The Newest Biomarker Of Aging: Breaking Down The GlycanAge Test In Detail Transcript

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Introduction and Speaker Background

Hello, I'm Doctor Joseph Rafael, your host of the Telomere Summit. Today I'm very pleased to be talking to Doctor Gordon Louse. If you're interested in telomere biology and its clinical applications, I guarantee you will be fascinated to hear about psychobiology and specifically how IG glycans can help you take better care of your patients aging processes.

Welcome, Gordon. Thank you for the intro, for the invitation. Pleasure to be here. I'm looking forward to talking to you. Doctor louse is a professor of biochemistry and molecular biology at the University of Zagreb and director of the National Center of Scientific Excellence in Personalized Health Care.

Honorary professor at the University of Edinburgh and the King's College London. And member of the Johns Hopkins Society of Scholars. In 2017, he initiated the launch of the human like project and is one of its two co-directors.

His research team is pioneering high throughput glycolytic analysis and application of glycan biomarkers in the field of precision medicine by combining iconic data with extensive genetic, epigenetic, and biochemical and physiological data in a systems biology approach.

They are trying to understand the role of glycans in normal physiology and disease. Professor glycan, sorry. We see your profession. Glycan. Professor Louse, has authored over 200 research articles that are cited over 5000 times.

He he was pi and co-pi for four NIH and two FP, six seven FP7 and six H 2020 and three DSI funded projects and coordinated five of them in 2007. He founded, you know, a biotech company that is currently the global leader in high throughput glaucoma.

Welcome again, Group. I'd like to start this conversation by having you introduce to our listeners some basic psychobiology, because they may not be familiar with it, as I wasn't until about a year and a half ago.

So glycosylation is the most elaborate and the most abundant post-translational modification. So glycans, chemical structures, complex soluble saturates which are being added to proteins, post-translational.

So they're not encoded in a single gene like the polypeptide, but they're encoded in the network of hundreds of genes which enable proteins to like human bodies to acquire novel functions, even after the gene for a specific immunoglobulin has already been defined.

And, I work in the field of glycan biology for, I think, over 30 years now. And we established a field called high throughput electronics, where we started to analyze thousands and thousands of, glycans from different people.

So kind of, similar to personalized medicine. We are trying to do personalized comics, and we already analyzed over 150,000 people.

What Glycosylation Is and Why It Matters

And by analyzing so many people from many really well-characterized cohorts from all around the world, we learned that glycans attach to when a global is, highly correlated with aging.

And other people also work on you glycosylation. And I'm going to Globulins are the the best selling drugs in the

world for a decade already. And we know that these glycans have many regulatory roles on immunoglobulins.

And one of these roles is the regulation of low grade chronic inflammation. So if there is a specific type of glycans, which usually we find in young people on immunoglobulins, these immunoglobulins actually suppress inflammation.

They do not allow this low grade chronic inflammation to be present everywhere. But if glycans are changed, if different glycans added to one of global is the pro-inflammatory glycans, which are usually shorter, they don't have a galactose in the cell like acid on the end, they become pro-inflammatory.

And this is something which we usually see in old people. We see that people have a glycans which are pro-inflammatory. So they're actually promoting low grade chronic inflammation.

And in this way they're significantly contributing to the inflammation. So they're doing damage to the tissues which is then manifest that that's aging.

But also it's age related diseases. Yeah. So it's a whole new area of biology. That's that's that's really fascinating. As a biomarker of aging, sort of, you know, telomeres are a biomarker basically you have epigenetic DNA methylation.

The correlation is it sort of linear across from, you know, say 20s to 80s, or is there kind of a, you know, an acceleration at some point? And what's the spread on either side?

So here's of year's different it's different than men and woman. So when you look at the men, men have more or less linear increase in glycans from their kind of early 20s when they're the most, suppressing inflammation to the old age, when they're more, more pro-inflammatory.

In women, the curve is a little bit different. So, the biggest change happened around menopause. So before menopause, women usually have less of these pro-inflammatory glycans than men.

But then in perimenopause it accelerates rapidly. And they quickly catch up with men and actually go above the men average for a short period of time.

And then they kind of kind of, look similar later. So it's, it's different men and women and, it does change with time a lot. And when you, when you give a like an age to, you they, they, you have to test in your lab and say a woman is 60 years old.

Is that her glycan age against a untreated postmenopausal? Group or. It's a guess. So it's a it's a, it's a, it's against no, no treatment because that's how you and I sort of met because I started ordering your test and we, saw that some of our patients, particularly men and women, but had much younger glycan ages.

And everybody in my practices is on some sort of hormone optimization. There's there's a big impact there. We were, you know, talking about I know a lot of our listeners practice hormone optimization and, and so talk a little bit about, you know, that, what happens with performance because I know there's other things that impact glycans like lifestyle, body fat, metabolic health, hypertension, etc..

But I think you know, one of the biggest impacts is hormones. So our baseline is the general population. And in the general population, a majority of people are not doing hormonal feminization.

So I would say the baseline would be people who do not do hormone optimization. And the the glycan age index we have is modeled based on these thousands of people.

We did in the past. So we kind of say your glycans look like an average glycans of a person of 58, 75 or whatever year old. As you mentioned, we got quite puzzled with your data.

And actually, my statisticians were initially wondering what went wrong and why. Why are all the the samples which

we are now analyzing coming from, from your lab so much younger until we started talking and doing more and more people and realized actually, that what you do in your practice is actually making people look younger on, I would like an age test.

And here I would like to stress one very important aspect, and this is that glycans and immunoglobulins. And I would like an age they're not only a biomarker.

For example, if you talk about epigenetics, methylation on a specific CPG site is just a biomarker. We don't know anything about its function and people original.

Steve's, Steve Horwitz, epigenetic clock is something like, I think, 373 CPG markers. Lichens are functional effectors. So these are molecules which either suppress or promote inflammation.

So if somebody has more of these glycans which suppress inflammation, we know that inflammation level will be lower. And if there is more of these glycans which promote inflammation, we know that they're actually promoting inflammation.

Glycan Age as a Biomarker of Aging

And now we know that this low grade chronic inflammation is behind so many different, chronic diseases that actually we can be very confident that having a lower glycan age is something which is good, which is associated with a lower risk of a disease or a milder disease, and something and something else, which is also very important when we look longitudinally, glycans usually change first.

In some diseases, they change up to ten years before the disease is actually diagnosed because, you know, disease. This is a name which was given by physicians for a condition when people appear to the hospital because something does not work, there is pain, some organ doesn't function and then you get a disease name.

This does not happen overnight. This is a long process where the body's first trying to compensating to compensate for a problem. And then when all the compensatory mechanisms fail, there is disease and synovial globulins are one of the early things which happen.

So before you get ill, your immunoglobulins become pro-inflammatory. They start to do damage and while we haven't proven in humans, we have some evidence in animals that if you improve glycans, disease does not happen for humans and only have correlation.

Glycans change first and then the disease appear. Which specific diseases are you're talking about? Just, So so we have one study where we have shown that by preventing these bad glycans, you can prevent hypertension.

And this was done on mice. Mice were fed, high fat diet and on high fat diet they became fat and they developed hypertension and their immunoglobulins were high positive.

Later they had less sialic acid, which is this Yankee venom. And when mice were fed and something which is the precursor for cyclic acid, their immunoglobulin glycans preserved this good glycosylation.

So they had young immunoglobulins. Of course, they got fat on a high fat diet, but they did not develop hypertension. So actually by by by preventing aging of immunoglobulin glycans, it's possible to save mice, obese mice from developing, hypertension for humans.

We do not know. We did study a small cohort of healthy people where we did not see a big change after taking menos amine, but we do not know whether actually in obese people taking menos I mean would improve glycosylation and and contribute to the decrease in hypertension.

Something what we published only a couple of days ago is that we were tracking, 2000 twins in UK for 20 years. And then we have shown in this study that, and actually there was a replication cohort in Germany that glycans

today are predictive of hypertension in the future. So maybe this could also work in, in humans that if you improve your glycans, you will not develop hypertension in the future.

And, well, that's that's really fascinating. Would that that I would imagine that would probably also, extend to atherosclerosis. And you looked at, and those mouse models of atherosclerosis as well, particularly with the high fat diet.

I wonder whether there's, an impact there, because particularly women, you see women going through menopause, they're very well protected. And we you know, we thought it was from the estrogen before menopause.

That, from getting atherosclerosis. And then afterwards, the corner calcium score start going up the carotid into the medial thickness goes up and their events start going up.

The catch up with men relatively rapidly. And I suppose that could be because of the change in the glycans that occurs with the loss of estrogen. And do we have any. Go ahead.

So, of course, hypertension and all cardiovascular or all other kinds of metabolic disease are very complex and they're very different in different individuals. So we cannot generalize.

But I guess that this is one of the important mechanisms because we know that inflammation is important. We know that these old items are pro-inflammatory.

For example, in woman, we definitely know that estrogen actually in both women and men, estrogen is improving the egg like, composition. We had one, proper, randomized, placebo controlled trial where the menopause was chemically induced.

Hormones, Menopause, and Estrogen Effects

And then in the placebo group, we saw a huge increase in, like, an age, I think average was nine years and six months. There was some woman who aged for 20 plus years in the few months while in, estrogen, groups of people where the estrogen was returned with, with this, estrogen patch, there was no change in the glycan age.

So definitely estrogen is causative. And, it does improve glycans. And in interestingly, in men, if you give testosterone like an age old, it improves.

But if you block aromatase, the enzyme which converts testosterone to estrogen, there is no effect. So it's actually estrogen which is improving energy like in men too.

Yeah. And that's a very, you know, when I heard that I had always been cautious with arithmetics or any anastrozole, any, aromatase inhibitors in my practice, but other, practitioners, I think they use it because they think estrogen is a bad thing in men.

But a certain level of estrogen is very important. And here's, you know, another reason why you don't want to block it down too much, because you're going to lose that benefit.

And and the benefit is, just turning to men for a second. The benefit is really quite significant. The average glycan age in my practice on men that are on testosterone replacement therapy with, you know, good youthful levels is 25 years younger than their chronological age.

And, you know, that is it's a fit group for sure. I mean, they're working out, but, we see a change when they come in, even if they are fit and with a low testosterone levels.

So, you know, that's we're up to about 160, 270 patients. Now we're looking at we try to see, you know, what other factors might be involved there. But it's interesting to me that it's even more in men.

I don't know if you saw that in your study. Whether there was a, a change, change, a bigger change. And like an age in men when they, knocked out the estrogen, from the testosterone.

So definitely if the. So this was not it was a different study. And in that study, we did not look like an age. Typically it was a little bit older study when the glycan age was not.

We're not able to measure it then. But what we did see is that this change from young to old, like, did happen if the other the hormones were blocked and it did happen is the conversion of testosterone to estrogen was blocked.

But if the testosterone was returned and it was and there was no inhibition of this, aromatase, then the glycan age did not change, not look like initially the the IG glycans did not change in the direction of older glycan age.

So, definitely, I think just blocking the conversion of testosterone to estrogen would not be beneficial in, in, in respect of inflammation and immunoglobulin like, affecting inflammation.

Yeah. I mean, I think that's and we know in other things for bone health and for arterial health that that's it's important, to maintain a certain level of, of, of estrogen.

I always tell my patients, when women come in with post-menopausal women that, you know, their husbands have 3 to 4 times the amount of estrogen circulating in their blood, than than they do.

And that's, you know, time to get back to at least a man's level of estrogen. So, I mean, I think that the, this test that you have available, which, by the way, is really great because it's a blood spot, can be sent to the patient and, and readily done.

Is, I think, going to transform menopausal and, and or causal medicines a certain degree. I know you're working with Louise Nissen in, in the UK. Looking at you're doing a trial, looking at, the effect of, of estrogen replacement therapy or on replacement therapy on glycans.

You know, it seems to me that all the benefits that we thought estrogen had prior to the Women's Health Initiative, you know, have been turned around with a, a reanalysis of that data, looking at it with a better lens and the timing hypothesis, etc.

but having this tool to know whether or not a woman has gotten back her anti-inflammatory glycans, I think, would be pretty revolutionary. You're looking at it as a marker for perimenopause and, and for, for even potentially the adequacy of therapy in menopause.

So we haven't published anything on that yet. We only have this study, which was the menopause. Was the chemical induced, but we have some initial data.

And something which seems fascinating to me is that, glycan age can deteriorate rapidly in women in their menopause, especially in women who were, who had very good like an age before.

So we have seen, patients changing for 30 years, within a year. And interested only glycans change before any other symptoms appear. So we had a situation where women were shocked with what happened to their glycan age, and they said that they have no symptoms, they have no problems. Everything is okay.

And then a couple of months later, all the symptoms of menopause appeared. And this is why, the reason why we see that is that, estrogen really directly regulates glycosylation, and it regulates it in a kind of a long term manner.

Because IgG we measure today is made in the last couple of weeks. So all the alterations in the hormone levels which happen at that period are kind of integrated in the glycan.

So you can still have spikes of hormones. You can keep other things functioning. But the glycan age in glycans we will be changed. And I think this is very similar to way HbA one C the Glycated hemoglobin can be used to track the

average level of glucose.

In the past weeks. In the same way, like an H can be used to track the level of estrogen. In the past weeks. And so it could be a very early warning signal that somebody that entering the the menopause.

And of course, we still have to do a lot of research. We have no idea whether it's better to start therapy early, whether you get the same results after a couple of months without hormones.

There are many questions which we are interested to address, and we are trying to do as as properly design studies as possible. And of course, we are extremely interested to collaborate, especially if somebody already has, you know, hundreds of samples in the fridge.

We can do a very quick study to see what happens with with, IG life insulation in women in this very sensitive period where there are so many changes happening in the body.

So, I'm just curious about the change of if you get a big increasing like an age at the loss of estrogen. I don't know if you've looked at this, but pre puberty, does a young girl get, a change in her IG like oscillation when she goes into, into menarche?

So we, you know, working with kids is a little bit more difficult. So we haven't done so many children, but we have done a couple of hundred. And for example, boys and girls look very similar before puberty.

Right. And then we with the onset of puberty, girls start to change very rapidly. And it's a little bit strange because actually kids, despite, before they develop this, hormonal, status of an adult actually have very pro-inflammatory gene.

So, young kids look like much older adults in their IG, like, composition. And, and we know from experience their kids are actually extremely pro-inflammatory.

Their, their immune response can be very explosive when there is some kind of, inflammation going on. And then this is suppressed with the hormones for the reproductive period of their lives, and then they go back as old and older individuals to be more, more pro-inflammatory.

So, I actually very enthusiastic about what you do with the hormone optimization. And I think this could actually help. Alleviate many problems related to inflammation, which is linked to all these, diseases which are now a burden for the planet because we all getting old.

Yeah. I mean, we, we see with testosterone, for instance, or, and as well with, with estrogen that things like insulin sensitivity improve. You know, you lose body fat.

And so all these metabolic changes that occur, you know, there may be, some kind of a, mechanism through the IG glycans, which is how this is taking place.

So, you know, I think it's a re validating this concept that, you know, humans, both males and females, need a certain level of, of estrogen, to, to have a, an optimal aging, particularly from an inflammatory standpoint.

Are there any other genetic factors that, figure into this? I mean, we've been talking a lot about hormones. I mean, is is there, what percent of it is heritable, you know, so we did a number of heritability studies.

And for the different glycans in aged, you like them who are heritability is between 30 and 75%.

Lifestyle, Exercise, and Weight Effects

So an average we can say maybe approximately half of the composition is genetic, meaning that, if your parents have kind of older, like, all the time, you will be in that direction.

Maybe approximately 50% of the variation could be explained by genes. And it's extremely complex network. We have already mapped over 40 genes which work together to regulate that glycosylation.

And they're not enzymes which actually put the glycans there. The different genes which regulate the the immune system. And another very important aspect is, lifestyle and environment.

Obesity is a very strong factor. So, with the increase in the body weight, glycans age faster. And we also did on these same 2000 people, which were tracked three times in, which were analyzed three times over 20 years.

We have noticed that. And these are mostly woman. They're from the twins UK cohort, which are mostly female. And we noticed that the women which were gaining weight over these time points, they were aging faster than the women who were losing weight or not changing their weight.

So by gaining weight, you actually accelerate this inflammatory process. And then by losing weight, you can improve it. So one of the easy things which we all can do is just take care of this extra body fat, which we don't need.

And this is also improving this as you like. But interestingly, there does not seem to be a magic diet. We did a study of 2000 people on five different diets, including the high glycemic index one and, and each of the diets were beneficial for some people, and they were very bad for other people.

So I did like them. We're changing in both directions on all types of that. It's actually one has to try what works for him or her. And the same goes for exercise.

So, we all tend to believe that, you know, eat so much, you just have to exercise a bit more and then you're fine. And this maybe works when your kids or when you are young.

But as you are getting older, you cannot without what you eat. And people who overtrain tend to get also pro-inflammatory and get very bad, like an inch.

For example, initially we were thinking that the gyms would be a good place to start working. We looked like an age and helping people improve like energy in the gym.

But then it turned out that most of the personal trainers and most of the people who are fanatic about going to the gym actually got worse. And if you take a middle aged people and try to work with them intensively, they also get worse.

So yes, exercise is important, but there has to be a sufficient relaxation time and there has to be sufficient time to compensate for all this pro-inflammatory aspects of, of exercise, because, you know, you do need some level of inflammation to start your muscle expanding.

But if you do this in a, in a, in a chronic way, then of course, you increase this low grade chronic inflammation, which is bad. So we are now trying also we are doing several studies to try to find, optimal way of exercising and relaxation, which would help you to improve your glycans.

So it's a very interesting field of study to. This is probably, sorry. Yeah. I mean, I have ultra endurance athletes in my, in my practice and then even, like, crossfitters and people who are really going at it and, and one could use it as almost a biological hoop.

You're familiar with the hoop device, and where it tells you about the strain on your body. This is sort of a molecular, sort of integrator of it over a longer period of time.

Like you said, it's 3 to 6 weeks for the glycans to change into their particular if they're, you know, premenopausal and you have relatively younger, you know, 30s or 40s, if their glycans are a lot higher and they're they don't have to carry a lot of body fat and they're probably overtraining.

And it's a good way, I'm thinking it be a good way to tell them, you know, maybe you need to put in some more days of rest. And we could track it to see whether you're like, an age is responding to that.

I think that could be another fantastic way. And people who not who are not even on hormone optimization, to see whether or not this is the opposite problem.

People aren't aren't exercising enough and are overweight and are eating too much. You do have the other side of it. I mean, I'd love to see people that sort of do Ironman triathlons and, you know, I sports one.

I did one a week, for, for a year around the globe. I mean, what is glycans look like? This kind of stuff is probably not good for you in the long run.

And it's it's good information to tell patients. You know, this is not surprising because the professional athletes are old in their 30s now. They. And you cannot put too much stress on your on your body and do not expect to have consequences.

And one thing which I forgot to mention also the psychological stress plays a game, plays a role. So it's also important to have, psychological relaxation, to feel good, and to have sufficient in our moment of exercise, but not too much healthy food, but not too much.

And then things are in kind of, balance, which is, you know, it's, it's there's no magic. We all know what is good and what is not good. The problem is that we all think that we are fine.

Now, you look yourself in the mirror. You are same as yesterday. You don't see anything. And unless you have some kind of pain and even you have, you can take a pill and the pain goes away and you just go on and go on and go on.

But there is the wear and tear in your body which you cannot see. And then usually, at least for men, you know, we stop after the first heart attack or stroke, but then it's often too late.

So ideally I want to get an early warning signal to tell me, you know, you are not going in the right direction. I mean, I don't want to wait for 20 years to get the feedback right.

I want to get feedback as soon as possible. So if I start losing my weight, I want to see an effect in a couple of months. And if it's not working, then I can try something else.

And this is where I see a huge potential of this test, which we have developed, is that to help people motivate themselves to do a difficult decision, because I was keeping that extra cookie is a difficult decision.

Skipping that extra beer or whatever. It's a difficult decision and people need rewards. And if you get a reward in the next after few months, you see your glycan age is going down.

I think it can help people. That's kind of a idea. Yeah. No. Of course. Did you see any because I know people practices. Do you see any relationship between intermittent fasting and, like an age?

Or is that going to be correlated to if there's weight loss or not? So we, we haven't done a proper study of intermittent fasting. My guess is that it would be beneficial.

At least we know that intermittent fasting is a good for your microbiome then your microbiome. Because know the problem with eating all the time is that in your gut there is always food.

And then the most aggressive bacteria grow, while when when your digestive tract is empty, then only bugs which can attach to your, gut and to kill you and actually graze on the glycol calyx survive.

And this is our evolutionary symbiosis between the bacteria we like and our, glycol colleagues, which is feeding

them. And if you do intermittent fasting, then you have this selection periods where you get rid of all the aggressive bacteria and only the ones you like to keep them.

And we know if you improve your microbiome, you will improve your glycans. So we had several studies with the fecal microbiome transplant. And yes, improving the microbiome improves the glycol.

Disease Prediction, Telomeres, and COVID

Well I would guess that the properly executed intermittent fasting after some period would improve the, the, the egg like but we haven't done a study yet.

So if, if you know somebody who might have some samples in the fridge, more than happy to look at it, I don't know, Walter Longo might have some, he's done the, the sort of fast mimicking diet, and he's done a lot of research on that.

Is a possible person for that. I don't I don't have, anybody else that I know that has samples. You know, you mentioned hormones. You mentioned, stress, but psychological and physical as things that affect the ECG, like, those are all sort of same sorts of things that affect telomere length and telomerase activation.

I'm wondering I did a quick look and I didn't see anything much. Is there any research on the relationship between tumor biology and glycan biology? So we did look in a couple of cohorts.

We haven't seen a huge, correlation. So I think one of the key problems with the telomeres is that, first how you measured them, some of the cohorts have telomere measurement, which is not extremely reproducible.

And the second thing is it's heavily biased with, with the composition of the the cells in, in the blood. So it's you know, telomeres are a fantastic biomarker for an individual cell, but on an organism level it's a little bit more complicated.

So guess I'm, we were talking to Bill Andrews a couple of times to try to do something together with him. He's also very enthusiastic about it, but we haven't done anything yet.

So eventually, as we will look, whether the same intervention has the beneficial effects for both telomeres and the glycans. Yeah. We just recently published a fact of 65 on, immuno senescence, Cd28 negative cells, and there was a reduction in them.

Presumably we think through telomerase activation and sort of send a lytic like effect, although, we don't know whether the cells went away or whether they were just turned back into C 28 positive cells.

But, you know, the senescence, immuno senescence, it takes place is, I guess, tracking a long or is there some relationship between that and the like a I think like an, change so that it becomes more inflammatory.

I mean, we are we are now, you know, collecting the samples of patients who have we have, you know, lymphocyte subsets with the senescent cells, the telomeres and the like.

An agent will see if there's something there as our sample size gets larger. But it's not, you know, of course, a controlled trial. And I wonder whether there's any, any thought about the that sort of correlation between the senescence that we know goes up because of replicative senescence, the loss of telomere length, and the change in the glycans, maybe in the I mean, this is a post-translational thing.

So it's not going to be in the B cell senescent cells. It's it's whatever whatever pathways are affecting that glycosylation of of of the, of the ATG.

And whether or not I think what we know that when you have cells in culture and where they're, when they're getting older, they change glycosylation of immunoglobulins, they produce.

So definitely they're I would expect to see an effect. But you know, cell culture and and the human body, they're two very different things. And you know, we cannot look you know, we are a complex machines.

We have evolved for billions of years to compensate for all type of problems, to fight all possible threats. And I think one of the most well, we have two very complicated systems.

One is of course, our brain, which is immensely complicated, and the other one is our immune system. Our immune system is keeping us alive against all these crazy bugs which mutate like, like like, you know, crazy.

They mutate all the time. And we still survive. So this is a very intricate and a complicated mechanism which has to balance. Fight against infectious agents against on the other side, there are tumors which can acquire the mutations cells.

So it's, you know, I think this is all very complicated. We cannot simplify it too much, I think. Yes, glycans and senescence and telomeres are correlated in a way, but I think there's still a separate aspects of this whole process.

So we have to look at telomeres. We have to look at we have to look at glycans and then try to integrate all these data. And you get more information.

You know they they measure different things and they're all important processes. And what's interesting is that there are ways to impact them different ways or different systems.

And I mean, I think you're like an age marker is great because, you know, even if you have a good lab, like repeat diagnostics doing, the telomere length and they can do also the neutrophils, which are not, you know, subject to changes because they're, they're really reflecting the bone marrow stem cell.

It's a longer process with glycans. It's I, I thought it was three months or you're saying really 3 to 4 weeks, you can get a significant change in the glycans.

How often do you think people should test to see, you know, what the what ending depends depending what happens. So if there is no major change in a body it's months.

They don't change very rapidly. So example now we were doing a lot of studies on Covid in the last year. And people who had, severe Covid, we saw a lot of changes in their attitude, like, in a matter of two weeks.

So they would gain, I don't know, ten, 15, 20 years in a couple of weeks. And it was the worse. So people who died actually had the most significant changes and still unpublished.

But this is what we have seen so far. So, when there is, rapid change in a body like a infection and maybe hormones, so what we are doing now is just looking how quickly the glycans would change after the start of the hormone replacement therapy.

Then it could be faster. So for example, we have a cohort of human which we are tracking now every two weeks to see how rapidly does it change. But in things like a weight loss or exercise, usually we don't see anything before two months.

And I think you also mentioned, when we talked before, or maybe it was in another with the Lena that there isn't that much change across the menstrual cycle.

So if you have a premenopausal woman, you don't necessarily have to to, to do your test at the same time of the cycle. Is that correct? For majority of women there are no huge change.

It's maybe a few percent. We have seen examples of some women where the changes were more, more, significant. So it would be better to try to kind of match the, the, the similar phase of a cycle.

But if it's a longer term, it's not so important. But oh, okay. So maybe try to do the luteal phase or the follicular phase and just keep that same one.

It doesn't matter necessarily which, which one. And speaking of hormones, are there any other hormones that impact glycans that you think's, significantly or is there any research on Abby?

I mean, I have quite a few patients on growth hormone IGF one increases. I don't know. You know, I haven't seen a signal yet, but we don't know cortisol, because cortisol is sort of the inflammatory, one.

We haven't seen huge effects of dexamethasone. Really? Yeah. So dexamethasone doesn't do much in a short term. So in the long term, of course it does.

But, for example, we know that, okay, TNF is not a hormone, but it's important signaling mechanism. So if there are if people are taking monoclonal drugs against TNF, we can see a very strong effects in some people.

In some people not so strong. So, I would guess that many of the immunomodulatory monoclonal could have a strong impact, but these are not things that people take, regularly deserve.

Right. That's for different conditions. So, you know, the thing is, glycans that very novel. So the technology to measure them in high throughput is here only for maybe a decade.

We managed to develop this, dried blood stain testing only two years ago because previously we had to have a frozen plasma. And this is a logistical complicated.

If you collect a sample and then you have to freeze it and ship it frozen, it's complicated. So once we started working with the dried blood stains, everything became much simpler.

You can actually ship it anywhere in the world. People can collect, sample and mail it back. And it's okay. We can we can work with with the data generated from the samples.

So it's, still not so many labs doing that. There are actually there there are over 100 labs in the world which can analyze egg glycosylation, but, not so many of them do it in the high throughput.

So this is why there's no, human not huge amount of data. It's more and more people working. We even have it the thing called the Human Glycogen Project, where we are trying to integrate our activities globally, but we still have to learn a lot because this is a very complicated part of biology and still not so many people working.

And interestingly, even at the beginning of this pandemic, the director of NIH was writing a blog about the S glycoprotein without a single glycan. He just showed the polypeptide part.

Well, there's more glycan on a surface than a peptide. And then just after that, people started thinking and saying, wow, well, there are so many glycans on this virus.

What are these glycans doing? And now we know that the glycans are very important, that they're integral part of not only SARS-CoV-2 but all other viruses.

So, you know, there will be more and more glycan work in the future. I'm very positive about that. And I know you're a very busy man, but I just want to ask one last, one last question with regard to Covid, you brought it up in terms of testing.

If a patient has had Covid recently, you would probably expect their glycan age to be older, I guess, and maybe take that into account. How long would you wait the three months if if the Covid was mild, we don't see much changes.

So, symptomatic Covid, nearly nothing, mild Covid, nearly nothing, severe Covid. Yes, it can be over a decade and

it can take months for this to come back to the normal level.

But it's, if it's not, you know, when I say severe, I mean, hospitalized in intensive care. So even even just hospitalized means moderate, not severe.

So for the majority of people, I would not expect to see a huge changes in how about after the vaccination? Do you have any data on that? There is yes we have.

We looked at some cohorts of people who were vaccinated. We don't see any change. So that prediction does not induce a change. Well, I mean, I know that you, are on the case, and I appreciate your speaking to me, and I, I know you have to get to to your family.

As always. Great. Great talking to you. Any last words you have to say to our listeners? It was pleasure chatting with you. And it's a pleasure to work together with you, because we are learning so much from your experience and how you can actually improve people.

And yeah, eventually I have to try something of myself. But also knowing you. Come on over. Yeah. It's. Yeah. I mean, it's great to work, with, you know, researchers and, and sort of put the clinical and the research and research together to sort of move things along more rapidly.

You know, I'm just very pleased to be working with you and, like a huge thank you very much, Gordon. Thank you. For.