Episode 4: No 'One Size Fits All': The Issue with Fat Tissue

KEYWORDS

fat cells, fat tissue, obesity, triglyceride, diabetes, adipose tissue, weight gain

SPEAKERS

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TRANSCRIPT

Gretchen Repasky 00:07

Did you know that 99.9% of the genetic makeup of all human beings is identical? It's that 0.1% remaining that makes us unique. And that 0.1% could hold clues about the causes of disease. Perhaps why one person with obesity may be predisposed to type 2 diabetes, but not another, or why one may gain weight differently than another. Today I'm sitting down in the studio with two experts who will help us understand some of these clues. First, Alison Ludzki, a Novo Nordisk postdoctoral fellow at Karolinska Institute in Sweden. Alison is uncovering the molecular regulation in adipose tissue that helps explained links between adipose and cardiometabolic disease such as diabetes, and Mads Tang- Christensen, who is former head of obesity and liver disease research at Novo Nordisk in Denmark, Mads has been examining the science behind the chronic disease of obesity, learning why 'eat less and move more' isn't always the solution, and searching for effective prevention and treatments. I'm your host, Gretchen Repasky, and this is Postdocs Talking, connecting diabetes and metabolism research to society.

Gretchen Repasky 01:29

Welcome to you both Alison and Mads, thanks so much for joining us today, and setting out to help our listeners understand the complexity of fat cells.

Alison Ludzki 01:38

Thanks for having us.

Mads Tang-Christensen 01:39

Yes, thank you very much. It's actually and honor being here. So thank you.

Gretchen Repasky 01:43

Before we get into any of this complexity of fat cells, Alison, can you paint a big picture for us? Can you kind of tell us in a nutshell, what real life problem your research deals with?

Alison Ludzki 01:55

My research focuses on understanding how our fat is important for the health of our whole body. And so not just complexity, we're talking about storage in adipose tissue of our excess energy, so that it's not ending up in other tissues in our bodies and causing problems there relating to insulin sensitivity.

Gretchen Repasky 02:20

What kind of problems would those be?

Alison Ludzki 02:24

So when we have lipids deposited in tissues, like our muscle and our liver, this is interfering with the normal function of those tissues, including insulin signaling responses, glucose uptake.

Mads Tang-Christensen 02:39

It's super interesting. I'm looking forward to the discussion because as you probably know, and appreciate that the fat is not as a stupid organ, right? It's actually quite intelligent, right? So I'm looking forward to hearing more, and maybe challenge you a little bit on how to understand it better and put it into a broader context.

Alison Ludzki 02:59

Yeah, it's always nice to get people who are actually interested in talking about our fat, so I also can't wait.

Gretchen Repasky 03:12

So before we get into your work, can we just lay a little bit of groundwork for our listeners, and maybe define some of the terms we'll use today? So I'm thinking terms like fat and fat tissue, fat cells, adipose tissue. Can you give us a bit of a rundown of how we should distinguish these terms when you use them?

Alison Ludzki 03:31

Yes, sounds good. This is pretty tough, so I'll also try to explain it as I talk throughout the podcast. But fat in general, is this energy substrate that we use and store and it itself is stored in something that we call our fat tissue, which is - you can grab it between your fingers at your belly, but it's also found in other locations throughout our body. So fat tissue's, pretty hard to understand because we have it in different parts of our body and it functions and is made up differently in those different parts of our body. Were there other words on the list?

Gretchen Repasky 04:13

Yeah, help us with how we should distinguish fat and the word 'adipose'.

Alison Ludzki 04:17

So adipose, we use to describe that tissue, that depot, that organ. So I'll try to always say fat tissue when I'm talking about that. And then 'fat' we most typically use to describe the biomolecule. So then we're talking about a structural energetic substrate.

Gretchen Repasky 04:37

Sounds good. And then when you're talking about adipocytes, then we're thinking about the cells that make up that tissue.

Alison Ludzki 04:42

So the most important player I'll always say fat cells for these cells that give the fat tissue its definition. And as we'll talk about, there's other cells within the fat tissue but the fat cells are really important there. These professional stores of fat.

Gretchen Repasky 05:01

Got it, sounds good. So now we're ready, let's step inside the big picture. And let's hear about your main research question.

Alison Ludzki 05:09

So I'm interested in understanding how our fat stores energy in this safe way within the tissue. So how our fat tissue stores fat, but also other ways that it impacts our health. And here, we can get into all the other cells that are present in the fat tissue. And those include immune cells, and blood vessels, and structural architecture. And my question overall, is linked to understanding new genes or other factors that we've never explored before, that could play a key role in the storage within this fat tissue of energy, so that it doesn't impact these other important tissues

like the liver. And it's a two-part equation - storage. So we take fat up into fat tissue, and we release it. And it's the balance of these two sides of the equation that I'm trying to understand. So that we can help people do a better job storing and result in less spillover into the other tissues in our body.

Mads Tang-Christensen 06:33

But maybe, you can, Alison, just sort of emphasize the precise action of the fat stored or the fat tissue that is an energy reservoir.

Alison Ludzki

Exactly.

Mads Tang-Christensen

So how does that play? So when you say reservoir, you say something that's just a pool, but we're talking about you see this going in - fat in and fat out? So how's that? Could you? You know, because that's, I think that's the crux of what you're doing, right?

Alison Ludzki 06:58

Yeah, exactly. So it's a super complicated process on both sides of the equation. So fat comes in, largely when we're storing and talking about the storage half of the equation. This is really important in the context of obesity, because we're talking about a situation where we have a surplus of energy. We're eating lots, we need to be able to store that. And that involves uptake into the fat cells and the synthesis of triglyceride, this basic form of fat that we like, because it's really stable. It's not so reactive. It doesn't cause problems and so many interactions with other players in the tissue. So that's the uptake side of the equation. And part of that process, in the case of obesity and weight gain is the fat cell getting bigger. So to fit more triglyceride in our fat cells, the cells have to expand. And that involves lots of responses within the tissue. So the fat cell gets bigger, the structural architecture that I mentioned, has to remodel and the fat cell expands, it kind of pushes on the surroundings, then you need to have a remodeling of blood vessels. You need more blood vessels, as things get bigger problems that we're trying to understand are whether you can still have oxygen reach the center of those big fat cells. So hypoxia is thought to be a big problem when we have really expanded fat cells. And you also have other cells changing their composition in the adipose tissue as it gets really big -immune cells coming to bring new hormones to the environment to respond.

Gretchen Repasky 08:50

Alison, you a little bit alluded to what can take place when you have this prolonged exposure of the larger fat cells and the triggering of an immune response. Might you be able to extend that into an answer to - tell us about what does it mean to have healthy adipose tissue?

Alison Ludzki 09:11

Yeah, so that's the goal is to be able to store fat and get bigger fat cells without the problems that come within the tissue, such as really high flux of release of fat from the tissue at the same time, or increased pro-inflammatory signaling. So this is signals that mess up our insulin response, which is there to stop the release of fatty acids out of the adipose tissue. So what this would look would look like is there are some mouse models where we can delete a gene and then achieve this. So an example would be the collagen-6 knockout mouse. And so this involves the deletion of a gene that provides structural support around the fat cells. And what that does in those mice is allows the fat cells to expand with basically no limit. And at the same time, the fat tissue can store tons and tons and tons of fat that the animals are eating. But there's not a really strong immune response and you don't develop tons of pockets of immune cells in the fat tissue. And you make that the mice maintain their insulin sensitivity.

Gretchen Repasky 10:50

Our fat tissue is an underappreciated organ that plays a major role in protecting us against the cardio metabolic consequences of overeating. Fat tissue sequesters the excess energy that we consume as triglyceride, in its professional fat storing cells. This action keeps fat out of other tissues in our body, such as the liver, pancreas, and skeletal muscle, tissues that control our metabolic health and response to insulin. During weight gain, fat cells get bigger and multiply. And this process involves complex gene programming and interactions with the different cell types that reside in fat tissue, including immune cells, stem cells, and more. Preventing and treating obesity is profoundly difficult because people respond to weight gain in vastly different ways. And fat tissue expansion is no exception. Often people who stay healthier in the presence of obesity, as measured by sensitivity to insulin, have more smaller cells in their adipose tissue, less inflammation, and less fibrosis, among other differences that are still being studied. But going even deeper than what the differences between healthy and unhealthy fat tissue and obesity are, is understanding how these processes are regulated at the molecular level. Because this will allow us to develop prevention and treatment strategies. It's been known for many years that there is a causal link between fat tissue health and metabolic disease. But what are the molecular underpinnings of this link? And how are they actually studied in these lipid filled cells?

Gretchen Repasky 12:42

You're going hunting for new genes that are important in fat cell function, right? So that's a main crux of what you're doing. Tell us how one goes about that.

Alison Ludzki 12:52

Yeah. So the very first step is to choose what function you're trying to change. So we've talked about a lot of them during this episode, because fat tissue is so interesting, and does have multiple functions, not just storing and releasing, but also signaling. So for my specific postdoc project, the function we chose is release and break down of triglyceride, which goes along with this release of fatty acids. So framing this in the context of discovery, you choose what specific process you're trying to explore. Here, we're talking fat breakdown, and then you can intervene so that you can capture many of the different players that could be involved in that pathway. So to give this specific example of my project, then we're trying to understand new players that could be impacting triglyceride breakdown and fatty acid release. And so we're choosing as our read-out this fatty acid release from fat cells. And then what we do to discover new genes regulating this pathway, is you can go big and knock down, in this case, 700 different genes in fat cells, and then we take this measurement, which is the readout to discover these new players and that is, we measure the breakdown of triglyceride. And then we see where we have big changes in that measurement. And those would be likely candidates that could be interesting, actually important in fat cells. And also at the same time, new were looking for new things that would expand our understanding of this.

Mads Tang-Christensen 14:43

So how do you sort of, because I think that's super interesting. But you sort of spoke to the sort of the different energy stages of the fat cell, right. So how do you...because basically what you're doing, you're taking a snapshot of a cell in a certain energy state. But how do you? How do you account for that? Are you sort of are you in energy surplus when you do experiment or in negative energy balance? Or are you trying to just trying to level it off? But because there can be totally different responses, when you're trying to look for new things that are downregulated? Right?

Alison Ludzki 15:19

Yeah. So part of that is you might not capture all of those at once with the same design. So then we just really need to think about how we're setting up our experiment to understand this breakdown. And, what I think is the most important is to combine different approaches. And so for the example of the study that maybe I'll be talking about more here, which is my specific project, what we do is measure triglyceride breakdown, in conditions of surplus, pick out things that look interesting, and then we add, then we play around with the conditions, and try to understand how this is changing. So instead of a situation of surplus, which would signal storage, like, after we eat. Then we trigger break down. And that allows us to look at a bigger range of regulation of the fat cell. And then we might discover something that's important in the condition of surplus, or the condition of energy stress, or triglyceride break down. Or we could find something that's important for both. So those are the specific conditions that we think about a lot in designing an experiment.

Mads Tang-Christensen 16:44

So all these experiments, are they done in mouse cells? Human cells? Or, what kind of? I assume that you are working with cell lines?

Alison Ludzki 16:54

Yeah, so a lot of my work is with cells. And importantly, for studying fat and translatability to humans, we use fat cells that were isolated from human subjects. And there are times that people have to go back and forth between using mouse cells or mice to add a level of control for things we can't do in humans. But we use only humans fat cells in our lab, because we're looking for these novel targets. We want to be starting with human cells.

Gretchen Repasky 17:30

Are you the first one to go hunting for novel targets in this way? And how does this compare to work that has been done before?

Alison Ludzki 17:36

Yeah, so fat cells are notoriously hard to work with. But there are lots of people trying to use different approaches to get, discover new important factors in fat cells. In terms of the project that I've started describing, what I did was knock down these huge panel of genes in fat cells that were taken from patients, and then plated and differentiated and fat cells don't stick to plastic when you take them out of a person. And the typical way that we often do cell culture experiments, we plate cells, and this means we can really control their environment. But for fat cells, a lot of work is done coming from these progenitor cell populations. So these are kind of like stem like cells we have in our adipose tissue, that we can turn into fat cells. So there's heavy work done on the transcriptional regulation of that process of what makes a fat cell a fat cell. And we still don't know all the components there. But what's really new and exciting about my work is doing this kind of knock-down experiment on a cell that is already turned into a fat cell. And then we knock down these players of transcriptional control in fat cells and measure the response and people have never done a big screen like that in fat cells differentiated in a dish to be fat cells.

Mads Tang-Christensen 19:20

So there must be a lot of technical issues here, right? We, Gretchen, talked about the heterogeneity that you have, but you say that you sort of do that by having frozen cells samples from the same patient at the same ages, but how do you control all these different aspects? Because if you want to, if you find something, you want to go back and repeat it into mature, but if you change the conditions, right, so how do you do that?

Alison Ludzki 19:47

Yeah. So this goes back again to this theme of combining different approaches to make sure we can answer a question. So we'll do experiments using this one cell model, so that we can really understand maybe what step in a metabolic pathway is changed in response to this gene that we knocked down. And then what's important to do is to also go look at how that is different between different people. And then what we have in our lab is a data bank of material from hundreds of people who have different environmental and genetic conditions. And then we're able to look at specific comparisons, like, how is this different in a cohort of people with diabetes compared with people who don't have diabetes?

Gretchen Repasky 20:44

And when you say this, are you referring to the fatty acid release? Are you referring to a transcriptional profile?

Alison Ludzki 20:51

It could be all of those depending on what our research question is. So for me, again, I'm focusing my project on triglyceride breakdown. But that's just this one process in fat cells. So we have people in the group studying fat cell insulin sensitivity, and we have people studying storage in fat cells. And those are all regulated differently. And though there are many complex pathways in fat cells that we're trying to understand, but for all of them, we need to go back and compare people who have these different diseases to ultimately be able to understand their role in diabetes, or cardiovascular disease or obesity.

Mads Tang-Christensen 21:42

So once you've sort of isolated or found new a factor or gene or something, what are the next steps? Because I think that's for you also very important that you're not looking at this in isolation. I guess. You have a point to all your research, right? Yeah,

Alison Ludzki 21:56

Exactly. So for me, that's why one of the themes I'm really talking about today is combining different tools to make sure that something's real, because we're not trying to discover things that are not important for human health. So one of the things we do to do that is use readouts that measure very different functions in fat cells, so that we can make sure that using different techniques in the lab, we find that this is important.

Mads Tang-Christensen 22:34

So if you just take me through that there's a nuts and bolts of going from one to the other. And so what's sort of all the steps until you have the golden protein in your hand.

Alison Ludzki 22:44

Yeah, you can do this in a few ways. So I just did this knock down screen, knocked down 700 genes in fat cells to find a target. The nuts and bolts of what I'm doing in this case would look like - then we combine experiments, which include blocking certain parts of the breakdown pathway. This is happening in isolated cells, and then we see it's important there, then we would go back to our patient data bank and measure expression of the different genes that we're looking at and see if they're changed in diabetes. Then you can go maybe high fat feed a mouse, and that's a model for weight gain and obesity, which allows us to control that gene in an in vivo situation in a living animal and see the response. And then hopefully, we hand it over to someone at a company who's able to run clinical trials for these targets. Combining cells and animals and human material is able to help us find something that is probably going to have a real effect.

Gretchen Repasky 23:59

Can you give us a teaser? Do you have any candidate genes now that are looking promising as you're taking them through all of these early stages of the preclinical work?

Alison Ludzki 24:06

Yeah, so I've been looking at a DNA binding protein that's never been studied before. That's in pretty early stages. And so we're at the cell stage for that experiment. So the next study would be to test that in mice. But for more specifics of how that works - it's a protein that binds to DNA. And when you bind to DNA, you can regulate the expression of different genes. So in the intro of this episode, we were we heard about how different people's genetic makeup could influence their weight gain or their response to weight gain. But these DNA binding proteins add a layer of control on top of our genetic makeup, which is something I'm really excited about because it might be an easier step to intervene at. And this is called epigenetic control. So this is influences on our DNA that aren't our DNA sequence. And those change the products of DNA, which is what changes the workings of our cells. Famous epigenetic regulator or transcription factor, which is what we call DNA binding proteins is *PPAR-γ*. So getting back to working towards how we can ultimately control obesity and diabetes in the clinic, one commonly used drug or one of the most the drugs with the highest efficacy for improving insulin sensitivity, turns on this *PPAR-γ* transcription factor. So this transcription factor, again, is that layer of control on top of our DNA, which changes the protein players in our cells. And we still don't understand super well how this works. But it's one of our best tools to reduce the consequences of obesity and to improve our blood glucose control. And the exciting thing about going for more of those candidates is, is all of these proteins that bind to our DNA have many consequences, because they target many different genes to dial them up and down. And so identifying new players is important because

they're all going to influence different, different genes. And so if we could discover something that has less consequences or different consequences, then this gives us new tools for obesity treatment.

Gretchen Repasky 26:56

And also isn't it true that some targets are a lot more easily druggable than other targets, too. So you kind of need a lot in your repertoire.

Alison Ludzki 27:05

We need tons to go with just because of how hard it is to find to get to that final stage of using a drug in humans.

Mads Tang-Christensen 27:15

But it's also super important when you mentioned *PPAR-γ*, that this is not said. It is not science fiction, it's actually make this druggable. So you're not that far away from the patient. So even though we talked about genes and epigenetics and control of DNA binders, and blah, blah, blah. In reality, we are talking about real drugs that can help real people. And that's I guess, that's also your motivation, your drive. Right?

Alison Ludzki 27:40

Exactly. There are some success stories in the end. And we know that these can work in people.

Gretchen Repasky 27:47

So I'm wondering how focused we might need to be on sex and race differences in regard to your research, and in particular, the findings that come out, because you mentioned that you're beginning even with primary cells.

Alison Ludzki 28:02

Yeah, so we can't control all of that in every individual study, but it matters. And so that has to come in at some stage. And in terms of discovery, you can use samples that come from people from different ethnicities and from different sexes. And that's the way we can identify things that are important in these different people. And then, of course, just including in our clinical studies, specific groups and different groups is essential to make it ultimately happen successfully for different people.

Mads Tang-Christensen 28:48

And I would say it is also as you say, Alison, it is a requirement that when you test your drugs. It needs to be on both females and males. And it also has to be in different ethnic groups, that is part of the requirements in order to get approval to launch a new drug.

Gretchen Repasky 29:05

But I think there's also space for this to also at the discovery stage as well. And I can imagine, though, that that brings with it a huge requirement for resources.

Alison Ludzki 29:17

Yes. And you hear people write, or I read people write in grant applications, different reasons for doing things in different groups largely being limited by money. And so that is a limiter for how much we can do things or it's a game changer for if we can double the throughput and check things in men and women.

Mads Tang-Christensen 29:42

And I would also just to add to that - it is up until this day, almost we are studying the male mouse, right? Because it's easier, right? than starting the female mouse. But I was at a Danish Diabetes Academy conference the other day, where we talked where there was one of the participants actually talking about sex differences and gene differences, and it is not a small thing, it's not just XY/XX thing it is actually it has broader implications. So you're absolutely right Gretchen that this warrants more research. But it could also be, as you say, a game changer or eye opener for things where we start treating - not that we should treat genders differently, but there are maybe different requirements depending on your gender.

Gretchen Repasky 30:31

Let's talk a little bit more about what difference your discoveries might make for society.

Alison Ludzki 30:36

So the ultimate goal is to help the many people who are trying to achieve weight loss but can't and it's so hard to lose weight and to control our body weight. And there are so many factors in society that are working against us. But, the hope is that we can reach a situation where we can help people control their blood glucose levels, so that they don't have the many consequences of obesity and diabetes, including microvascular complications and things that lead to reduced quality of life and death.

Mads Tang-Christensen 31:19

But I think it's - so you're really hitting on something that is, I'm really passionate about. One thing is treatment, but the biggest thing is actually prevention. Right? It's understanding, when we get into dire straits, as you describe sort of this imbalance in storage. It's how do we prevent getting there in the first place. And I think the research that you're providing or insight that you provide, and gives us hope, that understanding these processes, it could also sort of really push us to understand that we actually need to set in before that that's the case. And I'm not necessarily - I come from a pharmaceutical company, but I'm not necessarily talking about drugs. I'm talking about prevention in the broader term. Identifying those patients, as you say, that are susceptible to the sort of, sort of storage of fat in an unhealthy way. Yeah. So I think it's, it speaks to a much broader thing, also that what you're doing,

Alison Ludzki 32:22

Yeah, and this comes from, you know, using these some of these setups, like collecting many patient samples, the numbers that we need are high to be able to identify things in adipose tissue that are different between people and then going and checking all the steps of, okay, what is this doing that's leading to either weight gain, or one of the negative many negative responses that happen in our adipose tissue when we gain weight so that we can say, this is how this is working in this person, but it's different in someone else?

Gretchen Repasky 33:03

Yeah. So that's exactly what I was sitting here thinking about, too - what space is there here in precision medicine and personalized medicine from the perspective of prevention?

Alison Ludzki 33:14

Yeah, I think it's space is really high. Because it's such a complicated disease. And it's probably one of the areas of science where we're really at the beginning, because the studies are so hard to do. And because we just need more patient samples and more material and more time.

Mads Tang-Christensen 33:36

But when you say precision medicine, I always I start shaking a little bit, because we are dealing with a problem with the size of 650 million people, right? So when you talk about precision there, I would say not yet, right? We need the broader things. And that's also why I hope the research that you're doing are pointing to more things that are more general instead of more specific, and I think we can solve for the specific, right, as we've seen with obesity with the monogenetic and maybe one or two genes that are off for obesity. But for the vast majority of people living with obesity, it is a polygenic trait that we are trying to treat. So precision medicine in that case - it would be really hard and sort of too expensive to be honest. Gretchen, so yeah, it's the goal but

obesity is a much, excuse the pun, but a much bigger problem than what you're seeing. So, precision medicine, yes. For the minute, but we need to solve for the bigger the bigger question, which is not precision medicine.

Gretchen Repasky 34:40

And even solving for the bigger question that takes time. So what do we do while we wait?

Alison Ludzki 34:46

Keep working. Are you talking about what does society do?

Gretchen Repasky 34:50

Yeah, while we wait.

Alison Ludzki 34:54

So what we know now is mostly pointing towards lifestyle factors and this is not where I'm an expert. This is where I think it's working with physicians. It's hard, because a lot of the control of that is down to factors influencing society like policy changes on, that impact how easy it is to over consume.

Mads Tang-Christensen 35:29

Yeah, but I think so, Alison, I think one of the key things here is where your research is really sort of spearheading this movement is actually to describe that there is something wrong in the fat tissue of these people that are sort of storing more fat than they should and they can't regulate. So, I would say, getting to a point from a societal perspective, where you accept or recognize obesity as a disease, right, because that is the first step. And that's what your research right here is actually pointing to. So well, its facts are this, this and that, that basically shows everybody that it's nothing to do with people being lazy. It's nothing to do with people just eating like crazy. It is something that is different from person to person, and is sort of in our genes, right, combined, obviously, with the environment. So I'm absolutely agreeing with you. And so it's a broad panel of things we need to do, including on the societal level where you - why do we pay the same tax on candy, as we do on cucumbers? Right? So it's, so it is a big, big movement that we need to have here Gretchen.

Gretchen Repasky 36:35

But do we need to be concerned with where in the body the fat is distributed, either from the perspective of health, but also from the perspective of your studies as well, where you're taking adipose cells, adipocytes from?

Alison Ludzki 36:50

Both of those are important. And so we see that people who store their fat in different places can be protected or have a harder time and have more metabolic consequences, from fat, from increased fat mass. So for example, people who have this pear body shape where they're depositing their fat, more lower, and more lower body, leg, and gynoid are basically butt fat stores, those are more protective. It's more superficial compared to this apple shape body that we talked about, which has more fat deposited abdominally, or surrounding our important organs like our heart. And in this case, there are worse consequences of having fat in those locations. And the way we deal with this in the lab is by collecting fat samples from both locations, to study how the fat cells function differently in both locations, because things exactly like fat breakdown and release are different between different locations in the body. So it's extremely important to look at both and to be selective about where we're getting our fat from, depending on what our research question is.

Mads Tang-Christensen 38:23

The reason why we have fat stores is because that's where we need the fat to go. And one of the big problems with metabolic diseases is actually you start storing fat in other tissues than your fat stores, right, so like the heart, muscle and the liver. Could you just elaborate just a bit on that?

Alison Ludzki 38:41

Yeah, so the safest place it seems we can store our fat is in our subcutaneous stores, the store is just below our skin. And the biggest depot which we, if we're sampling from for our experiments, is the belly fat. And this contributes to the vast majority of fatty acid release to other tissues that use the fat in most situations. But when we overeat and gain weight, then the fat can't - there's a physical limit to how much can be stored there. And then it can be more preferentially deposited in these risky places like the abdominal fat stores, and in these other tissues like muscle and liver, and pancreas. And that's a big problem.

Gretchen Repasky 39:41

So is it actually possible to say that healthy adipose can actually protect a person from complications of cardio-metabolic disease?

Alison Ludzki 39:51

Yes, and that's one of the end goals of our research is to find ways to make our adipose tissue healthy and to make it store fat and keep it out of these other parts of our body.

Gretchen Repasky 40:04

So Alison and Mads, let's end where we started. We talked about the fact that only a very small percentage of our genome actually makes us different from one another. What should we take away today about this difference? What take home message do you want to leave for our listeners?

Alison Ludzki 40:22

So my take home message would be our responses to obesity and weight gain are super complicated. And, and within one person, they're complicated, and between people, they're complicated. So our goal in the lab is to use all the different technical tools available and a lot of thought in how we do our studies, to find new layers of control of this complicated disease, to identify ways that we can improve our adipose tissue health and thereby our whole body health.

Mads Tang-Christensen 40:59

I would say that after today, so I would say the biggest thing that I've sort of extracted from this is, there's a lot of hope, there's lots of hope, and the research that you're doing is pointing one direction, if we talk to another postdoc, it's yet another direction. So I think there's, you know, so many good things that are happening out there. So there's a lot of hope, you could say that, there's still a lot of things to discover there. There's still so much more to do. So, you know, please work. So I'm super optimistic about the future with postdocs like you.

Alison Ludzki 41:32

Thanks. Great to hear and we'll keep working on it.

Gretchen Repasky 41:35

Well, a very big thank you to both of you for spending time here with us today to explaining your work and to leaving us with a good amount of hope as well. It was great to have you here today.

Mads Tang-Christensen 41:47

Thank you.

Alison Ludzki 41:49

Thanks for inviting us and doing the work to get this out to the public.

Gretchen Repasky 41:54

Thousands of postdocs around the world are dedicating their careers to better understanding and improving diabetes prevention, care and treatment. You can learn more about Alison and Mads. The guests of our show today at our website, Danish Diabetes Academy.dk/podcasts, where we have short bios additional information about their research and photos of them at work. Our show today was produced by the podcast agency Kontekst & Lyd. A very warm thank you to the Danish Diabetes Academy for keeping Postdocs Talking. Thanks for listening!