

GENOS[®]

Glikani kao supragenomski markeri u personaliziranoj medicini

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University of Zagreb &
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KING'S COLLEGE LONDON

WO2014203010; US2016103137; WO2012042020; WO2011015944; WO2009044213

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1

Efficient patient stratification is the holy grail of precision medicine

Patient population

Treatment

Standard approach

Treatment A (effective in 20% of target population; 80% is waste)

Tailored approach

Treatment A
Treatment B
Treatment C
Treatment D

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2

Despite technical success, the Human Genome Project did not fulfill expectations of both general and scientific public

DECODING THE BOOK OF LIFE
A Milestone For Humanity

Science
THE HUMAN GENOME

nature
THE HUMAN GENOME

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3

Genes do not define everything

Only 20% of longevity and 30% of most complex diseases is genetic

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4

Genetic polymorphisms are very far away from the phenotype

Genome mapping

LOD score for Metabolite G

genotype **molecular** **networks** **phenotype**

Dumas, Mol Biosystems, 2012

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5

Glycans are important structural component of nearly all proteins

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6

2012: US National Academies

- “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”

Walt et al, National Academies Press, 2012

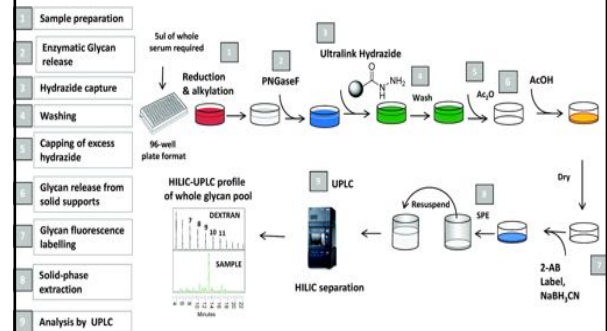
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7

Glycan analysis is very complex



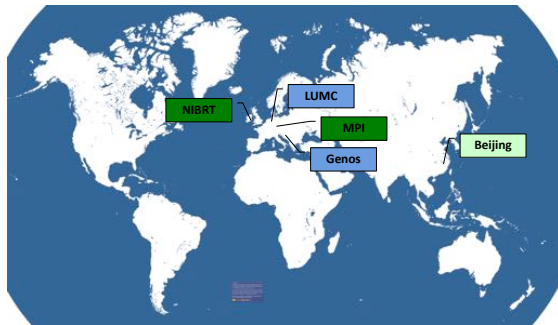
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8

High-throughput glycomics is globally deficient



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9

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

The screenshot shows the NIH Common Fund Glycoscience program website. The header includes the NIH logo and the text 'National Institutes of Health Office of Strategic Coordination - The Common Fund'. The main content area features a 'Glycoscience' section with a 'Program Snapshot' and a 'Save the date!' announcement for the 'Glycoscience 2019 Annual Meeting' on May 29-30, 2019, at the NIH campus in Bethesda, MD. The website also includes navigation links for 'Common Fund Programs', 'Common Fund Research Funding', 'News & Media', 'Common Fund Highlights', and 'About Common Fund'.

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10

With over 100,000 analysed samples Genos is the global leader in high-throughput glycomics



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	6,000	2,000
PTSD	600	600
Total	33,100	42,500

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11

Mining the gold from big glycomics datasets



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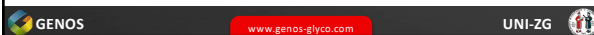
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12

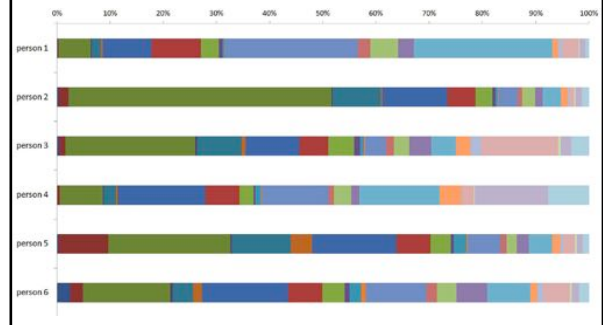
Glycomics is becoming a mainstream science

High-impact papers in 2017- 2019	IF	RANK	High-impact papers in 2017- 2019	IF	RANK
Suchre et al, Nature Communications 8:14357	12.4	3/64	Krištić et al, Nature Chemical Biology, 14:516.	15.1	5/290
Shen et al, Nature Communications 8:447	12.4	3/64	Šimurina et al, Gastroenterology, 154:1320	20.8	1/80
Benedetti et al, Nature Communications 8:1483	12.4	3/64	Clerc, Gastroenterology, 155:829-843	20.8	1/80
Lauc et al, Nature Communications 9:2916	12.4	3/64	Monaghan, Gastroenterology, published online	20.8	1/80
Bermingham et al, Diabetes Care, 41:79-87	13.4	5/143	Josipović et al, Nucl Acid Res, published online	11.1	14/298
Juszcak et al, Diabetes Care, dc180422	13.4	5/143	Klarić et al, Science Advances, in press	12.8	4/69
Menni et al, Circulation Research, 117.312174	14.0	1/70	Peng et al, Circulation, published online	23.1	1/65



13

Glycome composition differs significantly between individuals

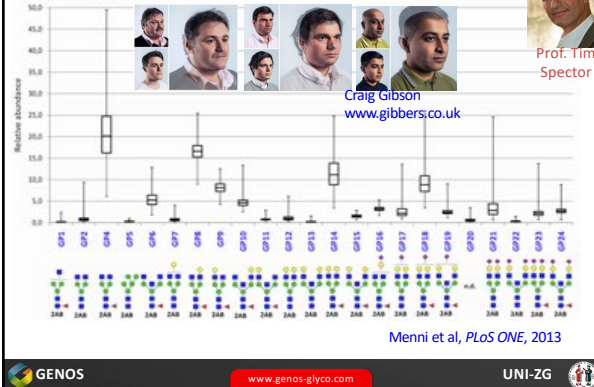


Lauc et al, Front Genet, 2014

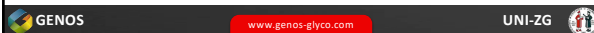


14

Levels of individual glycans in the IgG glycome are heritable between 30% and 80%

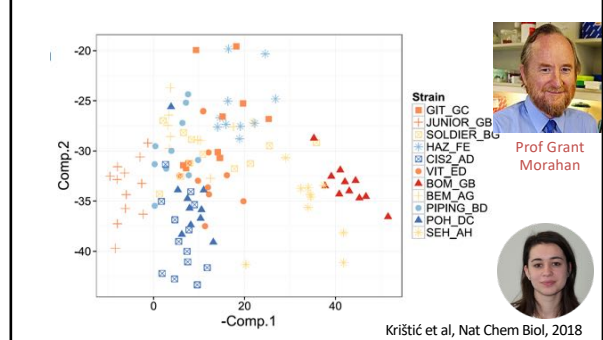


Menni et al, PLoS ONE, 2013

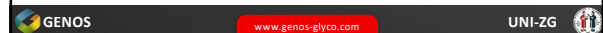


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IgG glycans are chemical structures that are being inherited as complex traits

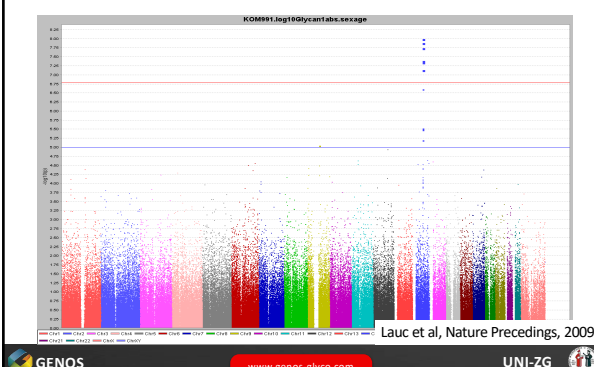


Krištić et al, Nat Chem Biol, 2018



16

Genome-wide association (GWA) studies can be used to map genes involved in glycosylation

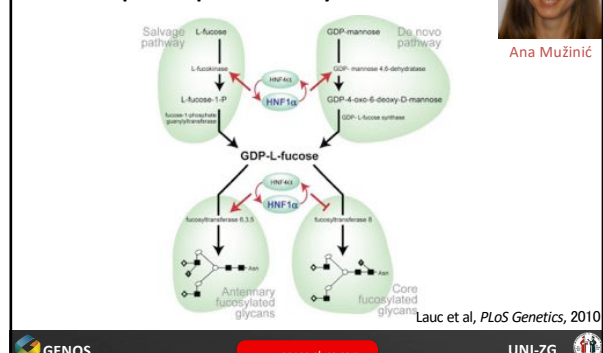


Lauc et al, Nature Precedings, 2009



17

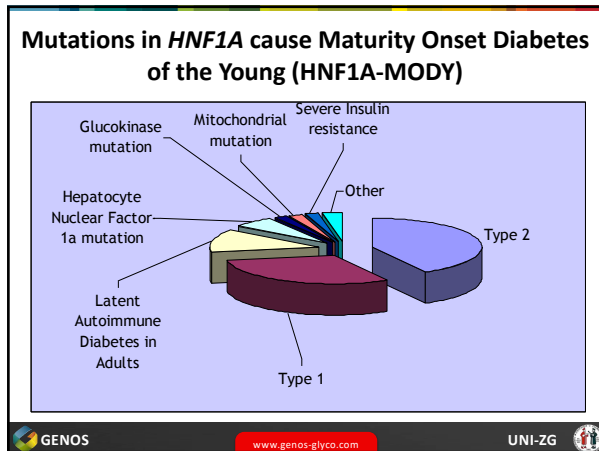
The first GWAS study of human glycome identified HNF1A as a master regulator of plasma protein fucosylation



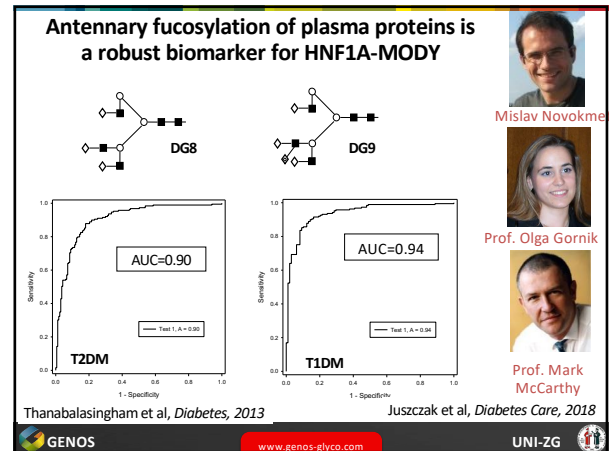
Lauc et al, PLoS Genetics, 2010



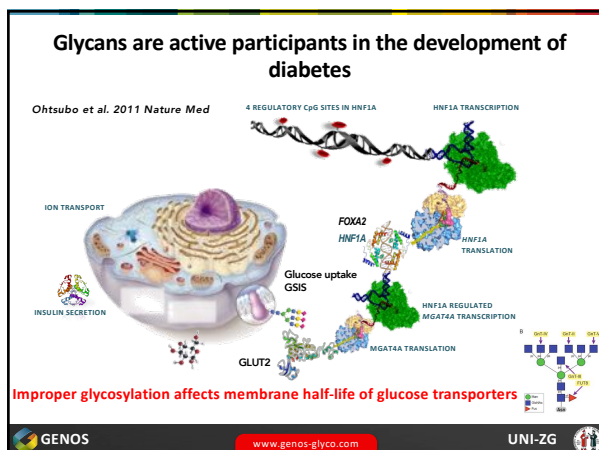
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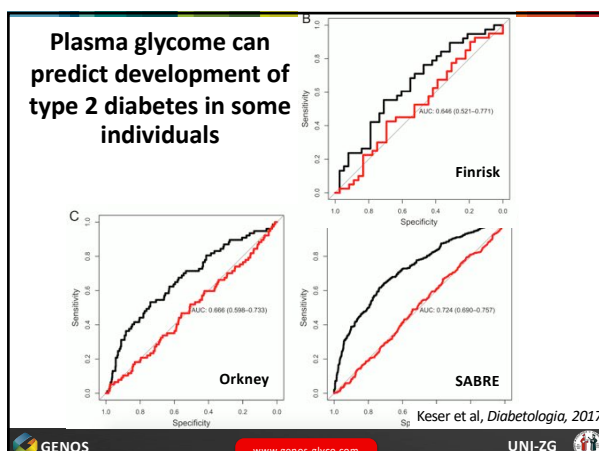
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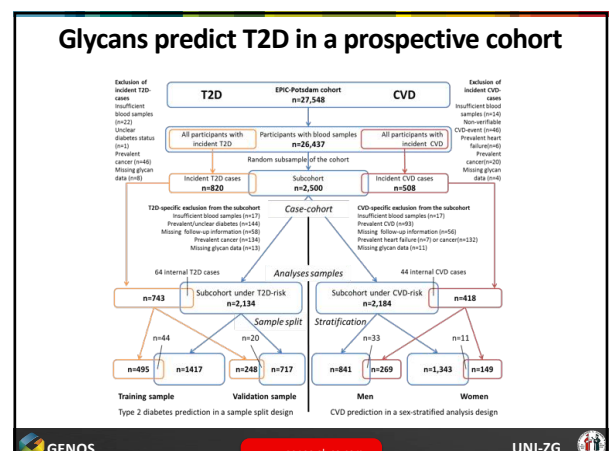
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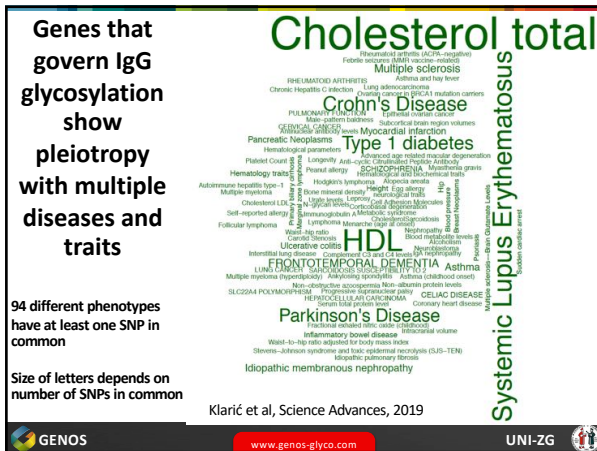
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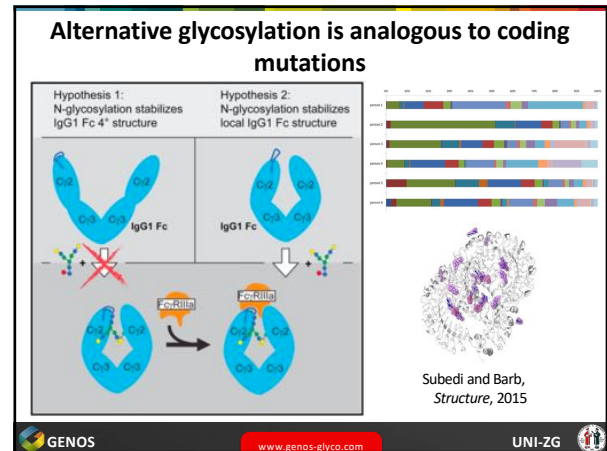
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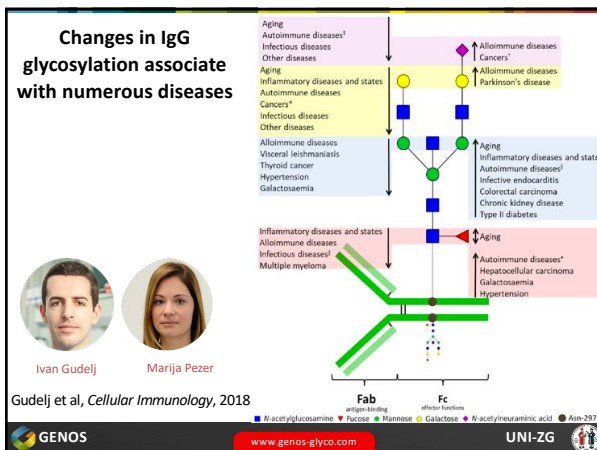
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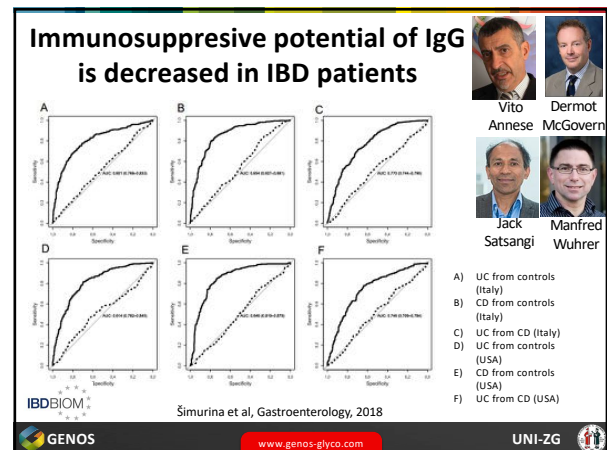
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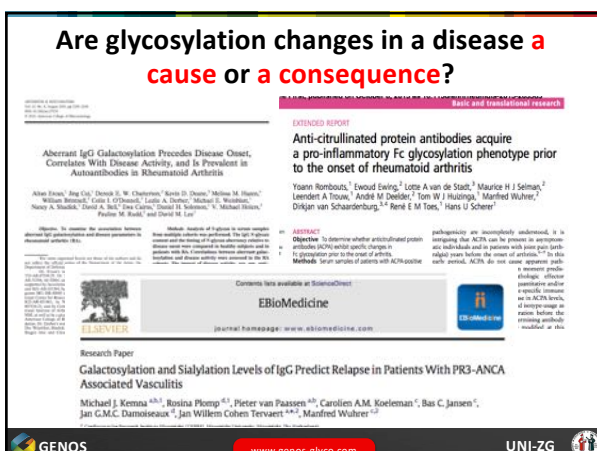
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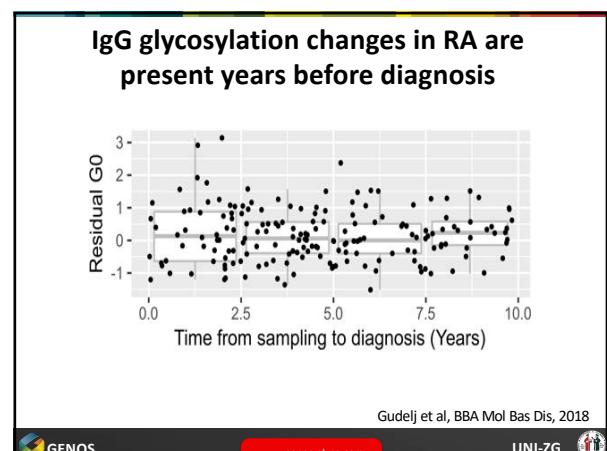
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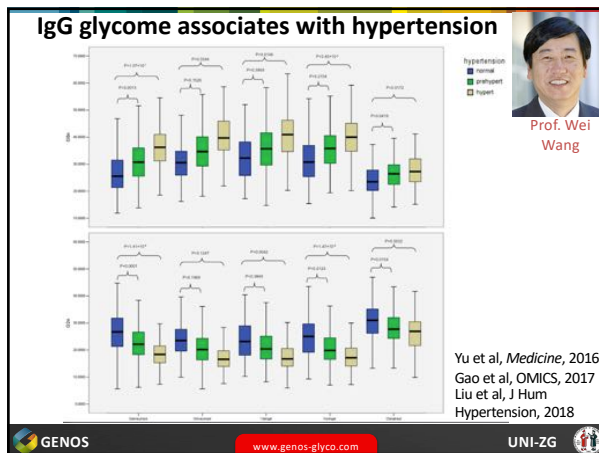
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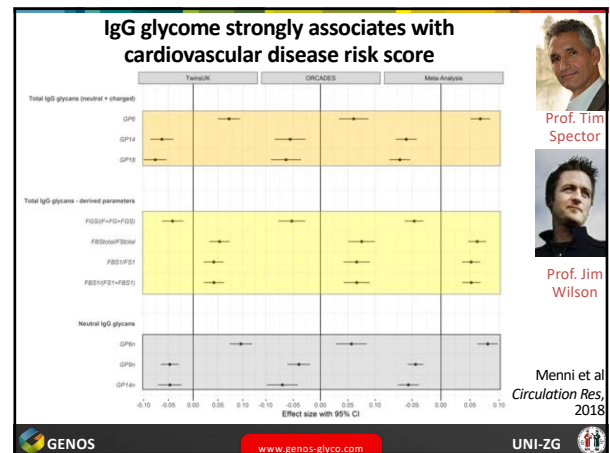
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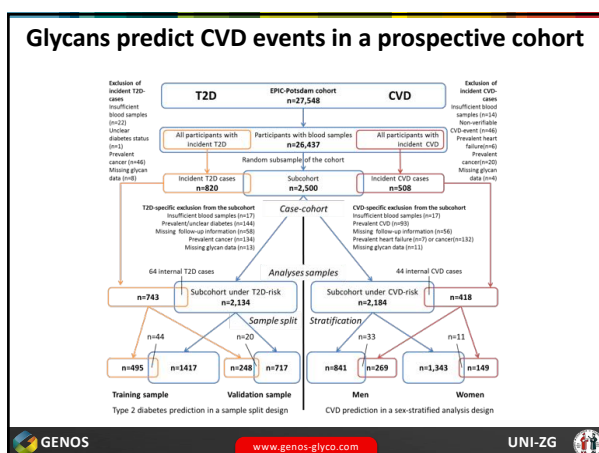
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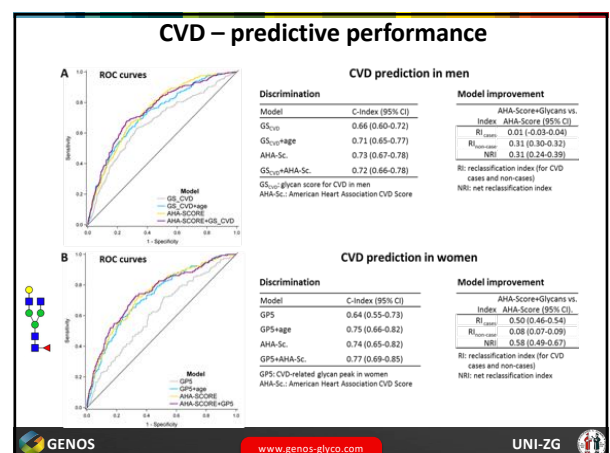
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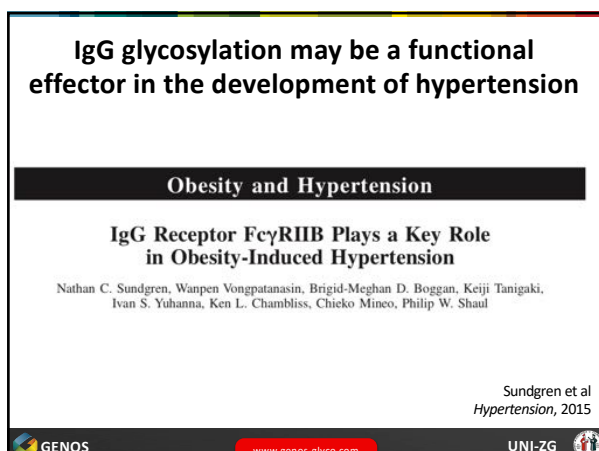
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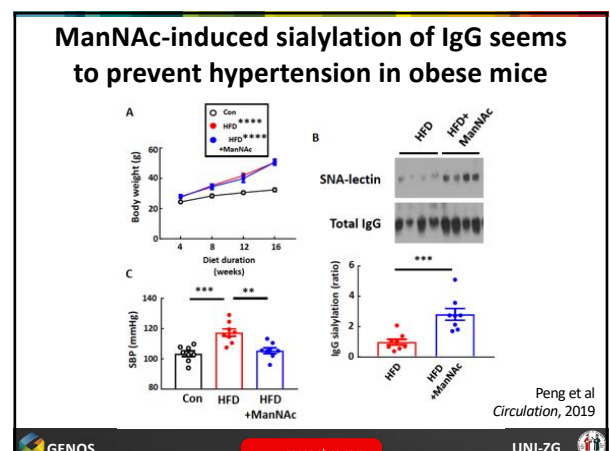
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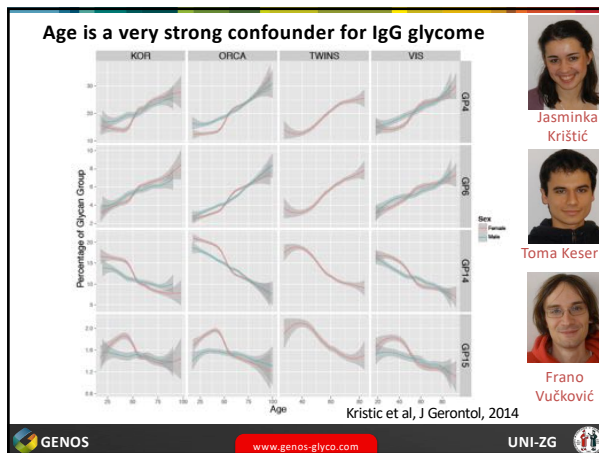
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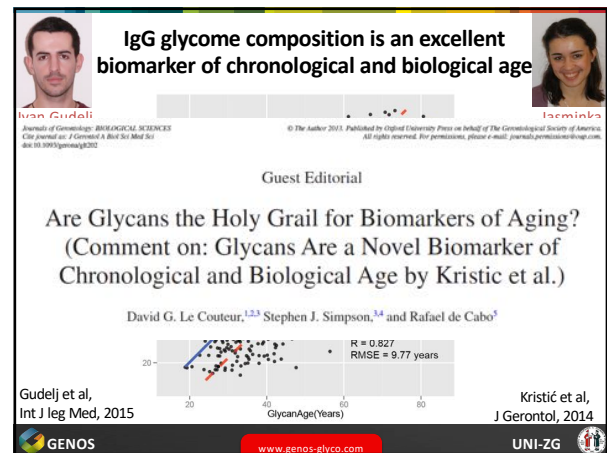
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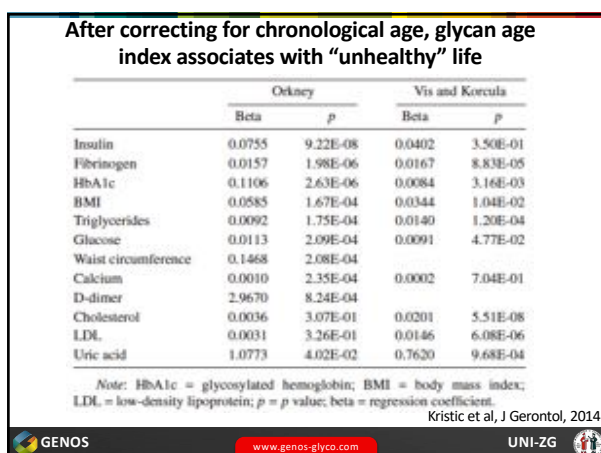
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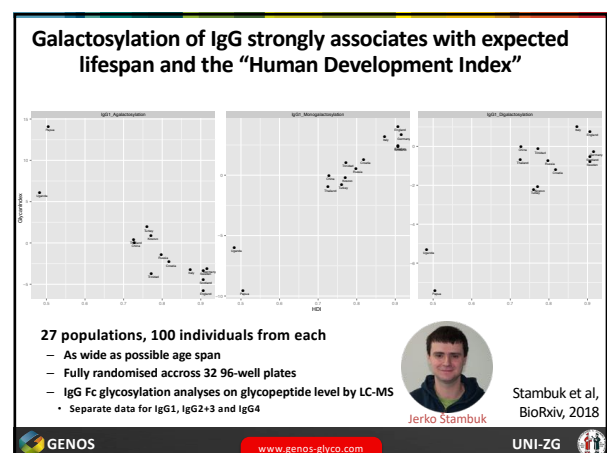
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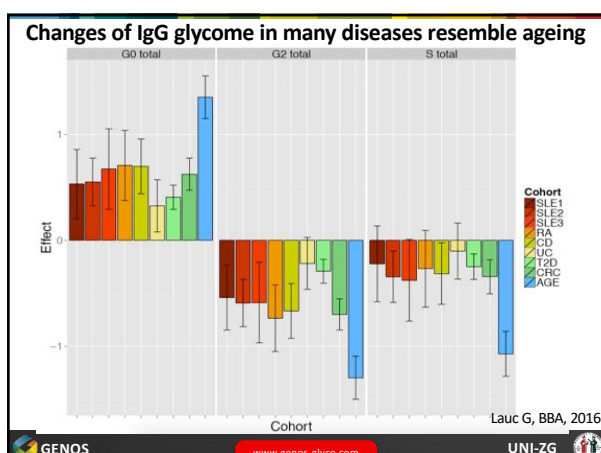
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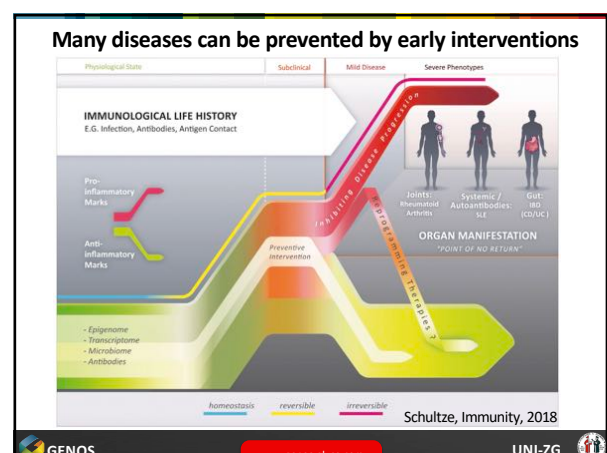
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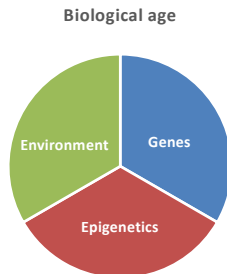


47



48

What contributes to the dynamics of changes in the biological age?



49

How can I change my biological age?

Factors contributing to biological age of person A



Factors contributing to biological age of person B



50

GlycanAge test is available commercially



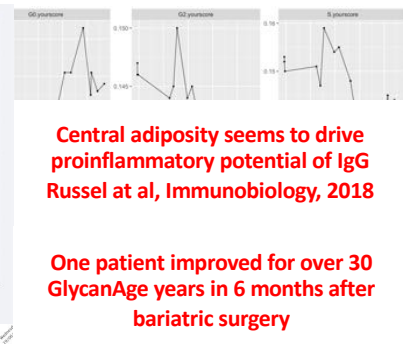
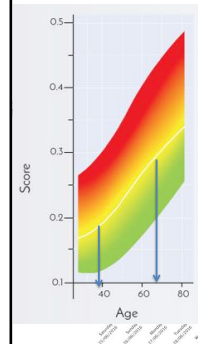
St. Catherine
SPECIALTY HOSPITAL



www.glycanage.com

51

How can we change our glycans?



52

Lifestyle interventions can change IgG glycome composition even in older adults



Prof. Eline
Slagboom

www.impactaging.com

AGING, January 2016, Vol. 8 No 1

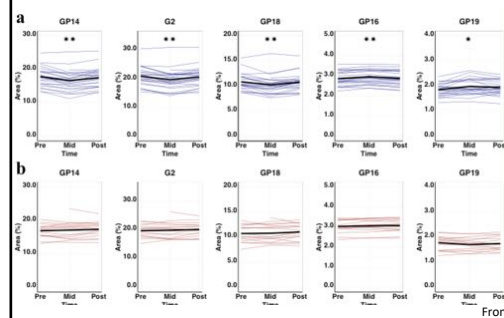
Research Paper

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

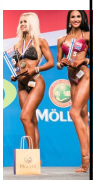
Ondine van de Rest^{1,2}, Bianca A.M. Schutte^{2,3}, Joris Deelen^{2,3}, Stephanie A.M. Stassen³, Erik B. van den Akker^{2,4}, Diana van Heemst³, Petra Dibbets-Schneider⁵, Regina A. van Duijten-van der Veen¹, Milou Kelderman¹, Thomas Hankemeier⁶, Simon P. Mooijaart³, Jeroen van der Grond⁵, Jeanine J. Houwing-Duistermaat⁷, Marian Beekman², Edith J.M. Feskens¹, and P. Eline Slagboom²

53

Intensive exercise makes IgG glycome more pro-inflammatory, but only transiently



Prof. Markus
Perola

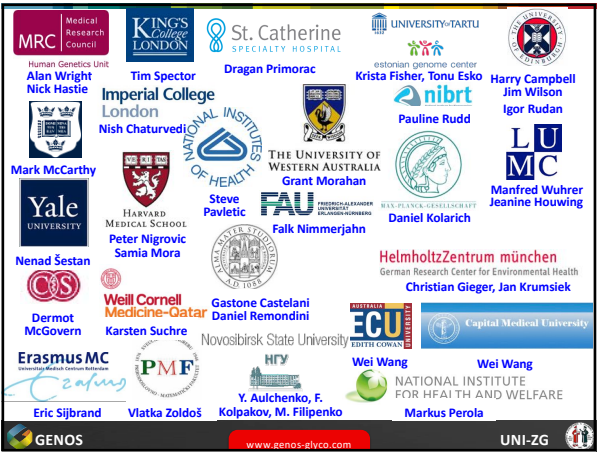


Sarin,
Front. Immunol, 2019

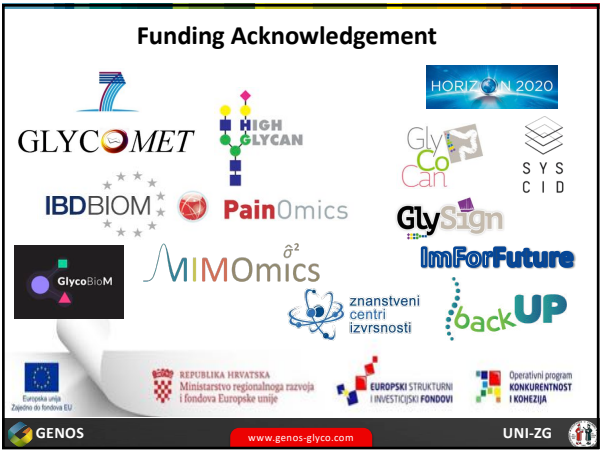
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56



57