I really just think of these polyunsaturated fats as just a different organisms fatty acids and I really don't think that there are too necessary to worry about getting enough of.

DANNY LENNON: That's certainly a really interesting viewpoint that I had thought from but it definitely does seem particularly when you look at intakes there's no one that's going to be in a shortage of consuming enough of these and of course people could probably make the same point about saturated fat considering that we can synthesize ourselves and only recently I was having actually a discussion with a few people around this more in the context of cardiovascular health but one of the interesting things with looking at saturated fat and even if we go with probably some people at least could probably do with limiting it amounts it probably comes down to number one the their food sources in general all of those is probably going to make a key determinant considering just the nutrient value that a given food is going to have in its totality as opposed to focusing hyper specifically on saturated fat content but more so if someone is going to limit that, the nutrient they choose to replace it with is probably going to have a big determine and I think

there's probably a lot of people on board with you in probably not being convinced that a good idea is to jack up your omega 6 or polyunsaturated fat intake super high. One question I've been interested to ask you and I think I've asked Chris Masters on this a bit before. Is looking at it outside of the context of hypothermic information but more so incorporation of fatty acids into the cell membrane for example and their potential to be oxidized more readily then maybe something like a stable foot like a saturated fat? Have you looked much in that area and again what would be your thoughts in that line of really high intakes of polyunsaturated fats in and potential impacts of their incorporation into say cell membranes for example?

KYLE MAMOUNIS: I haven't done any direct research but that's one of the things that I found when I was surveying the literature you know during the whole project and even while I was doing my dissertation a scientist came to Rutgers and he gave a talk and he focused his entire talk on heart damage, cardio damage being caused by excessive incorporation into heart mitochondria of these really long like twenty two and twenty four chain very unsaturated fatty acids. And so that information is out there and of course when it does get incorporated into different cell types and it can oxidize. And that seems to cause a problem but even if it doesn't oxidize and this is the most interesting thing that I found when I was surveying the literature.

It seems that when I was saying before that these fats are they work well in plants, plants make them and don't make them and mammals consume small amounts of them and perhaps use them in that form when you have a lot of them and you look at any enzyme system, so I found some literature in drug research, how the liver clears some drugs and it has a system where it tags the drugs and that tags it for excretion in the kidneys and these enzymes where their rate was dependent on the type of fatty acids that were in their cells of the liver that was producing these enzymes and the enzymes were working and

they found that the more unsaturated the fats were the slower the rate of those enzyme was. It is called the [Indiscernible 00:32:50] of drugs to deactivate them and then I found the same thing at various levels of the thyroid system. So in the production of thyroid hormone the cleaving of thyroid globular and the binding of its receptor all these enzymatic processes, there's papers out there that don't get a lot of press but. They don't specifically market themselves as fat research for obesity but you can cobble together a story that seems to suggest even before the polyunsaturated fatty acids are damaged by oxidation they seem to slow down the mammalian enzymes systems. And that could if taken to a certain level slow down thyroid hormone production or action and other things having to do with a metabolic rate.

DANNY LENNON: Yeah that's super interesting and like you just mentioned there I think a lot of this gets very interesting when you start looking at least these potential mechanisms that we could have for this stuff to come into play in when you start looking at some of the stuff that goes on a cellular level but for this to become more as from lack of better term concrete within the literature or at least for something that more obviously jumping out as that could help more explain or at least work out if there is something more to this story of polyunsaturated fats not only detrimental to health in those aspects but also to this obesogenic potential that we talked about earlier. What sort of trials and what sort of area would you like to see the research go into and what type of research questions that we need to further answer to try and move this thing along to see if there is something more to this and if there is something that is that would match up with potentially what we've been discussing?

KYLE MAMOUNIS: Well I think the two fields that I'd like to see more work in is this enzyme kinetics and the fatty acids mill of the cells actually right now working in a post doc that studies enzyme kinetics and the way enzyme

kinetics research works is ninety nine out of one hundred times you just drop enzymes into some buffer solution that you made that has the proper salts to keep the protein alive and then you put in it substrate and you measure the rate of its action on the substrate in basically in water or in a quasi-cell solution but not inside real cells and so these kinds of effects of the fatty acids or even vitamins and minerals and just all the stuff that's inside of cells is not understood for how it works with enzymes.

I'm sure you've heard some people say oh this is an anti-oxidant and then in the literature it will show that it is an antioxidant in vitro and then in vivo it seems to be a pro oxygen you know whether it's in an animal or humans and I can't say definitively why some of these things seem to flip but a lot of this research that gets eventually gets reported in as health recommendations for you know Vitamin C or resveratrol in wine. This stuff starts off in a petri dish and it's done in a very non cellular, non-life form so I would like to see a field of enzyme kinetics and for my particular interest and how fatty acid profile within a cell facts that that looks at the kinetics inside of a cell or inside of a very similar environment to a cell to actually see what happens to these things and how the metabolism would be changed from these different enzymes and their rates are being turned on or off from the different manipulations that currently are just sort of done in a test tube. And the other thing I'd like to see is just more honest big nutritional studies looking at fatty acids because it just seems like they kind of get stopped sometimes I don't know there hasn't been a big one for a while there was that veterans one I think Chris Masters wrote about it a long time ago. With the saturated fat versus the vegetable oil and they didn't really get the results they wanted and it looked like cancer rates started to pick up in the vegetable oil and they just stopped the study.

DANNY LENNON: Yeah I agree there's a lot to dive through and we're starting to see that I think emerged within saturated

fatty acids and effects and again back in the realm of cardiovascular disease of people at least starting now to ask if there's going to be a study you want to know what specific fatty acids we're looking for, the effects of because we know even within the one class of saturated fats not all of those fatty acids are created equal and never mind when you compare them to polyunsaturated or unsaturated even. So I agree there's a lot of deciphering that needs to go on and dig in to that in a bit more detail. Kyle before we start rounding up here with anything that we've discussed in this line of conversation and this general area. Is there anything that we didn't get into that you think this is a particular important point for people to know or anything that you would like to leave them with a few could have key points from these types of discussions and this area?

KYLE MAMOUNIS: Well I think I should if I didn't make it clear before and I know you mentioned it but a deficiency in polyunsaturated fatty acids is basically impossible. So one thing people should not worry about is getting enough it is very easy to get enough the only experiments that have ever been done on giving people no fat and seen if you could induce a deficiency were really not able to produce any kind of the symptoms that they can produce in lab animals and even the lab animal research is a little suspect because some of the papers back then in the middle of the twentieth century reduced the fat really, really low and got these symptoms that were reversed by adding a little bit of omega 6 buffer.

But you could also reverse the symptoms with Vitamin B6 I think they gave the animals. So it could just been effect of if indeed omega 6 fatty acids were suppressing the metabolism of the animals then removing them from the diet could have increased their metabolism such that the vitamin mix in their pre-determined experimental diet was no longer sufficient to support their health in the same way. So the main point there is that the literature that that

tells people you need this much omega three and omega 6 is good for this and it's better for heart health is very, very flimsy and pretty much falling apart. And there's not a ton of literature that saying saturated fat is great but at the same time the literature that originally demonized that on the heart health question and on the obesity question there's essentially no claim to make other than these studies that most of the time misreport the fats. So I would just say people shouldn't really worry about it too much and I think if people eat the foods that they're kind of attracted to like you know people like the fat on meat they tend to like dairy fats and cheese and I think it seems pretty natural that people gravitate towards those types of fats.

DANNY LENNON: Yeah it is interesting when you think about something like a piece of fat that still on a piece of steak is something that's quite palatable for someone whereas something like a vegetable oil is not something you're going to drink alone I don't think in any way so that's an interesting analysis for sure. Kyle, before we get to the very final question if people are interested in finding more of your work or finding you online or in any where they can connect to you further, where's a place for them to go online to find more about you?

KYLE MAMOUNIS: Alright I have a blog that I post extremely intermittently on. But I'm going to try and do better with that and that's Nutrio-chronology it's nutrition and endocrinology put together dot com and actually with a friend of mine who I met at H.S. last year 2016, we're starting a podcast we recorded a few episodes in the pipeline and we're going to get it online soon but it's going to be a philosophy of science from the starting point of nutrition and it's called nutrition deconstructed.

DANNY LENNON: Brilliant and forever on this thing I will link up to both of those things as well as some of the research papers that Kyle put out as well so all be in the show in this episode. Make sure you go and check all that stuff out

and with that we come to the Final question that I always end the show on call and this can be to do with something completely outside of today's topic and I realize it's quite generic broad question so forgive me for putting you on the spot but it's simply if you could advise people to do one thing each day that would have some positive impact on any area of their life what would that one thing be?

KYLE MAMOUNIS: To do some type of a mindful writing whether it's journaling, where if you start a blog or something or just write something that's a paragraph but write something down that you're thinking and then walk away for a few minutes and then go back and look at it again and make it better and that's the exercise.

DANNY LENNON: Awesome, I absolutely love that, that's a great answer and a great way to finish off the show and I've really enjoyed this conversation and your insights and like I said throughout the show I've been enjoying some of the questions you've been posing and looking to answer and really the attitude that you go on to try and do that I think it's quite refreshing. So Kyle thank you so much first of all for taking the time out to do this and for the work that you're doing and for being on the show so much appreciated.

KYLE MAMOUNIS: Thanks a lot it was fun.