



Visokoprotlačna glikomika u molekularnoj dijagnostici

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Genos Glycoscience Research Laboratory



WO2014203010; US2016103137, WO2012042020; WO2011015944; WO2009044213

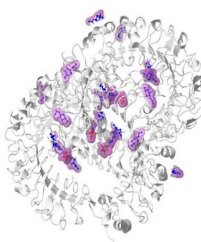
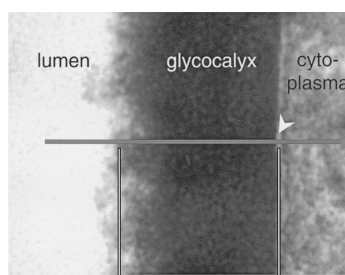
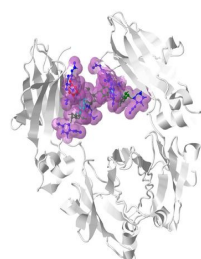


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Glycans are important structural component of nearly all proteins

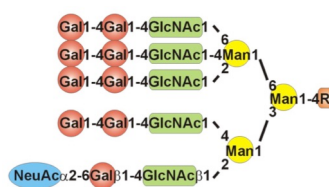
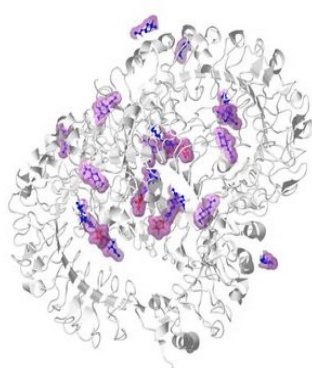
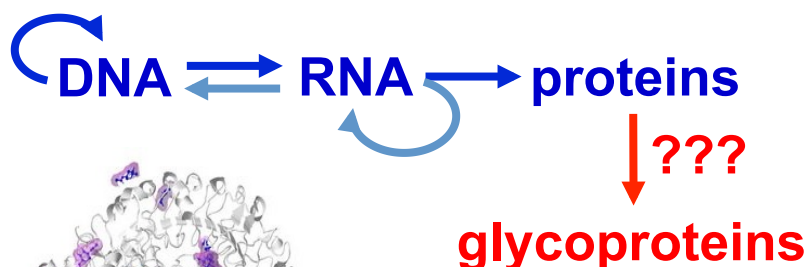


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Genome does not contain templates for synthesis
of glycan parts of glycoproteins



Cohort	Plasma glycome	IgG Glycome	
10001 Dalmatian	2,000	4,000	
Orcades	2,000*	2,000	
TwinsUK	4,000	4,500	
KORA	–	2,000	
SABRE	2,000	–	
Global population study	–	2,700	
FINNRISK	–	1,200	
Estonian biobank	–	1,300	
China	1,000	1,000	
CRC	2,000*	2,000	
IBD	3,000	5,700	
SLE	–	1,200	
Type 1 Diabetes	1,000	1,000	
Type 2 Diabetes	–	3,000	
Down syndrome	–	800	
PTSD	600	600	
Total	17,600	33,000	* Analysed in NIBRT

Mining the gold from big glycomics datasets



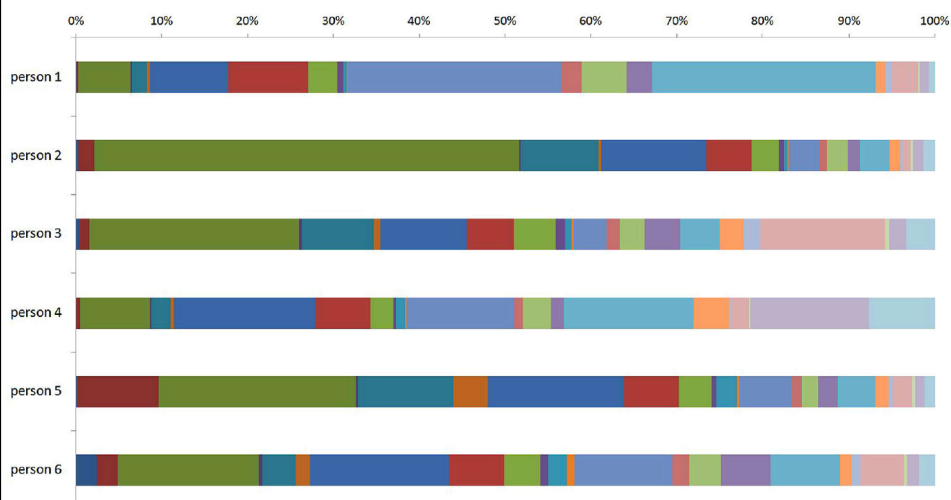
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Composition of IgG glycome differs significantly between individuals



Lauc et al, Front Genet, 2014

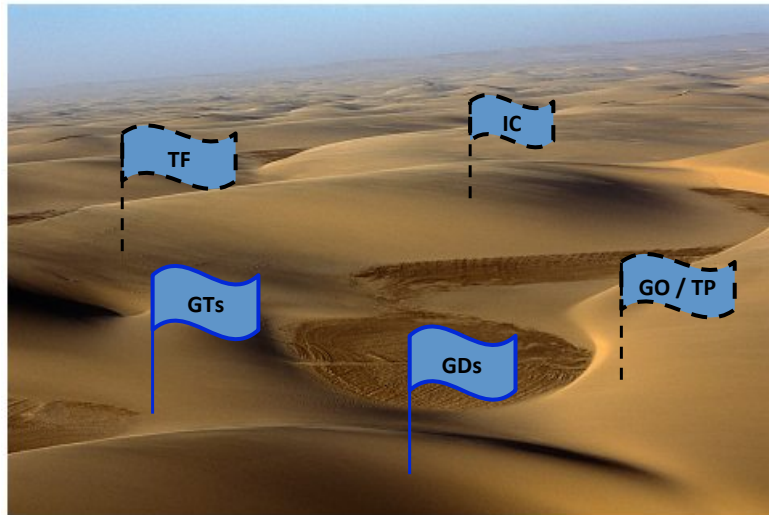
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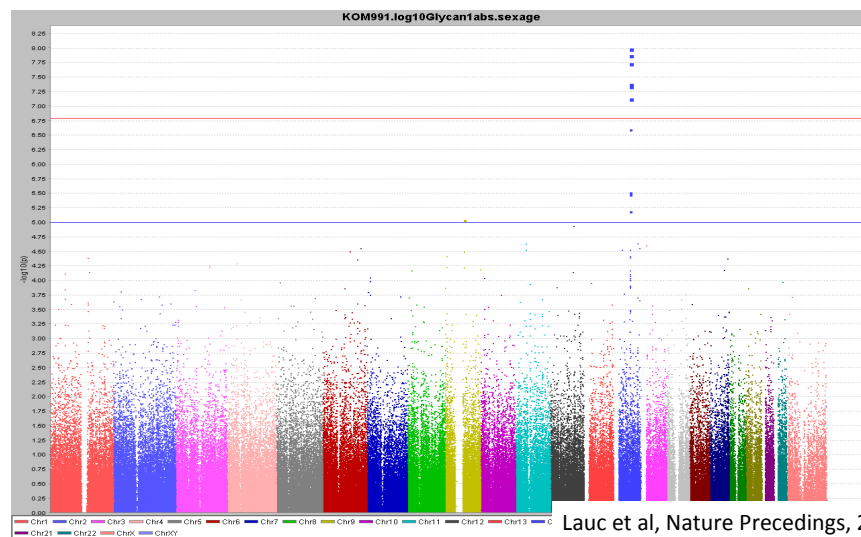
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The majority of genes that affect IgG glycosylation are still not known



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

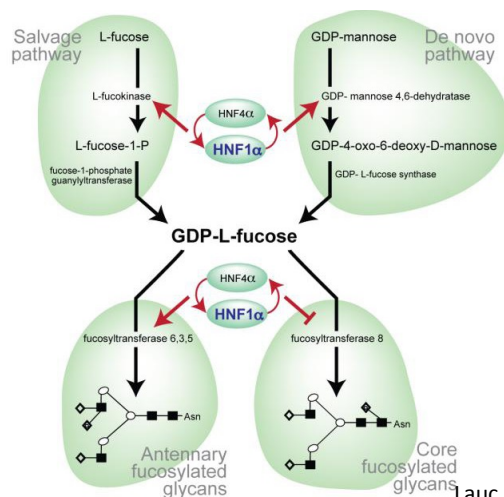


Lauc et al, Nature Precedings, 2009

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



Ana Mužinić

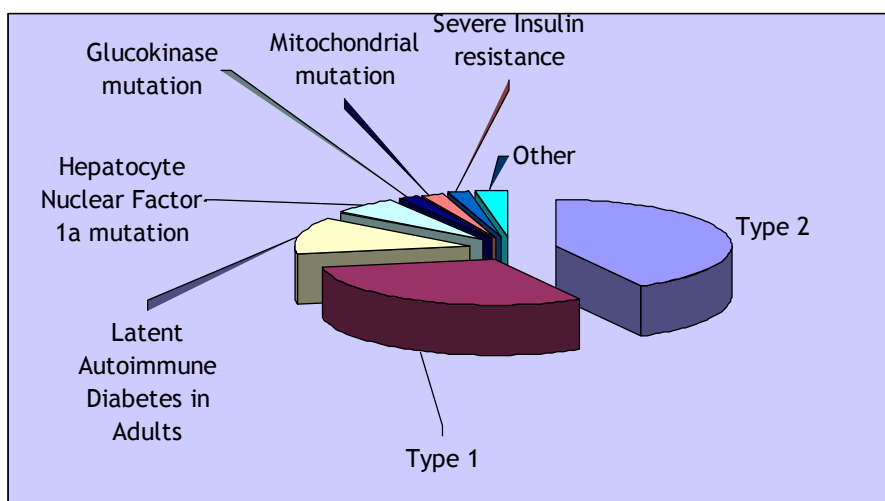
Lau et al, *PLoS Genetics*, 2010

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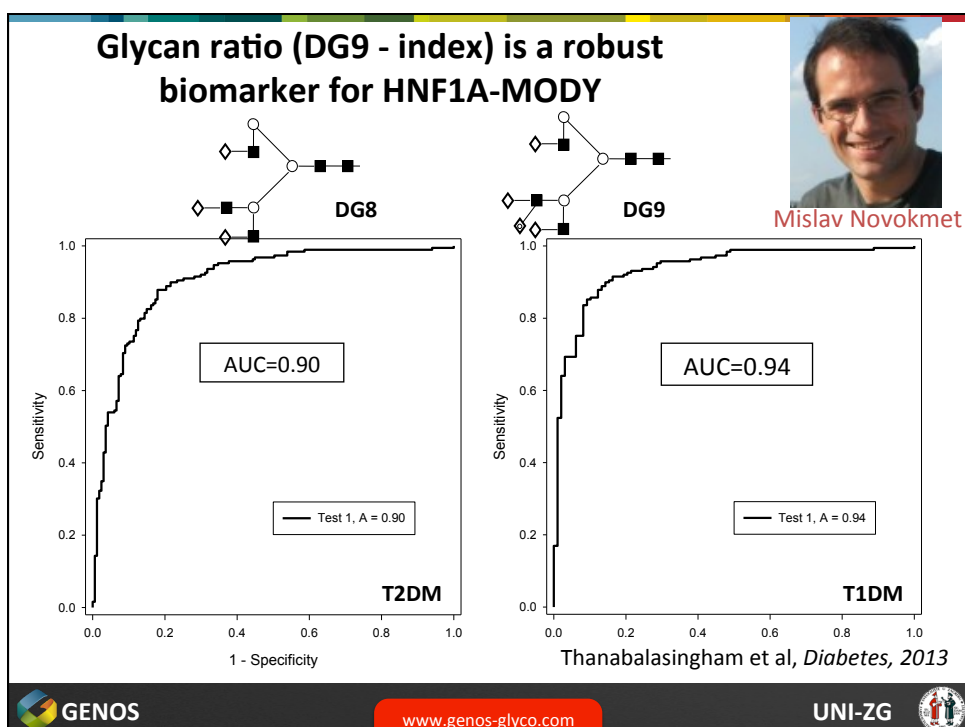
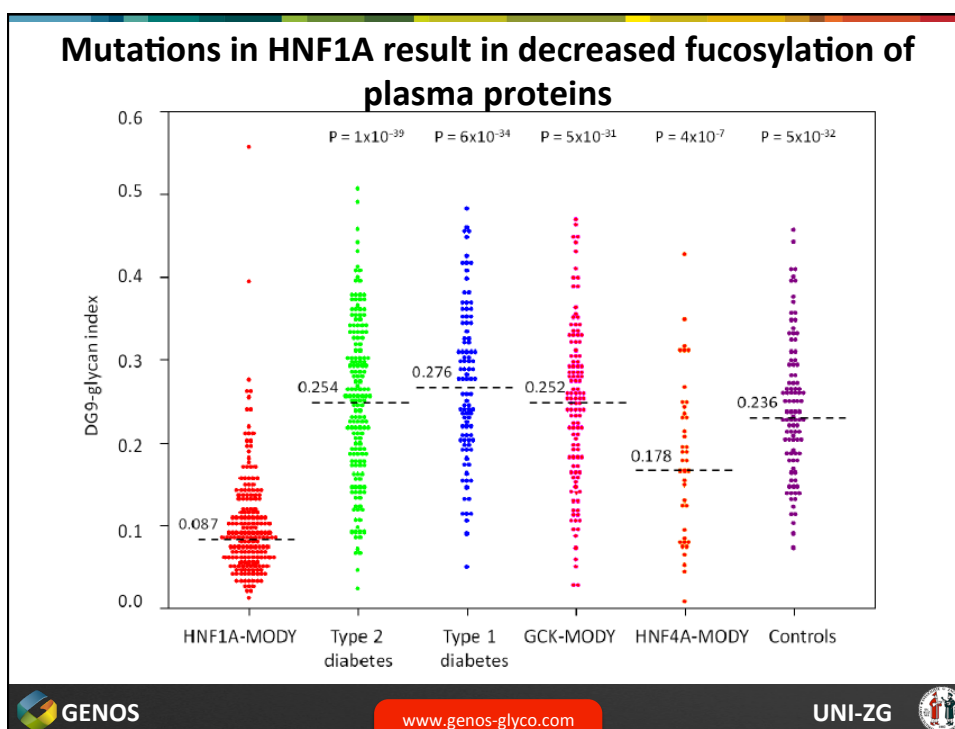
Mutations in *HNF1A* cause Maturity Onset Diabetes of the Young (HNF1A-MODY)



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Analysis in a prospective setting

- 1100 young onset diabetics recruited in Zagreb and Oxford
- Plasma glycome analysed by UPLC
- Sequencing of the entire HNF1a gene
 - 32 mutations (11 known to be pathological)
- Classification



Prof. Olga Gornik



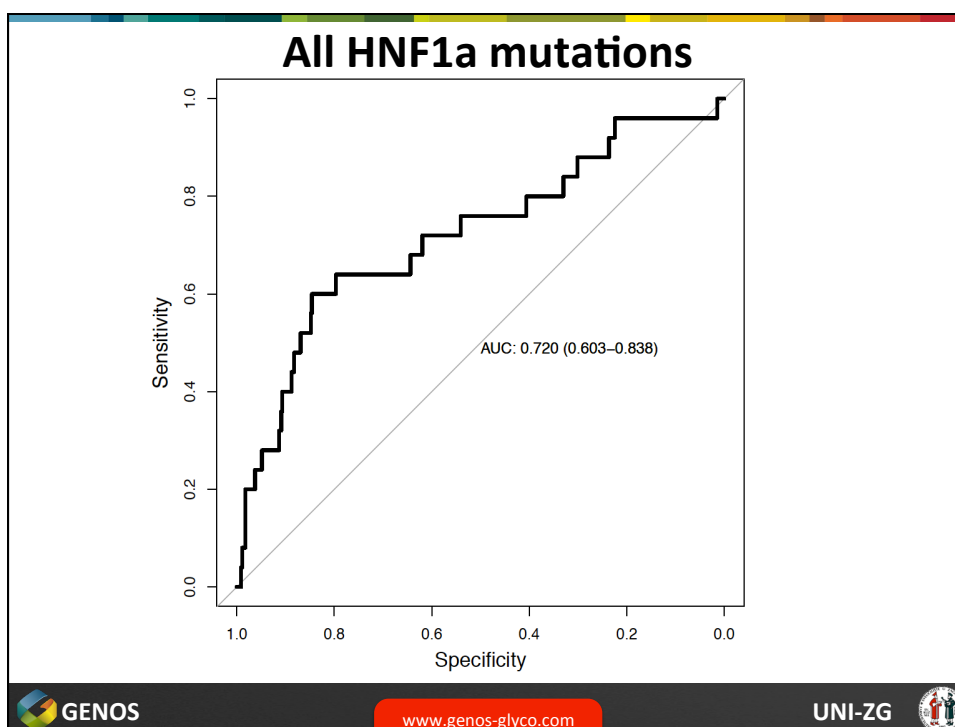
Frano Vučković



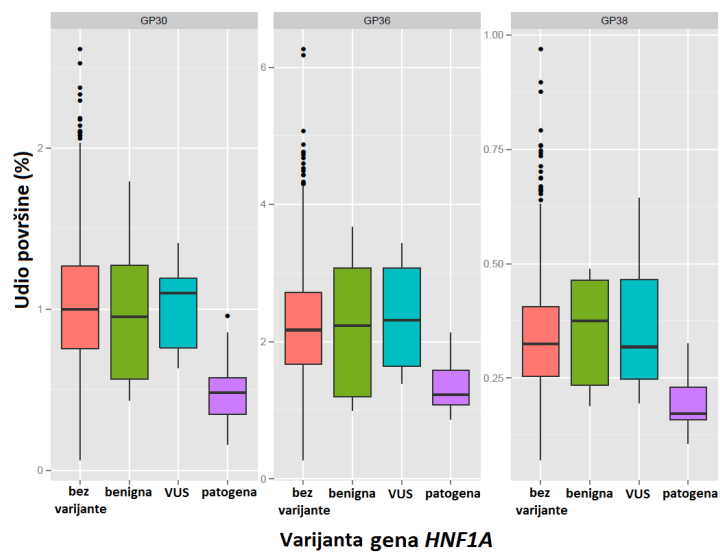
Tamara Pavić

EFSD European Foundation for the Study of Diabetes

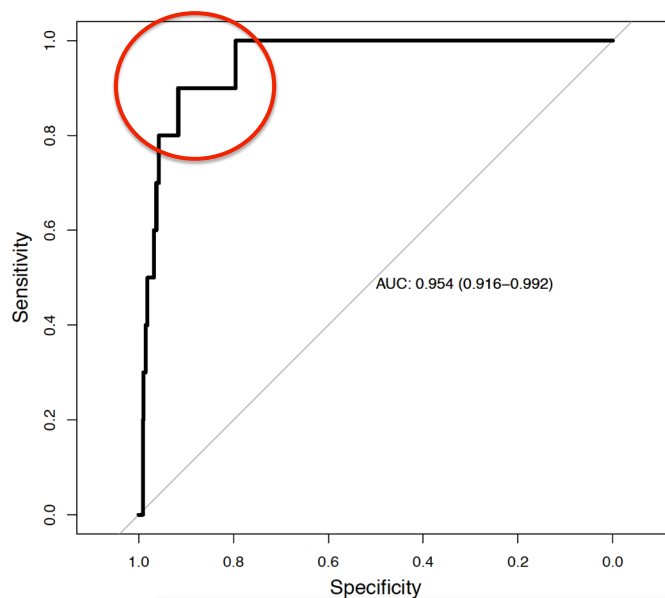
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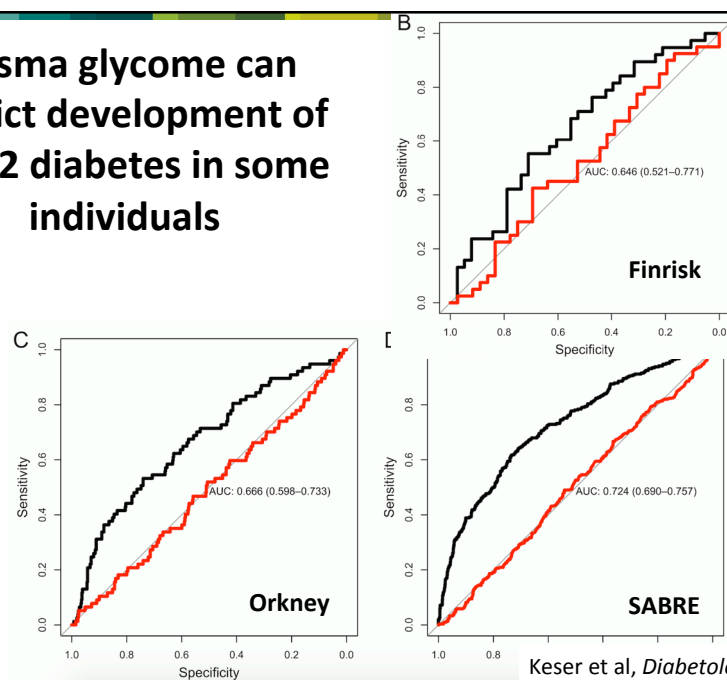
Glycan profiling can identify pathogenic mutations



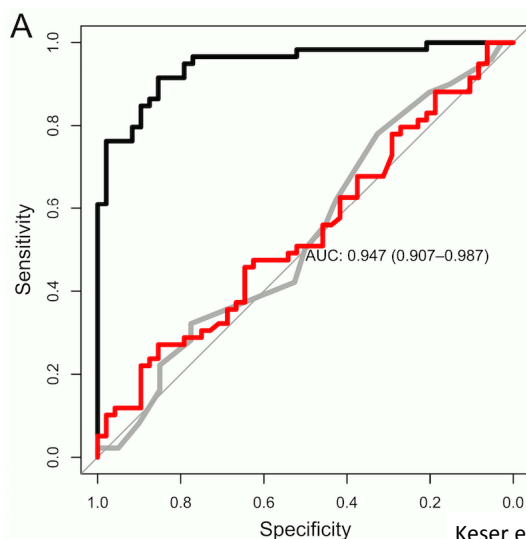
Known pathogenic mutations

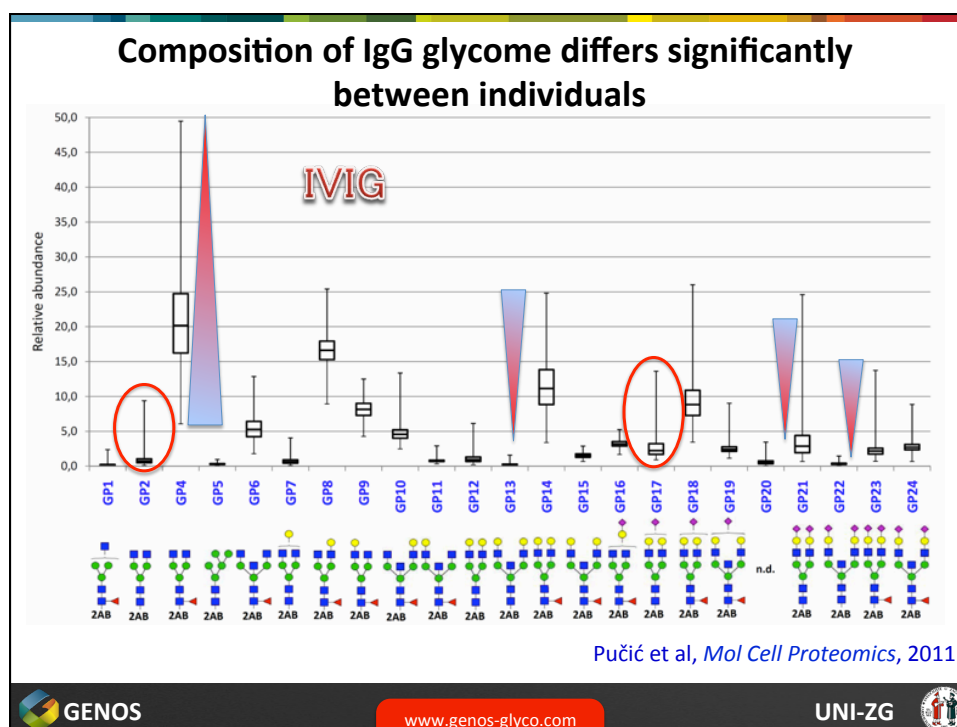
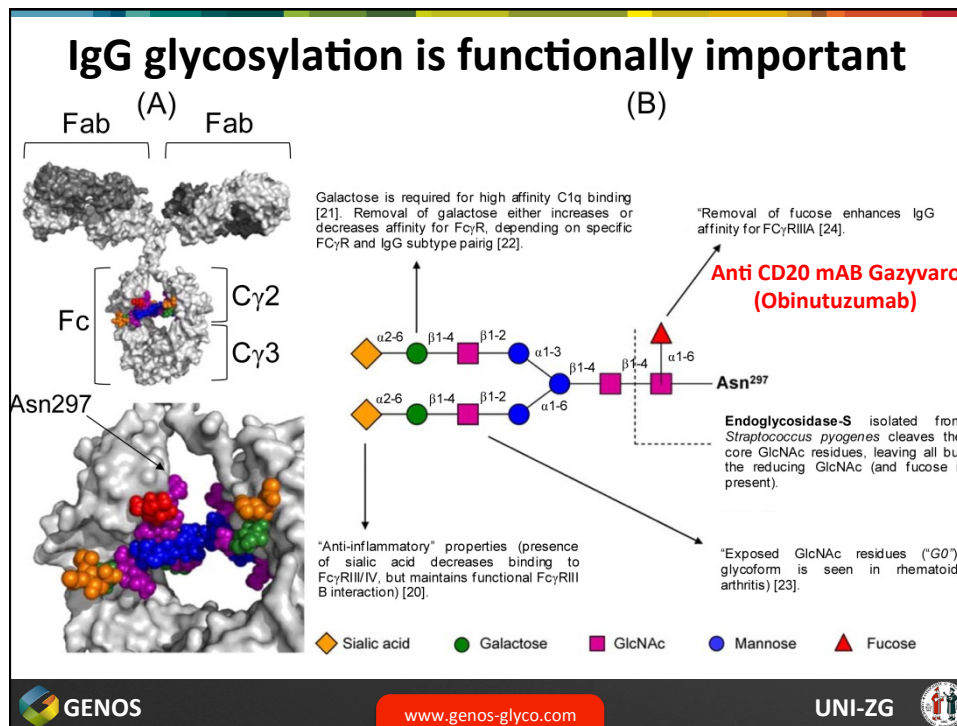


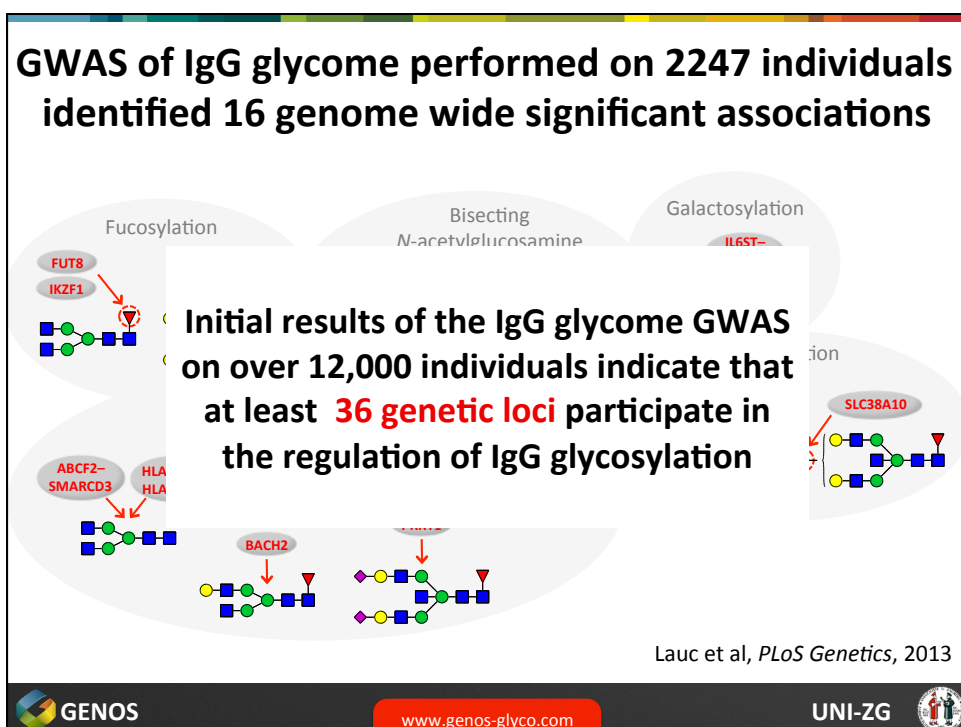
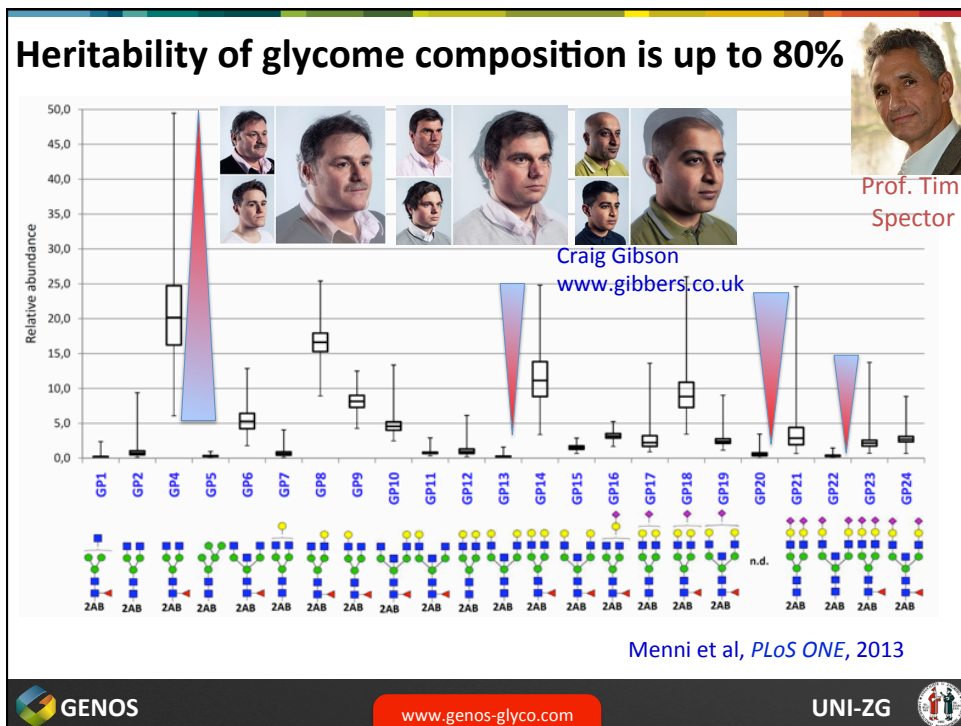
Plasma glycome can predict development of type 2 diabetes in some individuals

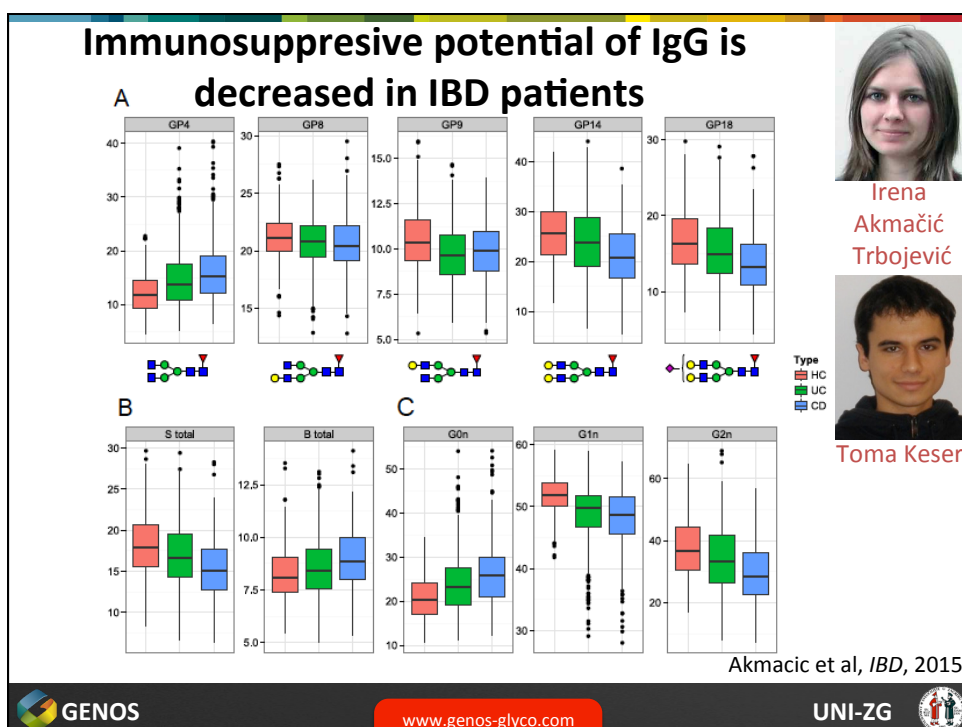
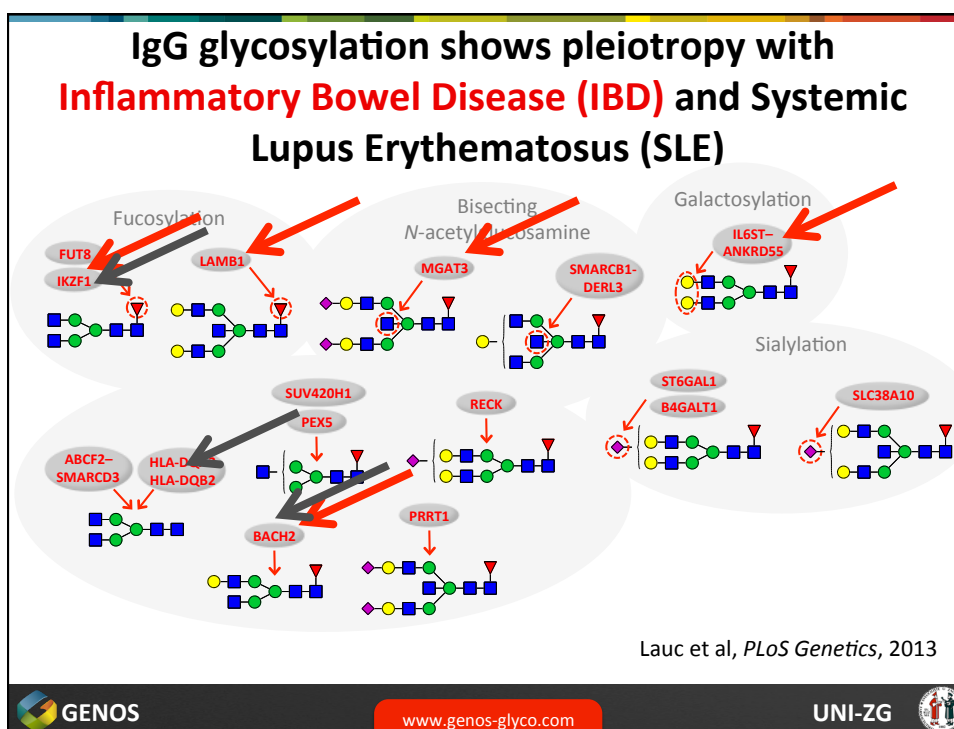
Keser et al, *Diabetologia*, 2017

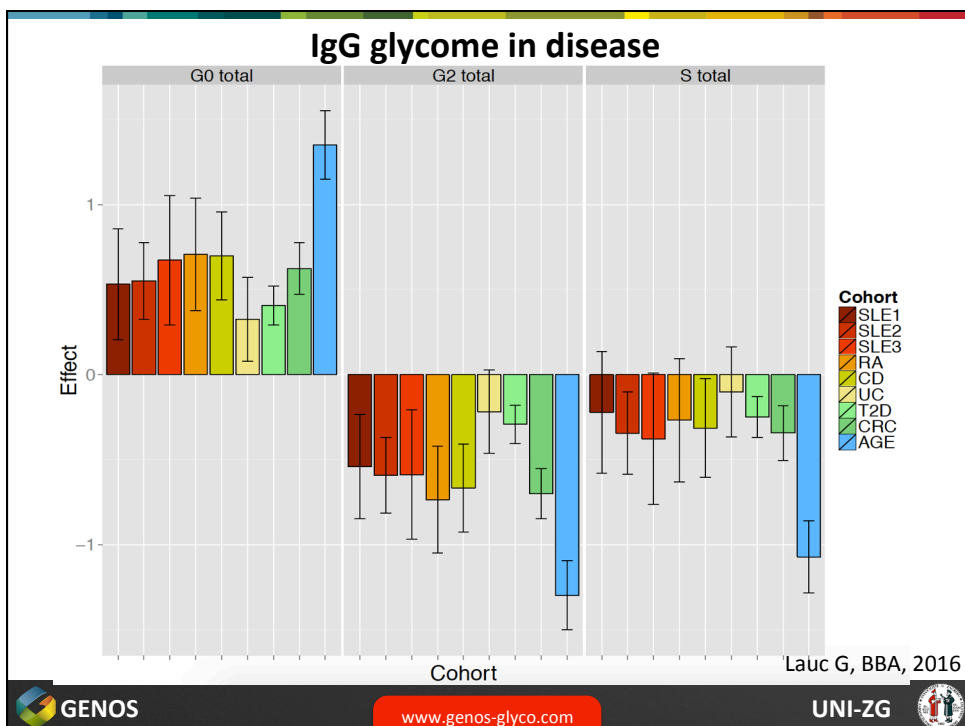
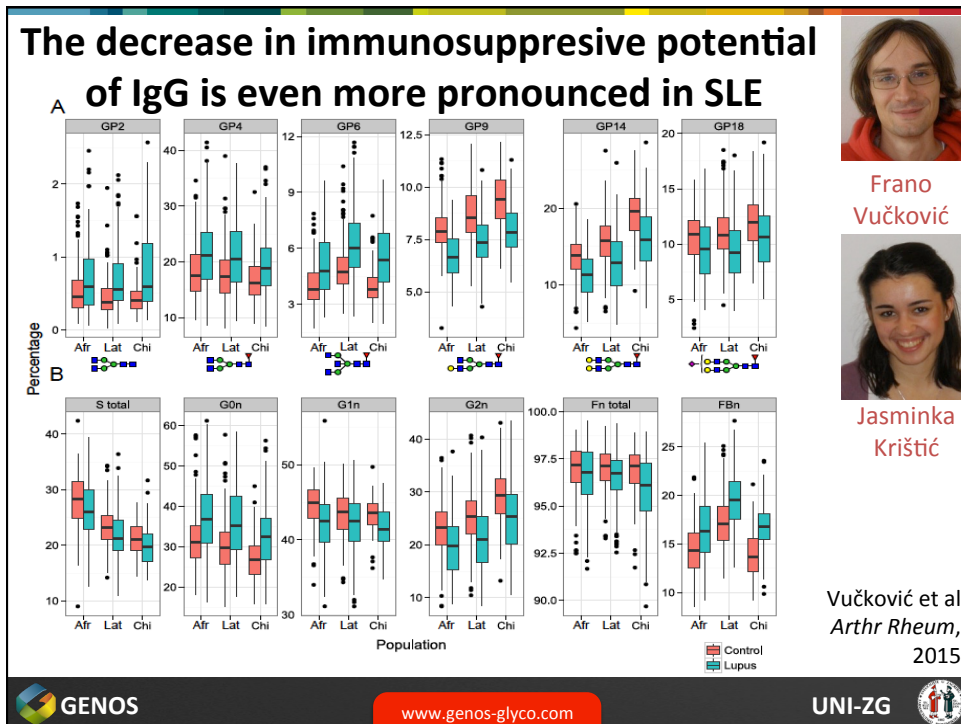
Plasma glycome is a very good predictor for hyperglycemia in acute disease

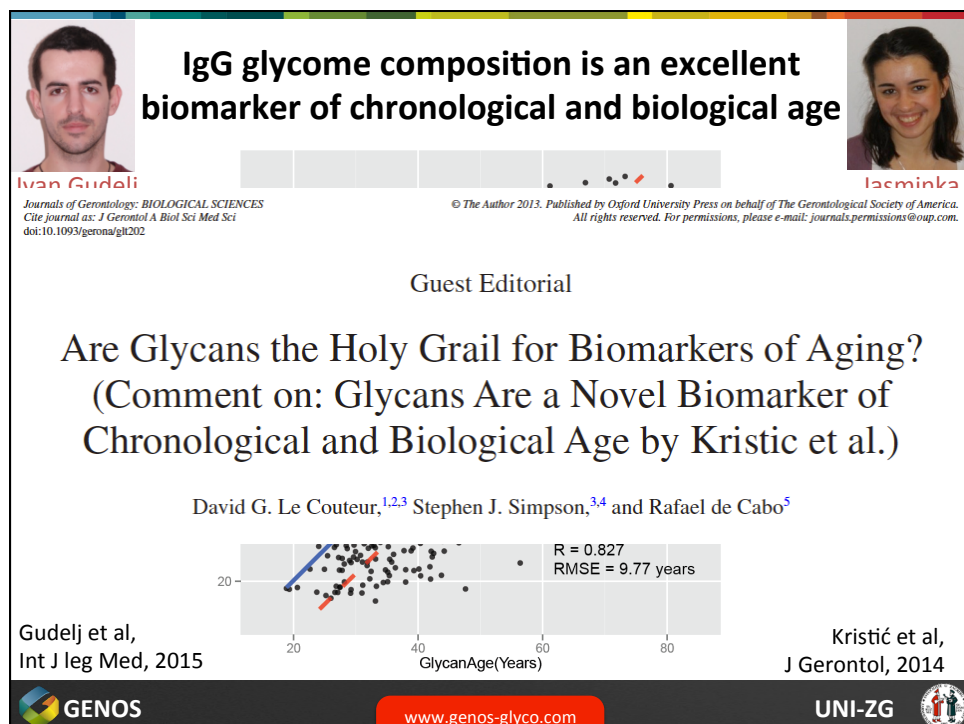
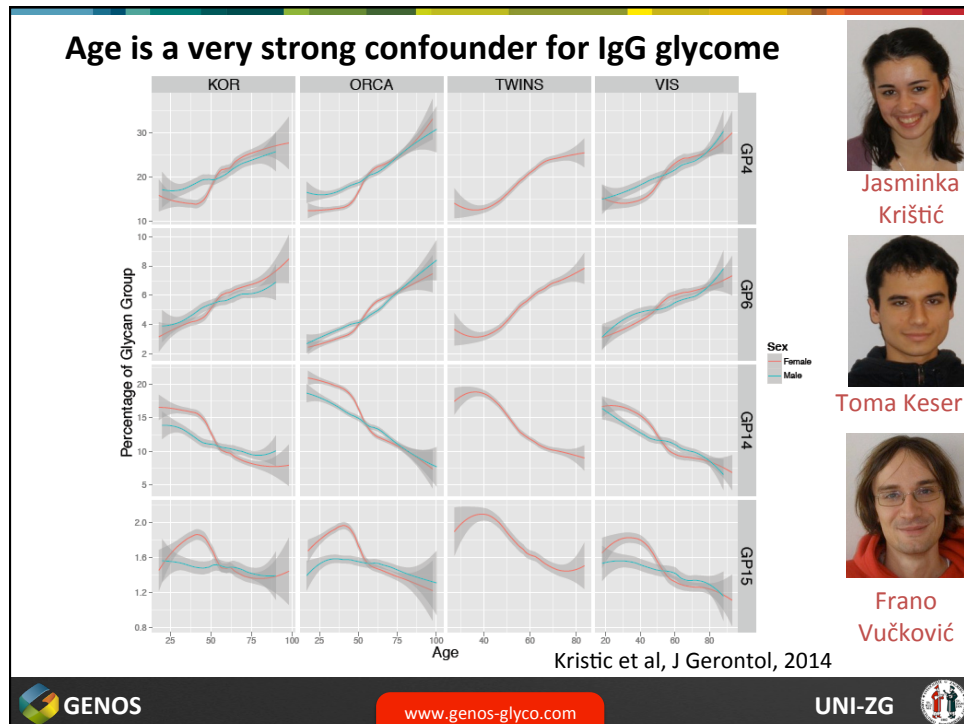
Keser et al, *Diabetologia*, 2017











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.

Kristic et al, J Gerontol, 2014

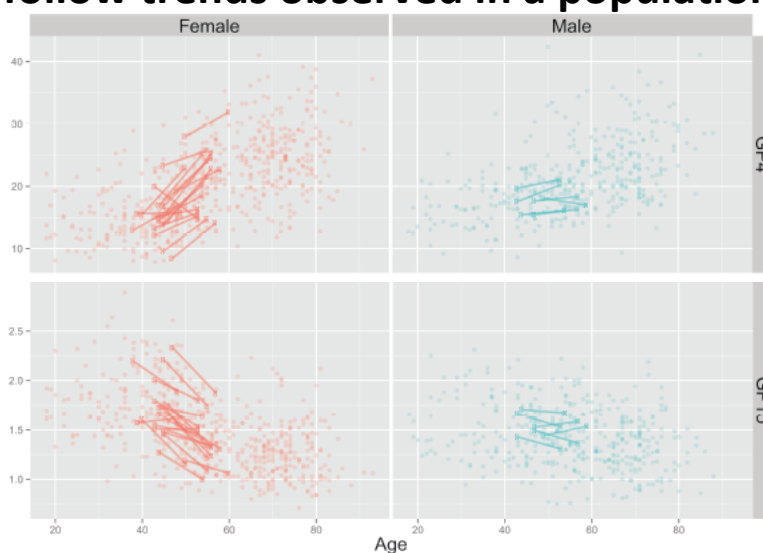


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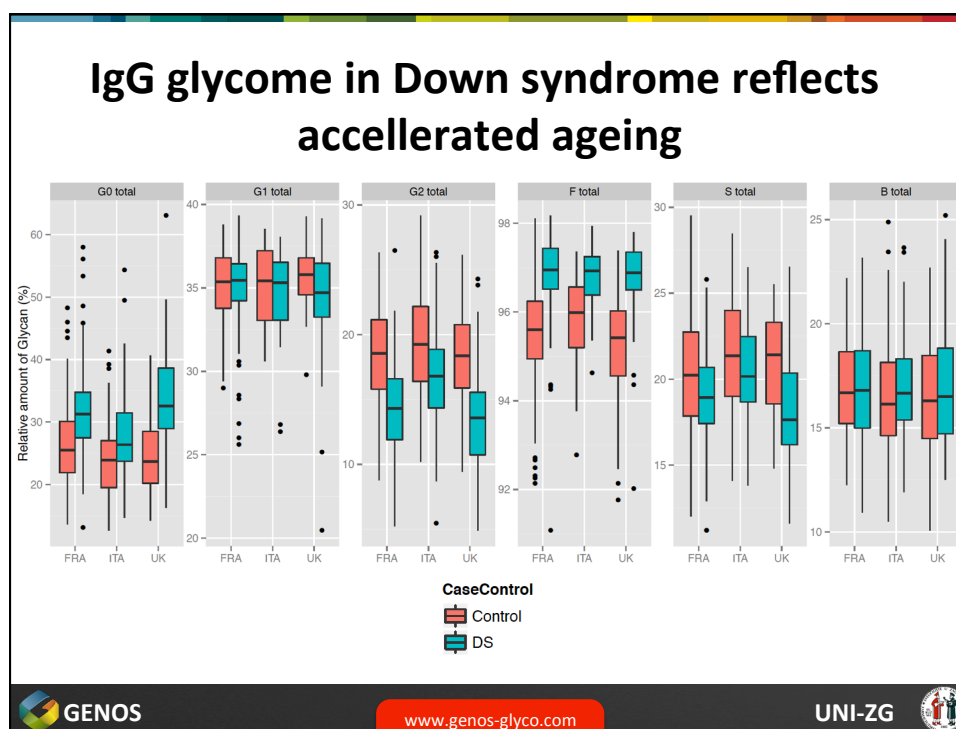
Changes within an individual generally follow trends observed in a population



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



Prof. Markus Perola

frontiers
in Physiology

ORIGINAL RESEARCH
published: 10 January 2017
doi: 10.3389/fphys.2016.00689

Check for updates

The Effects of Intensive Weight Reduction on Body Composition and Serum Hormones in Female Fitness Competitors

Juha J. Hulmi^{1,2*}, Ville Isola¹, Marianna Suonpää³, Nea J. Järvinen¹, Marja Kokkonen⁴, Annika Wennerström^{5,6}, Kai Nyman⁷, Markus Perola^{6,8,9}, Juha P. Ahtiainen¹ and Keijo Häkkinen¹

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IgG glycome is better predictor of mortality, than NMR biomarkers or methylation

Marioni et al. *Genome Biology* (2015) 16:25
DOI 10.1186/s13059-015-0584-6



Prof. Ian Deary

Genome Biology

RESEARCH Open Access

DNA methylation age of blood predicts all-cause mortality in later life

Riccardo E Marioni^{1,2,3†}, Sonia Shah^{3,4†}, Allan F McRae^{3,4†}, Brian H Chen^{5,6†}, Elena Colicino^{7†}, Sarah E Harris^{1,2}, Jude Gibson⁸, Anjali K Henders⁹, Paul Redmond¹⁰, Simon R Cox^{1,10}, Alison Pattie¹⁰, Janie Corley¹⁰, Lee Murphy⁸, Nicholas G Martin⁹, Grant W Montgomery⁹, Andrew P Feinberg^{11,12}, M Daniele Fallin^{11,13}, Michael L Multhaup¹¹, Andrew E Jaffe^{13,14}, Roby Joeanes^{5,15,16}, Joel Schwartz^{2,17}, Allan C Just⁷, Kathryn L Lunetta^{5,18}, Joanne M Murabito^{5,19}, John M Starr^{1,20}, Steve Horvath^{21,22†}, Andrea A Baccarelli^{7,17†}, Daniel Levy^{2,6†}, Peter M Visscher^{1,3,4†}, Naomi R Wray^{3,4†} and Ian J Deary^{1,10†}

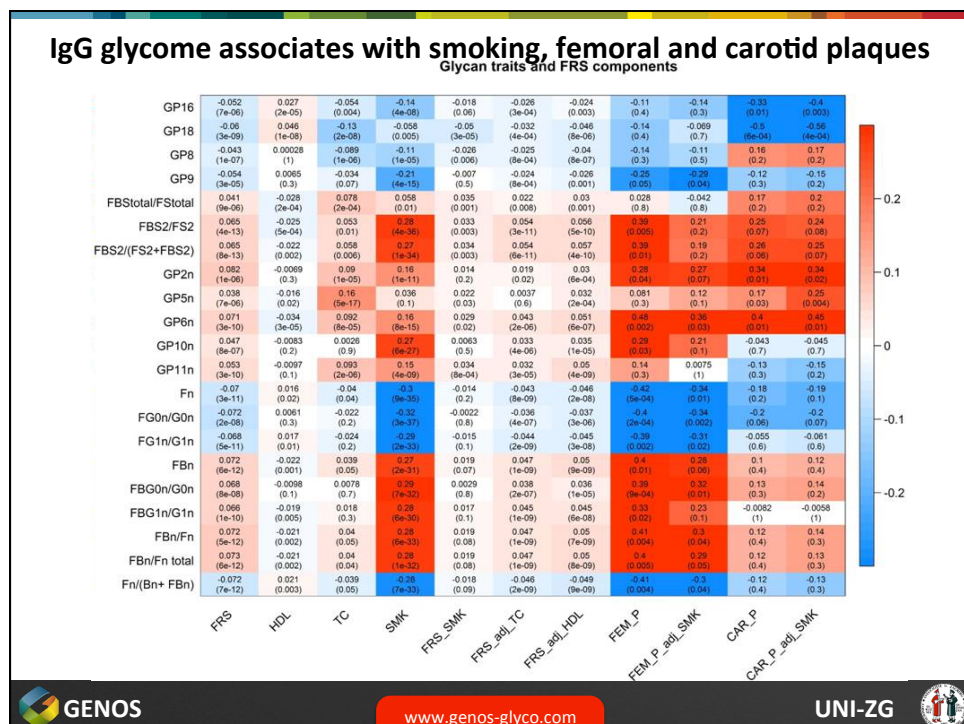
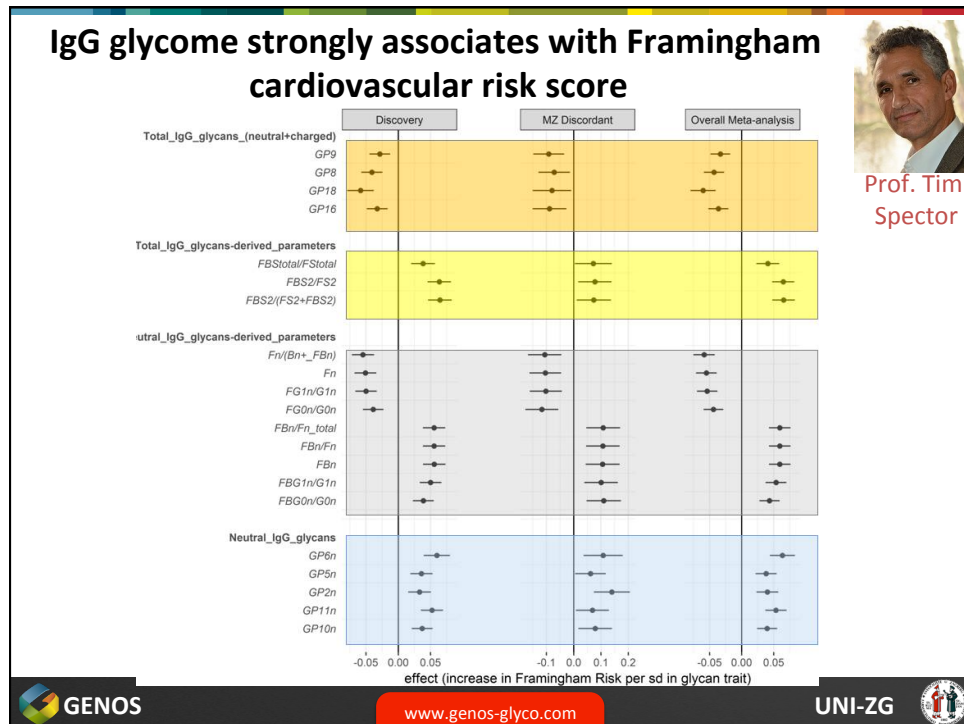
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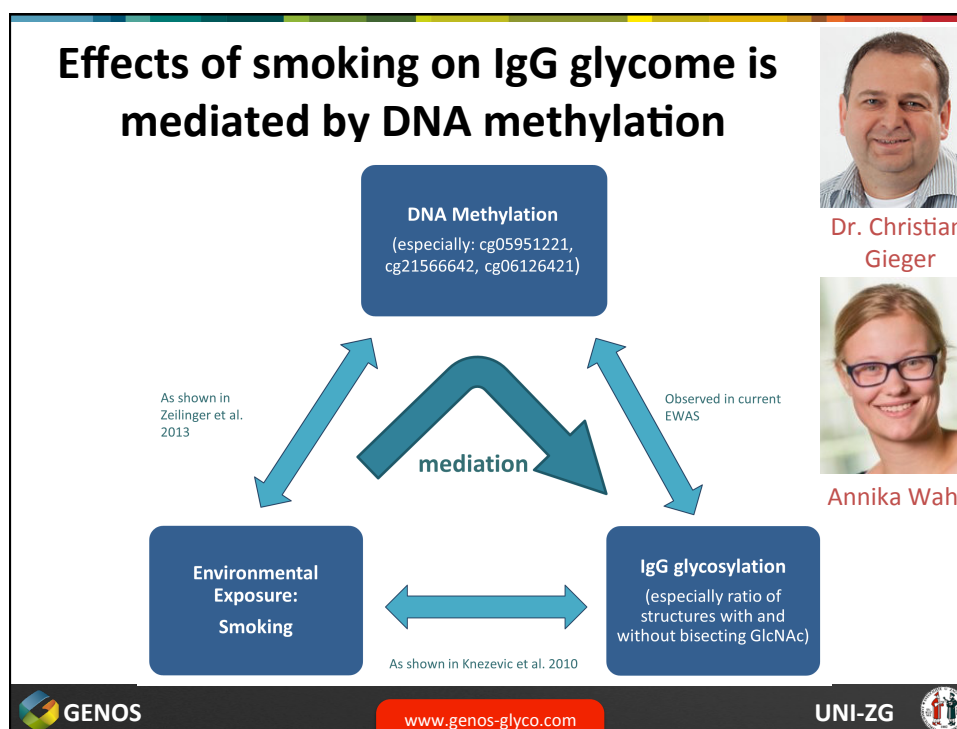
PLOS MEDICINE

Biomarker Profiling by Nuclear Magnetic Resonance Spectroscopy for the Prediction of All-Cause Mortality: An Observational Study of 17,345 Persons

Krista Fischer^{1,3*}, Johannes Kettunen^{2,3,4,5}, Peter Würtz^{2,4,5*}, Toomas Haller¹, Aki S. Havulinna³, Antti J. Kangas⁴, Pasi Soininen^{4,5}, Tõnu Esko^{1,6,7,8,9,10}, Mari-Liis Tammesoo¹, Reedik Mägi¹, Steven Smit¹, Aarno Palotie^{2,6,11}, Samuli Ripatti^{2,11}, Veikko Salomaa³, Mika Ala-Korpela^{4,5,12†}, Markus Perola^{1,2†}, Andres Metspalu^{1,13†}

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