Glycans As Biomarkers On Ageing And Disease Transcript

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Introduction to Glycans and Longevity

– Welcome to another episode of the reverse inflammation. Summit body and mind longevity medicine. And I'm your host Dr. Robert Lufkin today. In this episode we get to explore the fascinating area of glycogen cans and their role in longevity. And we are joined by one of the world's experts in the area. Professor. Gordon Lauc. Gordon.

Thanks for joining us today. – Thank you for the invitation and thank you for your interest in the fast Field of microbiology. Perhaps you could tell us a little more about your background and how you came to be interested in this area.

– So I'm in the field for 30 years and I stayed in the same field of microbiology because it is fascinating. It's actually glycol elation which enabled us to become multicellular organisms. And the glass icons provide another layer of complexity to protein because the protein sequence is determined by our genes and we cannot change it without random mutations which happens only in the next generation.

While in the same time glycans are chemical structures so they're part of a protein. They're part of the structure. They're part of the function but their composition is decided in the network of dozens or even hundreds of genes.

So it's a it's another layer of complexity which enables life in the way we know it today. But unfortunately the majority of scientists are still ignoring likens because they're complicated D. N. A linear protein arylene R icons are branched structures there is no genetic template, not easy to analyze and people tend to move away from difficult topics. – Yeah I've heard the what you said about black icons explain that D. N. A. Has four base pairs and their linearly arranged and and then they produce the proteins which are based on the menial assets which have about 20. And and then then these glycans though are infinitely almost infinitely more complex in a non linear arrangement.

So it's a it's a higher order level of complexity of the organism. And and um what's what's specifically glycans? Maybe just just back to basics, What is their chemical structure?

And does everybody have chemical? – So several monosaccharide in a branch chain of 10 15, 20 monosaccharide units every single living cell on this planet have glycans there is no life without glycans.

So everything looks like coagulated and even things like the blood groups are chemical glycans But we talk about A. B. O. Blood groups, we don't talk about the glycans structures which are behind them.

What Glycans Are and Why They Matter

The majority of tumor markers are also like isolated. So actually we interfere with likens often Just we don't think about them as a black man because glycans start difficult to quantify actually it was my lab who was first to start doing hydroponically comics, meaning analyzing likens in a large patient cohorts.

This was nearly 15 years ago when we started and we already analyzed over 200,000 people. So we really collected a lot of information about glycans and so – and now many of our a few of our speakers have mentioned in the longevity space A.

G. E. S. Sort of advanced glycation and products. And these are separate from glide consolation that you're referring to. Is that correct? – It is extremely important to make a very clear distinction between these two things. A. G. Or like oh like glycated proteins.

It's a random chemical damage. So when we have elevated glucose, glucose is a very reactive molecule. When it the ring opens it's another hideout right reacts with amino groups and then there is a rearrangement and there is a

chemical modification called called advanced location and products which is just a random damage to pro we usually quantified as a dedicated hemoglobin.

HB A one C. Or a one C. And this is kind of indicator how how much of too much glucose we had in the last couple of weeks glide consolation is sophisticated regulated process involving dozens and hundreds of genes.

Where the decisions are made based on the biological needs and then based on what our body needs. At the given moment we can make different icons, we can make our proteins different and we can make them function in a different way.

– Okay so the age the A. G. E. S. The advanced application and products are damaged too are proteins in our bodies done by glucose by sugar in our bloodstream, elevated sugar damages things. And that's pretty much universally bad.

But like oscillation with likens is um something that happens normally throughout life. And it's not necessarily good or bad. It's just what happens to the organism, right? And you can interrogate that somehow.

– So glad glycosylation is it provides a specific functions to different proteins and these functions can be beneficial or in some situations it could even be detrimental.

For example, information is one of the central elements of aging and glycogen is one of the key regulators of inflammation. And we need inflammation to kill pathogens.

So if if we have some kind of cuts and then bacterias come to our skin, we need to send our army there and kill those pathogens. So inflammation is necessary for survival. But today we live much longer than what, what was the median age only 100 50 years ago.

And we are not fine tuned to live that long because there is no evolutionary pressure to optimize our g networks beyond the reproductive age. So as we are getting older, inflammation is usually getting out of control.

So we have excessive inflammation which is often referred as a low grade chronic inflammation. So instead of acutely attacking the invader, we have a small fires burning all around our body where inflammation is actually destroying issues, we don't have to be rebuilt and so on.

So inflammation is first consuming huge amount of energy. This low grade chronic inflammation and secondly it's leaving micro scars, the damages which are not perfectly fixed.

Inflammation, Aging, and Lifestyle Damage

And then as it accumulates to aging two years, it leads to the tissue damage we usually associate with aging. So inflammation is one of the mechanisms how inflammation is promoting aging and the installation is important there because the insulation regulates inflammation and when everything is fine, when everything is functioning perfectly, we have activation inflammation when it is needed and then we have a suppression of inflammation when we don't need inflammation in it.

But if we lose these compensatory mechanisms or these regulatory mechanisms, if we don't suppress inflammation when we no longer need it, then we have this success, inflammation and inflammation and one of the key elements which is contributing to this inflammation is actually lifestyle.

We know that the diet and and all all the chemicals we introduce to our body and even the less of physical the lack of physical activity can lead to too much inflammation. And this is where the glycans are important because the glycans can help to regulate this inflammatory process. – And Gordon, I wanted to take a moment and acknowledge and thank you for coming all the way from the University of Zagreb where you're a professor there today um also um we ask all of our experts and you've already addressed this a little bit, but I just wanted to put the question out there about what their overall view of longevity is. That is why do we age, what are the mechanisms is

it just gradual wear and tear or is it quasi programmed?

How does that work? – I think that the frankest answer is we do not know because there are some indications there could be a program which could be beneficial for the population by eliminating the old individuals because we need to change for population to be adaptive. And there are also some indications that could be just the accumulation of the random damage and then malfunction with time.

So I think we still do not know and there might be a little bit of each of that component, but I think you know the the essential parts and are the most important part.

What we can do with the knowledge we have today is to try not to accelerate the process of accumulating damage because big part of the damage is determined by our lifestyle, by the environment, even by the things we think and if we can try to improve or at least not to do the wrong things, we can do a lot in prolonging our healthy life. And I think that the key thing in longevity is not living forever but enjoying the years that we are spending on this planet and we can only enjoy these years if we are healthy and if we are physically fit because if we are in pain, if we are sick then life is not a pleasure.

– Yes, the common theme we've heard emphasize over and over again throughout the program is it's not just about increasing lifespan but but the healthy years or the health span is so, so critically important. Um you mentioned glide Kansas the ultimate driver of inflammation and inflammation driving aging.

When does inflammation become? How do we know when inflammation is good? And how do we know it when it's bad? What's the difference there? – I think this is very, very hard to know and this is why mistakes happen.

This is why our immune system and the immune system is the most sophisticated uh system that we have. Probably the brain and the immune system are the to the most complicated system because immune system is keeping us alive against all these pathogens which are trying to eat us and they multiply like crazy, they we cannot fight them with the mutation rate, but we can fight them with our immune system and by looking from outside. So if a physician looks at a patient, I think the inflammation becomes bad when it is starting to cause damage, inflammation should be temporary. It should be rapidly activated to remove the threat and then it should be dampened.

So we shouldn't have inflammation if there is no threat. What happens with time is that somehow in different parts of our body from reasons which we don't fully understand.

There there are a lot of inflammatory processes and these processes both consume energy and cause damage. And if we find a way how to how to regulate them, it would degrade. The problem is if we use very aggressive approach, like for example, there are some biological drugs which can uh suppress uh touring across this factor, which is then suppressing inflammation a lot or kill the B cells. But then we are losing our defense and then we are becoming vulnerable to different tumors or different pathogens.

So it's um it's extremely complicated process. I'm not too optimistic about the current pharmacological interventions because we have no ideas what would be the side effect and what would be the damage that we are doing.

So personally, I think that at the current level of knowledge, we should try to minimize the damage that we are doing because we are doing a lot of damage.

We are eating too much. We are eating way too much carbohydrates because remember carbohydrates became available only with the agriculture. There was very little carbohydrates in our food because before we invented agriculture and on on evolutionary level on metabolic level because metabolically we are really not different than nice.

And so we didn't adapt to that pet much sugar. Or at least we didn't all adapt. And if you think about milk. So milk is available for thousands of years, more than than than the carbohydrates. And there are still people who are intolerant to lactose. So I would guess that the majority of the people on the planet can be considered as

carbohydrate intolerant meaning they cannot cope with the amount of carbohydrates we are eating regularly and then we have the obesity.

We have the metabolic syndrome. We have all the diseases which come with eating the wrong type of diet. Then we have stress which is uh supposed to be a short term response to danger.

Why We Age and the Role of Healthspan

And now our sources of stress are no internet, not working, uh not liking our boss or being late in traffic. And then we activate the stress response.

So if we find a way how to minimize the damage will make a big step forward. And one of the key problems here is that we're all different. You know, everything we know about medicine is based on an idea of a standard human.

So you take thousands, you take thousands of people, you do some research and then you calculate some kind of average things and then you decide what is good for an average person.

There is no standard human nobody's standards. So these standard recommendations do not apply to anybody. Each of us have their own personalized requirements, needs responses to therapy.

And I think the the medical community today appreciates or accepts the fact that we are wasting 80% of the smart drugs because we are giving them to people who do not respond to them. But we are still not aware of the fact that we're also wasting probably 80% of all lifestyle interventions because we are suggesting them or we are doing them Which are not optimized for a given person.

So one idea we have behind this glider contest which we are doing is that this test can actually tell you whether something you are trying is working for you or not not, whether it works in general, but whether it works for you for example, we did a large study in Europe with 1000 people on a low calorie diet for two months. There are 800 calories for two months.

You know? That's crazy. That's torture. Nobody can stay for 800 on 800 calories for a long time. But after these two months on low calorie diet and majority of people lost over 10 kg in these two months, they're put on five different maintenance diet, so different combinations of glycemic index protein and other nutrients and on each of the diet some people got better and some people got worse. So there is no standard diet which will work for everybody. We have to identify our optimal diet the same is the case for exercise. We have found out that the majority of people who start exercising especially if they do it in the midday at middle age when they decide to kind of live healthier, they over train and by overtraining they're doing damage to themselves again because you know, it's a kind of a dogma which was imposed on us by the by the food industry, it's not the junk food that you're eating, it's that you are lazy and you don't go to the gym and you have to go to the gym and then sweat out all the junk food we are selling to this is wrong.

There is no way we can sweat out all the junk food we are eating. So um, maybe by having this test which we promote, which is giving you feedback on things which you cannot see in the mirror can actually help people motivate themselves to live a healthier life. – Well, so many things to unpack here.

One thing I just wanted to underscore you said earlier was that the inflammation that we experience can be good if it's short and acute and it can be bad when it's chronic and lifelong with aging?

Personalized Medicine and Glycan Age Testing

And that sounds similar to other things like stress, Like uh, a little bit of stress can be very healthy, but chronic stress can be, can be very damaging.

And and also another point was about the programming um, programmed causes of aging or longevity if it is programming. Uh, many people doctors sitter off on this program and others like Dave Sinclair have mentioned that

epigenetic programming may be a mechanism for this and that we can reprogram our epic genome by the food we eat by even things like purpose in our lives.

Um, do you think of um, glide cans as something that is programmed also? Is that analogous to the epigenome? We program our glycans or is it more downstream from that or is that a reasonable way to look at them. – So we did a lot of research on the link between the epigenetic single comics and uh I would guess that significant part of the glycol composition is actually decided by epigenetic modifications of the South which produced them. So epigenetics is definitely information.

So we have a D. N. A. Sequence which is evolutionary knowledge. So all the knowledge accumulated in the millions of years. It's written in our D. N. A. Then we have epigenetic information which is more or less at least this environmental epigenetic part it's a lifetime experience.

So things which happen to us in prenatal life in early life in adulthood they stay written in the genetics. So genes become activated, deactivated by either DNA methylation but also the histone assimilation and other modifications which are going on. And uh if there is a program it's an epigenetic program, there's no doubt. The problem with epi genetics is that we still know very little about individual mutilation sites about the relationship between methylation and histone assimilation. So the the epigenetic reprogramming we see today is still very non selected. For example people are eating food which is providing more in in and then you have changes in methylation but this is not directed. So if you want to have a real epigenetic modulator which will affect any of the programs then you have to target a specific part of our genome and then modulate epigenetic information in that part and not globally and all drugs which are currently in development or being used are still global epigenetic re programmers and to know what would be the consequences of this reprogramming.

It will take very long time to to study that. But it's a good direction. So I think it's a good idea to try to reprogram epigenetics and try to make things better. But as I mentioned, you know, even with all these um if you read the literature I think we have over a dozen different epigenetic clocks being used today. Starting from the original Steve Horvath clock which was developed based on just the chronological age.

And then everybody was super excited because you can predict somebody's chronological age from ventilation and it's actually super accurate especially on a population level.

But then you know if you just prediction logical age, what is the value of that because we know chronological age. And then there is this new generation of epigenetic clocks which are calibrated based on some protein markers on some kind of uh physiological markets which then predicts some other things. But in majority of these clocks we still do not know what are we actually measuring. And if we change the clock, if we change this specific mutilation sites. Will it mean anything or not?

So this is something that we are still lacking in the field of epigenetics which is super exciting and I love epigenetic Stephen teach part of the genetics.

But we're still missing the understanding the big difference between blackens and epigenetic se's the glass icons are functional defectors. Their molecules which actually do the work.

They either promote inflammation or they suppress inflammation. So if we see glycans which promote inflammation, we know that they are promoting inflammation.

And if we improve these glass icons and then we change them in a way to suppress inflammation, we know that this will suppress inflammation. So I think this is the key benefit of google icons today of course, in addition To the fact that they're responding to intervention.

So one of the key problems with most of the agenda clocks is that you do something which is healthy. You know you lose 10, 15 extra kilos and nothing happens to your mutilation.

If you lose 10 or 15 extra kilos, your guidance will improve. Also if you do, for example, in a in a perimenopause if

you do uh common replacement, your guidance will improve. Epigenetic will not at least Steve Horwitz clock will not. – So if the defector level then glycans are for many lifestyle changes. A much more appealing biological clock than the DNA methylation. Epigenetic clocks.

Is that right? – So these are different clocks. For example, there was a recent paper published in aging which compared all these different clocks and the of course all these clocks correlate because they correlate with the chronological age. But when you look at acceleration, acceleration and google icon aging and the genetic agent did not correlate much.

So these are different biological processes. I will not say that one is better than the other. I think it's important to have both of them. And of course the advantage of google icons is they respond to intervention.

And there is also another paper published uh in late 2020, It's called the Molecular human. Where it was done in Qatar where they studied over 6000 different molecular phenotype meta bellum uh genome epi genome pro TEM glycone and out of these 6000 trades.

When you list 20 which most college with age nine out of these 20 google icons and most of the others are the hormones which we know the change with age.

So definitely there is a strong link between black icons and aging. – Yeah. And and two of the two of the big questions I guess with with the DNA methylation clocks are one.

Um how far back can you rewind the clock? Like people have, you know, shown a couple of years here and there. But how how much can you rewind it? And they've also shown that you get the greatest improvement in calculated biological age with the DNA methylation clock and the people who have the poorest poorest health and poorest lifestyle.

Um so one of the question is how far can you rewind them? And then the other question I guess is does rewinding the biological clock and lowering your biological age actually improve your survival uh improve your longevity. And I I imagine those two questions for or google icon related biological clocks are also unanswered at this point.

Is that right? – Well for glycans we have, we don't have much. We have one paper showing that if you actually improved likens you can prevent hypertension in mice because but what we know we know that you know in intervention which is beneficial for health is also improving glycans but we cannot, there is no positive confirmation that you know if you just take the glass icons things will get better. But there is 1 type of therapy called intravenous immunoglobulins I V I G. Where you actually give young immunoglobulin icons and this is known to suppress inflammation.

So I think for icons, we know that if you improved likens you are suppressing inflammation for epigenetic.

Epigenetics, Glycan Clocks, and Biological Aging

So I think the key problem we have today is that we still do not know Which of these ventilation start sites are actually functionally relevant because you know, Steve Horvath selected 373 CPG sites out of 400,000. There there are other 300 sites which would be equally good and completely different sites.

And the question is which of them are functionally important. Eventually we will learn that so we will learn which are important. And then if we improve these sites we will know that there are beneficial effects were now we don't know that. – one of the emphasis of this course is to talk not just about the body and the that role it plays in longevity but also bring the mind and mental issues in. Are you?

What sort of evidence do we have that the mind or stress related type things affect likens? Actually this was one of the reasons I entered the glycol biology field because I was in the nineties, we had a war in the former Yugoslavia and we were all trying to do things which will help people and stress was one of the key issues and I was really interested in the biochemistry of stress And the things which were changing mostly in people under extreme stress

Borg likens.

So then and this was in the 90s. So 30 years ago we learned that what we think can actually change our likens. And we have a number of experiments today, even with animals that that psychological stress can change your like.

And today it's it's widely accepted because you know what we think these are also chemicals, their chemical processes, their neurotransmitters released, their chemical reactions and our immune system is also linked with our stress response.

So if you're under stress, your inflammation goes up and I think one of the one of the ways to improve your girl icon is to reach some kind of a peace of mind and not be under stress which is not easy, you know it's it's it's easy to say but it's very easy.

It's not easy to actually achieve it. But I completely agree the part of well being, part of health is a psychological well being and feeling at least not being afraid and not being under stress.

That's kind of a minimum which I think is needed. – You mentioned before lifestyle effects on google icons. What are some of the lifestyle choices that we can make ourselves that you've seen positively favorably affect glycan measurements. – So one thing which definitely works is getting rid of the extra body weight. So obesity is very pro inflammatory. So not being obese is one of the best things we can do. Physical activity is also very important.

But it has to be optimized in a way that there is a sufficient amount of activity and relaxation stretching and such things. Because what we often see as a mistake is people actually trying too hard, especially if you try too hard by combining physical activity, some kind of oxygen therapies, keto diet, some kind of supplements.

You you practically burn yourself. So I think that what we learned so far and we haven't done that money. So glad can age I think has something like 15,000 customers. So it's not it's not hundreds of thousands but it's still a reasonable number Uh is that each of us have to find what actually works for us. And we have often seen individual clients trying something, finding it doesn't work trying something else and then it works.

And um and there are some clinics and glycogen ages today being sold in over 500 clinics who are really successful in making nearly all of their patients improving like an age while in program. And so this can be done.

There is no universal solution. So like an age is the test comes with with the counseling. So together with the test you get this um initial counseling where people who have experienced with other people trying to improve their like an age can try to help individual clients but it's got like an age is not a universal solution to a problem. It's it's a tool which can help a motivated person find a solution or which can help position guide their patients.

Stress, Mindset, and Glycan Changes

– for our audience glycan age, as the name suggests, is a biological clock that measures age instead of DNA methylation or something like that uses the glycans like we've been talking about and that is uh it's commercially available online. And as Gordon says, people are using this all over the world. How often um how fast google icons respond to changes in our lifestyle or changes in our health.

Will there ever be a continuous glycan monitor like we have for C. G. M's for glucose or it's a more involved process, isn't it? – It's a it's a it's a slow process.

So glycan ages based on glucose attached to I G I G immunoglobulin. G has a hard life for approximately three weeks. So nothing happens in a matter of hours or even days. It takes weeks to change.

And if changes are moderate meaning we change our diet, we change our exercise. It usually takes 2-3 months to see some effects with with some drugs. So if you take some kind of drugs which modulate your immune system then you can see effect in a couple of weeks. And if there is a extreme information going on like in in covid or

severe influenza than we can see changes even faster in maybe week or two weeks. But it it does take time for the icon to change.

So it's it's a chronic measure. It's not something which you measure day. Today we normally for example I test my glycogen age every two months but they have a lot doing it so I don't have to send it or paid. So customers usually don't do it more than every three months or six months. – I know it's hard to get information about errors and variants just because we're tracking things that are difficult to measure.

But do you have any information about the error variance in a test, like like an age compared to other types of biological clocks. – So I think one of the big advantages of glycan age is that it is really coming from a laboratory from my laboratory and we are primarily trying to do hard science.

So I do my like an age regularly and very rarely. It would change more than a year every two months. So the criminality of of biological differences and analytical differences would be a year in a couple of months. And one of the ways we achieve that is that we analyze every sample three times. So it's analyzed in triplicate so that there is no analytical variation um, for mutilation, depending how you do it, it can be problematic. So some technical approaches are very reliable, gather ones would give a different number each time you measure it.

So analytical reliability is one of the key elements of a good test.

Lifestyle Interventions and Future Research

You have to have a test which is giving the real result and not changing randomly just based analytical errors. So this is one of the reasons why this test is not cheap and it's probably never be cheap because you know, to measure something as complicated as a geek like on in triplicate.

It's it does cost money. – We've talked a lot about glycans today and that's your obviously your your specialty. I always, I wonder what in the longevity field outside google icons and areas that you're directly working in that are you most excited about. – So I'm excited about this.

All these new interventions, which people are people are trying to develop and we always try to use glycans to see what actually happens with icons and some of these companies get disappointed because we don't see any effect. Some get very excited because we see the effects and I think that the what I'm most excited about is just science and trying to understand what is going on and what can we actually do.

– Do you have any, have you done any studies with glycans with some of the most popular longevity drugs like rapamycin or Metformin. – So we haven't done any proper placebo controlled trial and I'm afraid to make any conclusions without proper randomized trial because things get confounded.

For example, you know if somebody starts an intervention and then start thinking about the diet and thinking about exercise and theological well being, it's very hard to pinpoint the effect. So once we do a proper study we will publish it.

We have some people changing a lot on Metformin but maybe it was not meant for me, Maybe it was something else. So still we are still lacking the hard times but we're doing a couple of studies now which are properly placebo controlled so we'll know relatively soon.

– Yeah, things are happening so fast and and changing so rapidly. It's such an exciting time in this longevity space. And uh I really look forward to the information that google icons can add to our our whole picture here. What's the best way for our audience to follow you on social media or your website? – So Glycan Ages.

The company is very active on instagram and also on their website. I am personally on all media, but instagram. So linkedin twitter would be places where I post about the research which we do. – Great, well thank you so much for taking an hour and spending time with us on this episode. Gordon and thank you so much for the great work that you're doing. – Thank you for the invitation again and I enjoyed chatting with you.