



Glikozilacija proteina i personalizirana medicina

Gordan Lauc
University of Zagreb &
Genos Glycoscience Research Laboratory



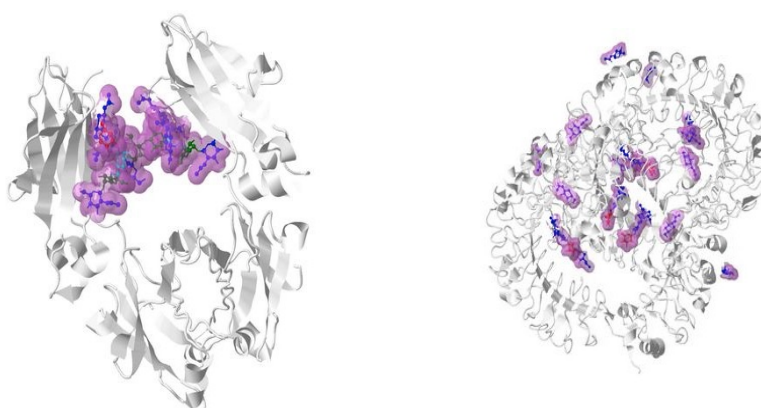
WO2014203010; US2016103137; WO2012042020; WO2011015944; WO2009044213



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Glycans are important structural component of nearly all proteins



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A number of different glycans can be attached to IgG

■ GlcNAc
● Man
◆ Gal
★ NeuNAc
◆ Fuc

Core fucose disables ADCC
Sialic acid converts IgG into anti-inflammatory agent

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Small local effects of glycans on protein structure can have dramatic physiological effects

Hypothesis 1:
N-glycosylation stabilizes IgG1 Fc 4° structure

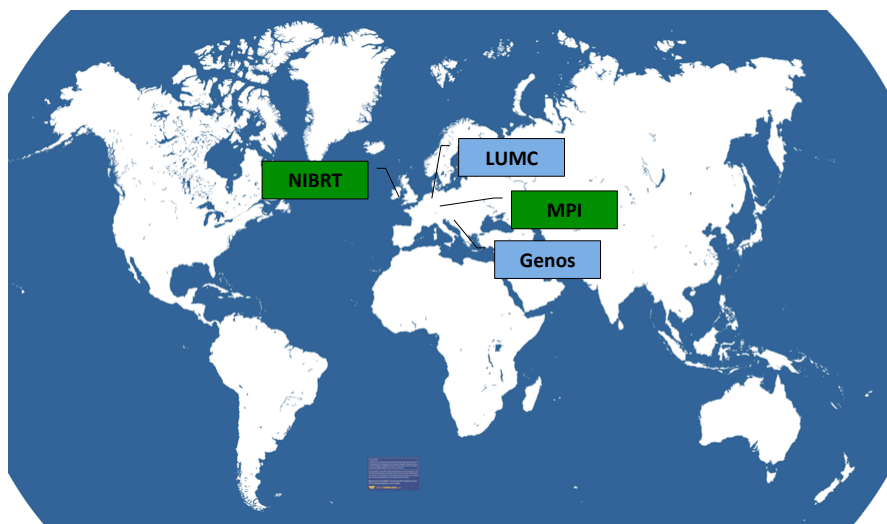
Hypothesis 2:
N-glycosylation stabilizes local IgG1 Fc structure

Alternative glycosylation is analogous to coding mutations

Subedi and Barb, *Structure*, 2015

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High-throughput glycomics is globally deficient



Osam od 10 najprodavanijih lijekova u Europi su glikoproteini

	2008	2009	2010	2012	2013
1	Lipitor (atorvastatin)	Lipitor (atorvastatin)	Seretide (fluticasone/ salmeterol)	Humira (adalimumab)	Humira (adalimumab)
2	Seretide (fluticasone/ salmeterol)	Seretide (fluticasone/ salmeterol)	Lipitor (atorvastatin)	Seretide (fluticasone/ salmeterol)	Seretide (fluticasone/ salmeterol)
3	Plavix (clopidogrel)	Plavix (clopidogrel)	Humira (adalimumab)	Herceptin (trastuzumab)	Enbrel (etanercept)
4	Herceptin (trastuzumab)	Enbrel (etanercept)	Enbrel (etanercept)	Enbrel (etanercept)	Herceptin (trastuzumab)
5	Enbrel (etanercept)	Herceptin (trastuzumab)	Herceptin (trastuzumab)	Lipitor (atorvastatin)	Mabthera (rituximab)
6	Zyprexa (olanzapine)	Humira (adalimumab)	Lovenox (enoxaparin)	Mabthera (rituximab)	Remicade (infliximab)
7	Lovenox (enoxaparin)	Lovenox (enoxaparin)	Mabthera (rituximab)	Lovenox (enoxaparin)	Lovenox (enoxaparin)
8	Glivec (imatinib)	Glivec (imatinib)	Avastin (bevacizumab)	Remicade (infliximab)	Avastin (bevacizumab)
9	Pantozol (pantoprazole)	Zyprexa (olanzapine)	Remicade (infliximab)	Avastin (bevacizumab)	Lucentis (ranibizumab)
10	Symbicort (budesonide/ formoterol)	Mabthera (rituximab)	Glivec (imatinib)	Spiriva (tiotropium)	Lyrica (pregabalin)
	Biological				

<http://gabionline.net/Reports/Biologicals-dominate-Europe-s-best-sellers>

2012: US National Academies

- “glycans are directly involved in the pathophysiology of every major disease”
- “additional knowledge from glycoscience needed to realize the goals of personalized medicine and to take advantage of the substantial investments in human genome proteome research and its impact on human health”



Walt et al, National Academies Press, 2012


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NIH office for Strategic Coordination launched The Common Fund programme for glycoscience

U.S. Department of Health & Human Services
National Institutes of Health
Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)

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Glycoscience


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Glycoscience

For the Public

Public Health Relevance

Highlights

For Researchers

Funded Research

Funding Opportunities

Program Resources

Other Resources

Publications

Glycoscience Program Tackles Human Milk Oligosaccharides

Learn More...



Program Snapshot

The Glycoscience program aims to create new methodologies and resources in the study of glycans that are accessible to the broader



Save the date!

Glycoscience 2019 Annual Meeting

The next annual meeting for the Glycoscience program will take place May 29-30, 2019 at the NIH campus in Bethesda, MD.

The 2018 annual meeting took place July 2 - 3. View the meeting [agenda pdf](#) and [group photo](#).

New Funding Opportunities!

The Glycoscience Program has two new


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Genos is global leader in high-throughput glycomics

nature|methods

TECHNOLOGY FEATURE

Metabolism: sweeter paths in glycoscience

Vivien Marx

Carbohydrates are tough molecules to study, but glycoscientists are developing and democratizing the needed tools.

Stanford: Carolyn Bertozzi; **Harvard:** Richard Cummings; **Genos:** Gordan Lauc



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Genos and our partners already invested over Euro 30 million in glycan analysis and analysed over 70,000 samples

Cohort	Plasma glycome	IgG Glycome
10001 Dalmatian	2,000	5,000
Orcades	2,000*	3,000
TwinsUK	4,000	4,500
KORA	–	2,000
SABRE	2,000	–
EPIC	3,500	3,500
Global population study	–	2,700
FINNRISK	–	1,200
Estonian biobank	–	1,300
China	1,000	2,000
CRC	2,000	2,000
IBD	3,000	5,700
SLE	–	1,200
Type 1 Diabetes	3,000	1,000
Type 2 Diabetes	3,000	4,000
Down syndrome	–	800
Low back pain	800	2000
PTSD	600	600
Total	27,900	42,500



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Main Genos research papers in 2017/2018

Rad	IF	RANK
Suchre et al, Nature Communications 8:14357	12.4	3/64
Shen et al, Nature Communications 8:447	12.4	3/64
Benedetti et al, Nature Communications 8:1483	12.4	3/64
Bermingham et al, Diabetes Care, 41:79-87	13.4	5/143
Šimurina et al, Gastroenterology, 154:1320	20.8	1/80
Krištić et al, Nature Chemical Biology, 14:516.	15.1	5/290
Clerc et al, Gastroenterology, 155:829-843	20.8	1/80
Menni et al, Circulation Research, 117.312174	14.0	1/70
Lauc et al, Nature Communications 9:2916	12.4	3/64



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The Human Glycome Project was launched on Oct 6th, 2018 in Dubrovnik

human-glycome.org  glycomehuman

The Human Glycome Project

"Glycans are directly involved in the pathophysiology of every major disease... Additional knowledge from glycoscience will be needed to realize the goals of personalized medicine and to take advantage of the substantial investments in human genome and proteome research and its impact on human health."

— US National Academies, 2012

The Human Glycome Project addresses this major societal challenge.

Full Members

Prof. Michael Pierce, University of Georgia

News

Oct 2, 2018

Official Launch of the Human Glycome Project

Following the successful meeting of the Human Glycome Project Initiative in May 2017, we are happy to announce that the Human Glycome Project will be officially launched in a beautiful city of Dubrovnik (Croatia). This will happen on Saturday, **October 6th 2018** during the GlycoCom conference attended by many of the brightest minds in the field of glycobiology. Any principal investigator dedicated to our cause can apply for the membership by sending the email to info@human-glycome.org while any company or institution can apply to info@human-glycome.org.

Latest Tweets

Tweets by @GlycomeHuman

Human Glycome Project Retweeted

HMSCG @HMSCIG

Less than 2 weeks before the Inaugural Symposium of the #HMS Center for Glycoscience. We are very close to full capacity for the event, please RSVP here to secure a seat and a free lunch: tinyurl.com/y9S4a4mk #Glycotime #Glycoscience #Harvard

Harvard Medical School Center for Glycoscience
Inaugural Symposium

Wednesday, October 24, 2018
7:00AM - 5:00PM

Joseph B. Martin Conference Center - HMS
(77 Avenue Louis Pasteur - Boston, MA)

Organizers: Richard D. Cummings, Eyal Chailuf & Robert Sachdev

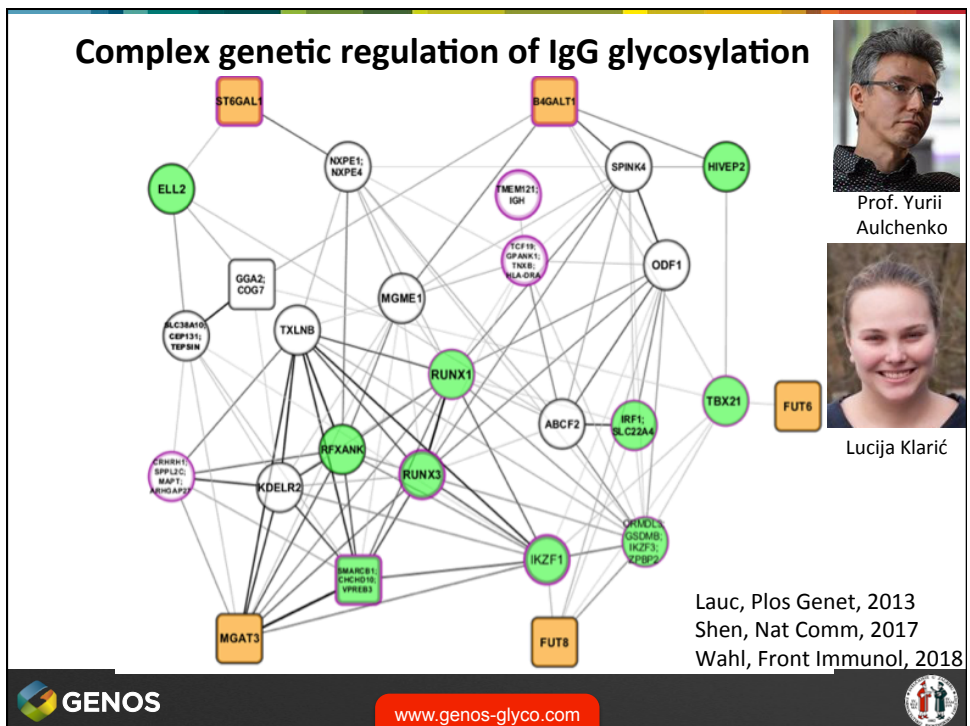
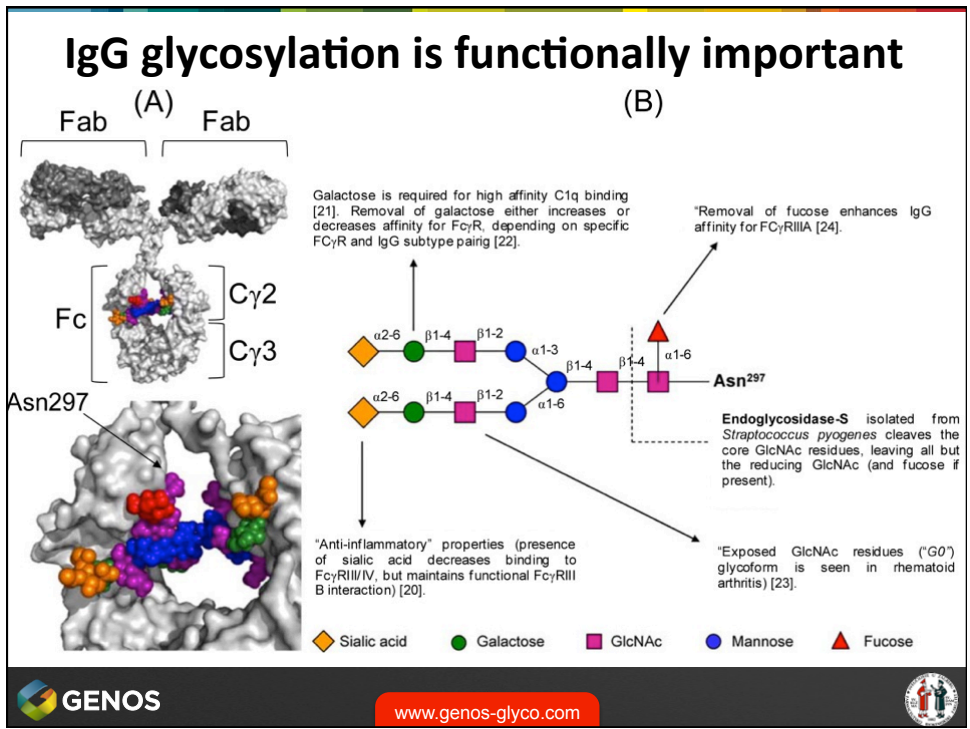
A full day of presentations by outstanding researchers will provide researchers and clinicians with the opportunity to hear about current glycoscience research, present a glycan structure related to medicine, and foster discussions among the local community.

Speakers
Knutson, Suzanne; Barbone, Frances; Pitt, Richard; Barbone, Frances; Medical Discovery Institute
Klein, P. Campbell, PhD, University of Iowa



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Glycan biomarkers developed in Genos

1. **GlycanAge** – biomarker of biological age
 - Awarded patents in EU, USA and China
 - Sales starting in EU and China
2. **DiabRisk** – predicts risk of type 2 diabetes
 - PCT patent application favourably evaluated
 - Entering national phases
3. **CardioRisk** – Predicts CVD risk
 - Patent application in preparation



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GlycanAge – the best biomarker of biological age

Home | Daily Mail Online 11/10/16 11:00

GLYCANAGE Like (6.1M) Follow @MailOnline DailyMail Tuesday, Oct 11th 2016 11AM 7°C @ 2PM 7°C 5-Day Forecast Book a test

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Your health

Our GlycanAge test... number and take con


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BODY AGE 34	BODY AGE 59	BODY AGE 51	BODY AGE 34	BODY AGE 76	BODY AGE 54

Just how differently our bodies age can be seen from a pioneering, but simple, new blood test developed by an international team of scientists. The test is said to be the most accurate method yet of determining our biological age - that is, the age of our body's cells. Pictured (from left): Karen La Borde, who runs a business training ski instructors with her husband and lives near Penzance, Cornwall; John Vylevel, a semi-retired investment adviser who lives in London with his wife; Helen Dee, a plus-size model and TV and film extra who is divorced and lives in Epsom, Surrey; Dave Watts, a retired civil servant who lives in Romford in Essex with his wife; Joanna Lamin, from West London, who works as a web business administrator, cook and food writer; and Sonia Scrimshire who runs a consultancy and training business with her husband and lives near Leamington Spa.


197 comments 2 videos 151 shares

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Ivan Gudeli
Journals of Gerontology: BIOLOGICAL SCIENCES
Cite journal as: J Gerontol A Biol Sci Med Sci
doi:10.1093/gerona/ght202

IgG glycome composition is an excellent biomarker of chronological and biological age

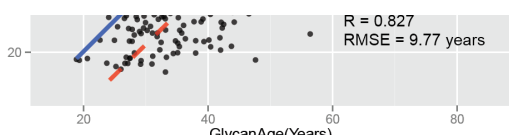


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Guest Editorial



Are Glycans the Holy Grail for Biomarkers of Aging? (Comment on: Glycans Are a Novel Biomarker of Chronological and Biological Age by Kristic et al.)

David G. Le Couteur,^{1,2,3} Stephen J. Simpson,^{3,4} and Rafael de Cabo⁵



Gudelj et al,
Int J leg Med, 2015



Kristić et al,
J Gerontol, 2014

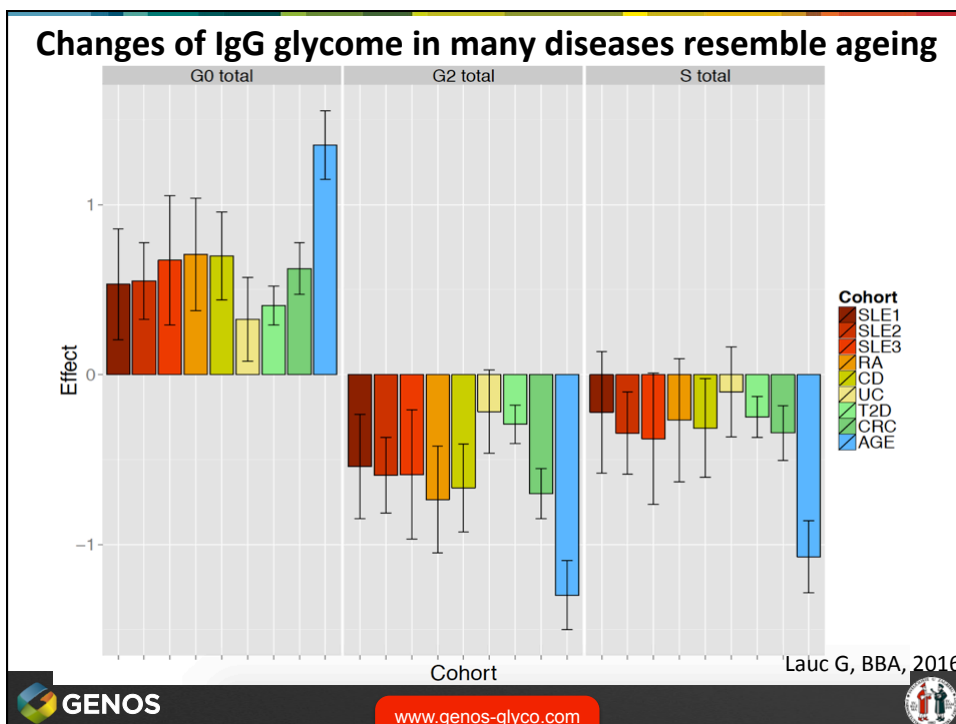
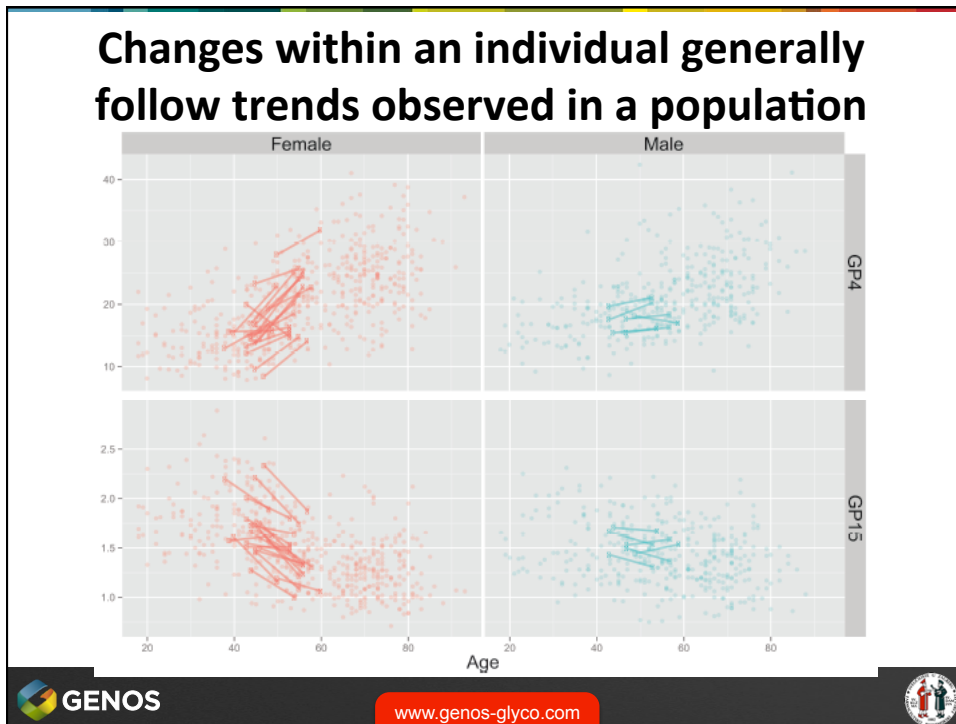

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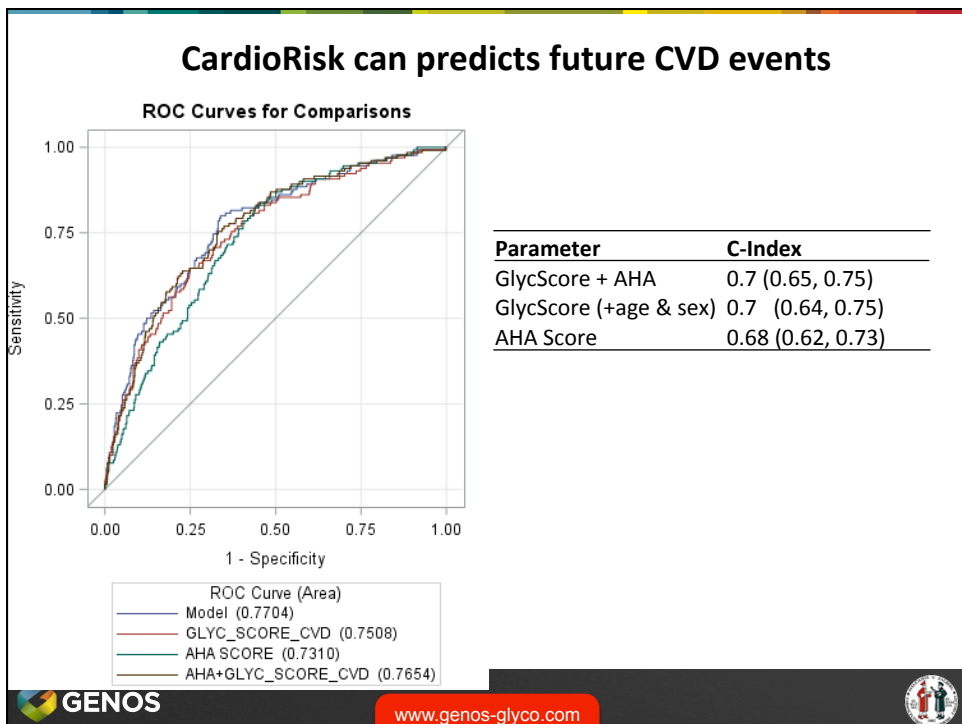
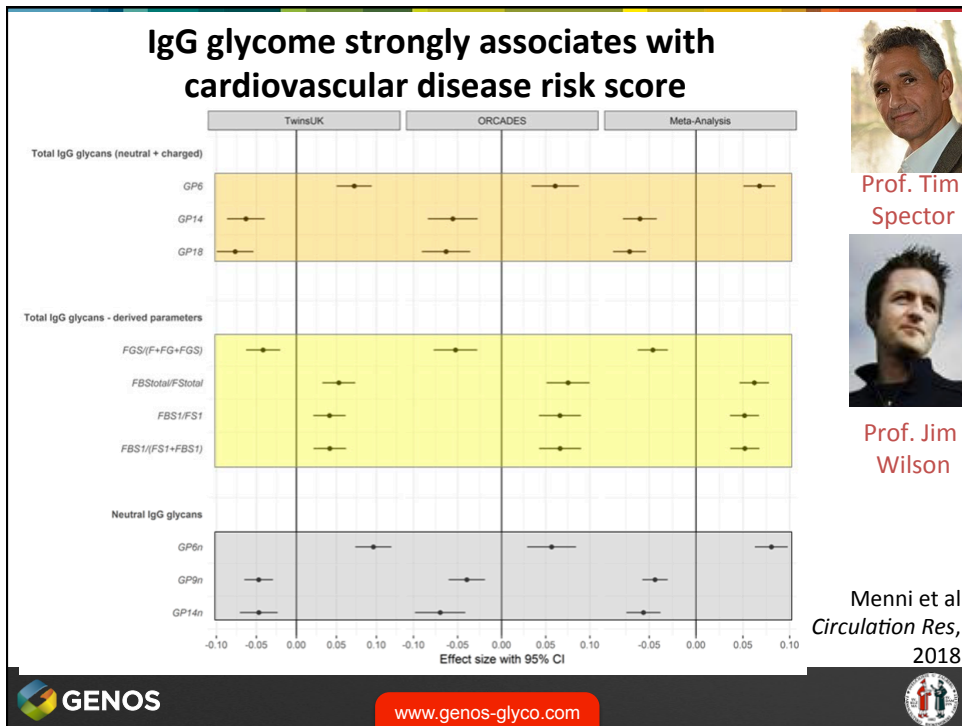
After correcting for chronological age, glycan age index associates with “unhealthy” life

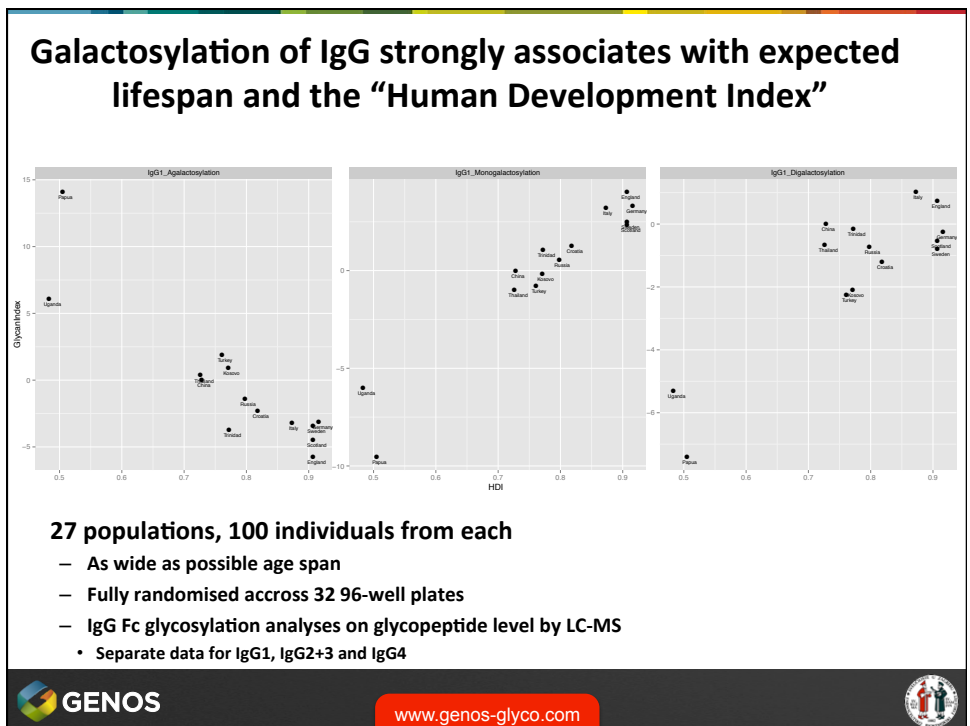
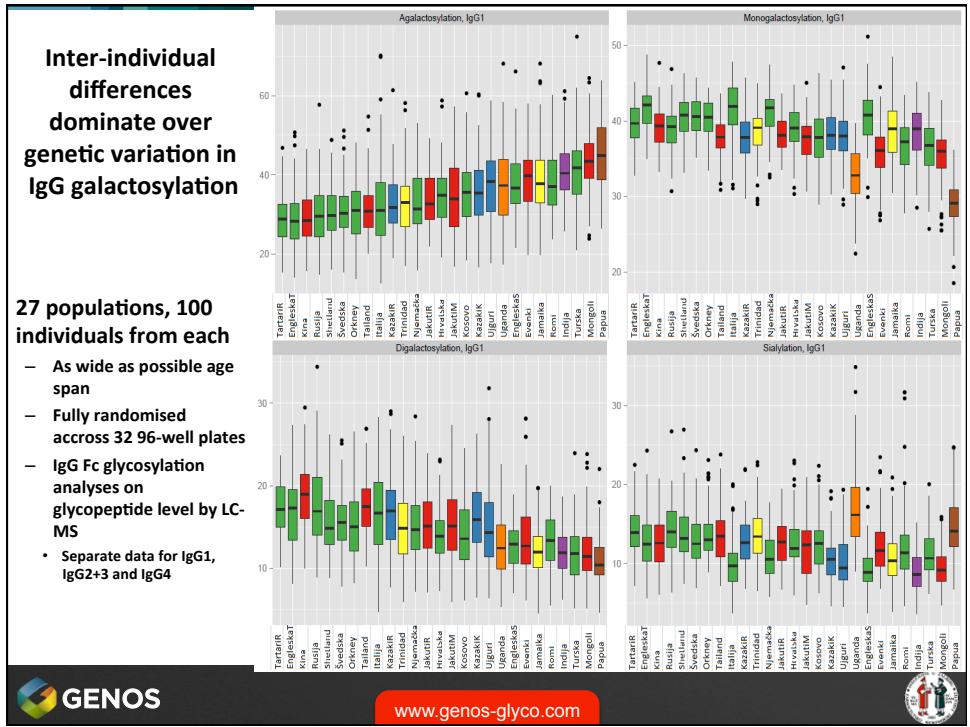
	Orkney		Vis and Korcula	
	Beta	<i>p</i>	Beta	<i>p</i>
Insulin	0.0755	9.22E-08	0.0402	3.50E-01
Fibrinogen	0.0157	1.98E-06	0.0167	8.83E-05
HbA1c	0.1106	2.63E-06	0.0084	3.16E-03
BMI	0.0585	1.67E-04	0.0344	1.04E-02
Triglycerides	0.0092	1.75E-04	0.0140	1.20E-04
Glucose	0.0113	2.09E-04	0.0091	4.77E-02
Waist circumference	0.1468	2.08E-04		
Calcium	0.0010	2.35E-04	0.0002	7.04E-01
D-dimer	2.9670	8.24E-04		
Cholesterol	0.0036	3.07E-01	0.0201	5.51E-08
LDL	0.0031	3.26E-01	0.0146	6.08E-06
Uric acid	1.0773	4.02E-02	0.7620	9.68E-04

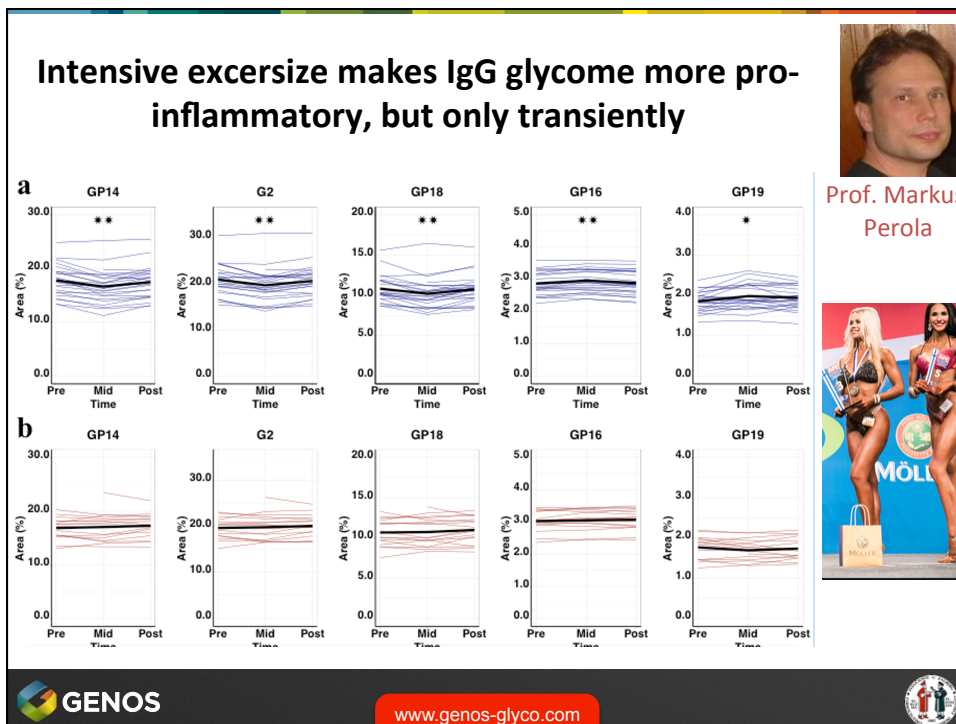
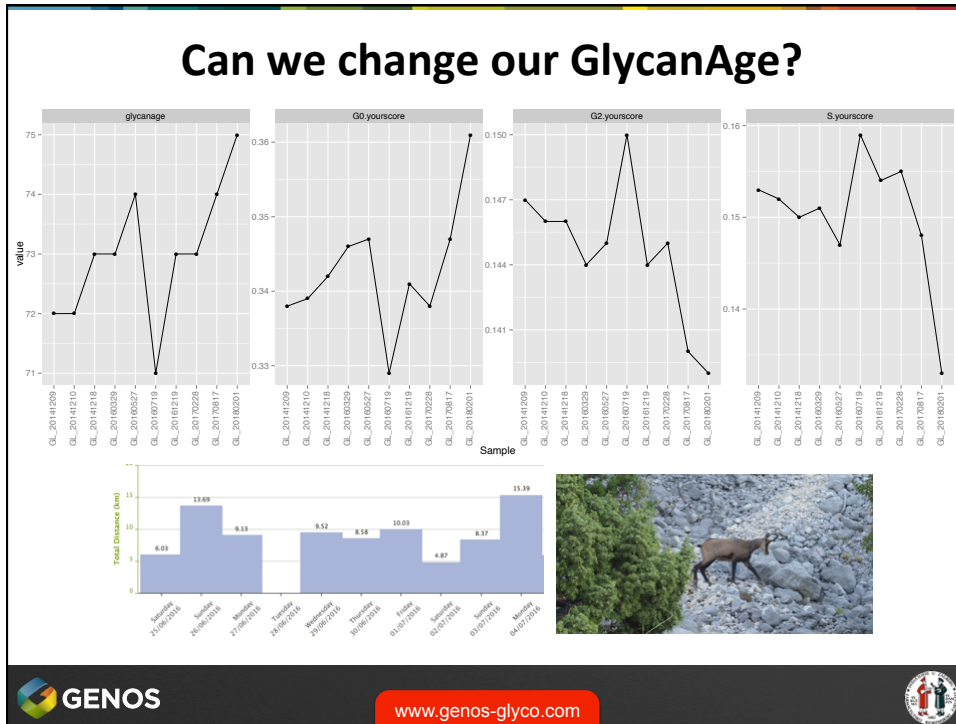
Note: HbA1c = glycosylated hemoglobin; BMI = body mass index; LDL = low-density lipoprotein; *p* = *p* value; beta = regression coefficient.


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Lifestyle interventions can change IgG glycome composition even in older adults



Prof. Eline Slagboom

www.impactaging.com

AGING, January 2016, Vol. 8 No 1

Research Paper

Metabolic effects of a 13-weeks lifestyle intervention in older adults: The Growing Old Together Study

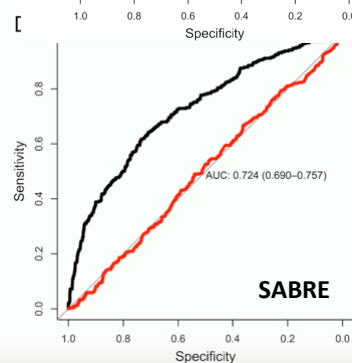
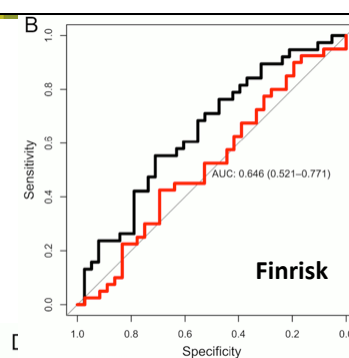
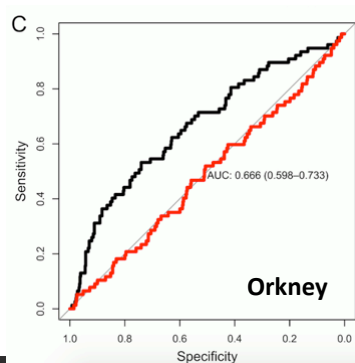
Ondine van de Rest^{1,#}, Bianca A.M. Schutte^{2,#}, Joris Deelen^{2,#}, Stephanie A.M. Stassen³, Erik B. van den Akker^{2,4}, Diana van Heemst³, Petra Dibbets-Schneider⁵, Regina. A. van Dipten-van der Veen¹, Milou Kelderman¹, Thomas Hankemeier⁶, Simon P. Mooijaart³, Jeroen van der Grond⁵, Jeanine J. Houwing-Duistermaat⁷, Marian Beekman², Edith J.M. Feskens¹, and P. Eline Slagboom²



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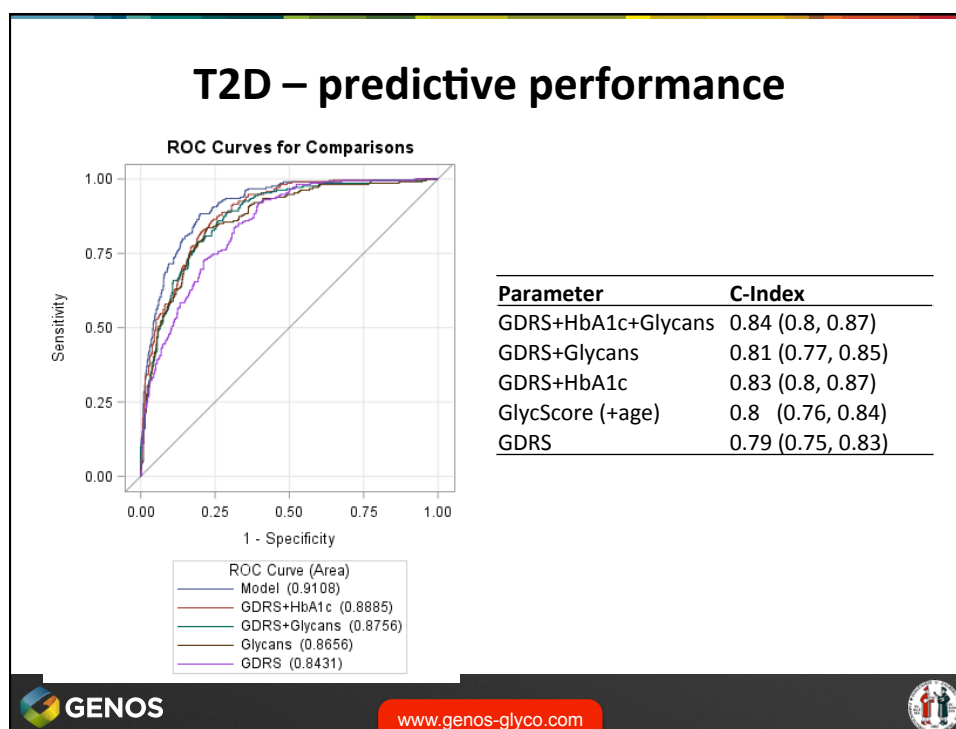


Plasma glycome can predict development of type 2 diabetes in some individuals



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Glycan biomarkes in prediction of diabetes

- Changes in the glycome (**the DiabRisk[®] test**) are visible several years before any other symptoms
 - elevated blood glucose of HbA1c
- Only a subgroup of future diabetes patients (10 – 20%) have this risk factor
 - **Altered glycans are not only a biomarker, but active effector in disease development**
 - **We need a new clasification of diseases**
- Ongoing clinical trials to see whether this risk is preventable by lifestyle or pharmacological interventions

Keser et al
Diabetologia, 2017

DiabRisk test is starting large clinical trials in China

A

Sensitivity

Specificity

AUC: 0.947 (0.907-0.987)

亿阳集团
Bright Oceans Corporation

Diab
Risk

Keser et al, *Diabetologia*, 2017

GENOS www.genos-glyco.com

Glyco-group in Zagreb

TheScientist
BEST PLACES
TO WORK
INDUSTRY 2013

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Funding Acknowledgement

GLYCOMET
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HORIZON 2020
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PainOmics
GlySign
GlycoBioM
MIMOmics
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