Genetic Analysis of Protein *N*-Glycosylation

Jennifer E. Huffman

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The University of Edinburgh
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Lay Summary

Over half of all human proteins have one or more complex sugar chains, known as glycans, attached to their surface. The arrangement of glycans is important for determining how individual proteins function within the body and genetic changes which dramatically affect these glycans are associated with serious diseases. Glycan profiles are also known to vary with age and in many medical conditions. This has attracted interest in their use for diagnosis and as targets for new treatments. Until recently, it has not been possible to measure glycans in a high-throughput manner, so investigations into the genetics underlying glycan manufacture and composition could not be done. In collaboration with groups at various European centres, this project aimed to investigate the genes influencing glycan structure and abundance through the use of genome-wide association studies (GWAS). These association studies are a method for determining if a particular region of the genome is associated with variation in a measured outcome. This outcome may be disease cases versus unaffected controls, or a continuous variable such as blood pressure, glucose levels, or here, plasma concentrations of a particular glycan. However, the results of these association studies do not inform about causality and generally require laboratory follow-up before conclusions about biology can be drawn.

Glycans were removed from all proteins within an individual plasma sample and 46 glycan structures measured. This was done for plasma samples collected from over 3,500 individuals from four European populations which also had genetic information available. GWAS was done for each of these 46 glycan structures. Statistically significant results were found in genes coding for proteins with known roles in glycosylation (such as enzymes that add a specific sugar at a particular location on a glycan chain). One unexpected and important result was the association of a gene whose protein product (HNF1A) is responsible for regulating the concentrations of many proteins produced in the liver. Laboratory work by collaborators found HNF1A to be a “master regulator” of several enzymes involved in addition of the sugar fucose to plasma glycans. Genetic changes in HNF1A are known to cause a form of diabetes (MODY3) which requires a different treatment than type-2 or type-1 diabetes. An important finding was that glycans could act as “biomarkers” to separate people with MODY3 from T2D and T1D.

After the success of the total plasma protein glycan GWAS, it was thought that more biologically interpretable associations may be found from the investigation of glycans isolated from a single protein. The addition of glycans to immunoglobulin G (IgG) influences which immune response is activated in the body when exposed to foreign molecules. To identify genetic networks that govern glycosylation of IgG, IgG glycans were measured in over 2000 individuals from the same populations as before. GWAS of the 77 glycan structures identified 16 statistically significant gene regions. Four of these contained genes with known functions in glycan synthesis, while the remainder were completely new findings.

Finally, several different methods for high-throughput analysis of glycans have been developed in the past few years but have not been thoroughly compared. To this end, comparison of IgG glycan structures generated by all four methods in the same dataset of 1,201 individuals was done by correlation of the raw trait values and by comparison of the results of GWAS studies. All methods performed well but have different advantages and disadvantages.

This work shows that new genetic regions that control glycan structure of plasma proteins can be identified using GWAS and shows the potential of glycans for disease diagnostics. It also provides some guidelines for method selection for future studies of glycans.

Abstract

The majority of human proteins are post-translationally modified by covalent addition of one or more complex oligosaccharides (glycans). Alterations in glycosylation processing are associated with numerous diseases and glycans are attracting increasing attention both as disease biomarkers and as targets for novel therapeutic approaches.

Using a recently developed high performance liquid chromatography (HPLC) method for high-throughput glycan analysis, genome-wide association studies (GWAS) of 33 directly measured and 13 derived *N*-glycan features were performed in 3533 individuals from four European isolated populations. Polymorphisms at six loci were found to show genome-wide significant association with plasma concentrations of *N*-glycans. Several of these gene products have well characterised roles in glycosylation, however, *SLC9A9* and *HNF1A* were two of the novel findings. Subsequent work performed by collaborators found HNF1A to be a "master regulator" of genes involved in the fucosylation of plasma *N*-glycans. Additionally, this work led to the discovery that *N*-glycans could act as biomarkers to discriminate HNF1A-MODY from type 1 and type 2 diabetes mellitus (T1D, T2D) patients.

After the success of the total plasma *N*-glycan GWAS, it was thought that stronger and more biologically interpretable associations may be found from the investigation of *N*-glycans isolated from a single protein. Glycosylation of immunoglobulin G (IgG) influences IgG effector function by modulating binding to Fc receptors. To identify genetic networks that govern IgG glycosylation, *N*-linked IgG glycans were quantitated using ultra performance liquid chromatography (UPLC) in 2247 individuals from the same four European populations from the previous study. GWAS of the 77 *N*-glycan measures identified 15 loci with a p-value$<5x10^{-08}$. Four loci contained genes encoding glycosyltransferases, while the remaining loci contained genes that have not previously been implicated in protein glycosylation. However, most have been associated with autoimmune and inflammatory conditions and/or hematological cancers.

Several high-throughput methods for the analysis of *N*-glycans have been developed in the past few years but thorough validation and standardization of these methods is required before significant resources are invested in large-scale studies. To this end, four of these methods were compared, UPLC, multiplexed capillary gel electrophoresis (xCGE), and two mass spectrometric (MS) methods, for quantitative profiling of *N*-glycosylation of plasma IgG in a subset of 1201 individuals recruited from two of the cohorts used in the previous GWAS studies. A "minimal" dataset was compiled of *N*-glycan structures able to be

measured by all four methods. To evaluate their accuracy, correlations were calculated for each structure in the minimal dataset. Additionally, GWAS was performed to test if the same associations would be observed across methodologies. Chromatographic methods with either fluorescent or MS-detection yielded slightly stronger associations than MS-only and xCGE, but at the expense of lower levels of throughput. Advantages and disadvantages of each method were identified, which should aid in the selection of the most appropriate method for future studies.

This work shows that it is possible to identify new loci that control glycosylation of plasma proteins using GWAS and the potential of *N*-glycans for biomarker development. It also provides some guidelines for methodology selection for future studies of *N*-glycans.

Declaration

I declare that I composed this thesis and the contributions of others to this work are clearly indicated. This work has not been submitted for any other degree or professional qualification.

Jennifer E. Huffman

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List of Abbreviations

%	percent
ºC	Degrees Celsius
1000G	1000 Genomes
2-AB	2-aminobenzamide
2-PB	2-picoline-borane
ABS	Arthrobacter ureafaciens sialidase
ACN	acetonitrile
ADCC	antibody dependent cell-mediated cytotoxicity
ADHD	attention-deficit hyperactivity disorder
APS	ammonium peroxodisulphate
APTS	aminopyrene-1,3,6-trisulfonic acid
BMI	Body Mass Index
CAaq	citric acid monohydrate
CDCV	Common disease-common variant
CE	Capillary Electrophoresis
CGE (xCGE)	Capillary Gel Electrophoresis (Multiplex CGE)
Cl-CCA	4-chloro-α-cyanocinnamic acid
cm	centimetre
CNTF	ciliary neurotrophic factor
CNV	Copy Number Variant
CV	column volume(s)
DMSO	dimethylsulfoxide
DNA	Deoxyribonucleic acid
ESI	Electrospray ionization
EtOH	Ethanol
FA	formic acid
Fab	fragment antigen-binding region
Fc	fragment crystallisable region
FLR	Fluorescence
eV	Electronvolt(s)
GAD	Glutamic Acid Decarboxylase
GGT	Gamma-glutamyl transferase
GlcNAc	N-acetylglucosamine
GWAS	Genome-wide Association Study
GU	glucose units
h	hour(s)
h^2	heritability
HILIC	Hydrophilic interaction liquid chromatography
HNF1A	Hepatic Nuclear Factor 1 Alpha
HPLC	High Performance Liquid Chromatography
HWE	Hardy-Weinberg equilibrium
Hz	Hertz
IBD	Inflammatory bowel disease
IBD	Identity by Descent
IBS	Identity by State
i.d.	internal diameter
IgG	Immunoglobulin G
IL2	interleukin 2
IL6	interleukin 6
indel	insertion deletion

IPA	isopropanol
kb	kilobase(s)
kV	kilovolt(s)
l	litre(s)
LD	linkage disequilibrium
LIF	Laser-Induced Fluorescence
LIF	leukaemia inhibitory factor
LLS	Leiden Longevity Study
nl	nanolitre(s)
nanoLC	nano Liquid Chromatography
M	molar
mg	milligram(s)
µg	microgram(s)
min	minute(s)
ml	millilitre(s)
µl	microliter(s)
mm	millimetre(s)
mM	milllimolar
mmHg	millimetres of mercury
µm	micrometre(s)
MAF	Minor Allele Frequency
MALDI	Matrix-assisted laser desorption/ionisation
MS	Mass Spectrometry
MS/MS	Tandem mass spectrometry
m/z	mass to charge ratio
MODY	Maturity Onset Diabetes of the Young
n	number
$NaHCO_3$	sodium bicarbonate
nM	nanometre
NIBRT	National Institute for Biotechnology and Training
NSPHS	Northern Swedish Population Health Study
o.d.	outer diameter
ORCADES	Orkney Complex Disease Study
OSM	oncostatin M
PBS	Phosphate buffered saline
P	probability
PA	propionic acid
PC	principal component
pHWE	Hardy-Weinberg equilibrium p-value
RP	reverse-phase
rpm	revolutions per minute
SD	standard deviation
SDS	Sodium dodecyl sulphate
SE	standard error
SLE	systemic lupus erythematosus
SNP	Single nucleotide polymorphism
SPE	solid-phase extraction
T1D	Type 1 Diabetes mellitus
T2D	Type 2 Diabetes mellitus
TEMED	*N,N,N,N'*-tetramethyl-ethylenediamine
TFA	trifluoroacetic acid
TEA	triethylamine
TOF	Time of Flight

UPLC	Ultra Performance Liquid Chromatography
V	Volt(s)
v/v	volume to volume
WAX	Weak Anion Exchange
w/v	weight to volume

Chapter 1 - Introduction

1.1 Success of Genome-wide Association Studies for Mapping Quantitative Trait Loci

Genome-wide association studies (GWAS) have come to the forefront in human genetics in the past 6-8 years. Linkage studies had great success identifying genes for Mendelian disorders but were not proving as fruitful for common diseases. This is due to the fact that linkage relied upon causal mutations of large effect which could be traced down a pedigree, and usually involved the analysis of relatively few markers per chromosome due to low recombination between generations within a family [1]. It is a low resolution technique, often pinpointing to regions of several megabases, and for common diseases, the effect sizes were too small to track [2]. In addition, linkage required families which limited the sample sizes available for those studies. In order to perform linkage, it is necessary to follow segments which are shared identity-by-descent (IBD). The probability of a segment being shared by descent is estimated using various algorithms that rely on assumptions that may not be accurate, especially for large extended pedigrees. These problems also apply for linkage analysis of quantitative traits using variance components.

GWAS is a simple regression technique of phenotypic value on genotype, which does not require evaluation of identity by descent status and works best under the common disease-common variant (CDCV) hypothesis. The latter holds that genetic variants contributing to the majority of the population risk for common diseases must themselves be common [3,4], rather than rare with high allelic heterogeneity. With the GWAS technique, the mapping resolution across the genome is increased, as many recombination events separate two random individuals who share a common susceptibility variant. By exploiting linkage disequilibrium (LD), the concept that alleles located close together on a chromosome tend to be inherited together, researchers were able to investigate much smaller blocks of the haploid genome or "haplotypes" simply by looking at an individual "tagging" single nucleotide polymorphism (SNP) [5]. This means that by analysing approximately 1 SNP per 5-10kb (or approximately 300,000 -500,000 SNPs across the genome) in non-African populations, the majority of common variants across the genome could be interrogated [6]. Additionally, this method no longer required families but could be used on a population scale which allowed increased sample sizes and therefore increased power to detect true associations. Another contribution to increased sample size was the rapidly decreasing cost of genotyping which, combined with increased throughput, allowed existing larger cohorts to acquire the genetic data required for analysis. These in turn have driven the development of better analytical and computational tools to handle data on this scale.

Like linkage, GWAS has the advantage of being "hypothesis free" in that it is an unbiased scan of the entire genome rather than using prior biological knowledge which may be flawed or incomplete. This allows for the discovery of genes not previously associated with a particular trait or disease and new avenues for further laboratory or clinically-based studies. However, one has to keep in mind that association with a trait does not imply causation and further studies into the function of loci in the association region will be required for a clear biological understanding. Also, due to the number of tests, multiple testing is an issue but increased sample sizes or clever study design can help to overcome this barrier. Finally, single marker GWAS is unlikely to identify rare variant associations unless very large samples and different genotype data are used (i.e. imputed dosages where a broad allele frequency spectrum is present or specially designed arrays for rare variants are used) but even then there are different analytical techniques that are better suited to this task.

To date, approximately 2000 GWAS papers have been published which report associations with P-values < $1x10^{-05}$ for over 13,000 common SNPs, covering a variety of quantitative traits and diseases illustrating the undeniable success of this technique [7]. Genetic architecture of the traits assessed varied from height, a polygenic trait with hundreds of associated loci of small effect, to von Willibrand factor (vWF), with one locus, ABO, able to alter vWF levels by 25 – 30% [8,9]. In general, quantitative traits seem to be highly polygenic and the traits that are outputs of a simple process, such as some biochemical measures or transcript levels, often have loci with large effects. Despite the majority of associated loci being found to be intronic or intergenic, it seems that intergenic associations are actually underrepresented when compared to a random set of SNPs. In addition, there appears to be an overrepresentation of associated loci in regulatory regions and non-synonymous sites [10].

1.2 Rare Variant Analysis

Despite the success of GWAS performed so far, the common variants associated with quantitative traits still do not explain all of the trait heritability. For example, in the vWF paper mentioned above, despite this massive phenotypic change caused by ABO blood group, the 8 loci reported in this paper only explain 12.8% of the trait variance [9]. It has been hypothesized that this may be due to additional loci of small effect that have not been measured, rare variants of possibly large effect that are not present in the data available to date, structural variants which are not well captured by current genotyping technology, gene-gene interactions, or inflated heritability estimates due to unaccounted for shared environment in the populations used to calculate these estimates [11].

In order to tackle one of these postulated causes, the "Exome Chip" was designed. This is a genotyping chip that is focussed on low-frequency and rare variants, identified through exome sequencing projects, that are predicted to be functional. In order to limit false candidates on the chip, only variants observed at least 3 times across two or more sequencing efforts were included on the chip (http://genome.sph.umich.edu/wiki/Exome_Chip_Design).

Due to the fact that these variants are rare, traditional analysis methods do not have much power to detect association with quantitative traits. For this reason, methods have been developed to aggregate the effect of multiple rare variants across a region then to test for association with this "burden" of rare variation. This results in a p-value for the region rather than for a variant. These are called burden tests and generally the region is defined as a gene, but in theory the genome can be partitioned in any way the analyst would like [12,13].

1.3 Studied Populations

The CROATIA study was initiated to investigate the use of isolated rather than urban populations for the identification of genes associated with medically-relevant quantitative traits. These include traits that are used to measure or predict a disease outcome such as blood pressure, body mass index (BMI) or cholesterol levels. The decision to use isolated populations was based on the prediction that the genetic make-up of a population, the more homogeneous environment, and the use of quantitative traits rather than disease end points would increase the ability to detect associated genetic loci [14]. Three cohorts have been recruited as part of the CROATIA study: CROATIA-Vis, CROATIA-Korcula and CROATIA-Split. Only CROATIA-Vis and CROATIA-Korcula were used in this study. CROATIA-Vis was the first to be collected when 1008 Croatians aged 18-93 were recruited from the villages of Komiza and Vis on the Dalmatian island of Vis. Recruitment occurred from 2003 to 2004 with participants donating blood for DNA extraction and biochemical measurements as well as undergoing some anthropometric measurements and physiological tests to measure traits such as height, weight and blood pressure, and finally completing several questionnaires relating to general health, medical history, diet and lifestyle. CROATIA-Korcula was recruited from 2007 to 2008 from several towns and villages on the island of Korcula, Croatia with 969 adults aged 18-98 agreeing to participate. This study followed the same recruitment procedures as CROATIA-Vis and the same samples and tests were collected.

The Orkney Complex Disease Study (ORCADES) was performed in the Scottish archipelago of Orkney. Genetic diversity is decreased, just as on the Croatian islands, compared to the Scottish mainland, consistent with high levels of historical endogamy [15]. Participants were recruited between 2005 and 2011 following similar procedures and collecting similar data as the CROATIA studies in order to have complementary phenotypes for analysis. Close to 2000 people were recruited into this study, aged 16-98.

The Northern Swedish Population Health Study (NSPHS) is a family-based population study including a comprehensive health investigation and collection of data on family structure, lifestyle, diet, medical history and samples for laboratory analyses from peoples living in the north of Sweden. Data from this population isolates was available from 700 participants aged 14–91 years [16].

The Leiden Longevity Study was designed to investigate genetic factors contributing to long life. Siblings aged 89 years and over for men and 91 years and over for women, were recruited along with their offspring and offspring spouses. Both parents of the nonagenarians had to be Dutch and Caucasian [17].

Geographic locations of all studied cohorts are presented in Figure 1.

1.4 Role of Glycosylation

Glycosylation is a common post-translational protein modification that modulates the structure and function of polypeptide components of glycoproteins [18,19]. It is estimated that the glycome (defined as the complete set of all glycans) of a eukaryotic cell is composed of more than a million different glycosylated structures [20], which contain up to 10,000 structural glycan epitopes for interaction with antibodies, lectins, receptors, toxins, microbial adhesins, or enzymes [21]. Over half of all known proteins are modified by covalently bound glycans, which are important for various physiological processes, including protein folding, degradation and secretion, cell signalling, immune function and transcription [22-25]. The configuration and composition of attached glycans significantly change the structure and activity of polypeptide portions of glycoproteins [19] and since this process is not template driven, the complexity of the glycoproteome is estimated to be several orders of magnitude greater than for the proteome itself [26]. Terminal variability in glycans is common (e.g. ABO blood groups) and helps to create the diversity that allows our bodies to evade

Figure 1: Location of Population Cohorts.
NSPHS: Northern Swedish Population Health Study; ORCADES: Orkeny Complex Disease Study; CROATIA: the CROATIA study; LLS: Leiden Longevity Study.

pathogens and adapt to changing environments [27]. Dysregulation of glycosylation isassociated with a wide range of diseases, including cancer, diabetes, cardiovascular, congenital, immunological and infectious disorders [22,23,28]. Enzymes that are involved in glycosylation may therefore be promising targets for therapy [29]. A recent report endorsed by the US National Academies concluded that "glycans are directly involved in the pathophysiology of every major disease and that additional knowledge from glycoscience will be needed to realize the goals of personalized medicine" [40].

There are two major classes of glycans, "*O*-" and "*N*-" linked based on the linkage of the glycan to the attached lipid or protein. This project concerned the analysis of *N*-linked glycans only. Preformed glycans are transferred onto proteins as they appear out of the ribosomes in the endoplasmic reticulum (ER). The *N*-linked glycans are then remade in the Golgi depending on the protein they have been attached to, the cell they are found within and enzyme concentrations. Figure 2 shows an overview of this process. All *N*-glycans contain two core N-acetylglucosamine (GlcNAc) residues, to which a ‘‘core’’ fucose can be α1,6-linked to the inner GlcNAc, which is directly linked to an asparagine residue on the protein. This asparagine must be followed by any amino acid other than proline, then by either a serine or threonine. Additional fucose residues can be transferred to different positions on antennas that have been added to the core glycan structure. A generic structure for an *N*-glycan is found in

Figure 3. *N*-glycans are essential for multicellular life, with complete absence being lethal [30], however a group of rare diseases named congenital disorders of glycosylation [31] have been identified where different mutations in the biosynthesis pathway of *N*-glycans cause significant mortality and extensive motor, immunological, digestive and neurological symptoms [32,33]. These can affect any point in the glycosylation pathway shown in Figure 2. Due to experimental limitations in quantifying glycans in complex biological samples, the current understanding of their role in biological processes lags significantly behind knowledge about proteins or DNA [38,39]. However, recent technological advances have allowed reliable, high-throughput quantitation of *N*-glycans [34], which now permits investigation of the genetic regulation and biological roles of glycan structures and brings glycomics into line with genomics, proteomics and metabolomics [35]. Recent population-based studies indicated that the composition of the human plasma *N*-glycome varies significantly between individuals [36,37]. Since glycans have important structural and regulatory functions on numerous glycoproteins [38] , the observed variability suggests that differences in glycosylation might contribute to human phenotypic variability.

1.5 IgG *N*-Glycosylation

Variation in protein glycosylation also has physiological significance, with immunoglobulin G (IgG) being a well-documented example. Each heavy chain of IgG carries a single covalently attached bi-antennary *N*-glycan at the highly conserved asparagine 297 residue in each of the C_H2 domains of the Fc region of the molecule (Figure 4). The attached oligosaccharides are structurally important for the stability of the antibody and its effector functions [39]. Thirty-six different glycans can be attached to the conserved Asn297 of the IgG heavy chain [40,41], leading to hundreds of different IgG isomers that can be generated from this single glycosylation site. In addition, some 15–20% of normal IgG molecules have complex bi-antennary oligosaccharides in the variable regions of light or heavy chain [42,43]. Figure 4 shows *N*-glycosylation sites on IgG molecules.

Glycosylation of IgG has important regulatory functions. The absence of galactose residues in association with rheumatoid arthritis was reported nearly 30 years ago [44]. The addition

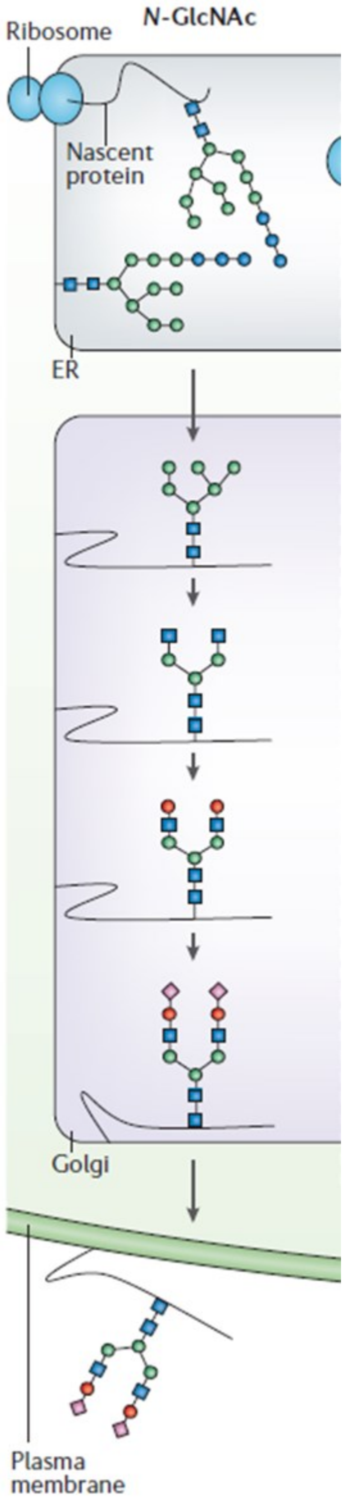


Figure 2: *N*-glycan biosynthetic pathway
(Modified figure from Freeze *et al*., 2006 [33]) The steps in the biosynthetic pathway for *N*-glycan synthesis are presented along with the cellular location. Preformed *N*-glycans are attached to the nascent protein as it is formed by the ribosome. Remodelling of the *N*-linked glycan starts in the endoplasmic reticulum (ER) but mainly occurs in the Golgi. The structures depicted here contain sialic acid (purple diamond), galactose (red circle), mannose (green circle), glucose (blue circle) and *N*-acetylglucosamine (GlcNAc, blue square).

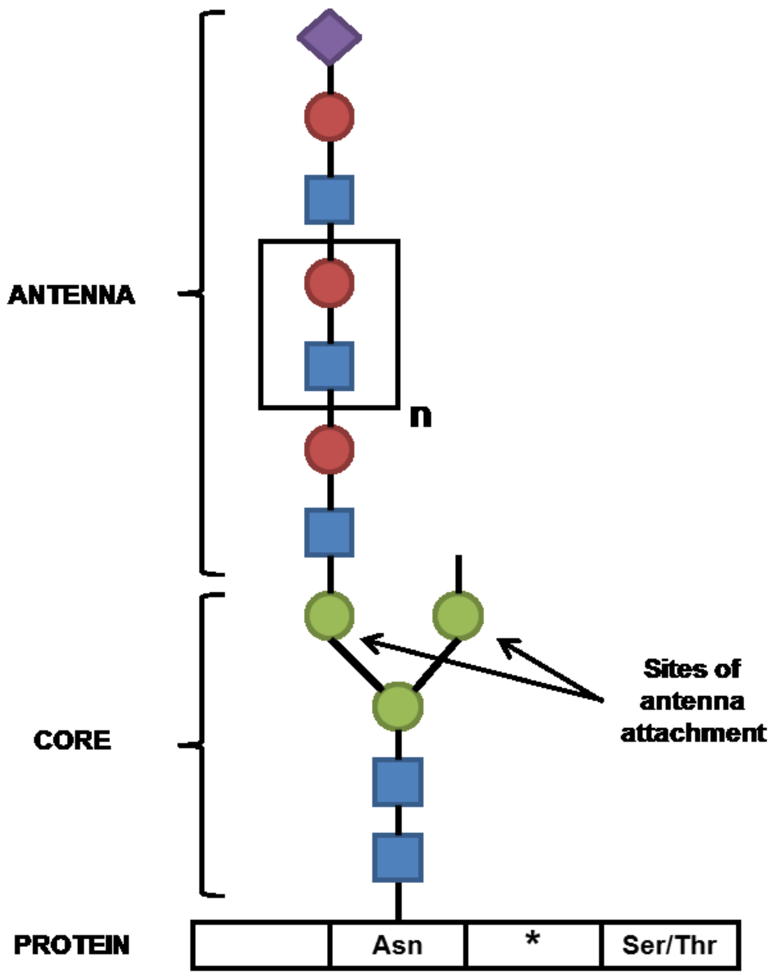


Figure 3: Generic *N*-glycan structure.
(Adapted from Ma *et al*., 2006 [45].) A generic *N*-glycan containing a tri-mannosyl core ("CORE") and an antenna ("ANTENNA"). An *N*-glycan can have up to four antennae with two attached to each of the mannoses indicated and can be lengthened as indicated by the box with "n". An *N*-glycan is attached to an asparagine (Asn) residue on the protein which must be followed by any amino acid other than proline (*), then by either a serine (Ser) or threonine (Thr). The structures depicted here contain Sialic acid (purple diamond), Galactose (red circle), Mannose (green circle) and *N*-acetylglucosamine (GlcNAc, blue square).

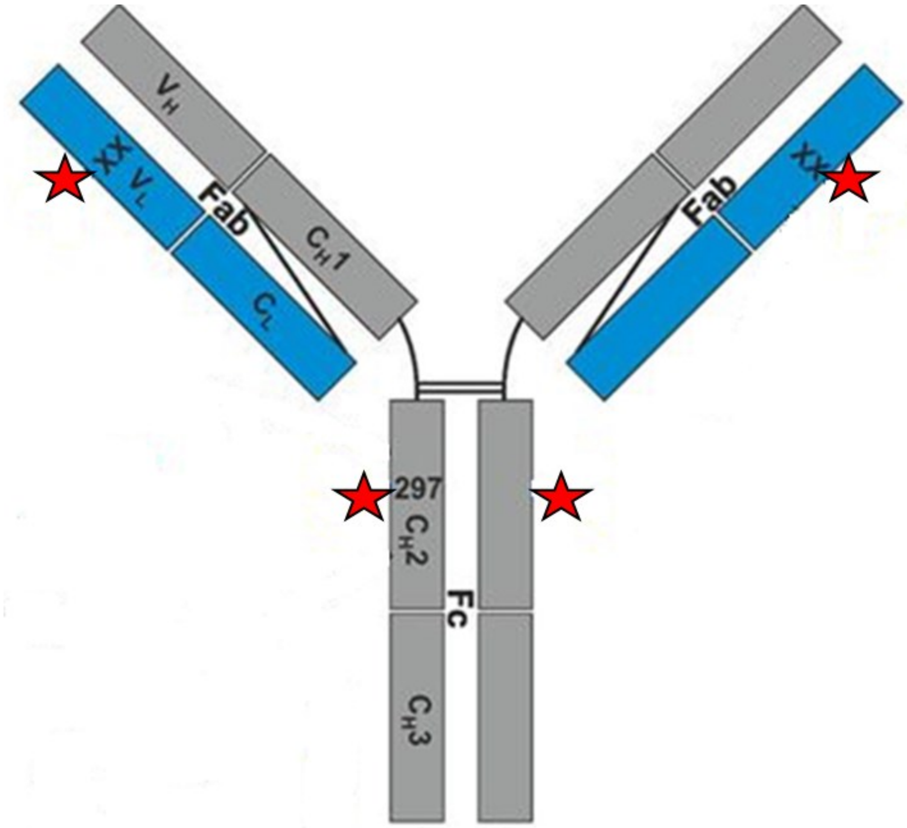


Figure 4: *N*-glycan attachment sites on Immunoglobulin G (IgG).
(Adapted from Zauner *et al.* (2013) [46].) The main *N*-glycosylation site at Asn297 is marked by 297. Stars represent *N*-glycosylation sites; Fab= fragment antigen binding region; Fc= fragment crystallisable region; V_H= variable heavy chain; V_L= variable light chain; C_H1 = constant heavy chain 1; C_H2 = constant heavy chain 2; C_H3 = constant heavy chain 3.

of sialic acid dramatically changes the physiological role of IgGs, converting them from pro-inflammatory to anti-inflammatory agents [47,48]. Addition of fucose to the glycan coreinterferes with the binding of IgG to FcγRIIIa receptors and greatly diminishes its capacity for antibody dependent cell-mediated cytotoxicity (ADCC) [49,50]. ADCC is a process whereby effector cells of the immune system (natural killer cells, macrophages, neutrophils and eosinophils) bind to and kill target cells which have been bound by antibodies. This is one of the major pathways by which the immune system prevents infection but requires prior knowledge that the target cell is dangerous in order to have antibodies directed against it [51]. Structural analysis of the IgG-Fc/FcγRIIIa complex has demonstrated that specific glycans on FcγRIIIa are also essential for this effect of core-fucose [52] and that removal of core fucose from IgG glycans increases clinical efficacy of monoclonal antibodies, enhancing their therapeutic effect through ADCC mediated killing [53-55].

1.6 Methodology for the Analysis of Glycans

A number of studies have investigated the role of glycans in human disease, including autoimmune diseases and cancer [56,57]. However, most human glycan studies have been conducted with very small sample sizes. Given the complex causal pathways involved in the pathophysiology of common complex disease, and thus the likely modest effect sizes associated with individual factors, the majority of these studies are very likely to be substantially underpowered. In the case of inflammatory bowel disease (IBD), only 20% of reported IBD glycan associations were replicated in subsequent studies, suggesting that most are false positive findings and that there is publication bias favouring the publication of positive findings [58]. This situation is similar to that which occurred in the field of genetic epidemiology in the past when many underpowered candidate gene studies were published and later found to consist of mainly false positive findings [59,60]. It is essential, therefore, that robust and affordable methods for high-throughput analysis are developed so that adequately powered studies can be conducted and the publication of large numbers of small studies reporting false positive results (which could threaten the credibility of glycoscience) be avoided.

Several methodologies have the capacity for high throughput glycan analysis including high performance liquid chromatography (HPLC), ultra performance liquid chromatography (UPLC), matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS), nano liquid chromatography electrospray ionisation mass spectrometry (LC-ESI-MS) and multiplex capillary gel electrophoresis with laser induced fluorescence detection (xCGE-LIF), but there is currently no “gold standard” [34,61-66].

UPLC and xCGE-LIF separate glycans based on structure whereas the MS-based methods separate glycans based on mass. Another important difference between UPLC and xCGE-LIF versus MS-based methods is that UPLC and xCGE-LIF analyse glycosylation at the level of released glycan while the MS-based methods presented here analyse glycopeptides. Although in-depth analysis of released glycans may provide a detailed picture of the glycan structure, no information on the original glycan attachment site is provided from UPLC or xCGE-LIF analyses. Such site-specific information can be obtained by the direct analysis of glycopeptides. This means that by analysing glycans at the glycopeptide level MS-based methods are able to give information about the protein from which the glycan was released.

However, unlike the MS-based methods used in this study, UPLC and xCGE-LIF provide branch-specific information.

1.7 Thesis Aims

The aim of this thesis was to investigate the genetic contributions to natural variation in concentrations of *N*-glycans in the above mentioned population cohorts. This was done through the use of GWAS to look at the contributions of common variants and burden tests to look at rare genetic variation. The initial investigation centred on the analysis of *N*-glycans isolated from total plasma proteins, then specifically of those attached to IgG. Finally, a comparison of the quantitative abilities of the different methodologies for *N*-glycan measurement was undertaken using correlation analysis and GWAS.

Chapter 2 - Materials & Methods

2.1 Studied Cohorts

All cohort recruitment, phenotyping and SNP genotyping was done by colleagues at the University of Edinburgh, the University of Zagreb, the University of Split Medical School, Uppsala University and Leiden University Medical Center.

2.1.1 The CROATIA Study

There are fifteen islands in the Adriatic Sea along the Croatian Dalmatian coast that have populations greater than 1000 which have been isolated from other villages and the mainland for many centuries. All have their own unique history and founder population and the anthropology of these population have been studied for many decades by colleagues at the Institute for Anthropological Research in Zagreb, Croatia [67].

A pilot study was initiated in 2002 in ten Dalmatian island villages selected for their differing population genetic history including founding times, admixture, bottleneck events and ethnic history. One hundred individuals from each isolate were collected to determine their suitability for recruitment into a larger population cohort to be used for further genetic studies of complex trait genetics. High levels of differentiation and structure were observed between most of the villages which was most likely due their geographic isolation as well as endogamy [68].

The island of Vis was selected for further recruitment with volunteers collected from the villages of Komiza and Vis between 2003 and 2004 (Figure 5). 1008 unselected adult participants aged 18-93 were recruited with almost even participation between villages. Blood was collected along with medical histories and various anthropometric and physical measures. Several questionnaires were completed covering the participant's medical history, general heath, lifestyle and diet. Both plasma and serum was collected and stored for use in various biochemical measurements and DNA was isolated for genotyping. For the rest of this thesis this population will be referred to as CROATIA-Vis.

The second population to be collected was from the town of Korcula and villages of Lumbarda, Zrnovo and Racisce on the island of Korcula (Figure 5). Recruitment occurred from 2007 to 2008 with 969 adults aged 18-98 agreeing to participate. This study followed the same recruitment procedures as Vis and the same samples and tests were collected. Some additional samples and tests were added to reflect the academic expertise in Edinburgh, including the collection of urine samples and an expanded battery of cognitive tests. In 2012 it was decided to continue recruitment on this island with the hope of eventually expanding the size of the cohort to 4000.

In order to have an “urban” population for comparison, volunteers were recruited from the Dalmatian mainland city of Split in 2009-2010 (Figure 5). This is the main ferry port to the islands and is the second largest city in Croatia and the largest along the Dalmatian coast. 1012 adults aged 18-85 were recruited using the same methodology and with the same samples collected as in Korcula. Samples from CROATIA-Split were not used for this work.

Ethical approval was given for recruitment of all CROATIA study populations by ethics committees in both Scotland and Croatia. All volunteers gave informed consent prior to participation.

Figure 5: Recruitment Sites for CROATIA cohort participants

2.1.2 The Orkney Complex Disease Study (ORCADES)

The Orkney Complex Disease study (ORCADES) is an ongoing family-based, cross-sectional study with adult participants recruited from the Scottish Orkney islands and was designed as a sister study to CROATIA-Vis. The Orkney islands are an archipelago found north of mainland Scotland (Figure 6). The Northern Isles of Orkney are comprised of a group of 10 inhabited islands with populations ranging from approximately 30-600 people. Despite recent improvements in transportation links between the Northern Isles and the rest of Orkney, they are still isolated and would have been more so in the past. Genetic diversity is decreased, just as on the Croatian islands, compared to the Scottish mainland consistent with high levels of historical endogamy[15]. All participants recruited into the study were residing in Orkney at the time of study recruitment (2005 - 2011) and had at least one grandparent who was born in the Northern Isles of Orkney. The final study sample size is just over 2000 people, however only data from the first two waves of genotyping were used for this study. This included 889 participants aged 16–98 years.

Ethical approval was given for recruitment of ORCADES participants by ethics committees in Scotland in 2004 and all volunteers gave informed consent prior to participation.

Figure 6: Location of Orkney Islands

2.1.3 The Northern Swedish Population Health Study (NSPHS)

The Northern Swedish Population Health Study (NSPHS) was designed to investigate the differences between individuals living a modern, sedentary lifestyle versus individuals following a traditional, semi-nomadic way of life based on reindeer herding. Participants recruited into this family-based population study completed a comprehensive health investigation and provided data on family structure, lifestyle, diet, medical history and samples for laboratory analyses. Individuals were recruited from the northern part of the Swedish mountain region (County of Norrbotten, Parish of Karesuando) in 2006 [16,69]. Approximately half of the eligible inhabitants of the parish agreed to participate in the study for a final sample size of 658 aged 14-91. Historic records indicated that there has been little immigration or other drastic population changes in this area in the last 200 years [70]. An additional 350 participants were recruited from Soppero and Vittangi, which are located just south of the initial collection area in the same County, in 2009. A map of the recruitment site locations is found in Figure 7.

The NSPHS study was approved by the local ethics committee at the University of Uppsala (Regionala Etikprövningsnämnden, Uppsala, Dnr 2005:325) in compliance with the Declaration of Helsinki. All participants gave their written informed consent and if the participant was not of legal age, a legal guardian also signed. In this study only participants from the first recruitment and aged over 18 were included.

2.1.4 The Leiden Longevity Study (LLS)

The Leiden Longevity Study was designed to investigate genetic factors contributing to long life. Siblings aged 89 years and over for men and 91 years and over for women, were recruited along with their offspring and offspring spouses. Both parents of the nonagenarians had to be Dutch and Caucasian. Siblings were recruited in order to decrease environmental cofounders and the offspring spouses provided population controls. In total, 3,359 individuals were included: 944 long-lived proband siblings with a mean age of 94 years (range 89–104 years), 1,671 offspring with a mean age of 60 years (range 39–81 years), and 744 controls with a mean age of 60 years (range 36–79 years) at baseline. Recruitment occurred between July 2002 and May 2006 and no additional selection based on health or demographic categories was performed. Non-fasting blood samples were taken at baseline for extraction of DNA and RNA and measurement of other serum and plasma parameters. Blood cell counts were performed using standard procedures. Additional information and biological samples were collected from the offspring and their spouses from November 2006 to May 2008. The LLS was approved by the Medical Ethical Committee of Leiden University Medical Centre, and all participants gave written informed consent [17,71].

Figure 7: Location of Recruitment Sites for NSPHS.

2.1.5 Diabetes Cohorts

All type 2 diabetes (T2D) and half of the Maturity Onset Diabetes of the Young 3 (MODY3) patients were obtained from the South of England. The first set of MODY3 patients were all found to harbour a mutation (confirmed by sequencing in a certified UK diagnostic centre) in *HNF1A* (n=19). T2D subjects were selected from the Young Diabetes in Oxford (YDX) study (n=41), comprising subjects diagnosed with diabetes ≤ 45 years of age. Criteria for diagnosis were: C-peptide positive, no requirement for permanent insulin within 3 months of diagnosis and negative glutamic acid decarboxylase (GAD) antibodies. Subjects with a clinical label of T2D did not meet clinical criteria for MODY diagnostic testing or had been tested and were negative for mutations in genes that are known to cause the most common types of MODY (*HNF1A*, *HNF4A* or *GCK*). The study was approved by the Oxfordshire Local Research Ethics Committee and all subjects gave informed consent.

The rest of the MODY3 samples comprise subjects who were collected in Edinburgh and had a mutation (confirmed by sequencing in a certified UK diagnostic centre) in *HNF1A* (n=14). All Edinburgh participants contributed plasma samples and were used in both the initial pilot and the expanded study. The study was approved by the Lothian Research Ethics Committee and all subjects gave written informed consent.

2.2 Genetic Data

All SNP genotyping and quality control was performed by colleagues at the University of Edinburgh, the University of Zagreb, the University of Split Medical School, Uppsala University and Leiden Univeristy Medical Center. HapMap2 imputation of all datasets was completed by Yurii Aulchenko (CROATIA-Vis & NSPHS), Christian Fuchsberger (CROATIA-Korcula) and Mirna Kirin (ORCADES). I performed genotype quality control of the CROATIA-Korcula data prior to starting my PhD. An overall descriptive chart of all participating population cohorts and genotying information is found in Table 1.

2.2.1 SNP Genotyping and Quality Control

SNP genotyping for CROATIA-Vis was performed by the Wellcome Trust Clinical Research Facility (WTCRF) at the Western General Hospital, Edinburgh, UK, using the Illumina Infinium HumanHap300 BeadChip. NSPHS and the majority of ORCADES samples were also genotyped using this chip (at Helmholz Zentrum München, GmbH, Neuherberg, Germany) with the remainder of ORCADES genotyped using the Illumina HumanHap370CNV duo chip (Integragen, Paris, France). CROATIA-Korcula was genotyped on the Illumina HumanHap370CNV duo chip as well by Helmholz Zentrum München.

SNP genotypes were clustered using BeadStudio. Verification that the correct individual had been genotyped was carried out by checking for sex discrepancies and verifying expected relationships, where known, using PLINK [72]. Individuals were removed if there was not an obvious solution (e.g. samples flipped on the genotyping chip). Final SNP quality control was undertaken using the GenABEL package for R (from the *ABEL suite of programs, www.genabel.org) [73]. Individuals with a call rate less than 97% were removed as well as SNPs with a call rate less than 98% (95% for CROATIA-Vis), minor allele frequency less than 0.02 or Hardy-Weinberg equilibrium p-value (pHWE) less than $1\text{x}10^{-06}$. 924 individuals passed all genotype quality control thresholds from CROATIA-Vis, 898 from CROATIA-Korcula, 889 from ORCADES, and 656 from NSPHS. After quality control was complete, an identity-by-state (IBS) matrix was computed for each cohort using the "ibs" function of

Table 1: Participating population cohort, genotyping, and imputation descriptions.

	CROATIA-Vis	CROATIA-Korcula	NSPHS	ORCADES	LLS
Study Type	Population-based	Population-based	Population-based	Population-based	Population-based
Population Type	Isolate	Isolate	Isolate	Isolate	General
Year of Recruitment	2003-2004	2007-2008	2006	2005-2011	2002-2006
Genotyping Platform	Illumina Infinium HumanHap300 BeadChip	Illumina HumanHap370CNV duo chip	Illumina Infinium HumanHap300 BeadChip	Illumina Infinium HumanHap300 BeadChip (majority) or HumanHap370CNV duo chip	Illumina660 W (1345) Illumina OmniExpress (503)
Quality Control Thresholds	ind call rate > 97% SNP call rate > 95% MAF > 0.02 HWE > 1E-06	ind call rate > 97% SNP call rate > 98% MAF > 0.02 HWE > 1E-06	ind call rate > 97% SNP call rate > 98% MAF > 0.02 HWE > 1E-06	ind call rate > 97% SNP call rate > 98% MAF > 0.02 HWE > 1E-06	ind call rate > 95% SNP call rate > 95% MAF > 0.01 HWE > 1E-04
N SNPs after QC	308,996	316,751	289,203	293,687	296,619
N ind after QC	924	898	656	889	1,848
% female	58.0%	63.8%	52.9%	54.6%	NA
mean age in years (sd)	56.4 (15.5)	56.3 (13.9)	47.0 (20.7)	53.5 (15.7)	NA
HapMap2 Imputation Software	MACH version 1.15	MACH version 1.15	MACH version 1.15	MACH version 1.15	IMPUTE2
Pre-Imputation Filters	ind call rate > 97% SNP call rate > 98% MAF > 0.01 HWE > 1E-06	ind call rate > 97% SNP call rate > 98% MAF > 0.01 HWE > 1E-06	ind call rate > 97% SNP call rate > 98% MAF > 0.01 HWE > 1E-06	ind call rate > 97% SNP call rate > 98% MAF > 0.01 HWE > 1E-06	ind call rate > 95% SNP call rate > 95% MAF > 0.01 HWE > 1E-04
GWAS Analysis Software	GenABEL/ProbABEL	GenABEL/ProbABEL	GenABEL/ProbABEL	GenABEL/ProbABEL	QTassoc

N=number, ind = individuals, SNP= single nucleotide polymorphism, MAF= minor allele frequency, HWE = Hardy-Weinberg equilibrium, sd= standard deviation, QC= quality control, GWAS= genome-wide association study

GenABEL (using weight= “freq” option), which uses genomic data to estimate the realized pair-wise kinship coefficient. This was used to verify pedigree information reported at recruitment. It is also the matrix which was used to account for relatedness in the genome-wide association analyses reported later.

The Leiden Longevity Study had 1345 individuals genotyped using Illumina660 W (Rotterdam, Netherlands) and 503 individuals genotyped using Illumina OmniExpress (Estonian Biocentre, Genotyping Core Facility, Estonia). LLS analysts performed all genotyping quality control, imputation and statistical analysis for their cohort data. The GenomeStudio algorithm was used for genotype calling. Sample call rates were >95%, and SNP exclusions criteria were Hardy-Weinberg equilibrium p-value < $1x10^{-04}$, SNP call rate < 95%, and minor allele frequency < 1%. The number of overlapping SNPs that passed quality controls in both samples was 296,619.

2.2.2 HapMap 2 Imputation

Imputation of approximately 2.5 million SNPs was completed for CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS using the release 22 HapMap CEU population as the reference. MACH version 1.15 (http://www.sph.umich.edu/csg/abecasis/MACH) [74] was used, after filtering out SNPs with MAF < 0.01, call rate < 98%, and pHWE < 10^{-6}. LLS used IMPUTE2 (http://mathgen.stats.ox.ac.uk/impute/impute_v2.html) [75] with the same reference panel for their imputation. Family structure was not accounted for during the imputation process as software had not been developed at the time to do so. Inclusion of population-specific phased sequence data has been shown to improve imputation, especially in isolated populations, but this was not available at the time the HapMap2 imputation was performed [76-78].

2.2.3 Rare variants

CROATIA-Korcula only was genotyped using the Illumina HumanExome BeadChip v1.0 (“Exome Chip”). The Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium [79] organised joint genotyping and SNP calling using this chip in 62,000 individuals of European, African, Asian and Hispanic ancestry. This allowed for reliable calling of variants where only one copy of the minor allele may have been present in a single cohort and these files were made available to all collaborating cohorts [80]. Since CROATIA-Korcula was not part of this joint calling, SNPs were clustered using GenomeStudio (Illumina) and cluster files provided from the CHARGE consortium. Further quality control was performed following procedures set out by the CHARGE consortium (detailed in [80,81]) to remove variants and people with low call rates (97% cutoff for both SNP and individual) and SNPs grossly out of Hardy-Weinberg equilibrium. Y-chromosome SNPs which were called in female participants were removed. Y and mitochondrial SNPs were also checked to ensure no heterozygous genotypes were present. Finally, X chromosome SNPs were checked for heterozygous male genotypes, if > 2 were present, the SNP was removed, if <2, the genotype was set to missing. Genotype data for 855 individuals and 236, 308 SNPs successfully passed all quality control procedures of which 67,417 SNPs were polymorphic.

2.3 Quantitation of *N*-Glycosylation

All methods presented here were performed by external collaborators. Isolation of plasma proteins and HPLC glycan measurement was performed at Genos, Zagreb, Croatia and NIBRT, Dublin, Ireland. I visited NIBRT for 3 months during the course of my PhD to learn how HPLC & UPLC analysis of *N*-glycans is performed, under the supervision of Barbara Adamczyk.

2.3.1 Glycan release and labelling

The *N*-glycans from plasma sample (5 µl) proteins were released and labelled with 2-aminobenzamide (LudgerTag 2-AB labelling kit Ludger Ltd., Abingdon, UK) as described previously [34]. Labelled glycans were dried in a vacuum centrifuge and redissolved in a known volume of water for further analysis.

2.3.2 Sialidase digestion

After initial HPLC quantification of *N*-glycans, sialidase digestion was performed to improve measurement precision. This removes sialic acid from glycan structures. Aliquots of the 2-AB-labelled glycan pool were dried down in 200-µl microcentrifuge tubes. To these, the following was added: 1 µl of 500 mM sodium acetate incubation buffer (pH 5.5), 1 µl (0.005 units) of ABS, Arthrobacter ureafaciens sialidase (releases a2–3, 6, 8 sialic acid, Prozyme, Leandro, CA, USA) and water to make up to 10 µl. This was incubated overnight (16–18 h) at 37ºC and then passed through a Micropure-EZ enzyme remover (Millipore, Billerica, MA, USA) before applying it to the HPLC column.

2.3.3 Hydrophilic interaction high-performance liquid chromatography (HILIC-HPLC)

Released glycans were subjected to hydrophilic interaction high performance liquid chromatography (HILIC-HPLC) on a 4.6 mm i.d. 5 µm particle packed TSKgel Amide 80 column (Tosoh Bioscience, Stuttgart, Germany) at 30ºC with 50 mM formic acid adjusted to pH 4.4 with ammonia solution as solvent A and acetonitrile as solvent B. 60 min runs were carried out on a 2795 Alliance separation module (Waters, Milford, MA). HPLCs were equipped with a Waters temperature control module and a Waters 2475 fluorescence detector set with excitation and emission wavelengths of 330 and 420 nm, respectively. The system was calibrated using an external standard of hydrolyzed and 2-AB-labelled glucose oligomerase from which the retention times for the individual glycans were converted to glucose units (GU) [62]. Glycans were analysed on the basis of their elution positions and measured in GUs, then compared to reference values in the National Institute for Biotechnology and Training's (NIBRT) ''GlycoBase v3.0 '' database (http://glycobase.nibrt.ie) for structure assignment [82]. HPLC analysis was performed partly at NIBRT in Dublin, Ireland, and partly at the Glycobiology laboratory of Genos Ltd in Zagreb, Croatia. Both laboratories used the same columns and separation conditions. Duplicate analysis of a number of samples was performed and confirmed full reproducibility of the analytical results both within and between laboratories.

Chromatography yielded a total of 33 directly measured traits. From the HPLC analysis, undigested *N*-glycans were separated into 16 structurally related groups of glycans, referred to as glycan peak (GP)1–16. Desialylated 2AB-labelled *N*-glycans were also separated into 13 structurally related groups of glycans, referred to as desialylated glycan (DG)1–13. Weak anion exchange (WAX) chromatography resulted in four peaks defining the amount of sialylation of structures: mono (MonoS), di (DiS), tri (TriS) or tetra (TetraS). The amount of *N*-glycans measured in each of these groups was quantified relatively, as a proportion of the total plasma *N*-glycome. An additional 13 parameters were gained by calculating some structural determinants from measured traits. A description of each glycan trait is presented in Appendix Table 15 along with equations for the additional 13 derived traits.

2.4 Quantitation of Immunoglobulin G *N*-Glycosylation

All methods presented here were performed by external collaborators. Isolation of IgG and UPLC glycan measurement was performed at Genos, Zagreb, Croatia. All mass spectrometry methods were performed by colleagues in Manfred Wuhrer's laboratory at LUMC, Leiden, Netherlands. xCGE-LIF methods were performed by colleagues in Erdmann Rapp's laboratory at MPI, Magdaburg, Germany and their associated company, glyXera, Magdaburg, Germany. Brief methods are presented here with full methods in the Appendix Section 9.1 and in Huffman *et al*., 2014 [83].

2.4.1 Isolation of IgG

Immunoglobulin G was isolated from plasma (50 µl) by affinity chromatography using 96-well protein G monolithic plates (BIA Separations, Ajdovščina, Slovenia). Aliquots were sent to each laboratory for IgG *N*-glycan analysis by the following four methods.

2.4.2 IgG *N*-Glycosylation by Hydrophilic Interaction Chromatography

2.4.2.1 Glycan release and labelling

The *N*-glycans from the protein G eluates (200 µl dried down and reconstituted to 5 µl) were released and labelled with 2-aminobenzamide (LudgerTag 2-AB labelling kit Ludger Ltd., Abingdon, UK) as described previously [34]. Labelled glycans were dried in a vacuum centrifuge and redissolved in a known volume of water for further analysis.

2.4.2.2 Hydrophilic interaction chromatography

2-AB labelled IgG *N*-glycans were separated by hydrophilic interaction chromatography on a Waters Acquity UPLC instrument consisting of a quaternary solvent manager, sample manager and a FLR fluorescence detector set with excitation and emission wavelengths of 330 and 420 nm, respectively. The instrument was under the control of Empower 2 software, build 2145 (Waters). Labelled *N*-glycans were separated on a Waters BEH Glycan chromatography column, 100 x 2.1 mm i.d., 1.7 µm BEH particles, with 100 mM ammonium formate, pH 4.4, as solvent A and ACN as solvent B. A linear gradient of 75-62% ACN was used at flow rate of 0.4 ml/min in a 20 min analytical run. Samples were maintained at 5°C prior to injection, and the separation temperature was 60°C. The system was calibrated using an external standard of hydrolyzed and 2-AB labelled glucose oligomers from which the retention times for the individual glycans were converted to glucose units (GU). Data processing was performed using an automatic processing method with a traditional integration algorithm after which each chromatogram was manually corrected to maintain the same intervals of integration for all the samples. The chromatograms obtained were all separated in the same manner into 24 peaks and the amount of glycans in each peak was expressed as % of total integrated area. Additional structures could be derived from these 24 peaks to give a total of 77 structures. All structures and formulas are described in Appendix Table 16 .

2.4.3 IgG *N*-Glycosylation by Mass Spectrometry

2.4.3.1 Trypsin digestion and reverse-phase solid-phase extraction (RP-SPE)

Aliquots (50 µl) of the protein G eluates were applied to 96-well polypropylene V-bottom microtitre plates. Trypsin digestion was performed overnight followed by reverse-phase desalting and purification of glycopeptides.

2.4.3.2 MALDI-TOF-MS

Purified and desalted tryptic IgG glycopeptides (3 µl) were spotted onto MTP 384 polished steel target plates (Bruker Daltonics, Bremen, Germany) and allowed to dry at room temperature. Subsequently 1 µl of 5 mg/ml 4-chloro-α-cyanocinnamic acid (Cl-CCA; 95 % purity; Bionet Research, Camelford, Cornwall, UK) in 50 % ACN was applied on top of each sample and allowed to dry. Glycopeptides were analyzed on an UltrafleX II MALDI-TOF/TOF mass spectrometer (Bruker Daltonics) operated in the negative-ion reflectron mode, since negative-ion mode has been found well-suited for the analysis of IgG glycopeptides and specifically for sialylated glycopeptides [84], while reflectron mode greatly improves the resolution and sensitivity of the analysis. Ions between m/z 1000 and 3800 were recorded. To allow homogeneous spot sampling a random walk laser movement with 50 laser shots per raster spot was applied and each IgG glycopeptide sum mass spectrum was generated by accumulation of 2000 laser shots. Mass spectra were internally calibrated using a list of known glycopeptides. Data processing and evaluation were performed with FlexAnalysis Software (Bruker Daltonics) and Microsoft Excel, respectively. Structural assignment of the detected glycoforms was performed on the basis of literature knowledge of IgG *N*-glycosylation [44,85-89]. The data were baseline subtracted and the intensities of a defined set of 27 glycopeptides (16 glycoforms for IgG1 and 11 for IgG2&3) were automatically defined for each spectrum as described before [90].

In Caucasian populations, IgG2 and IgG3 have identical peptide moieties (E_{293}EQFNSTFR_{301}) of their tryptic Fc glycopeptides and were, therefore, not distinguished by the profiling method [91]. Relative intensities of IgG Fc glycopeptides were obtained by integrating and summing four isotopic peaks followed by normalization to the total subclass specific glycopeptide intensities, as described previously [90]. Additional structures could be derived from these directly measured values to give a total of 103 structures. All structures and formulas are described in Appendix Table 17. The list of the assigned IgG1, IgG2&3 and IgG4 glycopeptides as well as the charge states corresponding m/z values is given in Appendix Table 18.

2.4.3.3 Reverse phase nano-LC-sheath-flow-ESI-MS (LC-ESI-MS)

Purified and desalted tryptic IgG glycopeptides were also analysed on an Ultimate 3000 HPLC system (Dionex Corporation, Sunnyvale, CA, USA), consisting of a degasser unit, binary loading pump, dual binary gradient pump, autosampler maintained at 5°C and fitted with a 10µl PEEK sample loop, and two column oven compartments set at 30°C. Samples (250-5000 nl) were applied to a Dionex Acclaim PepMap100 C18 (5 mm x 300 µm i.d.) SPE trap column conditioned with 0.1 % TFA (mobile phase A) for 1 min at 25 µl/min. After sample loading the trap column was switched in-line with the gradient and Ascentis Express C18 nano-LC column (50 mm x 75 µm i.d., 2.7 µm HALO fused core particles; Supelco, Bellefonte, USA) for 8 min while sample elution took place. The separation was coupled to a quadrupole-TOF-MS (micrOTOF-Q; Bruker Daltonics, Bremen, Germany) equipped with a standard ESI source (Bruker Daltonics) and a sheath-flow ESI sprayer (capillary electrophoresis ESI-MS sprayer; Agilent Technologies, Santa Clara, USA). The software used to operate the Ultimate 3000 HPLC system and the Bruker micrOTOF-Q were Chromeleon Client version 6.8 and micrOTOF control version 2.3, respectively.

Each LC-MS dataset was calibrated internally using a list of known glycopeptides, exported to the open mzXML format by Bruker DataAnalysis 4.0 in batch mode [92] and aligned to a master dataset of a typical sample (containing many of the (glyco)peptide species shared between multiple samples) using msalign2 [93] and a simple warping script in AWK [94]. From each dataset a list of 402 pre-defined features defined as peak maximum within a mass window of + m/z 0.04 and a retention time window of +10 [95] , were extracted using the in-house developed "Xtractor2D" software and merged to a complete data matrix as described previously [65]. The software and ancillary scripts are freely available at www.ms-utils.org/Xtractor2D. The complete sample-data matrix was finally evaluated using Microsoft Excel.

Structural assignment of the detected glycoforms was performed on the basis of literature knowledge of IgG *N*-glycosylation [44,85-89]. Relative intensities of 20 IgG1, 20 IgG2/3 and 10 IgG4 glycopeptide species were obtained by integrating and summing the first three isotopic peaks of both doubly and triply charged glycopeptide species followed by background correction and normalization to the total IgG subclass specific glycopeptide intensities. The list of the assigned IgG1, IgG2&3 and IgG4 glycopeptides as well as the charge states corresponding m/z values is given in Appendix Table 19 as well as in [65]. Additional structures could be derived from these directly measured species to give a total of 205 structures. All structures and formulas are described in Appendix Table 20.

2.4.4 IgG *N*-Glycosylation by Multiplex Capillary Gel Electrophoresis with Laser-Induced Fluorescence (xCGE-LIF)

2.4.4.1 Glycan release and labeling

Approximately 10 µg of the protein G monolithic plate IgG eluates were redissolved in 3 µl 1× PBS (Sigma-Aldrich) and dispensed into a 96-well microtitre plate (Greiner Bio-One, Solingen, Germany). IgG samples were denatured and *N*-glycans were released using PNGase F (BioReagent ≥ 95 %, Sigma-Aldrich). After *N*-glycan release samples were dried in a vacuum centrifuge and stored until labeling at -80°C. *N*-glycans were labelled with 2-picoline-borane (2-PB; Sigma-Aldrich). Post derivatization sample clean-up was performed by HILIC-solid phase extraction (SPE). Samples were further cleaned to remove free APTS, reducing agent and other impurities. The cleaned and labelled *N*-glycans were either analysed immediately by xCGE-LIF or stored at -20°C until required.

2.4.4.2 xCGE-LIF

For xCGE-LIF measurement, 1 µl of *N*-glycan eluate was mixed with 1 µl GeneScan 500 LIZ Size Standard (Life Technologies, Darmstadt, Germany; 1:50 dilution in Hi-Di Formamide) and 9 µl Hi-Di Formamide (Life Technologies). The xCGE-LIF measurement was performed in a 3130xl Genetic Analyzer, equipped with a 50 cm 16-capillary array filled with POP-7 polymer (all from Life Technologies). After electrokinetic sample injection, samples were analysed with a running voltage of 15 kV. Data were collected for 45 min. Raw data files were converted to .xml file format using DataFileConverter (Life Technologies) and subsequently analysed using the MATLAB (The Mathworks, Inc., Natick, MA, USA) based glycan analysis tools glyXtool and glyXalign. GlyXtool was used for structural identification by patented migration time normalization to an internal standard and *N*-glycan database driven peak annotation [96]. The data comparison was performed by glyXalign [97]. Additional structures could be derived from to give a total of 92 structures. All structures and formulas are described in Appendix Table 21.

2.4.5 Comparison of Methods for IgG *N*-Glycosylation Analysis

UPLC and xCGE-LIF separate glycans based on structure whereas the MS-based methods separate glycans based on mass. Another important difference between UPLC and xCGE-LIF versus MS-based methods is that UPLC and xCGE-LIF analyse glycosylation at the level of released glycan while the MS-based methods presented here analyse glycopeptides. Although in-depth analysis of released glycans may provide a detailed picture of the glycan structure, no information on the original glycan attachment site is provided from UPLC or xCGE-LIF analyses. Such site-specific information can be obtained by the direct analysis of glycopeptides. This means that by analysing glycans at the glycopeptide level MS-based methods are able to give information about the protein from which the glycan was released. However, unlike the MS-based methods used in this study, UPLC and xCGE-LIF provide branch-specific information. Figure 8 shows an example IgG spectrum from each of the four methods discussed above. This figure was prepared by colleagues at Genos, LUMC and MPI and is taken from Huffman *et al*., 2014 [83].

2.5 Statistical Analysis

2.5.1 GWAS using GenABEL & ProbABEL

GenABEL and ProbABEL are from the GenABEL suite of programs for association analysis (www.genabel.org) [73,98]. GenABEL is a package for R designed for use with directly genotyped SNP data whereas ProbABEL is a stand-alone program for use with imputed dosages or probabilities. One of the main benefits is their ability to account for relatedness among individuals using a kinship matrix rather than requiring a defined pedigree. This is especially suited for our populations since, due to their isolated nature, there tends to be more complex relatedness then traditional pedigree-based programs allow. It also allows us to account for distant, unknown or unreported relatedness that would not exist in a pedigree. Association analysis, while accounting for relatedness, is achieved using the “polygenic” and “mmscore” functions. The “polygenic” function estimates the parameters of the fitted linear mixed model using a maximum likelihood method. This function uses the genomic identity-by-state kinship matrix generated using the “ibs” function of GenABEL, (described in Section 2.2.1). The output produced can be directly used in GenABEL for association analysis, or the residuals (“residualY”) and the inverse of the variance-covariance matrix (“InvSigma”) can be extracted for use with ProbABEL, using the “mmscore” function. This is a score test for family-based association which takes into account relationship structure and allows unbiased estimations of SNP allelic effects when relatedness is present between examinees. If association analysis is not the next step, residuals with the polygenic effects removed can be extracted as well (“pgresidualY”).

2.5.2 Meta-Analysis with MetABEL

MetABEL is a meta-analysis program from the GenABEL suite of programs for association analysis (www.genabel.org) [73]. Inverse-variance weighted meta-analysis was carried out for all analyses using this program. SNPs with poor imputation quality ($R^2 < 0.3$) were excluded prior to meta-analysis.

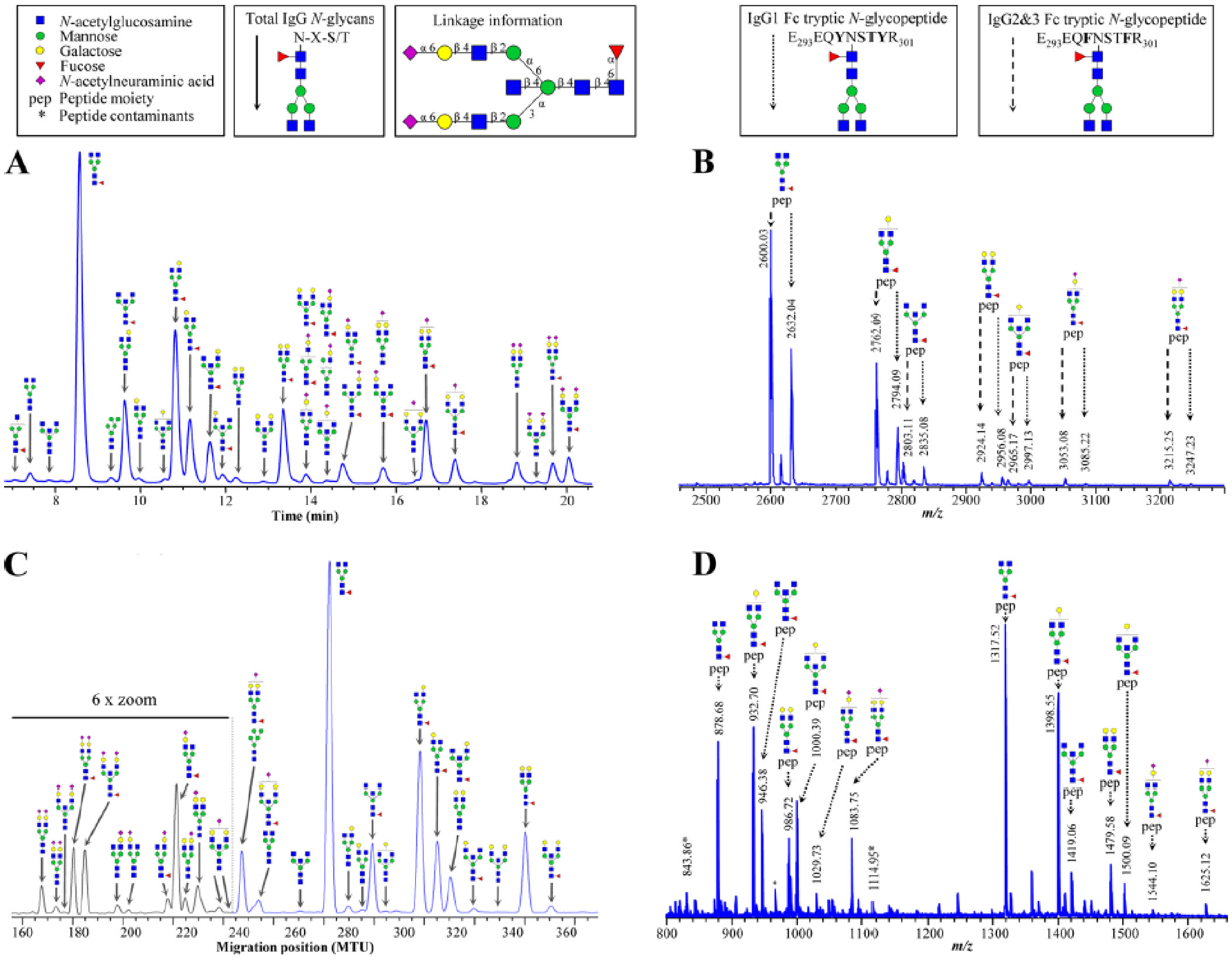


Figure 8: Spectrum from four methods for analysis of IgG glycosylation in the same individual. (Taken from Huffman *et al*., 2014 [83]). Data from IgG *N*-glycosylation analysis of the same individual by (A) UPLC (continuous lines - total IgG *N*-glycans), (B) MALDI-TOF-MS (dotted lines - IgG1, striated lines - IgG2&3, (C) xCGE-LIF (continuous lines - total IgG *N*-glycans), and (D) LC-ESI-MS (dotted lines - IgG1). Structures include: pep (peptide moiety), blue square (N-acetylglucosamine), red triangle (fucose), green circle (mannose), yellow circle (galactose), and purple diamond (N-acetylneuraminic acid). Linkage information is given to indicate separation of linkage isomers by UPLC and xCGE-LIF. Glycan structures are assigned to most of the signals.

2.5.2.1 Transformations and Correction for Population Stratification

Extensive testing was performed on the total *N*-glycan traits to find best trait-specific models with normally-distributed residuals, an essential assumption of the test statistics used for GWAS but these often were involving different transformations and adjusted covariates depending on the cohort investigated (results not included). In the end it was found that quantile normalization was the only transformation that worked consistently across cohorts. It allowed a “high-throughput analysis pipeline” to be developed that could be used for all traits. Additionally, the properties of the quantile normalisation allowed for comparison of effect sizes across traits, and across methods in the case of Chapter 7, since the units are the same for all traits after transformation. Quantile-normalisation was performed after adjustment for covariates because they may change the shape of the distribution of the residuals so would have required a second transformation to ensure normality of the residuals for analysis. We have tested the results of performing the adjustments for covariates before or after quantile normalisation when the residuals of a model after adjustments for covariates are not normally distributed and found very little impact on the GWAS results.

Principal components (PCs) derived from the IBS kinship matrix (described in Section 2.2.1) were included as fixed effects to account for population stratification. We have found that it is often not necessary but that for some traits some of the first PCs are still significantly associated with the phenotype in the mixed model used for analysis i.e. despite inclusion of a random polygenic effect derived from the same IBS matrix the PCs are calculated from. It is known that very first PCs usually capture geographic locations so may be accounting for some unknown environmental confounder. This being said, correlation between the PCs and the glycan traits was not tested systematically for all traits and cohorts. I therefore acknowledge that this may be an over-correction but is likely to result in a slight loss of signal rather than false positives. The choice to include 3 PCs (rather than 2 or 4) is common practice in GWAS where it has been shown that 3 PCs generally account for most of the population stratification in European populations [99].

2.5.2.2 Multiple Testing Correction for Total Plasma *N*-glycans

To account for the number of traits analysed, a multiple testing correction was applied based on the number of directly measured structures (n=33) since the rest were derived, therefore are not entirely independent. An association was considered statistically significant at the genome-wide level if the P-value for an individual SNP was less than 1.52×10^{-09} and “strongly suggestive” if the P-value was between 1.52×10^{-09} and 5×10^{-08}. The effect of the most significant SNP in each gene region expressed as a percentage of the variance explained was calculated for each glycan trait after adjustment for sex, age and the first three PCs in each cohort individually, using the ‘polygenic’ function of the GenABEL package for R [73].

2.5.2.3 Multiple Testing Correction for IgG *N*-glycans

Principal component analysis was performed using R to determine the number of independent traits used for these analyses. 21 principal components explained 99% of the variance so an association was considered statistically significant at the genome-wide level if the p-value for an individual SNP was less than 2.27×10^{-09} (5×10^{-08}/22 traits) [100]. SNPs were considered strongly suggestive with p-values between 5×10^{-08} and 2.27×10^{-09}.

2.5.3 IgG *N*-glycan Replication by Leiden Longevity Study

All genotyping, quality control, imputation, statistical analysis and IgG *N*-glycan measurement was performed by colleagues in Leiden, the Netherlands.

The Leiden Longevity Study (LLS) cohort and genotyping methods are described in Section 2.1.4 and 2.2.1. 1848 individuals with available genotypic and IgG measurements data were included in the replication sample. HapMap2 imputed dosages were used for analysis of all SNPs from the discovery analysis listed in Table 3. The only exception was rs11621121, which had low imputation accuracy and did not pass quality control criteria. For this SNP, a set of 11 proxy SNPs from HapMap r. 22 (all with $R^2 > 0.85$) were studied. All studied SNPs had imputation qualities of 0.3 or greater. In LLS, all IgG measurements were log-transformed. The score statistic for testing for an additive effect of a diallelic locus on quantitative phenotype was used. To account for relatedness in offspring data the kinship coefficients matrix was used when computing the variance of the score statistic. Imputation was dealt with by accounting for loss of information due to genotype uncertainty [101]. For the association analysis of the GWAS data, a score test was applied for the quantitative trait correcting for sex and age using an executable C++ program QTassoc (http://www.lumc.nl/uh, under GWAS Software).

IgG was isolated from plasma samples of 1848 participants. Glycosylation patterns of IgG1 and IgG2 were investigated by analysis of tryptic glycopeptides using MALDI-TOF MS. Six glycoforms per IgG subclass were determined by MALDI-TOF-MS. Since the intensities of all glycoforms were related to the monogalactosylated, core-fucosylated biantennary species (glycoform B), five relative intensities were registered per IgG subclass [102]. Detailed methods are contained in Section 2.4.3.

2.5.4 Results Interpretation

Regions of association were visualized using the web-based software LocusZoom [103] to display the LD relationship between SNPs in the region. The effect of the most significant SNP in each gene region expressed as a percentage of the variance explained was calculated for each glycan trait after adjustment for sex, age and the first 3 principal components in each cohort individually, using the ‘‘polygenic’’ function of the GenABEL package for R. Conditional analysis was undertaken for all significant and suggestive regions. GWAS was performed as described above but with the dosage of the top SNP in the region included as an additional covariate. This was run only for the chromosome containing the association locus. Subsequent meta-analysis was performed as described previously and the results visualised using LocusZoom to ensure that the association peak had been removed.

A preliminary literature search for each associated gene was performed using the NHGRI GWAS Catalog [7] for associations reaching genome-wide significance within a study or reasonably suggestive, if the sample size was large (≥10 000). Additional associations were reported if they were suggestive in a study with a smaller sample size but replicated by another population either within the original publication or in another study. SNAP [104] was used to look at LD between SNP associations from the literature and this study. 1000 Genomes Pilot 1 data from the CEU population was used to calculate LD, and SNPs were accepted to be tagging the same region if D’ = 1 and $r^2 > 0.8$.

2.5.5 Rare Variant Burden Analysis with seqMeta

All statistical analyses were performed using the seqMeta package for R version 1.3 (no paper published but discussed in [81] and uses methodology from [12,13,105,106]) and Exome Chip genotypes. The same phenotypic models were run as for the common variant GWAS. This package is able to account for relationship between individuals using an IBS kinship matrix. This matrix was generated using only Exome Chip SNPs with a MAF > 5% (n~30,000). SNP-to-gene allocations and variant consequences were taken from the SNP Information file compiled within the CHARGE consortium [80,81].

The unidirectional burden tests [107] assume that all variants collaped into an indicator variable are causal and have the same magnitude and direction of effects. Variants considered are often restricted to those with low minor allele frequency (cut-off set at 1% or 5%) presumed likely to be more deleterious and/or those having a “functional” annotation (ie. missense, stop-gain, stop-loss or splice site) also indicating a deleterious effect.

Therefore these tests are more powerful when these assumptions hold and their power declines if they do not. Bidirectional [13] tests are more robust when the variants may have effects on a phenotype in opposite directions and thus are more powerful when this is true. As the traits' underlying genetic architecture is unknown and functional effect somewhat of a guess, both unidirectional and bidirectional tests were performed to capture both situations. Bidirectional (SKAT) and unidirectional (T5) burden tests were performed using only variants with a minor allele frequency (MAF) < 5%. Unidirectional burden tests were also performed using a 1% MAF threshold (T1). The unidirectional tests were unweighted, so were simply based on the number of rare-variants present within an individual in the defined "gene". All genes needed to contain more than one SNP to be included in the analysis and have a cumulative minor allele frequency (cmaf) greater than the frequency calculated for 5 minor alleles within the meta-analysis sample size. A Bonferroni corrected gene-based p-value threshold of 1.85×10^{-06} was used for burden tests (0.05/26,965 genes).

Single variant tests were also run on all SNPs, but only used to further elucidate regions which attained significance in the burden tests.

2.5.6 MODY3 Biomarker Analysis

Standardised residuals were obtained from the linear regression of each *N*-glycan trait adjusting for age, sex and HbA1c. HbA1c was included as a covariate in order to remove any differences between the groups potentially caused by elevated glucose in the blood due to diabetes in T2D and MODY3 patients. Non-diabetic controls were selected from the ORCADES study and were age and sex-matched to the MODY3 cases to have approximately 2 non-diabetic controls for each MODY3 case. One-way ANOVA was performed on each trait to compare the means of different treatment groups (Controls; T2D; MODY3). This analysis was done including all groups (3 stratum test) as well as for all pairwise comparisons in order to determine exactly which groups were statistically different. All glycan groups reaching statistical significance were included together in a backwards linear regression to determine which glycan groups were required to build the best disease prediction model. All analysis was performed in SPSS 17.0.

2.5.7 Correlation Analysis of IgG *N*-glycan Analytical Methods

All glycan traits from the IgG minimal dataset were adjusted for sex, age and relatedness using the "polygenic" function of the GenABEL package for R. The "pgresiduals", which have the polygenic effect removed, were used to calculate Pearson's product-moment correlation coefficients and corresponding p-values using the "cor.test" function in the stats package for R [108]. Correlation coefficients were computed using the same individuals used for GWAS as the genetic data was required to account for relatedness within the population. The correlations were then compared for the same structure from the minimal dataset measure by different methods.

Chapter 3 - Genetic analysis of total plasma protein *N*-glycosylation

3.1 Introduction

Recent technological advances have allowed *N*-glycan structures to be measured in a high-throughput manner. Methods, such as high/ultra performance liquid chromatography (HPLC/UPLC), MALDI-TOF mass spectrometry (MS) and capillary electrophoresis (CE), allow us to quantitate *N*-linked glycans from an individual or a pool of proteins in various biological samples. Colleagues from the Rudd laboratory at NIBRT in Dublin, Ireland and the Lauc laboratory in Zagreb, Croatia, pioneered these high-throughput methods for HPLC & UPLC and have found that the variability of glycans far exceeds the variability of proteins and DNA [36]. However, within a single individual the composition of the plasma *N*-glycome is rather stable over a short period of time [109]. The majority of these *N*-glycans can be influenced to a moderate extent by environmental factors such as smoking, alcohol consumption and diet [110]. Heritabilities ranging from <0.010 to 0.581 were reported [36] suggesting that the discovery of genes regulating variation in the amount of specific *N*-glycan features may be possible. In this Chapter I will present the first GWAS of plasma *N*-glycans in four population isolates [111,112].

3.2 Methods

The CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS cohort data used for this study are described in the Methods Chapter (Section 2.1). SNP genotyping and quality control methods are described in Section 2.2.1.

In all four populations plasma protein *N*-glycans were isolated then analysed by HPLC in 3367 individuals. Detailed methods are contained in Section 2.3. Chromatography yielded a total of 33 measured traits: glycan peak (GP)1–16, desialylate glycan (DG)1–13 and four traits based on the number of sialic acids (MonoS, DiS, TriS and TetraS). An additional 13 parameters were gained by calculating some structural determinants from measured traits. A description of each glycan trait is presented in Appendix Table 15 along with equations for the additional 13 derived traits.

Data were checked for any extreme values which would indicate gross measurement error. After phenotype quality control the number of individuals with complete phenotype, covariate and genotype information for the meta-analysis was 3104 for GP, 3093 for DG and 3148 for WAX. For the maximum sample size (WAX) this consisted of 894 from

CROATIA-Vis, 896 from CROATIA-Korcula, 886 from ORCADES and 652 from NSPHS, with slightly more women than men (approximately 60:40 split across all cohorts).

In the discovery populations, genome-wide association analysis was firstly performed for each population and then combined using an inverse-variance weighted meta-analysis for all traits. Each trait was adjusted for sex, age and the first 3 principal components. The residuals were transformed to ensure their normal distribution using quantile normalisation. Initially GWAS was performed on directly genotyped data then later rerun using HapMap2 imputed genotype dosages. Analysis results for this association only are presented in the results section. Results from the initial analysis of directly genotyped data were published in Lauc *et al*. (2010) [112] and Huffman *et al*. (2011) [111]. Inverse-variance weighted meta-analysis was performed using the MetABEL package [73] for R. All methods used for statistical analysis are described in more detail in the Methods Chapter (Section 2.5.1).

Rare variant analysis was undertaken for only the *N*-glycan traits which achieved a p-value < $5x10^{-08}$ in the common variant GWAS using Exome Chip genotypes. This data was available in CROATIA-Korcula only (n=855). Analysis was performed using the seqMeta package (v1.3) for R. A bidirectional burden test (SKAT) at a 5% MAF threshold and unidirectional burden tests using a 5% (T5) or 1% (T1) MAF threshold were performed. A Bonferroni corrected gene-based p-value threshold of $1.85x10^{-06}$ was used for burden tests (0.05/26,965 genes). See Sections 2.2.3 and 2.5.5 for more detailed information on the genotyping chip and statistical methods.

A table describing which samples contributed to which analysis is found in Appendix Table 22.

3.3 Results

3.3.1 Genome-wide Association Study

A meta-analysis of genome-wide association results was conducted for 46 plasma *N*-glycan traits (Table 15) measured in four population-based samples, CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS. Initial results from genotype (rather than imputed data) suggested that there were no sex-specific differences that could reliably be attributed to sex, rather than the sample size difference so sex-specific analyses were not undertaken for the imputed dataset (Appendix Table 23). Descriptive statistics and heritabilities for all traits are presented in Table 2. Heritability estimates were variable between populations, as might be expected given the isolated nature of the populations. However, all traits had at least one population displaying a heritability > 0.2, with most having at least one population in which heritability was > 0.4. DG10 showed a fairly consistent heritability across populations (h^2 = 0.37–0.46), whereas GP10 was much more variable (h^2 = 0.23–0.70).

Meta-analysis summary data for each significantly associated gene region are presented in Table 3. Summary data for all SNPs achieving a P-value<$1x10^{-07}$ are presented in Appendix Table 24. Quantile–quantile plots for each association were consistent with an excess of true genetic associations, with low genomic control inflation for each population (inflation factor < 1.05 for all traits in each population (range=0.97-1.04, mean=1.00) as well as the meta-analysis (range=0.98-1.02, mean=1.00)), suggesting that the observed results were not due to population stratification.

The most statistically significant association was found with several SNPs located on chromosome 19. GP13, GP14, DG7, DG8, DG9, DG11, DG12 and A-FUC were all significantly associated with SNPs in this region. The most significant association was found with DG9 for SNP rs3760775 (P = $2.92x10^{-45}$), located 1.6 kb 5′ of *fucosyltranferase 6* (*FUT6*, Entrez GeneID: 2528). The effect size of the T allele of rs3760775 was the largest of all traits, -0.74 (SE 0.05) for DG9 [z-score units, after adjustment for sex, age and principal components (PC)]. Figure 9 shows the cohort level beta values along with their contribution to the meta-analysis effect size. The association region for this SNP contains the *NRTN*, *FUT6* and *FUT3* genes between two recombination hotspots (Figure 9). *FUT6* encodes the enzyme fucosyltransferase VI, which was reported to be the key enzyme responsible for the antennary fucosylation of plasma proteins [113], thus the causal variant(s) probably affect this gene. SNP rs3760775 explained 2.3, 8.8, 8.2 and 8.5% of the variance of DG9 (adjusted for sex, age and PC) in CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS, respectively. After conditioning on this top SNP for DG9, another SNP (rs10406157) in the same region was still significant (P_{COND}=$9.05x10^{-13}$) (Figure 10a). It explained an additional 0.3, 2.1, 1.1 and 9.0% of the variance of DG9 (adjusted for sex, age, PC) on top of rs3760775 in CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS, respectively. This SNP was not well imputed (mean RSq across cohorts = 0.40) therefore these estimates should be treated with caution. After adjusting for rs3760775 and rs10406157, a second peak remained with the top SNPs covering *FUT5* and *NDUFA11* which lie adjacent to the *FUT6/FUT3* region (Figure 10b). The top SNP (rs10421538) does not achieve significance but there is an obvious peak which did not appear in the discovery analysis. It explained an additional 1.5, 0.9, 1.2 and 0.1% of the variance of DG9 (adjusted for sex, age, PC) on top of rs3760775 and rs10406157 in CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS,

Table 2: Mean, standard deviation and heritabilities for total *N*-glycan traits.

Trait	Cohort	N	Mean	SD	h^2*	se(h^2)	p(h^2)
age	Vis	918	56.36	15.54	NA	NA	NA
	Korcula	898	56.27	13.94	NA	NA	NA
	ORCADES	889	53.49	15.73	NA	NA	NA
	NSPHS	656	46.98	20.70	NA	NA	NA
GP1	Vis	872	0.18	0.09	0.4227	0.0989	1.90E-05
	Korcula	893	0.16	0.13	0.5919	0.1124	1.39E-07
	ORCADES	878	0.22	0.30	0.3804	0.0743	3.03E-07
	NSPHS	646	0.12	0.07	0.5295	0.0659	9.15E-16
GP2	Vis	872	4.15	1.58	0.2304	0.0963	1.68E-02
	Korcula	893	3.41	1.21	0.3031	0.1043	3.65E-03
	ORCADES	878	4.01	1.92	0.2237	0.0640	4.75E-04
	NSPHS	646	4.08	1.62	0.5503	0.0580	2.19E-21
GP3	Vis	872	2.12	0.45	0.1251	0.0803	1.19E-01
	Korcula	893	2.03	0.45	0.3671	0.1223	2.69E-03
	ORCADES	878	2.50	0.86	0.3046	0.0707	1.63E-05
	NSPHS	646	2.03	0.43	0.5761	0.0826	3.06E-12
GP4	Vis	872	5.94	1.16	0.1941	0.0826	1.88E-02
	Korcula	893	5.06	1.13	0.4594	0.1015	6.06E-06
	ORCADES	878	6.46	2.03	0.3134	0.0650	1.44E-06
	NSPHS	646	5.91	1.33	0.4467	0.0499	3.42E-19
GP5	Vis	872	2.28	0.41	0.3896	0.0992	8.57E-05
	Korcula	893	2.48	0.45	0.4247	0.0990	1.78E-05
	ORCADES	878	3.87	1.00	0.1417	0.0496	4.30E-03
	NSPHS	646	2.16	0.41	0.5511	0.0673	2.66E-16
GP6	Vis	872	4.10	0.86	0.2163	0.0835	9.61E-03
	Korcula	893	3.61	0.82	0.4900	0.0940	1.86E-07
	ORCADES	878	5.11	1.18	0.2821	0.0691	4.47E-05
	NSPHS	646	4.24	0.88	0.4275	0.0609	2.28E-12
GP7	Vis	872	10.58	2.30	0.1215	0.0706	8.53E-02
	Korcula	893	11.11	3.05	0.1659	0.0714	2.02E-02
	ORCADES	878	15.18	2.48	0.2162	0.0497	1.39E-05
	NSPHS	646	9.32	1.44	0.4154	0.0684	1.23E-09
GP8	Vis	872	9.97	1.54	0.2067	0.0869	1.74E-02
	Korcula	893	9.10	1.45	0.3823	0.0816	2.82E-06
	ORCADES	878	10.18	1.70	0.5071	0.0736	5.43E-12
	NSPHS	646	9.64	1.44	0.3986	0.0680	4.51E-09
GP9	Vis	872	36.92	3.01	0.2766	0.1002	5.79E-03
	Korcula	893	38.02	3.05	0.5443	0.1043	1.80E-07
	ORCADES	878	33.95	4.70	0.0480	0.0405	2.36E-01
	NSPHS	646	37.71	2.95	0.4769	0.0598	1.47E-15
GP10	Vis	872	7.55	1.77	0.2298	0.0977	1.87E-02
	Korcula	893	7.52	1.47	0.4901	0.0830	3.46E-09
	ORCADES	878	5.87	2.53	0.3664	0.0774	2.19E-06
	NSPHS	646	7.96	1.49	0.6962	0.0838	9.80E-17
GP11	Vis	872	2.35	0.67	0.2916	0.0996	3.42E-03
	Korcula	893	1.67	0.44	0.3362	0.0757	8.83E-06
	ORCADES	878	2.59	0.61	0.2297	0.0580	7.46E-05
	NSPHS	646	1.50	0.20	0.1230	0.0553	2.63E-02
GP12	Vis	872	1.48	0.29	0.4744	0.1021	3.38E-06
	Korcula	893	1.91	0.52	0.5393	0.0885	1.09E-09
	ORCADES	878	2.56	0.99	0.1916	0.0617	1.90E-03
	NSPHS	646	1.78	0.32	0.4650	0.0743	3.90E-10

Trait	Cohort	N	Mean	SD	h^2*	se(h^2)	p(h^2)
GP13	Vis	872	4.92	1.41	0.5732	0.1047	4.38E-08
	Korcula	893	5.55	1.52	0.4723	0.0949	6.41E-07
	ORCADES	878	3.03	1.41	0.2583	0.0607	2.11E-05
	NSPHS	646	5.64	1.57	0.6405	0.0757	2.55E-17
GP14	Vis	872	6.33	1.42	0.4792	0.0953	4.90E-07
	Korcula	893	6.66	1.56	0.4247	0.1009	2.54E-05
	ORCADES	878	3.77	1.85	0.3338	0.0692	1.41E-06
	NSPHS	646	6.19	1.54	0.4446	0.0728	1.01E-09
GP15	Vis	872	0.45	0.17	0.3487	0.0962	2.89E-04
	Korcula	893	0.61	0.19	0.4933	0.0878	1.95E-08
	ORCADES	877	0.33	0.48	0.2501	0.0624	6.18E-05
	NSPHS	646	0.62	0.20	0.5401	0.0809	2.44E-11
GP16	Vis	872	0.67	0.23	0.2330	0.0836	5.33E-03
	Korcula	893	1.09	0.27	0.3510	0.1041	7.49E-04
	ORCADES	874	0.38	0.28	0.2677	0.0644	3.19E-05
	NSPHS	646	1.11	0.25	0.2952	0.0679	1.39E-05
DG1	Vis	893	0.19	0.09	0.5359	0.1172	4.82E-06
	Korcula	884	0.20	0.12	0.5244	0.1132	3.64E-06
	ORCADES	850	0.22	0.24	0.3824	0.0694	3.61E-08
	NSPHS	646	0.15	0.07	0.5491	0.0673	3.55E-16
DG2	Vis	893	4.21	1.53	0.2809	0.0981	4.19E-03
	Korcula	884	3.59	1.15	0.2675	0.1013	8.26E-03
	ORCADES	850	3.77	1.38	0.1896	0.0564	7.71E-04
	NSPHS	646	4.29	1.58	0.5477	0.0578	2.68E-21
DG3	Vis	893	2.71	0.51	0.1621	0.0842	5.42E-02
	Korcula	884	2.72	0.50	0.4032	0.1225	9.97E-04
	ORCADES	850	3.18	0.70	0.2752	0.0605	5.46E-06
	NSPHS	646	2.65	0.51	0.4444	0.0796	2.41E-08
DG4	Vis	893	7.00	1.27	0.1569	0.0756	3.80E-02
	Korcula	884	6.27	1.18	0.3812	0.1007	1.54E-04
	ORCADES	850	6.58	1.36	0.3287	0.0529	5.36E-10
	NSPHS	646	7.12	1.48	0.4774	0.0535	4.70E-19
DG5	Vis	893	49.19	3.58	0.0062	0.0085	4.67E-01
	Korcula	884	50.51	3.97	0.2749	0.0902	2.32E-03
	ORCADES	850	51.26	2.86	0.3157	0.0755	2.92E-05
	NSPHS	646	48.89	3.43	0.4168	0.0553	4.93E-14
DG6	Vis	893	16.00	2.94	0.1693	0.0738	2.18E-02
	Korcula	884	14.22	2.61	0.4431	0.0930	1.90E-06
	ORCADES	850	13.87	2.33	0.3715	0.0815	5.14E-06
	NSPHS	646	15.26	2.55	0.5114	0.0780	5.54E-11
DG7	Vis	893	1.55	0.41	0.4590	0.0993	3.78E-06
	Korcula	884	1.62	0.50	0.2456	0.0775	1.54E-03
	ORCADES	850	1.49	0.40	0.5588	0.0804	3.65E-12
	NSPHS	646	1.61	0.73	0.4618	0.0595	8.13E-15
DG8	Vis	893	10.92	2.07	0.5337	0.0951	1.99E-08
	Korcula	884	11.90	2.25	0.4307	0.1000	1.66E-05
	ORCADES	850	11.70	2.61	0.3506	0.0641	4.57E-08
	NSPHS	646	11.96	2.29	0.6243	0.0732	1.49E-17
DG9	Vis	893	3.67	1.31	0.4860	0.0941	2.44E-07
	Korcula	884	3.80	1.41	0.4484	0.0956	2.71E-06
	ORCADES	850	3.43	1.46	0.4401	0.0727	1.40E-09
	NSPHS	646	3.37	1.46	0.5928	0.0676	1.92E-18
DG10	Vis	893	1.08	0.18	0.3876	0.0995	9.83E-05
	Korcula	884	1.16	0.19	0.4571	0.0998	4.64E-06

Trait	Cohort	N	Mean	SD	h^2*	se(h^2)	p(h^2)
	ORCADES	850	1.02	0.40	0.3884	0.0667	5.73E-09
	NSPHS	646	1.01	0.17	0.3692	0.0685	7.09E-08
DG11	Vis	893	2.18	0.54	0.4542	0.0878	2.34E-07
	Korcula	884	2.45	0.55	0.4045	0.0985	4.04E-05
	ORCADES	850	2.23	0.77	0.1779	0.0612	3.62E-03
	NSPHS	646	2.41	0.58	0.4712	0.0671	2.13E-12
DG12	Vis	893	0.71	0.31	0.3446	0.0831	3.36E-05
	Korcula	884	0.79	0.31	0.3633	0.0908	6.32E-05
	ORCADES	849	0.67	0.35	0.3486	0.0712	9.65E-07
	NSPHS	646	0.67	0.32	0.5331	0.0651	2.55E-16
DG13	Vis	893	0.58	0.30	0.1128	0.0697	1.06E-01
	Korcula	884	0.78	0.25	0.3057	0.0915	8.31E-04
	ORCADES	843	0.61	0.32	0.1667	0.0661	1.17E-02
	NSPHS	646	0.61	0.20	0.2943	0.0655	6.91E-06
MonoS	Vis	900	24.60	3.26	0.3824	0.0994	1.19E-04
	Korcula	896	23.65	3.90	0.3657	0.1037	4.21E-04
	ORCADES	886	27.48	3.99	0.3163	0.0753	2.66E-05
	NSPHS	652	22.59	2.57	0.4633	0.0769	1.68E-09
DiS	Vis	900	58.43	2.32	0.5289	0.0983	7.48E-08
	Korcula	896	57.30	2.47	0.3808	0.1174	1.18E-03
	ORCADES	886	57.35	2.76	0.4434	0.0686	1.02E-10
	NSPHS	652	60.00	1.97	0.3395	0.0599	1.44E-08
TriS	Vis	900	14.86	2.07	0.3880	0.0954	4.78E-05
	Korcula	896	15.06	2.34	0.4334	0.0997	1.38E-05
	ORCADES	886	13.34	2.65	0.1575	0.0639	1.37E-02
	NSPHS	652	15.15	2.00	0.4191	0.0710	3.56E-09
TetraS	Vis	900	2.11	0.69	0.3962	0.1025	1.11E-04
	Korcula	896	3.99	1.29	0.4152	0.0896	3.55E-06
	ORCADES	886	1.71	0.67	0.0438	0.0398	2.71E-01
	NSPHS	652	2.26	0.54	0.4352	0.0753	7.65E-09
BAMS	Vis	863	30.77	3.11	0.3662	0.0961	1.39E-04
	Korcula	879	30.40	3.59	0.2429	0.0954	1.09E-02
	ORCADES	840	38.10	4.19	0.1593	0.0491	1.17E-03
	NSPHS	646	28.46	3.96	0.3269	0.0629	2.01E-07
BADS	Vis	863	70.25	3.86	0.3057	0.0990	2.01E-03
	Korcula	879	71.29	4.33	0.3453	0.0989	4.82E-04
	ORCADES	840	63.71	6.87	0.0000	0.0000	4.92E-01
	NSPHS	646	70.92	8.64	0.3833	0.0725	1.22E-07
BA	Vis	893	80.85	2.39	0.3095	0.0861	3.26E-04
	Korcula	884	79.12	2.76	0.4419	0.1100	5.91E-05
	ORCADES	850	80.36	3.64	0.1924	0.0542	3.88E-04
	NSPHS	646	79.96	2.54	0.3887	0.0750	2.21E-07
TRIA	Vis	893	15.67	1.88	0.3525	0.0915	1.17E-04
	Korcula	884	16.85	2.20	0.4536	0.1108	4.23E-05
	ORCADES	850	16.15	2.75	0.1968	0.0529	2.00E-04
	NSPHS	646	16.35	2.00	0.4347	0.0777	2.22E-08
TA	Vis	893	3.48	0.85	0.2741	0.0758	2.97E-04
	Korcula	884	4.03	0.78	0.3721	0.0970	1.25E-04
	ORCADES	850	3.49	1.16	0.1700	0.0606	5.06E-03
	NSPHS	646	3.69	0.73	0.3241	0.0678	1.73E-06
C-FUC	Vis	893	24.54	4.35	0.1061	0.0629	9.14E-02
	Korcula	884	22.00	4.10	0.3835	0.0933	3.95E-05
	ORCADES	850	21.27	3.37	0.3915	0.0832	2.51E-06
	NSPHS	646	23.80	3.87	0.4972	0.0732	1.11E-11

Trait	Cohort	N	Mean	SD	h^2*	se(h^2)	p(h^2)
A-FUC	Vis	893	3.06	0.82	0.4338	0.1043	3.18E-05
	Korcula	884	3.12	0.99	0.2855	0.0794	3.23E-04
	ORCADES	850	2.84	0.77	0.5015	0.0781	1.34E-10
	NSPHS	646	3.18	1.41	0.4539	0.0658	5.42E-12
A2	Vis	863	0.19	0.09	0.5117	0.1159	1.00E-05
	Korcula	879	0.18	0.12	0.5671	0.1131	5.33E-07
	ORCADES	840	0.22	0.27	0.3791	0.0742	3.23E-07
	NSPHS	647	0.14	0.07	0.5387	0.0654	1.75E-16
G0	Vis	893	4.40	1.57	0.2747	0.0990	5.53E-03
	Korcula	884	3.79	1.19	0.2624	0.1046	1.21E-02
	ORCADES	850	3.99	1.44	0.2043	0.0573	3.64E-04
	NSPHS	647	4.43	1.62	0.5331	0.0575	1.74E-20
G1	Vis	893	9.71	1.48	0.1576	0.0825	5.62E-02
	Korcula	884	8.99	1.37	0.3513	0.1044	7.66E-04
	ORCADES	850	9.75	1.75	0.3089	0.0538	9.68E-09
	NSPHS	647	9.75	1.66	0.5015	0.0575	2.71E-18
G2	Vis	893	66.74	2.81	0.1504	0.0719	3.64E-02
	Korcula	884	66.34	3.03	0.2573	0.0893	3.96E-03
	ORCADES	850	66.62	2.63	0.2217	0.0681	1.14E-03
	NSPHS	647	65.65	3.88	0.3982	0.0499	1.49E-15
G3	Vis	872	12.73	1.92	0.3933	0.1023	1.22E-04
	Korcula	893	14.13	2.31	0.4157	0.1107	1.74E-04
	ORCADES	878	9.37	3.58	0.2646	0.0648	4.44E-05
	NSPHS	654	13.45	2.50	0.3638	0.0679	8.41E-08
G4	Vis	872	1.12	0.36	0.2457	0.0854	4.00E-03
	Korcula	893	1.70	0.43	0.4267	0.1005	2.16E-05
	ORCADES	878	0.72	0.66	0.2436	0.0625	9.57E-05
	NSPHS	654	1.71	0.45	0.3406	0.0675	4.55E-07

N: number of samples with both genotype and trait data available; Mean: trait mean, SD: trait standard deviation; h^2: heritability estimate; se(h^2): standarad error of the heritability estimate; p(h^2): p-value for heritability estimate

* heritabilities are calculated after adjustment for sex and age

Table 3: Genome-wide significant ($P<1.52x10^{-09}$) or strongly suggestive ($P<5x10^{-08}$) SNP associations with total plasma *N*-glycans analysed by HPLC.

Chr	SNP with lowest P-value	Lowest P-value	Effect Size* (s.e.)	MAF	Mean RSq	nHits	nTraits	Genes in Region	Trait with lowest P-value+	Other Associated Traits
Genome-wide Significant										
2	rs2442046	$1.79x10^{-10}$	0.187 (0.029)	0.261	0.983	9	2	*MIR3679; MGAT5*	TA	DG11
3	rs10470450	$1.23x10^{-13}$	0.229 (0.031)	0.232	0.980	17	1	*CHST2; SLC9A9; SLC9A9-AS1*	TetraS	
12	rs7310409	$2.63x10^{-13}$	-0.198 (0.027)	0.444	0.941	31	7	*HNF1A-AS1; HNF1A; C12orf43; OASL*	DG7	GP13$, GP15$, DG8$, DG9, DG11$, A-FUC
14	rs11847263	$7.57x10^{-31}$	0.314 (0.027)	0.392	0.986	249	7	*MIR4708; FUT8-ASI; FUT8*	DG1	A2, C-FUC$, GP1, GP10$, DG6$, DG10$
16	rs217181	$2.49x10^{-14}$	0.257 (0.034)	0.195	0.923	8	5	*DHODH; HP; HPR*	G3	GP7$, DG8, DG11, MonoS$, TriS, BA$, BAMS$, TRIA
19	rs3760775	$2.92x10^{-45}$	-0.744 (0.053)	0.082	0.794	4	8	*NRTN; FUT6; FUT3*	DG9	GP13$, GP14, DG7, DG8$, DG11$, DG12, A-FUC
Strongly Suggestive										
1	rs1984769	$2.54x10^{-08}$	-0.237 (0.043)	0.228	0.483	1	1	*FCGR2C*	GP4	
2	rs2681019	$3.73x10^{-08}$	-0.144 (0.026)	0.448	0.991	4	1	no genes +/- 400kb	DG3	
2	rs13030345	$2.66x10^{-09}$	-0.210 (0.035)	0.186	0.868	7	1	*MRPL33; RBKS*	DG3	
4	rs13107325	$4.73x10^{-09}$	0.284 (0.048)	0.076	0.903	1	1	*BANK1; SLC39A8*	GP5	
6	rs3094093	$1.69x10^{-08}$	0.247 (0.044)	0.101	0.755	1	1	*MDC1*	GP1	
11	rs7948031	$3.93x10^{-08}$	-0.233 (0.042)	0.116	0.930	2	1	*B3GAT1*	DG13	

nHits:number of SNPs with GW-significant or strongly suggestive association; nTraits:number of *N*-glycan traits associated with the region at GW-significant level; MAF: minor allele frequency; Mean RSq: average imputation quality (RSq) across meta-analysis populations
* effect size is for the minor allele in standard deviation units after adjustment for sex, age and first 3 principle components; + description of the traits provided in Table 15; $ SNP effect is in the opposite direction to the most significant trait

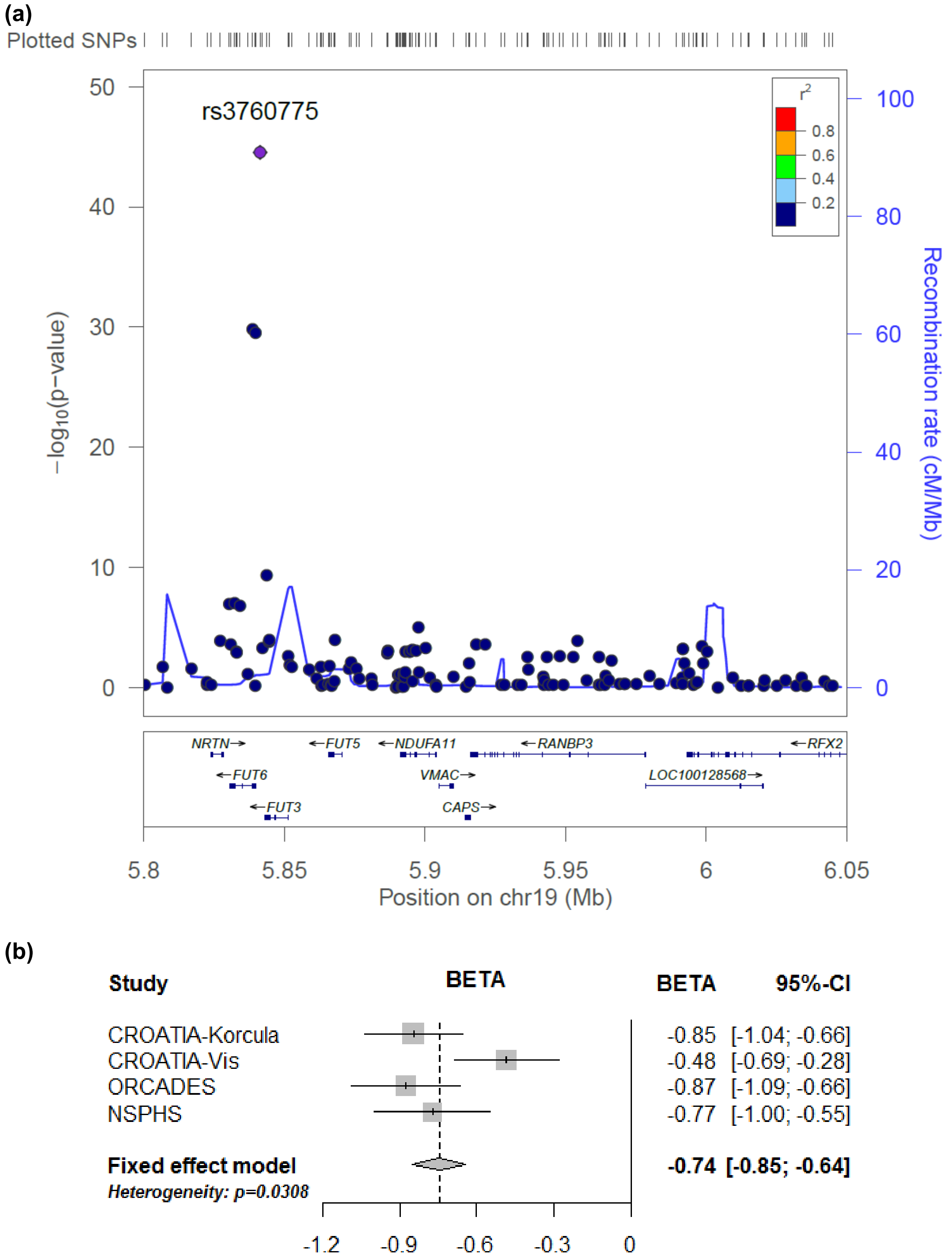
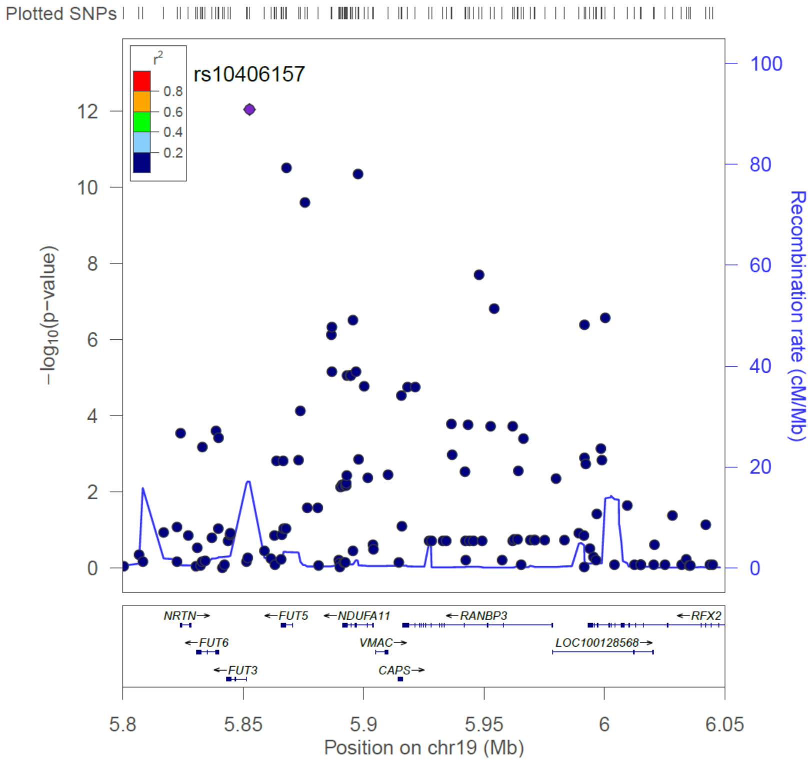


Figure 9: Significance (a) and Forest (b) plots for chromosome 19 region of the DG9 meta-analysis.
(a) -Log_{10} of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

(a)



(b)

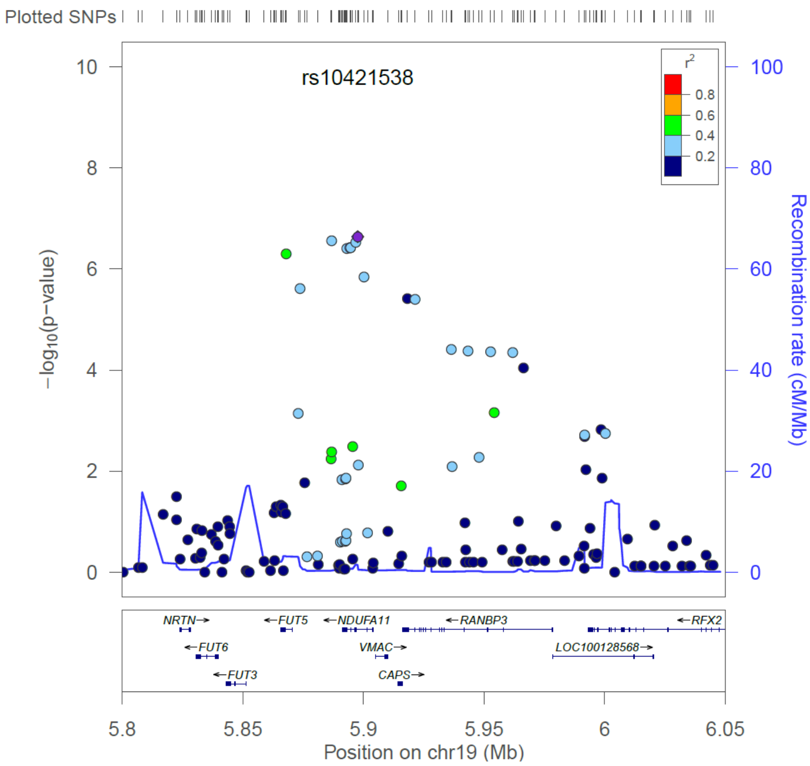


Figure 10: Significance plot for chromosome 19 region of the DG9 meta-analysis after conditioning on (a) rs3760775 and (b) rs3760775 + rs10406157.
-Log^{10} of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.

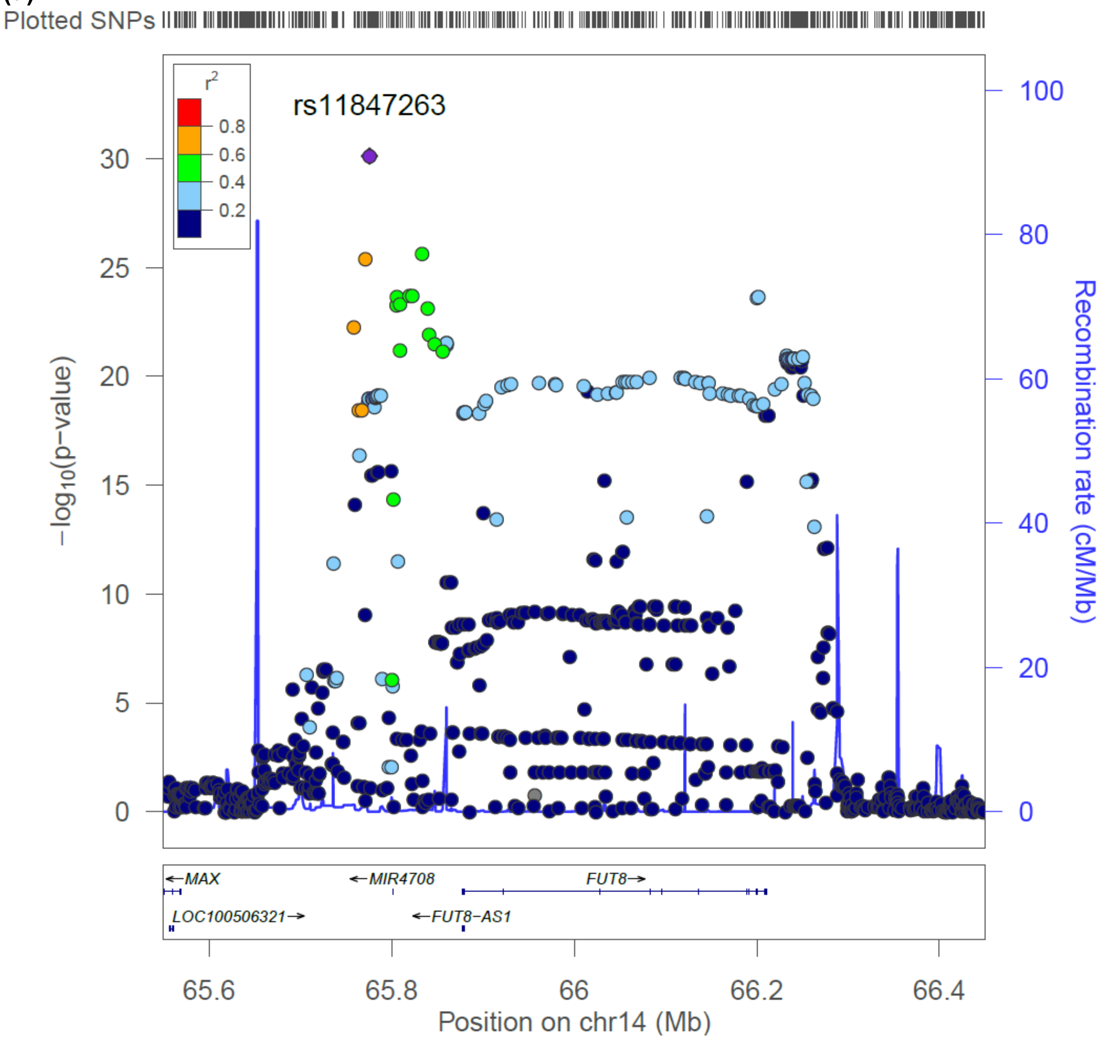
respectively. A final analysis of DG9 conditioning on all three SNPs removed all signal from the region. This was the only association which had a secondary association peak after conditional analysis.

An association peak containing 248 SNPs was located in the region encompassing the *fucosyltranferase 8* (*FUT8*, Entrez GeneID: 2530) gene on chromosome 14 (Figure 11). SNPs in this region were associated with DG1, DG6, DG10, GP1, GP10, C-FUC and A2. The *FUT8* gene product, fucosytransferase VIII, is responsible for the core fucosylation of *N*-glycans and all SNP association effects were in a manner consistent with the biological role of the FUT8 enzyme [45]. The most significant signal for DG1 was located 102kb 5′ of the gene (rs11847263, $P = 7.57x10^{-31}$). It explained 2.8, 9.3, 3.0 and 3.0% of the variance of DG1 (adjusted for sex, age and PC) in CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS, respectively. All SNPs significantly associated with DG1 levels were in high LD (r^2 >0.5) and located between two recombination hotspots, while no associations were found with SNPs located outside these boundaries nor with other genes located within this association interval.

Five SNPs on chromosome 12, the most significant being rs7310409, showed genome-wide significant associations with DG7 ($P = 2.63x10^{-13}$). SNPs within this region were also associated with GP13 ($P = 3.47x10^{-09}$), GP15 ($P = 3.96x10^{-08}$), DG9 ($P = 1.06x10^{-12}$), DG11 ($P = 9.16x10^{-09}$) and FUC-A ($P=1.31x10^{-11}$). All SNPs are located within or 5′ of the *HNF1 homeobox A* (*HNF1A*, Entrez GeneID: 6927) gene region, with rs7310409 located intronically. Four other genes are located between the recombination hotspots that comprise the boundaries of the association interval, *C12orf27*, *HNF1A-AS1, C12orf43* and *OASL* (Figure 12); however, none of the most significantly associated SNPs are located in these genes. An antisense transcript (*HNF1A-ASI*) is present in this region so even though the top SNP is in *HNF1A*, it is possible that it is affecting the regulation of the antisense transcript. Further functional work would need to be undertaken to investigate this fully. SNP rs7310409 explained 3.5, 1.2, 1.0 and 2.5% of the variance of sex-, age- and PC-adjusted DG7 in CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS, respectively.

An association peak on chromosome 2 was associated with DG11 and TA, a derived trait quantifying tetra-antennary glycans. The top SNP, rs2442046, ($P = 6.09x10^{-10}$, $P = 1.79x10^{-10}$) is intronic within the gene encoding mannosyl (alpha-1,6)-glycoprotein (beta-1,6)-N-acetylglucosaminyltransferase (*MGAT5*, Entrez GeneID: 4249). There is an area of high recombination in the middle of the *MGAT5*, indicating that the causal variant is most likely in the region 5′ of this hotspot (Figure 13). The effect size of the minor allele of rs2442046 is

(a)



(b)

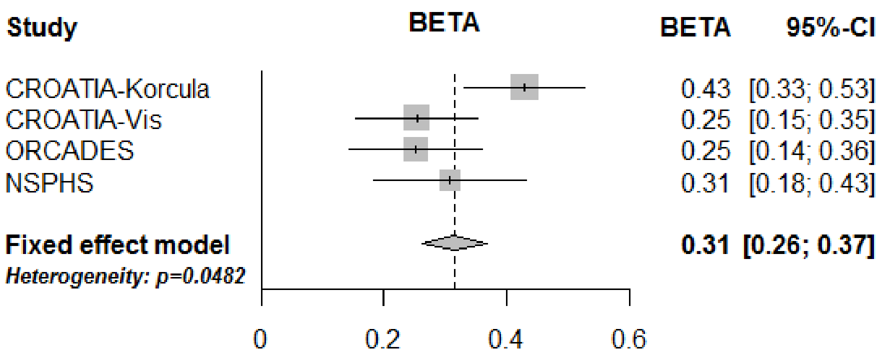


Figure 11: Significance (a) and Forest (b) plots for chromosome 14 region of the DG1 meta-analysis.

(a) -Log_{10} of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

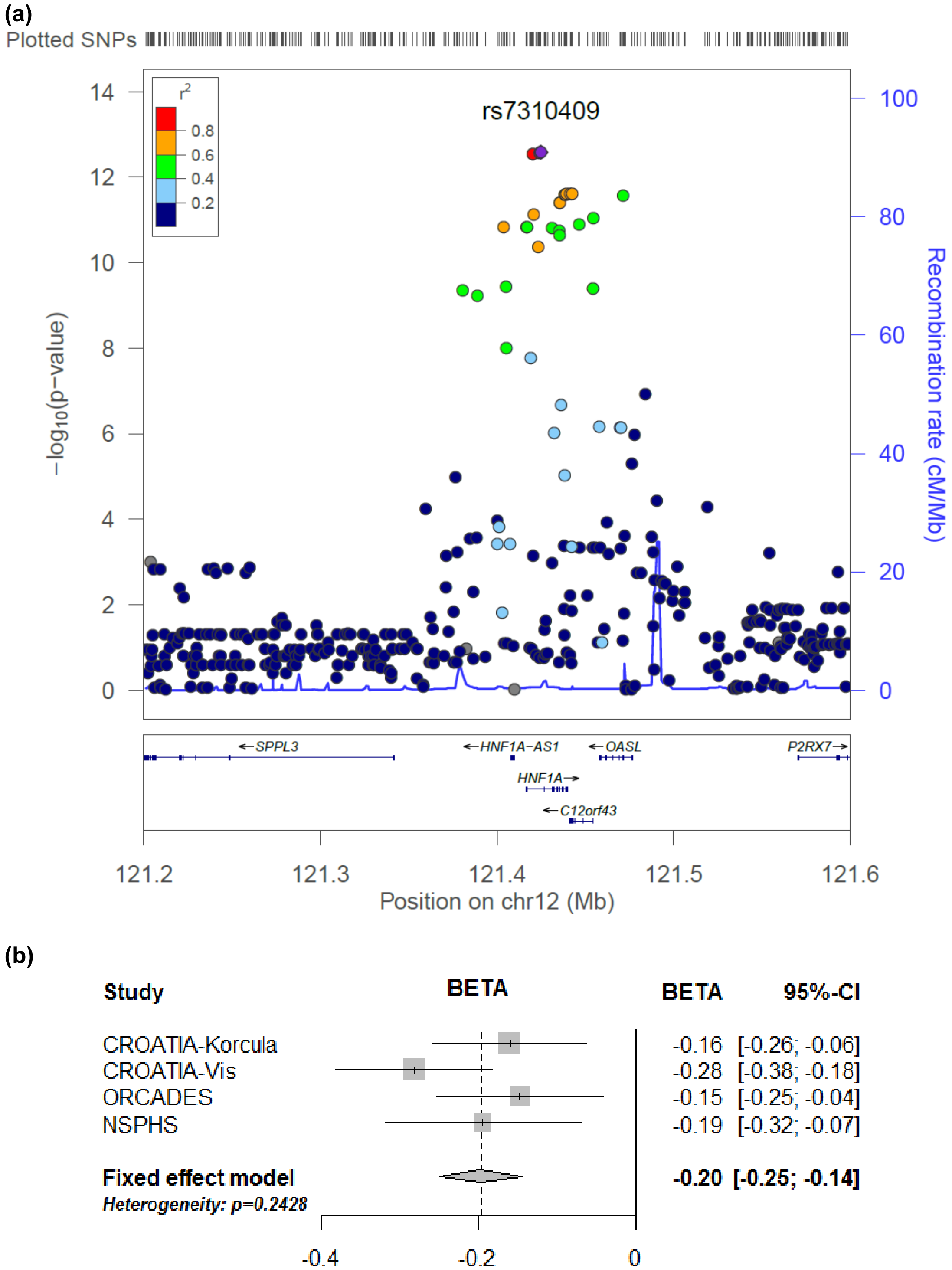


Figure 12: Significance (a) and Forest (b) plots for chromosome 12 region of the DG7 meta-analysis.

(a) -Log$_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

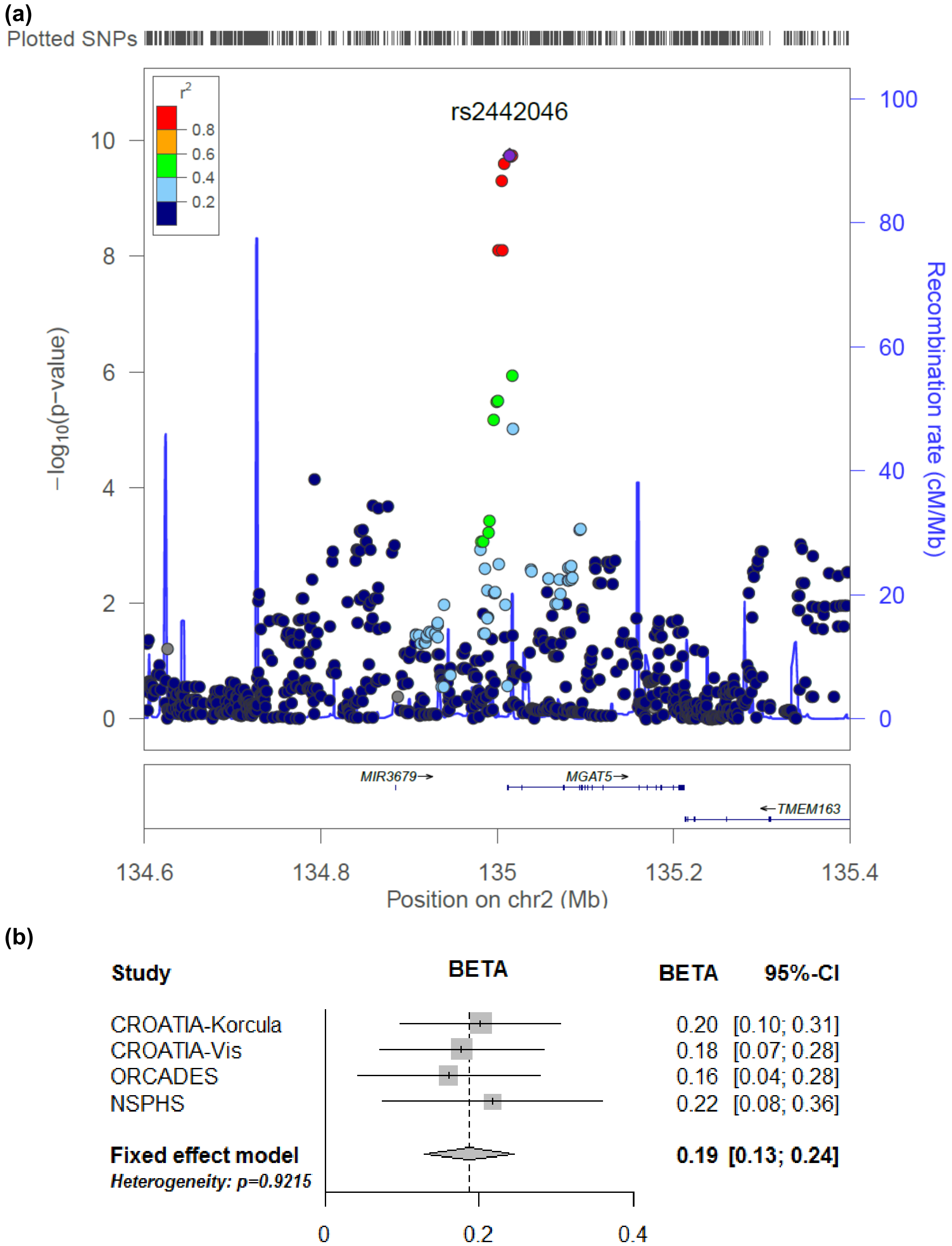


Figure 13: Significance (a) and Forest (b) plots for chromosome 2 region of the TA meta-analysis.

(a) -Log_{10} of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

0.184 (SE 0.030) for DG11 and 0.187 (SE 0.029) for TA (z-score units, after adjustment for sex, age and PC). SNP rs2442046 explained 1.2, 1.6, 0.8 and 1.7% of the variance of sex-, age- and PC-adjusted TA in CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS,respectively.

A group of SNPs on chromosome 3 were significantly associated with tetrasialylated glycans (TetraS) with top SNP rs9829667 ($P = 2.12 \times 10^{-12}$). All associated SNPs are found 3′ of *solute carrier family 9, member 9* (*SLC9A9* Entrez GeneID: 285195). The effect size for the minor allele rs9829667 is 0.217 (SE 0.031) (z-score units, after adjustment for sex, age and PC). All significant SNPs fall between the 3′ end of the *SLC9A9* gene and just before the 3′ end of *CHST2* but not within *CHST2*, which is oriented tail-to-tail with *SLC9A9* (Figure 14). There is a large spike in the recombination rate separating the region of association from the 3′ end of *CHST2* so the causal variant most likely falls in the region closer to *SLC9A9*. SNP rs9829667 explained 3.1, 1.4, 0.9 and 2.4% of the variance of tetrasialylated glycans (adjusted for sex, age and PC) in CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS, respectively.

Finally, a region on chromosome 16 was associated with levels of GP7, TriS, BAMS, BA and G3. The top SNP in the region was rs217181 and was most significantly associated with G3 ($P= 8.58 \times 10^{-13}$), explaining 2.9, 2.0, 0.7 and 3.1% of the variance (adjusted for age, sex and PCs) in CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS. This SNP is located just 3’ of *haptoglobin-related protein* (*HPR*, Entrez GeneID: 3250) (Figure 15). Other genes in the region include *hatoglobin* (*HP*, Entrez GeneID: 3240) and *dihydroorotate dehydrogenase* (*DHODH*, Entrez GeneID: 1723). There are many genes in this region without a recombination spike, but none have any obvious relation to *N*-glycosylation, therefore it is not certain what functional unit (gene, miRNA, regulatory region, etc.) is causing this association.

A peak on chromosome 1 achieved strongly suggestive p-values with the association of GP4 (Figure 16). This region contains many genes, several of which belong to thelow-affinity immunoglobulin gamma Fc receptor family. LD information was not available within the EUR 1000G dataset used for plotting. The top SNP was rs1984769 ($P=2.54 \times 10^{-08}$) which is located within *Fc fragment of IgG, low affinity IIc* (*FCGR2C*, EntrezGeneID: 9103) which is a receptor for CD32.

Two additional peaks on chromosome 2 were strongly suggestively associated with DG3. The first had no genes located +/- 400kb of the top SNP (rs2681019, $P=3.73 \times 10^{-08}$) as

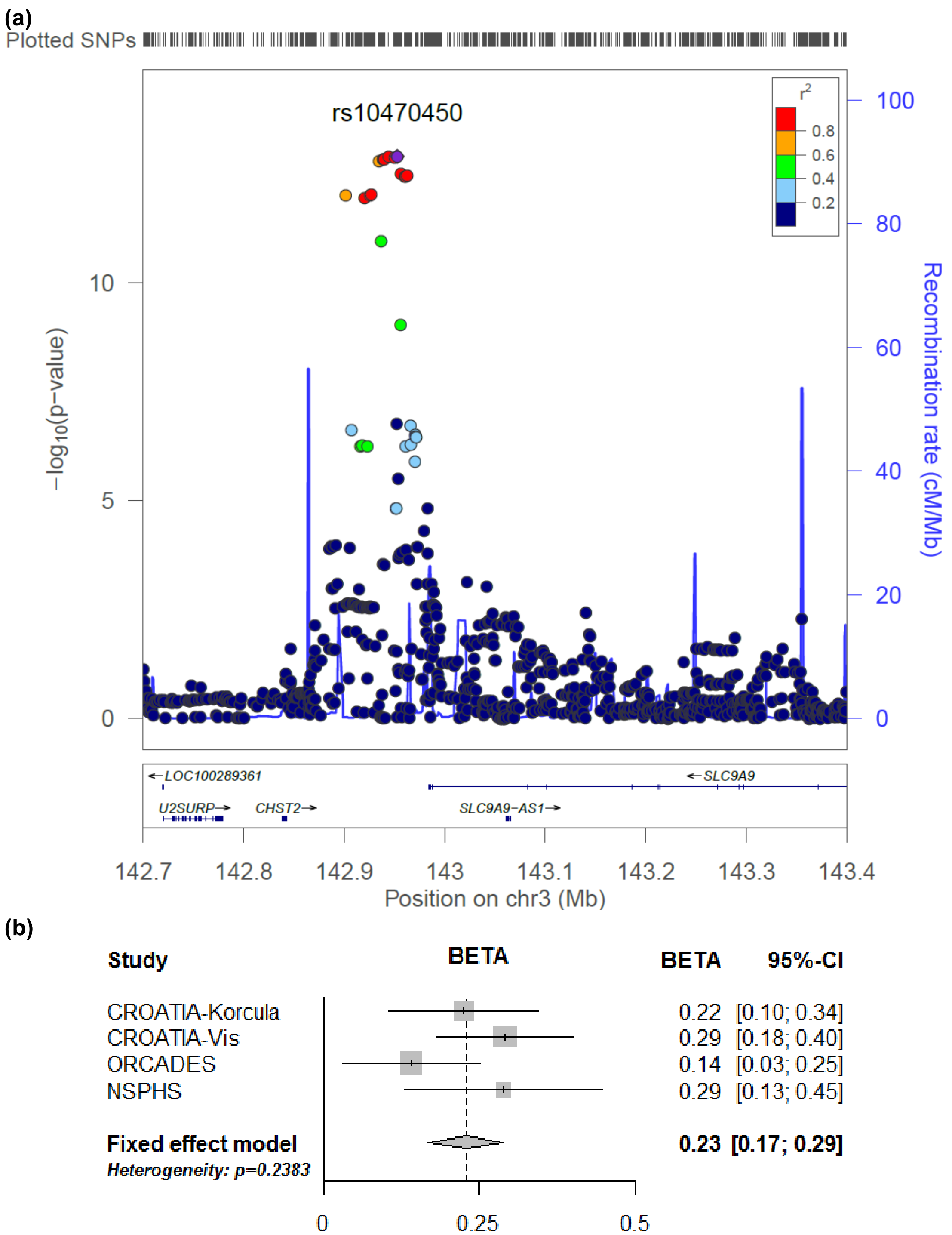


Figure 14: Significance (a) and Forest (b) plots for chromosome 3 region of the TetraS meta-analysis.

(a) -Log_{10} of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on "1000 Genomes Mar 2012 EUR".(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it's weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

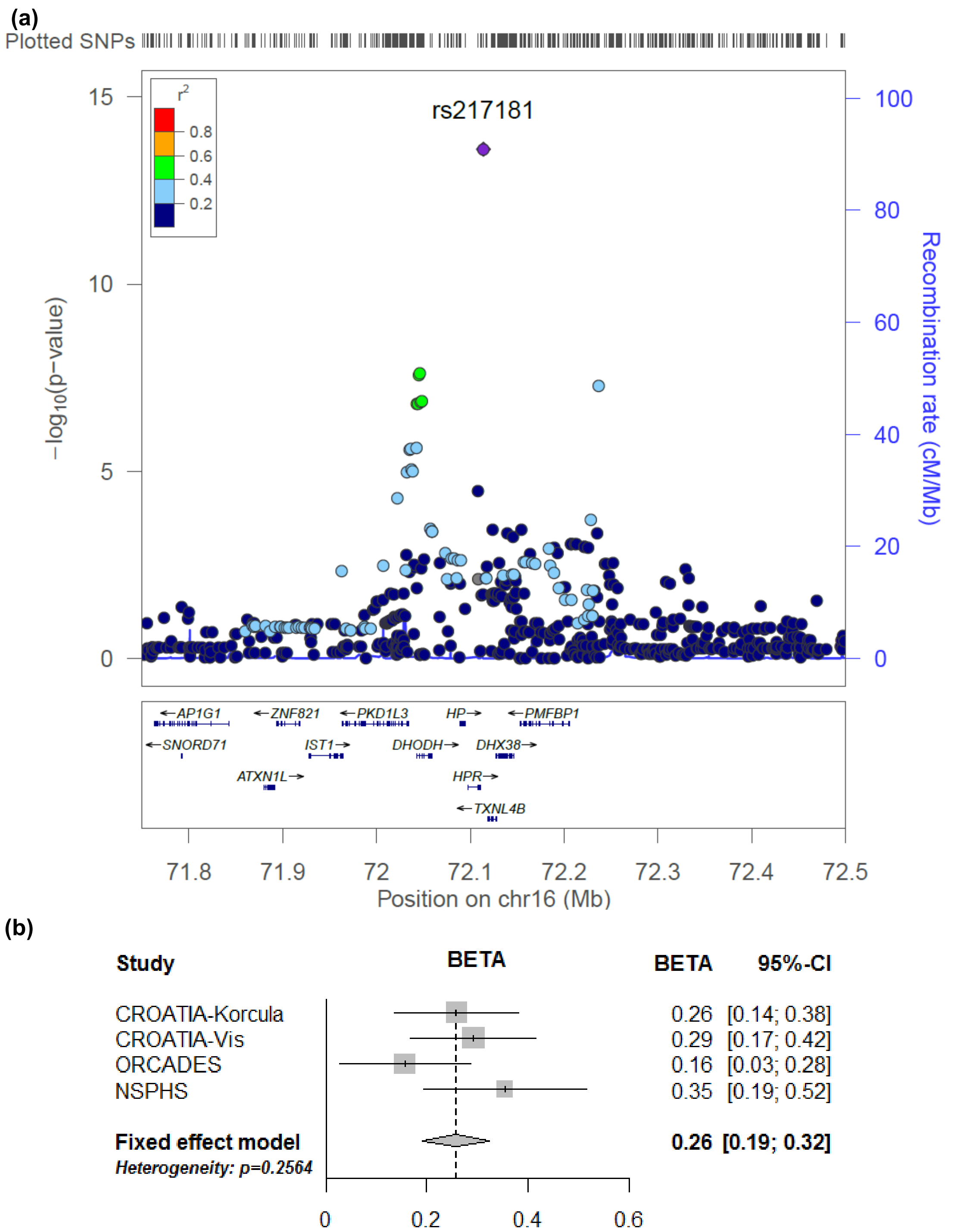


Figure 15: Significance (a) and Forest (b) plots for chromosome 16 region of the G3 meta-analysis.

(a) -Log$_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

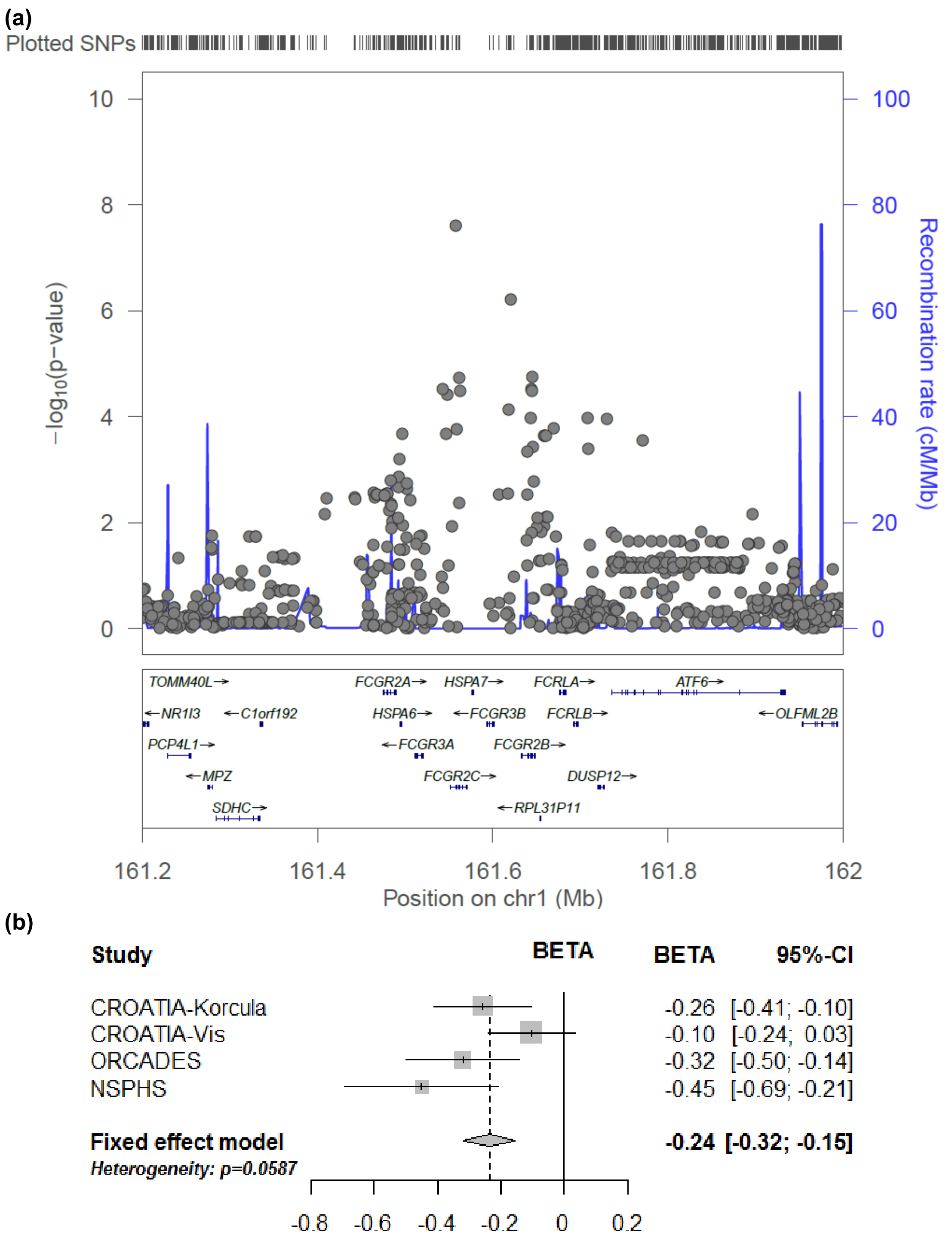


Figure 16: Significance (a) and Forest (b) plots for chromosome 1 region of the GP4 meta-analysis.

(a) -Log_{10} of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

(a)

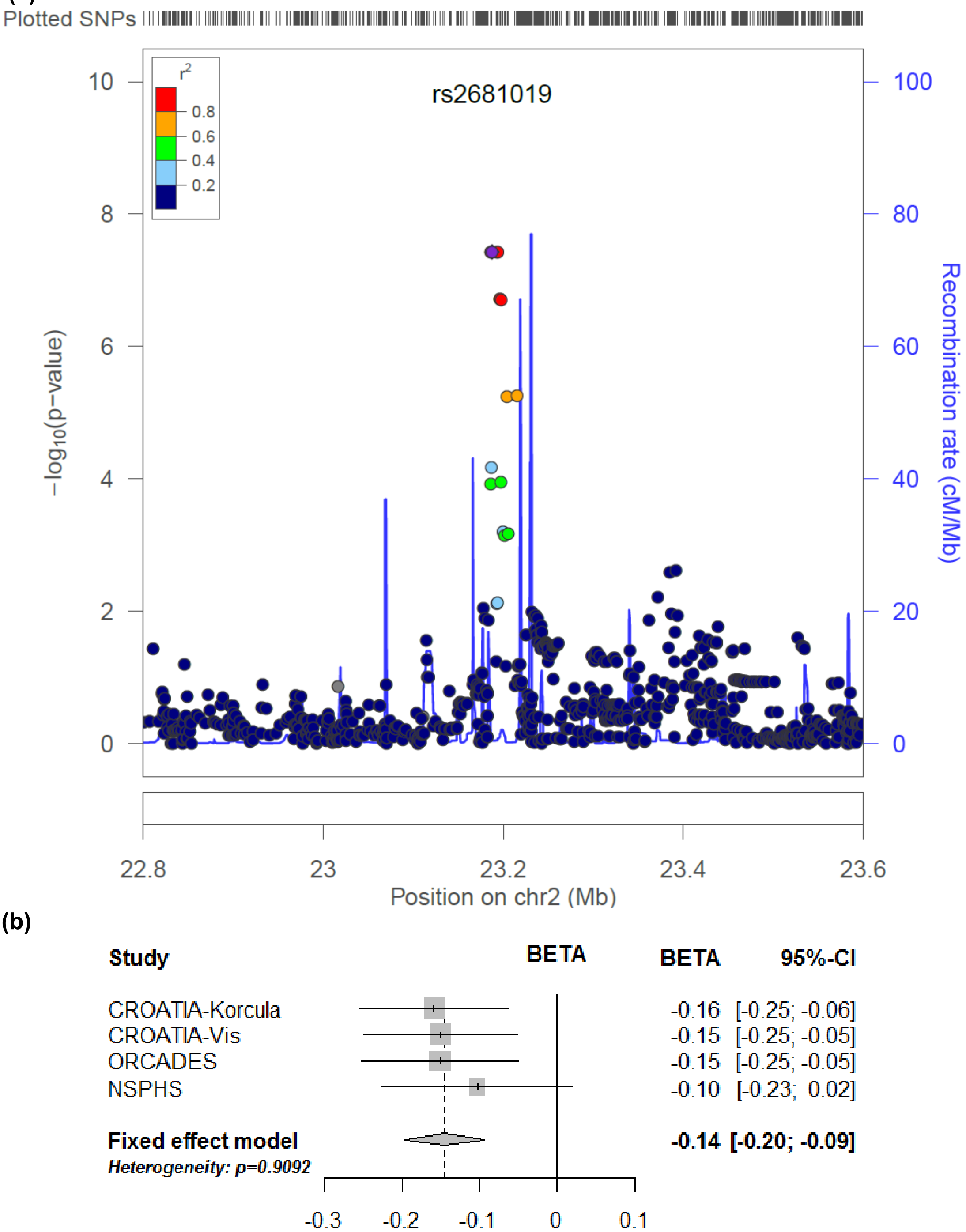


Figure 17: Significance (a) and Forest (b) plots for the first chromosome 2 region of the DG3 meta-analysis.

(a) -Log_{10} of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on "1000 Genomes Mar 2012 EUR".(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it's weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

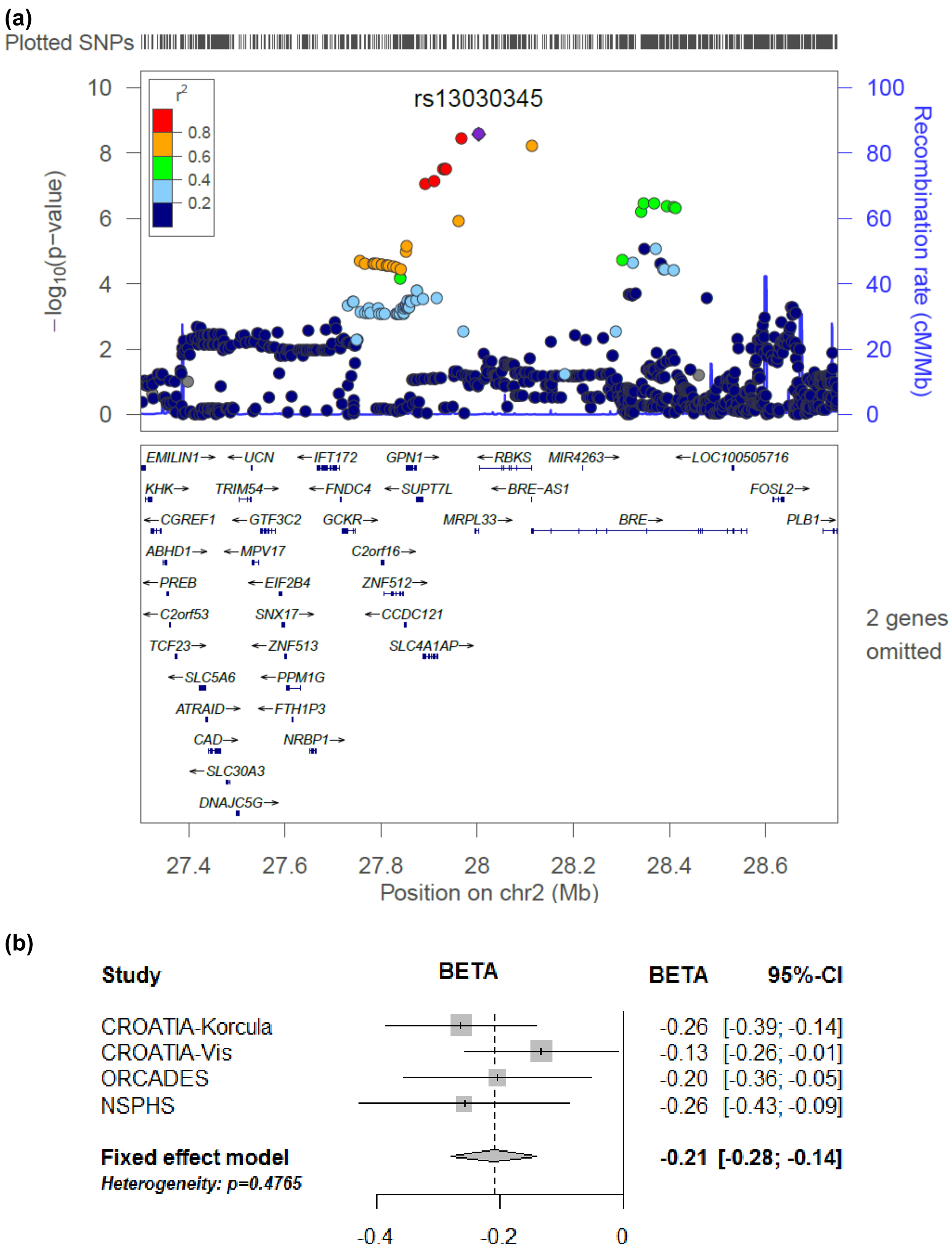


Figure 18: Significance (a) and Forest (b) plots for the second chromosome 2 region of the DG3 meta-analysis.
(a) -Log$_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

depicted in Figure 17. The second peak was located in another region containing many genes with widespread LD so the true associated gene cannot be determined from these analyses alone (Figure 18). The top SNP, rs13030345 (P=2.66 x10^{-09}), is located between the 3' ends of *mitochondrial ribosomal protein L33* (*MRPL33*, Entrez GeneID: 9553) and *ribokinase* (*RBKS*, EntrezGeneID: 64080).

A single missense mutation in *solute carrier family 39 (zinc transporter), member 8* (*SLC39A8* Entrez GeneID: 64116) on chromosome 4 was strongly suggestively associated with levels of GP5 (rs13107325, P=4.73 x10^{-09}) (Figure 19). The minor allele (T) encodes an Ala to Thr change at amino acid 391. It explained 1.9, 2.3, 0.1 and 0.7% of the variance of GP5 (adjusted for sex, age and PC) in CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS.

A single region on chromosome 6 was strongly suggestively associated with levels of GP1. A single intronic SNP rs3094093 in *mediator of DNA-damage checkpoint 1* gene (*MDC1*, Entrez GeneID: 9656 achieved suggestive significance with GP1 (P=1.69x10^{-08}). There are many genes in this region with widespread LD which makes it difficult to pinpoint the locus causing the association (Figure 20).

A single SNP located on chromosome 11, rs7948031, was strongly suggestively associated with DG13 (P = 3.93x10^{-08}). This SNP is located in the final intron of the *b-1,3-glucuronyltransferase1* (*B3GAT1*, Entrez GeneID: 27087) gene. There is a spike in the recombination rate towards the end of B3GAT1; therefore, the variant causing the association is most likely located 5′ of this spot (Figure 21). Some functional follow-up was undertaken based on the intial GWAS results from genotyped rather than imputed data and this gene was selected due to the known biological role of B3GAT1.

3.3.2 Rare Variant Analysis

Rare variant burden tests were successfully run for all 10 *N*-glycan traits which gave genome-wide significant or strongly suggestive p-values in the common variant GWAS. There were approximately 791 people with both genotype and phenotype information (depending on the phenotype) which is approximately 90 people less than with HapMap2 imputed data.

No genes achieved the Bonferroni-corrected threshold for any trait or analysis. When looking only at the genes that achieved a p-value < 5x10^{-08} in the common variant GWAS, only *FUT8* achieved a p-value < 0.05, however, only one SNP in this gene region had a MAF < 5% (rs2229678, MAF= 0.030, P= 2.13x10^{-03}) so it was not a true burden association

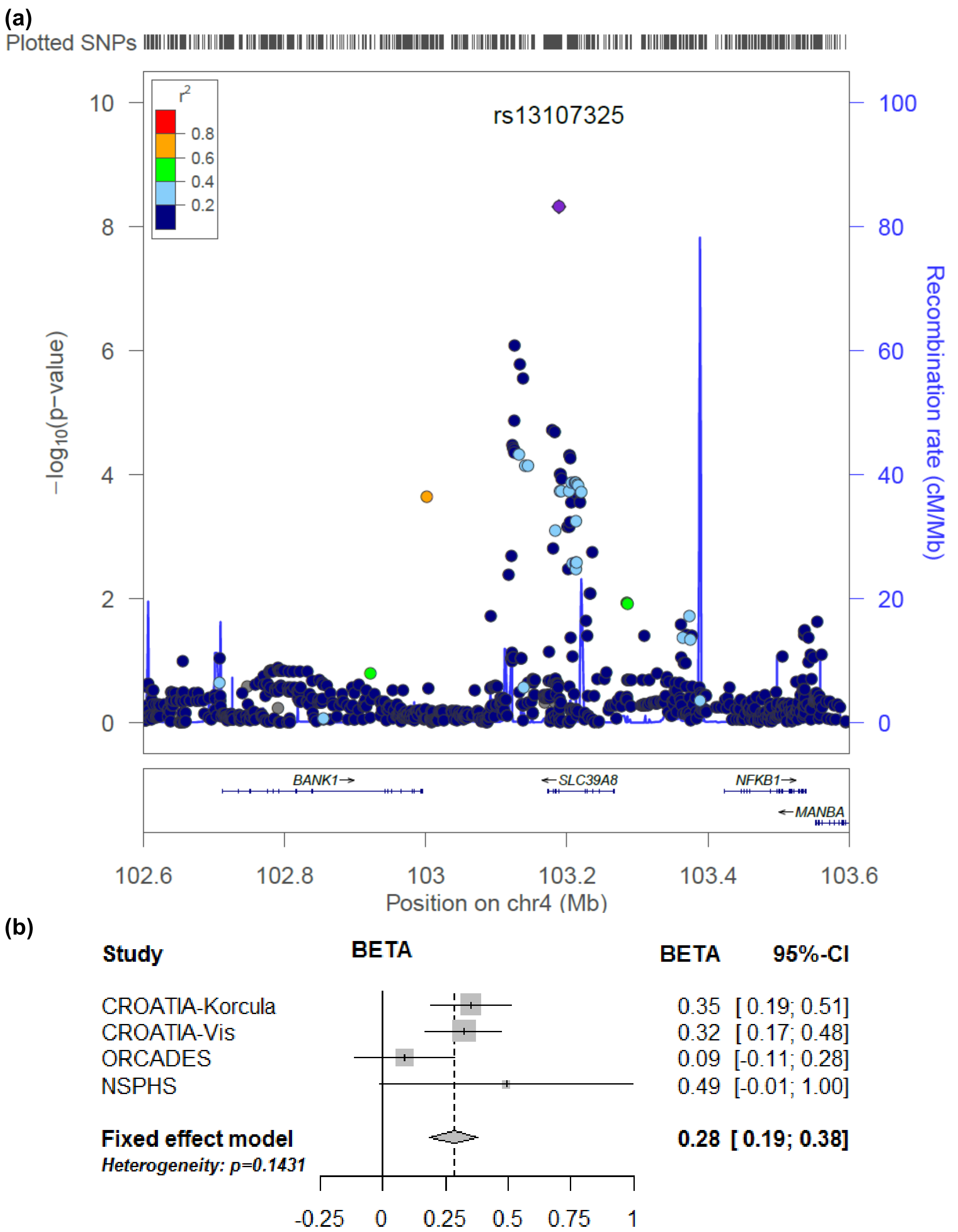
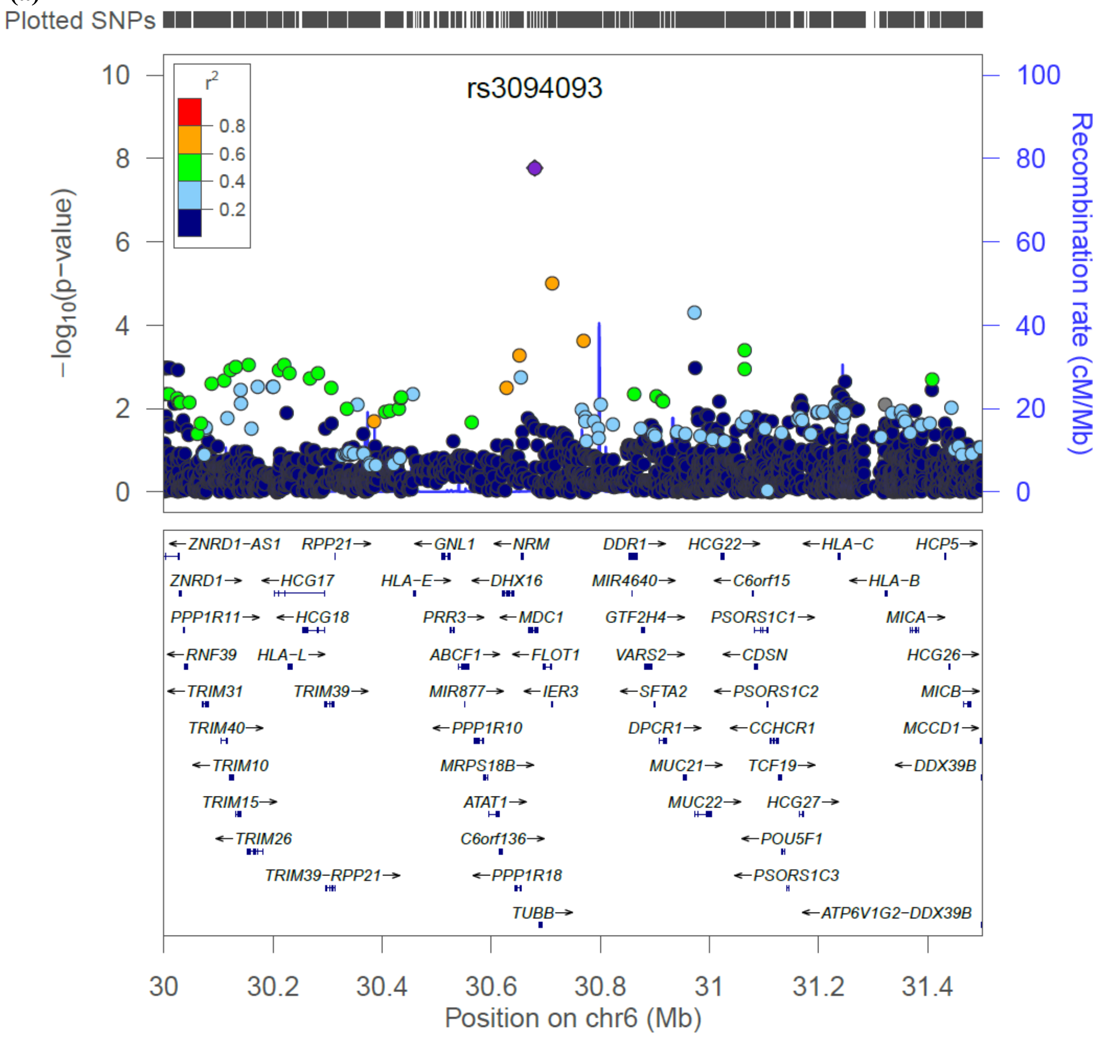


Figure 19: Significance (a) and Forest (b) plots for chromosome 4 region of the GP5 meta-analysis.

(a) -Log_{10} of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

(a)



(b)

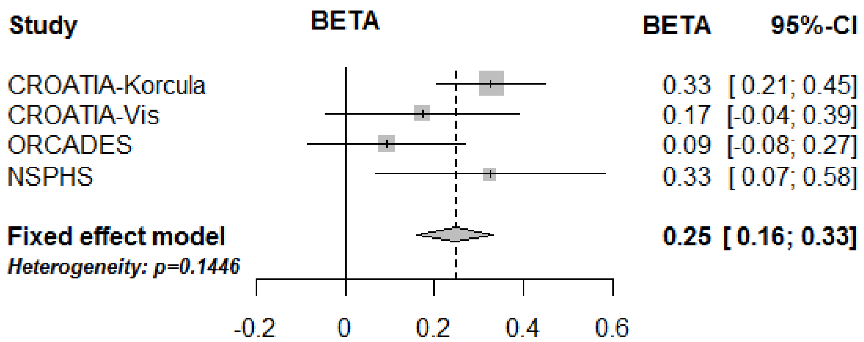
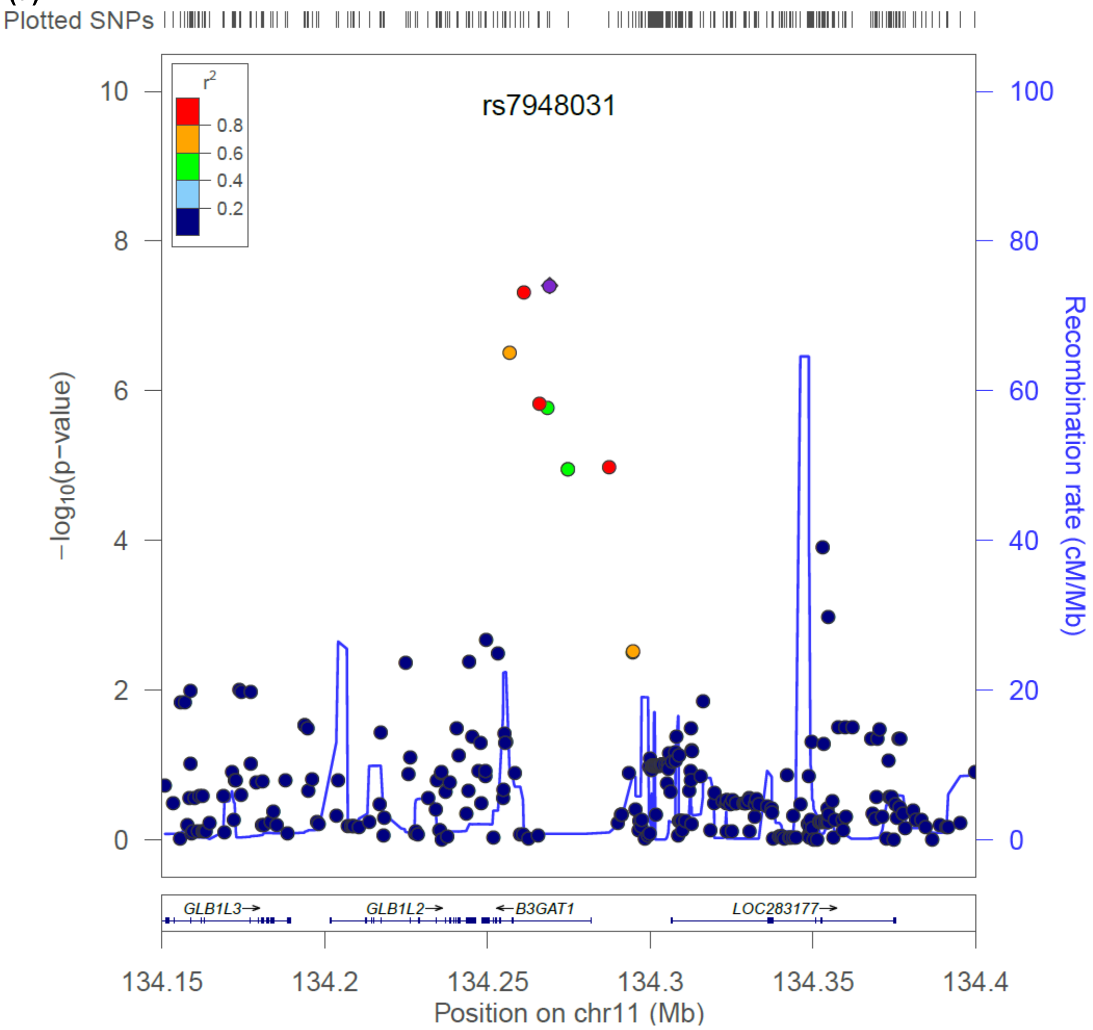


Figure 20: Significance (a) and Forest (b) plots for chromosome 6 region of the GP1 meta-analysis.

(a) -Log$_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

(a)



(b)

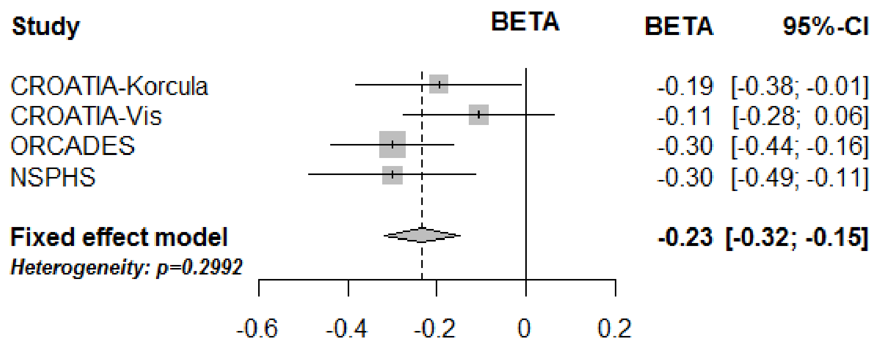


Figure 21: Significance (a) and Forest (b) plots for chromosome 11 region of the DG13 meta-analysis.

(a) -Log$_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

but a single (low-frequency) SNP association. The P-value presented is for the single SNP analysis, but is equivalent to the SKAT and T5 gene-based P-values for *FUT8* since this was the only SNP tested. After conditioning on the most significant common variant in the region (rs7159888, MAF=0.464, $P=1.45 \times 10^{-11}$), the effect for this SNP is still nominally significant ($P_{cond}=1.6313 \times 10^{-02}$). Conditioning on the rare SNP has little effect on the common variant ($P_{cond}=8.87 \times 10^{-11}$). This low-frequency variant is not present in the HapMap2 imputed data and codes for a lysine to glutamine change at amino acid 101 of FUT8. This finding is interesting by potentially highlighting a second contributing signal independent of the common signal but needs to be taken with caution until replicated due to the extremely small sample size.

3.4 Discussion

This study represents the first analysis of *N*-glycans in a population sample of this size. For some traits, there appears to be some differences in both the sample mean and variance, and heritability estimates between populations. Since all populations were isolates this could be down to population-specific differences (environmental or genetic) as well as differences in cohort plasma sample collection, processing and storage. It is also possible that this is due to the measurements themselves caused by uncorrected batch effects (operator/machine/laboratory) or subtle differences in the laboratory procedure between cohorts. Recent work within the glycobiology laboratory group has identified batch effects and several collaborating groups have been investigating the best practices for correcting these in glycan data. These had not been established at the time these data were analysed so it is acknowledged that there are batch effects within this dataset which have not been accounted for. Due to collection procedures in the Croatian cohorts, individuals tended to come to the recruitment centre with their family members, so in the process of accounting for relatedness, the batch effects are likely to have been also partially removed. This is not the case for ORCADES where sample order does not correlate with relatedness. Preliminary reports that batch correction methods show more of an effect on GWAS p-values in ORCADES than in the CROATIA cohorts support this. Presence of batch effects also has implications for the heritability estimates which may potentially be inflated in the CROATIA cohorts. Regardless, initial reports of results after correction for the batch effects indicate that GWAS is quite robust to these batch effects since GWAS meta-analysis p-values changed, in general, by one order of magnitude so will primarily only affect the detection of signals that were close to the significance threshold rather than causing hugely significant false positives.

This first genome-wide association meta-analysis of the human plasma *N*-glycome, represented by 46 *N*-glycosylation traits analysed from the plasma of 3148 individuals from four European populations , yielded several genome-wide significant loci associated with quantitation of *N*-glycans subtypes despite the modest sample size.

FUT8 encodes the fucosyltransferase responsible for the alpha-(1,6)-fucosylation of the core N-acetylglucosamine (GlcNAc) structure of *N*-glycans [114]. *N*-glycan groups associated by GWAS with the gene region surrounding *FUT8* contain fucose attached to their glycan core, or were associated with effects in the opposite direction for structures without core fucose, so the results are consistent with the known biological role of FUT8. In contrast, groups DG7, DG9 and DG12 include glycans containing antennary fucose, and A-FUC was derived as an overall measure of antennary fucosylation on biantennary glycans. *FUT6* encodes the enzyme fucosyltransferase VI, which was reported to be the key enzyme responsible for the alpha-(1,3)-fucosylation of plasma *N*-glycans [113] and is involved in the creation of sialyl-Lewis X, an E-selectin ligand. *FUT3* encodes the enzyme fucosyltransferase III, which has both alpha-(1,3)-fucosyltransferase and alpha-(1,4)-fucosyltransferase activities reported [115] and has a role in the synthesis of Lewis blood group antigens. Both FUT6 and FUT3 add fucose to the antenna of an *N*-glycan structure, therefore the association of *FUT8*, *FUT6* and *FUT3* with *N*-glycan structures containing core and antennary fucosylation is supported by their known biological functions [45]. Recently, the same top SNP in the *FUT6* region has been associated with tumour biomarkers cancer antigen 19-9 and carcinoembryonic antigen in Chinese individuals [116]. In addition, another SNP in this region, rs3760776, has been associated with vitamin B12 levels in Chinese men [117]. Although not in high LD with our top SNP (CEU: r^2=0.358, D'=0.711; CHB/JPT: r^2=0.038, D'=0.288), this was the same top SNP that was associated in our initial GWAS using genotyped rather than imputed data. Both reported associations are consistant with the reported roles of FUT6 and FUT3 in the synthesis of these tumour biomarkers and postulated mechanisms influencing absorption of vitamin B12 through the gut. A figure showing where these fucosyltransferases act on the generic *N*-glycan structure from

Figure 3 is found in Figure 22.

SNPs within *HNF1A* were associated with several glycan traits but the mechanism for this association was not obvious. Functional studies performed by Dr. Abdelkader Essafi, working in Prof. Nicholas Hastie's laboratory, showed that HNF1A and HNF4A act to co-regulate the expression of most fucosyltransferase genes (FUT3–11) in liver-derived HepG2 cells, as well as gene expression levels of key enzymes needed for synthesis of GDP-fucose, the substrate for fucosyltransferases. Through this mechanism HNF1A is able to regulate both core and antennary fucosylation [112]. Common polymorphisms in *HNF1A* have been associated with many traits now, including variation of the plasma concentrations of C-reactive protein (CRP) [118-126], low-density lipoprotein [127-129] and total cholesterol [128,129], homocysteine [130], urate [131], and gamma-glutamyl transferase (GGT) [132-134], and have been found to be susceptibility loci for type 2 diabetes [135,136], coronary heart disease [137] and pancreatic cancer [138]. Although only one of the GGT studies and two of the CRP studies reported the same top SNP as our study, none could be discounted from tagging the same region. There is support for the lipid (rs1169288) and coronary heart disease loci (rs1169310) to be tagging the same regions as was associated with *N*-glycan concentrations because the reported SNPs are in moderate linkage disequilibrium (LD) with our top SNP (rs1169288: $r^2 = 0.532$, $D' = 0.945$; rs1169288: $r^2 = 0.583$, $D' = 0.834$). The top SNPs in the type 2 diabetes studies (rs7957197: $r^2 = 0.122$, $D' = 1$; rs7305618: $r^2=0.138$, $D'=0.871$) are most likely not tagging the same pleiotropic signal but due to the very high D′ value this cannot be completely ruled out without further investigation.

The *MGAT5* gene codes for the enzyme mannosyl (alpha-1,6-)-glycoprotein (beta-1,6)-N-acetyl-glucosaminyltransferase V (GnT-V), which adds GlcNAc residues to mannose in a beta-1,6 orientation on the antennary structure of *N*-glycans. This is an essential step in the generation of tetra-antennary glycans. The majority of structures contained within the DG11 peak are tetra-antennary glycans [36]; therefore, the associations with DG11 and TA (a derived trait quantifying total tetra-antennary glycans) are biologically plausible. Tetra-antennary glycans are important regulators of membrane function [24] since they affect the half-life of numerous receptors on the cell membrane [139]. This has important implications for many dynamic processes, from immunity to cancer progression and metastasis. The *MGAT5* gene product synthesizes cell-surface ligands for galectins—proteins involved in the proliferation of T-cells and apoptosis. Loss of *MGAT5* expression lowers the threshold needed for T-cell activation, and as *Mgat5*-deficient mice displayed several autoimmune phenotypes, it was hypothesized that *MGAT5* expression might be implicated in autoimmune disorders in humans [140]. Recently, polymorphisms within *MGAT5* have been tentatively associated with the severity of multiple sclerosis [141,142] in two small studies which may support this theory; however, the SNPs reported in these studies do not appear to be tagging the same LD blocks as our glycan associated SNPs ($r^2=0.097$, $D'=0.487$). Expression of *MGAT5* is upregulated in oncogenic cells, and an increased production of galectin ligands on the cell surface allows the tumour cell to retain growth factors such as epidermal growth factor and transforming growth factor-beta [143].

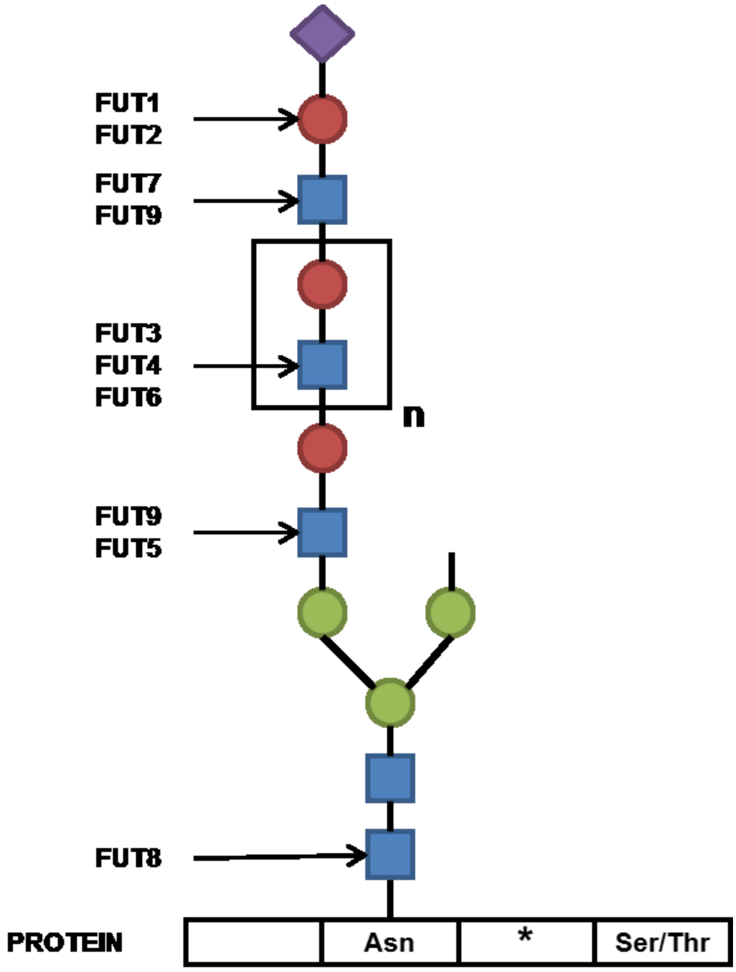


Figure 22: Sites of human *N*-glycan fucosylation.
Adapted from Ma et al., 2006 [45]. A generic *N*-glycan showing sites of fucosylation along with the fucosyltransferases responsible. The structures depicted here contain Sialic acid (purple diamond), Galactose (red circle), Mannose (green circle) and *N*-acetylglucosamine (GlcNAc, blue square).

SLC9A9, solute carrier family 9 (sodium/hydrogen exchanger), is a proton pump which affects pH in the endosomal compartment [144]. This gene was not previously linked to glycosylation, but it was recently reported that changes in Golgi pH can impair protein sialylation [145], thus the association between *SLC9A9* and tetrasialylated glycans makes biological sense. Sialic acids are found in cell secretions and are usually the terminal component of glycoproteins and glycolipids on the outer cell surface and therefore are involved in cell communication and defence. They act to shield recognition sites that may be antigenic in order to prevent autoimmunity but also function as ligands for many molecules such as hormones, inorganic cations and antibodies [146]. Microorganisms are able to exploit the prominent role of sialic acids within the human body by either coating themselves with or binding to sialic acid in order to penetrate and infect the cell. A better understanding of processes and pathways underlying sialylation could lead to new avenues for the treatment of infection and disease [147]. Polymorphisms in *SLC9A9* have recently been suggestively associated with attention-deficit hyperactivity disorder (ADHD (MIM:143465)) [148,149]. The first study reported only a gene-based P-value so it cannot be determined if the variant underlying the reported signal could be the same as for the glycosylation signal, whereas in the latter study, the reported SNP tagging the disease signal is not in strong LD with our top SNP (rs9810857, r^2= 0.106, D′ = 0.727). Plasma *N*-glycosylation analysis in ADHD patients has also revealed a difference in tetrasialylated glycans between children with ADHD and matching controls [150]. Although disease causality cannot be ascertained by this data, the associations still provide a novel set of molecules which could act as clinical markers of disease.

SLC39A8 (also know as ZIP8) is located in the plasma membrane and mitochondria and is one of the transporters responsible for the cellular import of zinc at the onset of inflammation. It is reported to act as a transcriptional target of NF-κB and is involved in a negative feedback loop to downregulate proinflammatory responses via IκB kinase activity [151]. The same SNP associated here with GP5, has been associated by GWAS with HDL cholesterol [128,129], diastolic blood pressure, systolic blood pressure, hypertension [152], mean arterial pressure [153] and BMI [154]. The gene itself has been implicated as a pleiotropic gene involved in adiposity/obesity related phenotypes, lipids and inflammation [155].

B3GAT1 is a member of the glucuronyltransferase gene family. This gene product functions as the key enzyme in a glucuronyl transfer reaction during the biosynthesis of the carbohydrate epitope HNK-1. It acts to add a glucuronic acid (GlcA) to the terminal N-acetyl-lactosamine (Lac) disaccharide to form the HNK-1 epitope precursor [156,157]. The HNK-1 epitope is expressed on a subset of human lymphocytes, including natural killer cells, but it was not previously reported to exist on plasma proteins. Colleagues from Dr. Manfred Wuhrer’s laboratory in Leiden were able to show through mass spectrometry (MS) analysis that glucuronic acid is present on some glycans which make up the DG13 plasma glycan pool, explaining this association [111].

Rare variant analysis yielded little results but was very under-powered due to the small sample size and limited to SNPs present on the exome chip. This also meant that many of the rare variants were not present in the cohort therefore many genes only contained one or two rare SNPs that were polymorphic. Further studies with larger samples sizes are warranted before any conclusions can be drawn. Despite the decision to include only SNPs predicted to alter the final protein product, it is possible that not all of these SNPs had an effect on the phenotype therefore reduced the power to detect an association. The inclusion of reliable information about tissue specific expression and differential transcription may help to determine which variants to include in these tests. Both of these issues need to be addressed before coming to any strong conclusions with regards to the effect of rare variants on the genomic regulation of *N*-glycans.

3.5 Conclusion

Recent advances in high-throughput methods of analysing *N*-glycans have now made it possible to measure these traits in large cohorts. GWAS analyses revealed several associations of large effect illuminating the genetic control of distinct biological pathways, including fucosylation, sialylation and glucuronyl transfer. Some of these biological processes are known to be altered in several disease states. For example, fucosylation of acute phase proteins is modified in many diseases, such as acute inflammation [158,159], rheumatoid arthritis [160] and diabetes [161], and changes in the levels of fucosylated glycans have been shown to be associated with several important pathological processes, including cancer and inflammation [162]. Although not the same variant, the finding that loci associated with disease (e.g. *SLC9A9* in ADHD or *HNF1A* in MODY3) are modulating various glycan species offers novel insight into disease mechanisms and pathways and offers new avenues for biomarker discovery. Variation in the glycosylation of plasma proteins caused by the polymorphisms identified here could be a predisposing or prognostic factor in numerous diseases and warrants further examination of these effects in plasma samples from specific disease cohorts.

Chapter 4 - Maturity Onset Diabetes of the Young 3 (MODY3) *N*-glycan Biomarker Analysis

4.1 Introduction

Since SNPs in *HNF1A* were shown to be associated with plasma concentrations of various *N*-glycan species, it was hypothesized that *N*-glycans might provide biomarkers for Maturity Onset Diabetes of the Young 3 (MODY3, (MIM: 600496)) which is caused by mutations in *HNF1A*.

MODY3 is the most common form of monogenic diabetes and is caused by mutations in *HNF1A* [163]. Often MODY3 patients are misdiagnosed as having T2D or type 1 diabetes (T1D) [164] and the optimal treatment differs from these other more common disorders with MODY3 patients optimally treated with low dose sulfonylurea drugs [165]. The only way to reliably diagnose MODY3 is by sequencing the *HNF1A* gene to look for causal mutations [166]. Therefore, *N*-glycans were tested to determine if they could act as biomarkers to prioritise potential MODY3 patients for definitive diagnostic gene sequencing and reduce the rate of mis-diagnosis. The results presented here are for the pilot dataset only.

4.2 Methods

Plasma *N*-glycans were analysed by HPLC (by Jayesh Kattla from NIBRT, Dublin, Ireland) in 33 MODY3 patients (22 female, 11 males) and 41 T2D patients (22 females, 19 males) from the United Kingdom. Age and sex-matched non-diabetic controls were taken from the ORCADES dataset (n=59, 40 females, 19 males) to have approximately two non-diabetic controls for each MODY patient. The controls were checked to ensure that there were no relationships within this group. Analyses were undertaken to determine which *N*-glycan species was able to distinguish either just the MODY3 patients from the other two groups, or classify all three groupings. Only the directly measured traits were tested. Detailed methods are described in Sections 2.1.5, 2.3 and 2.5.6 and a table describing which samples contributed to this analysis is found in Appendix Table 22.

4.3 Results

Results of the ANOVA analysis are reported in Table 4. All structures with a P-value<0.05 and MODY3 as the category that was different were taken forward for backwards linear regression to try to build the best predictive model to discriminate MODY3 from T2D patients. The best full model included GP13, DG8, DG9 and DG11. These glycans, as well as the full model, were used to test their classification accuracy and generate receiver operator characteristic (ROC) curve statistics. The full model gave a correct classification of 85.9% compared to the null model 57.7% and gave a C-statistic of 0.961. These results are shown in Table 5 and Figure 23.

Table 4: ANOVA results for MODY3 biomarker testing.

TRAIT	SIG. GWAS	P-Value from ANOVA				CATEGORY DIFFERENT*
		C, T, M	C, T	C, M	T, M	
GP1	NO	0.08	0.058	0.455	0.033	
GP2	NO	0.15	0.104	0.699	0.041	
GP3	NO	0.16	0.056	0.533	0.237	
GP4	NO	0.12	0.056	0.345	0.343	
GP5	NO	0.19	0.511	0.113	0.104	
GP6	NO	0.18	0.084	0.303	0.575	
GP7	NO	0.25	0.777	0.195	0.039	
GP8	NO	0.09	0.04	0.087	0.975	
GP9	NO	0.94	0.761	1.000	0.728	
GP10	NO	7.10×10^{-06}	0.265	3.60×10^{-05}	3.01×10^{-06}	MODY3
GP11	E-03	1.32×10^{-03}	0.443	1.45×10^{-03}	8.95×10^{-04}	MODY3
GP12	E-03	0.02	0.073	0.013	0.207	DIABETICS (same)
GP13	YES	9.27×10^{-08}	0.633	1.47×10^{-06}	4.89×10^{-07}	MODY3
GP14	E-06	3.42×10^{-04}	2.83×10^{-03}	0.219	2.48×10^{-04}	T2D
GP15	YES	8.72×10^{-13}	0.277	1.33×10^{-13}	1.06×10^{-07}	MODY3
GP16	E-03	9.72×10^{-05}	2.29×10^{-03}	2.27×10^{-07}	0.360	DIABETICS (same)
DG1	NO	0.25	0.166	0.587	0.161	
DG2	NO	0.21	0.372	0.293	0.070	
DG3	NO	0.23	0.152	0.712	0.112	
DG4	NO	0.28	0.141	0.941	0.205	
DG5	NO	0.25	0.193	0.694	0.132	
DG6	NO	0.08	0.526	0.026	0.102	
DG7	YES	2.88×10^{-09}	0.686	5.80×10^{-11}	6.49×10^{-07}	MODY3
DG8	E-07	3.40×10^{-04}	0.452	9.62×10^{-04}	3.15×10^{-04}	MODY3
DG9	YES	2.22×10^{-11}	0.059	2.20×10^{-09}	7.54×10^{-11}	MODY3
DG10	E-04	$1.29 \times 10E^{-11}$	0.957	1.40×10^{-12}	2.51×10^{-09}	MODY3
DG11	YES	2.98×10^{-14}	0.360	1.69×10^{-12}	2.59×10^{-10}	MODY3
DG12	E-06	6.84×10^{-06}	0.023	2.62×10^{-04}	1.28×10^{-05}	DIABETICS (opp)
DG13	NO	1.70×10^{-03}	7.93×10^{-03}	2.12×10^{-04}	0.448	DIABETICS (same)
MonoS	NO	0.91	0.737	0.747	0.964	
DiS	NO	0.52	0.408	0.362	0.768	
TriS	NO	0.18	0.226	0.102	0.513	
TetraS	NO	0.17	0.997	0.098	0.062	

SIG GWAS= were SNPs in *HNF1A* region significantly associated with this *N*-glycan structure; C=Control, T= T2D, M= MODY3
* DIABETICS (opp) = both T2D and MODY different from controls but in different directions
* DIABETICS (same) = both T2D and MODY different from controls in the same direction

Table 5: Percentage of correct classification and receiver operator characteristic (ROC) statistics to discriminiate MODY3 from T2D patients using plasma *N*-glycans.

Trait	% Correct Classification		ROC Statistics	
	Null Model	Test Model	AUC (se)	P-value
GP10	57.7	74.6	0.820 (0.049)	$5x10^{-06}$
GP11	57.7	62.0	0.720 (0.060)	$2x10^{-06}$
GP13	57.7	73.2	0.841 (0.048)	$1x10^{-06}$
GP15	57.7	80.3	0.864 (0.044)	$<1x10^{-06}$
DG7	57.7	77.5	0.859 (0.046)	$<1x10^{-06}$
DG8	57.7	66.2	0.691 (0.064)	$6x10^{-03}$
DG9	57.7	83.1	0.889 (0.041)	$<1x10^{-06}$
DG10	57.7	81.7	0.848 (0.050)	$<1x10^{-06}$
DG11	57.7	78.9	0.866 (0.045)	$<1x10^{-06}$
Full Model	57.7	85.9	0.961 (0.019)	$<1x10^{-06}$

AUC: area under the ROC curve
* Full Model = GP13 + DG8 + DG9 + DG11

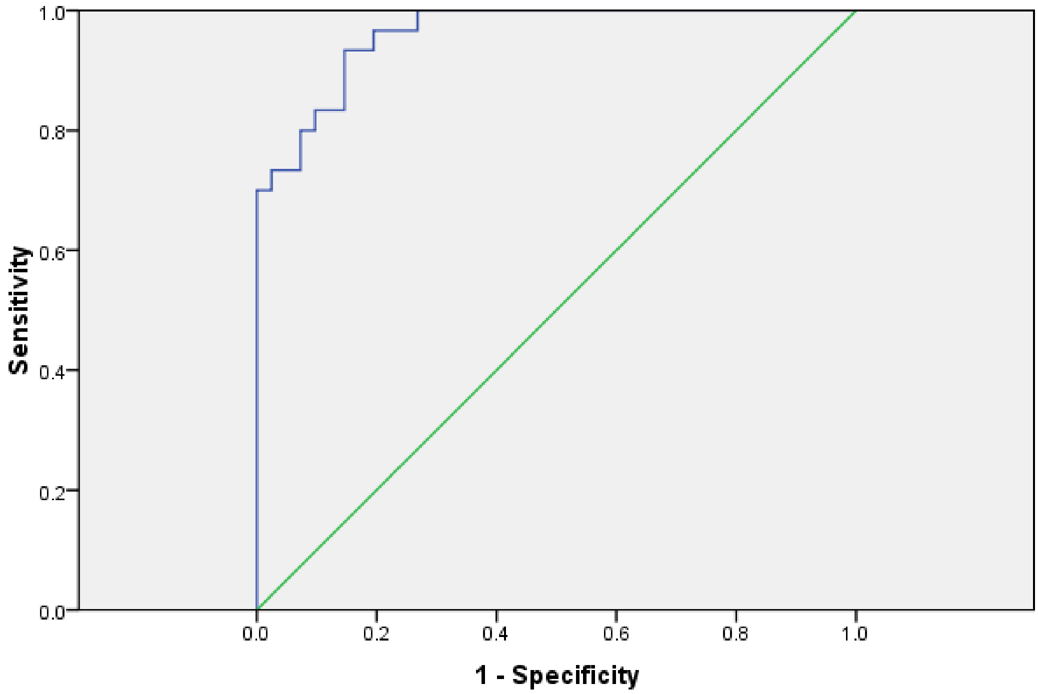


Figure 23: Receiver Operator Characteristic (ROC) Curve for full model to discriminate MODY3 from T2D patients.
ROC plot for the discrimination of MODY3 (blue line) from T2D patients (green line) using the full model of GP13+DG8+DG9+DG11. C-statistic = 0.961

4.4 Discussion

It is acknowledged that the study design was not ideal, with MODY3 cases from Edinburgh and Oxford, T2D cases from Oxford and non-diabetic controls from ORCADES. It was attempted to get T2D cases from Edinburgh to match the Edinburgh MODY3 cases but none of the available cohorts were willing to contribute samples for *N*-glycan analysis unless the entire large cohort was analysed which was not feasible for this pilot study. ORCADES was used as it was the only British cohort with *N*-glycans measured that was available at the time despite the potential allele frequency differences due to its isolated nature. In order to prevent some of these potential confounders only N-glycan traits were taken forward that were significantly different between MODY3 cases and both the T2D cases and the age- and sex-matched ORCADES non-diabetic controls. In doing this, it is noted that this may have introduced a bias in feature selection leading to biased estimates of classification accuracy. A resampling approach such as bootstrap or cross validation would have been more appropriate however, since the main study was undertaken almost immediately after preliminary pilot results were presented, further work on this dataset was not pursued.

The MODY3 biomarker pilot study showed promising results and was taken forward by Gaya Thanabalasingham, from Katharine Owen's group in Oxford, to include T1D patients as well as patients with other types of MODY (HNF4A, GCK). *N*-glycan analysis was performed between NIBRT and Genos, Zagreb, Croatia. In contrast to the pilot study, the expanded study included patients with either plasma or serum measured, so not all promising glycan biomarkers from the pilot (which was plasma-only) could be taken forward. However, encouraging results were found using DG9/(DG8+DG9), which represents the ratio of fucosylated to nonfucosylated triantennary glycans. This "DG9-index" was able to distinguish between MODY3 and T2D patients (C-statistic=0.91, 88% sensitivity, 81% specificity) as well as T1D patients (C-statistic=0.94, 88% sensitivity, 88% specificity) [167]. Previous studies published by the Oxford group using the same patient samples, found high-sensitivity C-reactive protein (hsCRP) to discriminate very well between T2D and MODY3 patients (C-statistic=0.94, 83% sensitivity, 86% specificity), but it was not as accurate in distinguishing between T1D and MODY3 (C-statistic=0.83) [168,169]. The assay for measuring hsCRP is already in use in clinical laboratories, however the methodology required for *N*-glycan analysis is labour intensive and not routinely available in a clinical setting. Also, there is no current method for measuring just one or two *N*-glycan structures, although this is not the most time-consuming or labour-intensive step in the process. Therefore, the glycan measure is unlikely to be implemented in a clinical setting unless it can show much greater diagnostic utility and/or selective assays are developed. This is also influenced by the falling cost of targeted gene sequencing so very soon it will be possible to simply sequence anyone who fits the typical diagnostic criteria of MODY (age of onset, family history of disease).

4.5 Conclusion

By starting from a GWAS hit, in which the disease causing gene (*HNF1A*) has also been shown to directly regulate the biomarker (*N*-glycan) structure, we have removed much of the confounding that usually surrounds biomarker discovery. These results show that regardless of their role in disease pathogenicity, *N*-glycans have the potential for use as biomarkers but some technical hurdles may need to be addressed before they are implemented into a clinical laboratory setting.

Chapter 5 - Genetic analysis of Immunoglobulin G *N*-glycosylation

5.1 Introduction

Following on from the success of the total plasma *N*-glycan GWAS, it was hypothesized that refining the analysis to *N*-glycans from a single protein may increase the ability to identify genetic markers and make interpretation of the biological function of resulting genes more tractable. Using UPLC, colleagues from the Lauc laboratory in Zagreb showed exceptionally high individual variability in *N*-glycans isolated from IgG and substantial heritability of the observed measurements [61]. In this Chapter, I will provide the results from the first GWAS of the human IgG *N*-glycome.

5.2 Methods

The CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS cohort data was used for the discovery study and are described in Methods Section 2.1. HapMap2 imputed dosages were used for the genome-wide association studies. Genotyping and imputation methods are described in Section 2.2.

IgG was isolated using protein G plates and its glycans analysed by UPLC in 2247 individuals, using methods reported previously ([61] and in Sections 2.4.1 and 2.4.2.). Glycans were separated into 24 chromatographic peaks and quantified as relative contributions of individual peaks to the total IgG glycome. On the basis of these 24 directly measured glycan traits, an additional 54 derived traits were calculated. These are described in Appendix Table 16 and were calculated to capture further glycan structural categories that were not directly assayed. Extreme outliers (those with values more than 3 times the interquartile distances away from either the 75th or the 25th percentile values) were removed for each glycan measure to account for errors in quantitation and to remove individuals not representative of normal variation within the population. After phenotype quality control, the number of individuals with complete phenotype and covariate information for the meta-analysis was 2247, consisting of 906 men and 1341 women (802 from CROATIA-Vis, 851 from CROATIA-Korcula, 415 from ORCADES, 179 from NSPHS).

GWAS was firstly performed for each population and then combined using an inverse-variance weighted meta-analysis for all traits. Each trait was adjusted for sex, age and population substructure using the first 3 principal components. The residuals were transformed to ensure their normal distribution using quantile normalisation. ProbABEL [98] was used for the association test under an additive model against HapMap2 imputed genotype dosages. Inverse-variance weighted meta-analysis was performed using the MetABEL package [73] for R. All methods used for statistical analysis are described in more detail in the Methods Chapter (Section 2.5).

Replication of GWAS hits was undertaken within the Leiden Longevity Study (LLS). Cohort and genotyping methods are described in Section 2.1.4 and 2.2.1, *N*-glycan measurement methods in Section 2.4.3 and statistical methods in Section 2.5.3. All genotyping, quality control, imputation, statistical analysis and IgG *N*-glycan measurement was performed by colleagues in Leiden, the Netherlands. 1848 individuals with available genotypic and IgG *N*-glycan data (measured by MALDI-TOF-MS) were included in the replication sample. HapMap2 imputed dosages were used for analysis of all SNPs from the discovery analysis listed in Table 7. For the association analysis of the GWAS data, a score test was applied for the quantitative trait correcting for sex and age using an executable C++ program QTassoc (http://www.lumc.nl/uh, under GWAS Software).

Rare variant analysis was undertaken for only the *N*-glycan traits which reached genome-wide significance in the common variant GWAS using Exome Chip genotypes. This data was available in CROATIA-Korcula only (n=855). Analysis was performed using the seqMeta package (v1.3) for R. A bidirectional burden test (SKAT) at a 5% MAF threshold and unidirectional burden tests using a 5% (T5) or 1% (T1) MAF threshold were performed. A Bonferroni corrected gene-based p-value threshold of $1.85\text{x}10^{-06}$ was used for burden tests (0.05/26,965 genes). See Sections 2.2.3 and 2.5.5 for more detailed information on the genotyping chip and statistical methods.

A table describing which samples contributed to which analysis is found in Appendix Table 22.

5.3 Results

5.3.1 Genome-wide association study and meta-analysis

Quantitative measurements of 77 IgG *N*-glycan structures were performed using ultra performance liquid chromatography (UPLC) in 2247 individuals from four European discovery populations (CROATIA-Vis, CROATIA-Korcula, ORCADES, NSPHS). A description of these traits is presented in Appendix Table 16. This list comprises of 23 directly measured quantitative IgG glycosylation traits and 54 derived traits. Descriptive statistics and heritabilities for all traits are presented in Table 6. Heritability estimates of IgG

N-glycan traits (adjusted for sex and age) were variable between populations, just like those measured from total plasma. Again, all traits had at least one population displaying a heritability > 0.2, with most having at least one population in which heritability was > 0.4. In fact, the mean heritability across all traits and all populations was 0.42. Due to the small samples sizes in both NSPHS and ORCADES, the heritability estimates for these populations may not accurately reflect the true heritabilites.

Aiming to identify genetic loci involved in IgG *N*-glycosylation, I performed a GWAS on all measures. Associations at 9 loci reached genome-wide significance ($p < 2.27\text{x}10^{-09}$) in the discovery meta-analysis and a further 7 loci were strongly suggestive ($2.27\text{ x}10^{-09} < p < 5\text{x}10^{-08}$) (Table 7). Summary data for all SNPs achieving a P-value<$1\text{x}10^{-07}$ are presented in Appendix Table 25.

Among the nine loci that passed the genome-wide significance threshold, four contained genes encoding glycosyltransferases (*ST6GAL1*, *B4GALT1*, *FUT8* and *MGAT3*), while the remaining five loci contained genes that have not previously been implicated in protein glycosylation. In general, the implicated genes were associated with several IgG *N*-glycan traits. Summary data for each gene region showing genome-wide association or found to be strongly suggestive are presented in Table 7. The structures for these associated traits are found in Figure 24, where possible. Summary data for all single-nucleotide polymorphisms (SNPs) and traits with suggestive associations ($p<1\text{x}10^{-07}$) are presented in Table 25. All analyses were checked for inflation remaining within reasonable limits (meta-analysis range=0.96-1.02, mean=1.00). NSPHS was a bit more variable (range=0.87-1.01) which is not surprising due to the small sample size.

The most statistically significant association was observed in a region on chromosome 3 containing the gene *ST6 beta-galactosamide (alpha-2,6)-sialyltranferase 1* (*ST6GAL1*, Entrez GeneID: 6480) (Figure 25). *ST6GAL1* codes for the enzyme sialyltransferase 6 which adds sialic acid to galactose-containing residues on various glycoproteins including IgG glycans, and is therefore a biologically plausible candidate. In this region of about 70 kilobases (kb) we identified 37 genome-wide significant SNPs associated with 14 different IgG glycosylation traits, generally reflecting sialylation of different glycan structures. The strongest association was observed for the percentage of monosialylation of fucosylated digalactosylated structures in total IgG glycans (IGP29), with SNP rs11710456 explaining 17%, 16%, 19% and 3.5% of the trait variation for CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS respectively (meta-analysis $p = 6.12\text{x}10^{-75}$). NSPHS had a very small sample size in this analysis (N =179) and may not provide an accurate portrayal of the

Table 6: Mean, standard deviation and heritabilities for IgG *N*-glycan traits.

Trait	Cohort	N	Mean	SD	h^2*	se(h^2)	p(h^2)
age	Vis	918	56.36	15.54	NA	NA	NA
	Korcula	898	56.27	13.94	NA	NA	NA
	ORCADES	889	53.49	15.73	NA	NA	NA
	NSPHS	656	46.98	20.70	NA	NA	NA
IGP1	Vis	785	0.22	0.18	0.2776	0.0889	1.80E-03
	Korcula	839	0.17	0.10	0.5202	0.0713	3.07E-13
	ORCADES	404	0.17	0.08	1.01E-08	1.49E-08	5.00E-01
	NSPHS	174	0.26	0.15	1.17E-08	1.73E-08	5.00E-01
IGP2	Vis	794	0.84	0.45	0.3261	0.0846	1.17E-04
	Korcula	842	0.82	0.47	0.4510	0.1096	3.86E-05
	ORCADES	409	0.81	0.44	0.7377	0.1390	1.11E-07
	NSPHS	178	0.90	0.63	0.7415	0.1354	4.34E-08
IGP3	Vis	802	20.93	6.28	0.2479	0.0914	6.66E-03
	Korcula	851	20.38	5.92	0.5761	0.1130	3.41E-07
	ORCADES	414	20.65	6.10	0.0571	0.0603	3.43E-01
	NSPHS	179	24.81	8.06	0.4289	0.1639	8.88E-03
IGP4	Vis	797	0.32	0.11	1.53E-08	2.27E-08	5.00E-01
	Korcula	842	0.31	0.11	0.4727	0.1243	1.43E-04
	ORCADES	405	0.28	0.07	0.2057	0.1092	5.97E-02
	NSPHS	175	0.35	0.14	1.16E-08	1.73E-08	5.00E-01
IGP5	Vis	801	5.42	1.61	0.2628	0.0960	6.22E-03
	Korcula	851	5.59	1.61	0.4006	0.1140	4.44E-04
	ORCADES	415	5.08	1.61	0.2962	0.1484	4.60E-02
	NSPHS	179	5.75	1.95	0.5941	0.1690	4.39E-04
IGP6	Vis	797	0.77	0.42	0.2104	0.0763	5.83E-03
	Korcula	845	0.75	0.37	0.6217	0.1124	3.14E-08
	ORCADES	413	0.52	0.24	0.5980	0.1365	1.18E-05
	NSPHS	179	0.66	0.33	0.3545	0.1056	7.87E-04
IGP7	Vis	802	16.35	1.92	0.1789	0.0760	1.86E-02
	Korcula	851	16.10	1.88	0.5698	0.1028	3.00E-08
	ORCADES	415	18.05	1.79	0.6371	0.1375	3.63E-06
	NSPHS	179	18.49	2.27	0.2922	0.1870	1.18E-01
IGP8	Vis	802	7.91	1.15	0.1941	0.0879	2.73E-02
	Korcula	851	7.99	1.26	0.6201	0.1043	2.76E-09
	ORCADES	415	8.94	1.24	0.6423	0.1490	1.62E-05
	NSPHS	179	8.75	1.54	0.3835	0.1736	2.71E-02
IGP9	Vis	801	4.72	0.91	0.2964	0.1114	7.77E-03
	Korcula	851	4.67	0.93	0.6427	0.1119	9.33E-09
	ORCADES	414	4.58	0.87	0.6877	0.1354	3.77E-07
	NSPHS	179	4.55	0.90	0.6201	0.1725	3.24E-04
IGP10	Vis	801	0.76	0.15	0.3512	0.1042	7.49E-04
	Korcula	847	0.78	0.16	0.4426	0.1079	4.13E-05
	ORCADES	415	0.78	0.15	0.5147	0.1322	9.84E-05
	NSPHS	177	0.68	0.15	0.6359	0.1832	5.17E-04
IGP11	Vis	798	1.06	0.51	0.1812	0.0754	1.62E-02
	Korcula	844	1.10	0.54	0.7184	0.1230	5.22E-09
	ORCADES	412	0.89	0.44	0.4803	0.1662	3.85E-03
	NSPHS	179	1.16	0.64	0.6072	0.1336	5.45E-06
IGP12	Vis	793	0.29	0.15	0.2180	0.0876	1.28E-02
	Korcula	848	0.23	0.06	0.5256	0.1119	2.62E-06
	ORCADES	406	0.24	0.06	0.1767	0.1135	1.19E-01
	NSPHS	176	0.28	0.09	0.2417	0.1043	2.05E-02

Trait	Cohort	N	Mean	SD	h^2*	se(h^2)	p(h^2)
IGP13	Vis	802	11.39	3.55	0.3572	0.0970	2.30E-04
	Korcula	851	11.24	3.41	0.6376	0.1264	4.59E-07
	ORCADES	415	12.51	3.67	0.3795	0.1223	1.91E-03
	NSPHS	179	12.37	4.34	0.3106	0.1685	6.53E-02
IGP14	Vis	802	1.44	0.35	0.2812	0.0946	2.97E-03
	Korcula	851	1.54	0.34	0.4569	0.1231	2.06E-04
	ORCADES	415	1.67	0.32	0.3170	0.1148	5.78E-03
	NSPHS	179	1.52	0.38	0.5514	0.1712	1.28E-03
IGP15	Vis	802	3.19	0.50	0.3612	0.1025	4.27E-04
	Korcula	851	3.23	0.45	0.6169	0.1022	1.57E-09
	ORCADES	415	3.24	0.47	0.5797	0.1476	8.57E-05
	NSPHS	178	2.84	0.50	0.3004	0.1699	7.70E-02
IGP16	Vis	794	3.05	1.53	0.0763	0.0512	1.36E-01
	Korcula	838	2.80	1.34	0.2799	0.0935	2.76E-03
	ORCADES	410	1.65	0.42	0.3894	0.1446	7.09E-03
	NSPHS	179	1.22	0.37	0.5021	0.1352	2.04E-04
IGP17	Vis	802	8.88	2.54	0.2287	0.0897	1.08E-02
	Korcula	851	9.30	2.58	0.5762	0.1190	1.28E-06
	ORCADES	415	9.59	2.62	0.3323	0.1257	8.21E-03
	NSPHS	179	8.14	3.00	0.4546	0.1784	1.08E-02
IGP18	Vis	799	2.49	0.51	0.3777	0.1019	2.09E-04
	Korcula	850	2.48	0.50	0.5331	0.1029	2.20E-07
	ORCADES	413	2.42	0.43	0.3756	0.1377	6.38E-03
	NSPHS	177	2.03	0.50	0.4588	0.1768	9.45E-03
IGP19	Vis	791	0.50	0.34	0.0018	0.0026	4.88E-01
	Korcula	842	0.69	0.39	0.4446	0.0910	1.02E-06
	ORCADES	407	0.54	0.20	0.1188	0.0886	1.80E-01
	NSPHS	175	0.33	0.12	0.2229	0.1159	5.46E-02
IGP20	Vis	792	3.88	1.98	0.0889	0.0567	1.17E-01
	Korcula	842	3.96	2.36	0.2206	0.1079	4.09E-02
	ORCADES	407	1.72	0.61	0.1254	0.0978	2.00E-01
	NSPHS	179	0.83	0.32	0.3500	0.1273	5.98E-03
IGP21	Vis	800	0.40	0.17	0.1621	0.0696	1.99E-02
	Korcula	847	0.32	0.11	0.5516	0.1032	9.16E-08
	ORCADES	413	0.31	0.11	0.4413	0.1262	4.71E-04
	NSPHS	179	0.24	0.10	0.3891	0.1111	4.63E-04
IGP22	Vis	801	2.03	0.59	0.1529	0.0771	4.75E-02
	Korcula	851	2.32	0.64	0.3436	0.1116	2.07E-03
	ORCADES	415	2.32	0.64	0.3450	0.1373	1.20E-02
	NSPHS	179	1.67	0.68	0.7021	0.2140	1.03E-03
IGP23	Vis	799	2.75	0.62	0.4302	0.0925	3.33E-06
	Korcula	848	2.80	0.61	0.3791	0.0940	5.52E-05
	ORCADES	413	2.66	0.52	0.6782	0.1441	2.51E-06
	NSPHS	179	2.04	0.70	0.2980	0.1750	8.86E-02
IGP24	Vis	801	28.20	3.31	0.1501	0.0752	4.59E-02
	Korcula	851	29.48	3.33	0.4830	0.1042	3.57E-06
	ORCADES	415	27.55	2.96	0.6397	0.1418	6.43E-06
	NSPHS	178	23.94	3.74	0.5930	0.1846	1.32E-03
IGP25	Vis	801	43.08	6.50	0.2642	0.0969	6.41E-03
	Korcula	851	43.04	5.88	0.4492	0.1205	1.93E-04
	ORCADES	413	42.09	5.41	0.5210	0.1368	1.40E-04
	NSPHS	179	37.43	7.60	0.6419	0.1721	1.92E-04
IGP26	Vis	801	19.95	4.10	0.1666	0.0817	4.15E-02
	Korcula	851	21.07	4.13	0.4918	0.1159	2.22E-05

Trait	Cohort	N	Mean	SD	h^2*	se(h^2)	p(h^2)
	ORCADES	415	20.08	3.93	0.3701	0.1371	6.95E-03
	NSPHS	179	16.38	4.65	0.5664	0.1880	2.59E-03
IGP27	Vis	801	30.07	6.01	0.1675	0.0878	5.64E-02
	Korcula	851	29.86	5.71	0.3593	0.1191	2.54E-03
	ORCADES	415	29.95	5.47	0.2673	0.1257	3.34E-02
	NSPHS	179	24.88	6.50	0.6641	0.1802	2.28E-04
IGP28	Vis	800	11.69	1.96	0.1971	0.0894	2.74E-02
	Korcula	851	11.90	1.76	0.7396	0.1145	1.04E-10
	ORCADES	415	10.75	1.54	0.6117	0.1443	2.26E-05
	NSPHS	178	9.48	1.68	0.3001	0.1585	5.83E-02
IGP29	Vis	802	39.81	2.42	0.3511	0.1041	7.40E-04
	Korcula	851	40.69	2.36	0.4905	0.1049	2.90E-06
	ORCADES	414	39.37	2.45	0.8013	0.1314	1.07E-09
	NSPHS	178	36.65	2.97	0.3513	0.1458	1.60E-02
IGP30	Vis	800	9.41	2.73	0.3184	0.0976	1.11E-03
	Korcula	850	10.48	2.78	0.4844	0.1115	1.40E-05
	ORCADES	414	9.73	2.21	0.4694	0.1225	1.28E-04
	NSPHS	179	7.76	2.59	0.3649	0.1879	5.21E-02
IGP31	Vis	802	37.22	3.51	0.3354	0.1095	2.19E-03
	Korcula	851	36.30	3.30	0.5103	0.0984	2.14E-07
	ORCADES	415	35.82	2.97	0.3589	0.1327	6.82E-03
	NSPHS	178	36.40	3.80	0.4903	0.1771	5.63E-03
IGP32	Vis	802	40.94	4.39	0.5241	0.0975	7.64E-08
	Korcula	851	40.92	4.11	0.3274	0.0911	3.24E-04
	ORCADES	413	39.27	3.49	0.5465	0.1327	3.84E-05
	NSPHS	179	35.54	6.06	0.0806	0.0906	3.74E-01
IGP33	Vis	801	3.13	0.63	0.3699	0.0906	4.47E-05
	Korcula	850	2.99	0.54	0.5106	0.1060	1.46E-06
	ORCADES	414	3.10	0.54	0.3580	0.1317	6.55E-03
	NSPHS	178	3.74	1.11	0.0492	0.0599	4.12E-01
IGP34	Vis	801	6.24	1.54	0.2224	0.0913	1.48E-02
	Korcula	850	5.62	1.28	0.4888	0.1169	2.88E-05
	ORCADES	414	5.72	1.20	0.3502	0.1305	7.30E-03
	NSPHS	178	7.16	2.38	0.4529	0.1967	2.13E-02
IGP35	Vis	799	0.92	0.14	0.5397	0.1089	7.22E-07
	Korcula	851	0.90	0.13	0.4184	0.0909	4.11E-06
	ORCADES	415	0.92	0.12	0.5004	0.1453	5.73E-04
	NSPHS	178	1.05	0.21	1.20E-08	1.78E-08	5.00E-01
IGP36	Vis	801	0.39	0.10	0.5524	0.1085	3.57E-07
	Korcula	850	0.37	0.09	0.5699	0.1040	4.24E-08
	ORCADES	412	0.35	0.09	0.5885	0.1492	8.04E-05
	NSPHS	177	0.34	0.12	0.1991	0.1239	1.08E-01
IGP37	Vis	800	0.22	0.06	0.5325	0.1170	5.37E-06
	Korcula	850	0.21	0.06	0.6132	0.1029	2.56E-09
	ORCADES	414	0.20	0.06	0.3951	0.1416	5.28E-03
	NSPHS	177	0.20	0.07	0.3147	0.1566	4.45E-02
IGP38	Vis	801	0.18	0.04	0.5404	0.1170	3.85E-06
	Korcula	850	0.17	0.04	0.5777	0.1021	1.52E-08
	ORCADES	415	0.16	0.04	0.4107	0.1477	5.41E-03
	NSPHS	177	0.16	0.05	0.3074	0.1581	5.18E-02
IGP39	Vis	801	1.42	0.35	0.2881	0.0962	2.76E-03
	Korcula	849	1.26	0.33	0.2646	0.0968	6.25E-03
	ORCADES	414	1.21	0.32	0.6311	0.1532	3.81E-05
	NSPHS	177	1.30	0.41	0.5878	0.1657	3.88E-04

Trait	Cohort	N	Mean	SD	h^2*	se(h^2)	p(h^2)
IGP40	Vis	802	0.58	0.06	0.2992	0.0973	2.11E-03
	Korcula	851	0.55	0.06	0.2719	0.0973	5.18E-03
	ORCADES	415	0.54	0.06	0.5739	0.1521	1.61E-04
	NSPHS	179	0.56	0.09	0.4870	0.1602	2.36E-03
IGP41	Vis	782	0.30	0.24	0.2784	0.0932	2.81E-03
	Korcula	839	0.24	0.14	0.5169	0.0719	6.32E-13
	ORCADES	403	0.23	0.11	1.47E-08	2.18E-08	5.00E-01
	NSPHS	172	0.31	0.18	1.08E-08	1.60E-08	5.00E-01
IGP42	Vis	795	1.15	0.59	0.2941	0.0845	4.98E-04
	Korcula	843	1.14	0.63	0.4882	0.1082	6.46E-06
	ORCADES	409	1.07	0.56	0.7596	0.1405	6.42E-08
	NSPHS	178	1.11	0.75	0.7296	0.1294	1.73E-08
IGP43	Vis	802	28.57	7.34	0.2939	0.0935	1.67E-03
	Korcula	851	28.14	6.96	0.6549	0.1120	5.03E-09
	ORCADES	415	27.21	7.09	0.1099	0.0901	2.23E-01
	NSPHS	179	30.42	8.55	0.3807	0.1575	1.56E-02
IGP44	Vis	797	0.45	0.17	0.0538	0.0504	2.85E-01
	Korcula	838	0.43	0.17	0.4000	0.1229	1.13E-03
	ORCADES	405	0.38	0.10	0.2622	0.1139	2.13E-02
	NSPHS	173	0.43	0.16	0.0740	0.0663	2.64E-01
IGP45	Vis	802	7.42	1.91	0.3128	0.0986	1.51E-03
	Korcula	851	7.73	1.93	0.4628	0.1136	4.64E-05
	ORCADES	415	6.68	1.87	0.4502	0.1697	7.97E-03
	NSPHS	179	7.06	2.16	0.5360	0.1572	6.49E-04
IGP46	Vis	792	1.06	0.56	0.1539	0.0724	3.35E-02
	Korcula	843	1.06	0.53	0.5946	0.1136	1.66E-07
	ORCADES	414	0.70	0.33	0.5813	0.1405	3.50E-05
	NSPHS	179	0.82	0.42	0.3381	0.0987	6.17E-04
IGP47	Vis	802	22.59	2.62	0.3178	0.0996	1.42E-03
	Korcula	851	22.48	2.48	0.5617	0.1016	3.28E-08
	ORCADES	415	24.01	2.69	0.4979	0.1364	2.61E-04
	NSPHS	179	23.04	3.27	0.5230	0.2607	4.48E-02
IGP48	Vis	802	10.92	1.52	0.1978	0.0984	4.44E-02
	Korcula	851	11.14	1.63	0.5773	0.1015	1.27E-08
	ORCADES	415	11.88	1.64	0.5485	0.1464	1.80E-04
	NSPHS	179	10.87	1.87	0.4434	0.1683	8.43E-03
IGP49	Vis	801	6.51	1.18	0.3562	0.1167	2.27E-03
	Korcula	851	6.51	1.22	0.6657	0.1111	2.07E-09
	ORCADES	414	6.07	1.12	0.7325	0.1329	3.58E-08
	NSPHS	179	5.66	1.12	0.6510	0.1924	7.14E-04
IGP50	Vis	801	1.06	0.22	0.1912	0.0998	5.55E-02
	Korcula	841	1.09	0.25	0.3905	0.1035	1.62E-04
	ORCADES	414	1.04	0.19	0.5239	0.1302	5.72E-05
	NSPHS	177	0.84	0.17	0.6364	0.1785	3.63E-04
IGP51	Vis	798	1.48	0.74	0.1240	0.0690	7.24E-02
	Korcula	846	1.57	0.82	0.6697	0.1203	2.63E-08
	ORCADES	409	1.18	0.58	0.4217	0.1622	9.30E-03
	NSPHS	178	1.44	0.82	0.5667	0.1239	4.76E-06
IGP52	Vis	786	0.40	0.20	0.2126	0.0964	2.74E-02
	Korcula	848	0.32	0.09	0.4958	0.1146	1.51E-05
	ORCADES	406	0.33	0.09	0.2045	0.1167	7.97E-02
	NSPHS	176	0.35	0.12	0.2707	0.1059	1.06E-02
IGP53	Vis	802	15.91	5.46	0.3645	0.0938	1.02E-04
	Korcula	851	15.83	5.26	0.5980	0.1249	1.70E-06

Trait	Cohort	N	Mean	SD	h^2*	se(h^2)	p(h^2)
	ORCADES	415	16.81	5.51	0.3179	0.1198	7.98E-03
	NSPHS	179	15.60	6.10	0.3738	0.1788	3.65E-02
IGP54	Vis	802	2.01	0.54	0.2524	0.0929	6.58E-03
	Korcula	851	2.17	0.55	0.4670	0.1220	1.28E-04
	ORCADES	415	2.24	0.51	0.3030	0.1153	8.60E-03
	NSPHS	179	1.90	0.54	0.5821	0.1772	1.02E-03
IGP55	Vis	802	37.50	8.95	0.3032	0.0936	1.20E-03
	Korcula	851	37.31	8.45	0.5860	0.1208	1.24E-06
	ORCADES	415	35.27	8.68	0.1577	0.1043	1.31E-01
	NSPHS	179	38.97	10.34	0.3456	0.1705	4.27E-02
IGP56	Vis	801	42.21	3.51	0.2482	0.0989	1.21E-02
	Korcula	851	42.33	3.30	0.4275	0.1047	4.41E-05
	ORCADES	411	43.80	3.07	0.3927	0.1342	3.44E-03
	NSPHS	178	41.33	4.09	0.5875	0.2103	5.20E-03
IGP57	Vis	802	19.85	6.34	0.3393	0.0944	3.27E-04
	Korcula	851	19.92	6.18	0.6181	0.1224	4.37E-07
	ORCADES	415	20.60	6.28	0.2473	0.1158	3.27E-02
	NSPHS	179	19.33	7.13	0.5140	0.1891	6.55E-03
IGP58	Vis	799	95.37	1.88	0.1809	0.0741	1.46E-02
	Korcula	848	95.41	1.80	0.7308	0.1146	1.83E-10
	ORCADES	412	96.28	1.40	0.6320	0.1496	2.41E-05
	NSPHS	179	95.76	1.81	0.5307	0.1111	1.77E-06
IGP59	Vis	798	96.87	1.48	0.2945	0.0831	3.96E-04
	Korcula	848	96.86	1.66	0.6095	0.1053	7.02E-09
	ORCADES	411	96.90	1.48	0.7740	0.1617	1.69E-06
	NSPHS	178	97.17	1.68	0.8115	0.1343	1.54E-09
IGP60	Vis	792	97.48	1.37	0.1476	0.0730	4.31E-02
	Korcula	842	97.50	1.27	0.6121	0.1151	1.04E-07
	ORCADES	413	98.40	0.75	0.5930	0.1352	1.15E-05
	NSPHS	179	97.99	1.05	0.3523	0.1026	5.98E-04
IGP61	Vis	801	90.12	4.02	0.1465	0.0681	3.15E-02
	Korcula	848	90.38	3.34	0.6438	0.1187	5.90E-08
	ORCADES	415	92.35	2.86	0.6803	0.1415	1.52E-06
	NSPHS	179	90.44	3.50	0.5317	0.1194	8.54E-06
IGP62	Vis	802	78.33	3.33	0.1775	0.0890	4.62E-02
	Korcula	850	77.87	3.55	0.7191	0.1122	1.49E-10
	ORCADES	415	80.17	3.31	0.5647	0.1449	9.76E-05
	NSPHS	179	80.29	3.63	0.7180	0.1417	4.01E-07
IGP63	Vis	802	76.86	4.04	0.2136	0.1003	3.31E-02
	Korcula	850	75.92	4.67	0.7762	0.1025	3.56E-14
	ORCADES	414	77.79	4.22	0.4430	0.1595	5.49E-03
	NSPHS	179	78.88	4.69	0.5488	0.1175	3.01E-06
IGP64	Vis	802	79.39	3.31	0.1613	0.0909	7.58E-02
	Korcula	851	79.37	3.39	0.5980	0.1064	1.89E-08
	ORCADES	415	81.99	3.18	0.6865	0.1444	2.00E-06
	NSPHS	179	82.11	3.21	0.8743	0.1967	8.79E-06
IGP65	Vis	801	79.68	4.73	0.1548	0.0698	2.66E-02
	Korcula	851	79.03	4.53	0.5635	0.1224	4.18E-06
	ORCADES	415	80.99	4.19	0.5321	0.1326	6.03E-05
	NSPHS	179	80.01	4.76	0.4622	0.1249	2.14E-04
IGP66	Vis	802	17.01	2.51	0.3072	0.1074	4.23E-03
	Korcula	851	17.51	2.73	0.6316	0.1175	7.61E-08
	ORCADES	415	16.06	2.68	0.6655	0.1498	8.84E-06
	NSPHS	179	15.47	2.77	0.6675	0.1675	6.79E-05

Trait	Cohort	N	Mean	SD	h^2*	se(h^2)	p(h^2)
IGP67	Vis	802	19.97	3.27	0.2328	0.1062	2.83E-02
	Korcula	851	20.91	3.65	0.7315	0.1020	7.55E-13
	ORCADES	415	19.07	3.27	0.4770	0.1610	3.05E-03
	NSPHS	179	18.25	3.55	0.5009	0.1357	2.23E-04
IGP68	Vis	802	18.00	2.83	0.2872	0.1063	6.90E-03
	Korcula	851	18.04	3.04	0.6377	0.1181	6.66E-08
	ORCADES	414	16.35	2.98	0.9379	0.1473	1.91E-10
	NSPHS	179	15.87	2.95	0.7327	0.1963	1.89E-04
IGP69	Vis	801	10.42	1.75	0.4648	0.1083	1.76E-05
	Korcula	849	11.26	2.30	0.4652	0.1219	1.35E-04
	ORCADES	415	11.36	2.49	0.4976	0.1423	4.71E-04
	NSPHS	178	10.37	2.24	0.4267	0.1964	2.98E-02
IGP70	Vis	802	0.22	0.04	0.2441	0.1027	1.75E-02
	Korcula	851	0.23	0.05	0.6686	0.1149	5.92E-09
	ORCADES	415	0.20	0.04	0.6188	0.1493	3.40E-05
	NSPHS	179	0.19	0.04	0.7108	0.1557	4.99E-06
IGP71	Vis	802	17.85	2.69	0.2782	0.1054	8.30E-03
	Korcula	851	18.38	2.95	0.6649	0.1168	1.24E-08
	ORCADES	415	16.70	2.85	0.6217	0.1472	2.39E-05
	NSPHS	179	16.18	2.98	0.7018	0.1620	1.48E-05
IGP72	Vis	802	4.61	0.85	0.2715	0.1054	9.98E-03
	Korcula	851	4.50	0.89	0.6719	0.1163	7.67E-09
	ORCADES	414	5.05	1.03	0.6003	0.1502	6.44E-05
	NSPHS	179	5.26	1.14	0.7386	0.1641	6.75E-06
IGP73	Vis	786	4.25	2.14	0.2159	0.0961	2.47E-02
	Korcula	847	3.38	0.97	0.5260	0.1146	4.44E-06
	ORCADES	407	3.39	0.95	0.1990	0.1181	9.20E-02
	NSPHS	176	3.68	1.33	0.2817	0.1068	8.38E-03
IGP74	Vis	800	0.13	0.03	0.3415	0.0991	5.67E-04
	Korcula	846	0.14	0.04	0.4360	0.1225	3.73E-04
	ORCADES	414	0.14	0.04	0.5597	0.1435	9.63E-05
	NSPHS	178	0.13	0.03	0.3529	0.1806	5.07E-02
IGP75	Vis	800	11.59	2.12	0.3317	0.0973	6.55E-04
	Korcula	849	12.50	2.70	0.4650	0.1253	2.07E-04
	ORCADES	415	12.34	2.83	0.4396	0.1340	1.04E-03
	NSPHS	179	11.58	2.79	0.3788	0.1860	4.17E-02
IGP76	Vis	802	6.58	1.55	0.2742	0.0860	1.43E-03
	Korcula	851	6.39	1.58	0.5120	0.1220	2.70E-05
	ORCADES	415	6.54	1.65	0.3697	0.1266	3.50E-03
	NSPHS	179	6.86	1.94	0.3958	0.1848	3.22E-02
IGP77	Vis	783	24.00	12.67	0.1734	0.0831	3.69E-02
	Korcula	846	18.96	6.05	0.4856	0.1178	3.74E-05
	ORCADES	410	18.34	6.20	0.2352	0.1166	4.36E-02
	NSPHS	177	21.83	8.00	0.1186	0.0885	1.80E-01

N: number of samples with both genotype and trait data available; Mean: trait mean, SD: trait standard deviation; h^2: heritability estimate; se(h^2): standarad error of the heritability estimate; p(h^2): p-value for heritability estimate

* heritabilities are calculated after adjustment for sex and age

Table 7: Genome-wide significant ($p<2.27x10^{-09}$) or strongly suggestive ($p<5x10^{-08}$) SNP associations with IgG *N*-glycans analysed by UPLC.

Chr	SNP with lowest p-value	Lowest p-value	Effect Size* (s.e.)	MAF	Mean RSq	nHits	nTraits	Genes in Region	Trait with lowest p-value+	Other Associated Traits
Genome-wide Significant										
3	rs11710456	$6.12x10^{-75}$	0.64 (0.04)	0.30	0.880	20	14	*ST6GAL1*	IGP29	IGP14$, IGP15, IGP17, IGP23, IGP24, IGP26, IGP28, IGP30, IGP31$, IGP32, IGP35$, IGP37$, IGP38$
5	rs17348299	$6.88x10^{-11}$	0.29 (0.04)	0.16	0.847	4	6	*IL6ST; ANKRD55*	IGP53	IGP3, IGP13, IGP43, IGP55, IGP57
7	rs6421315	$1.87x10^{-13}$	0.23 (0.03)	0.37	0.954	11	13	*IKZF1*	IGP63	IGP2$, IGP6$, IGP42$, IGP46$, IGP58, IGP59, IGP60, IGP62, IGP67$, IGP70$, IGP71$, IGP72
7	rs1122979	$2.10x10^{-10}$	0.31 (0.05)	0.12	0.906	3	4	*ABCF2; SMARCD3*	IGP2	IGP5, IGP42, IGP45
9	rs12342831	$2.70x10^{-11}$	-0.24 (0.04)	0.26	0.971	28	11	*B4GALT1*	IGP17	IGP13, IGP24, IGP26, IGP36$, IGP37$, IGP38$, IGP39$, IGP40$, IGP53, IGP57
11	rs4930561	$8.88x10^{-10}$	0.19 (0.03)	0.49	1.000	5	2	*CHKA; SUV420H1*	IGP41	IGP1
14	rs11847263	$1.08x10^{-22}$	-0.31 (0.03)	0.39	0.985	167	12	*FUT8*	IGP59	IGP2$, IGP6$, IGP11$, IGP42$, IGP46$, IGP51$, IGP58, IGP60, IGP61, IGP63, IGP65

Chr	SNP with lowest p-value	Lowest p-value	Effect Size* (s.e.)	MAF	Mean RSq	nHits	nTraits	Genes in Region	Trait with lowest p-value+	Other Associated Traits
22	rs2186369	8.63×10^{-17}	0.35 (0.04)	0.19	0.881	10	20	*SMARCB1; DERL3*	IGP72	IGP9$, IGP10$, IGP14$, IGP39$, IGP40$, IGP49$, IGP50$, IGP62, IGP63, IGP64, IGP66$, IGP67$, IGP68$, IGP69$, IGP70$, IGP71$, IGP74$, IGP75$, IGP76
22	rs909674	9.66×10^{-25}	0.34 (0.03)	0.30	0.991	60	17	*SYNGR1; TAB1; MGAT3; CACNA1I*	IGP40	IGP5, IGP9, IGP22$, IGP34, IGP39, IGP45, IGP49, IGP62$, IGP63$, IGP64$, IGP66, IGP67, IGP68, IGP70, IGP71, IGP72$
Strongly Suggestive										
6	rs1049110	1.64×10^{-08}	0.19 (0.03)	0.35	0.976	1	2	*HLA-DQB2*	IGP42	IGP2
6	rs404256	7.49×10^{-09}	-0.21 (0.04)	0.44	0.699	1	1	*BACH2*	IGP7	–
7	rs2072209	1.16×10^{-08}	-0.37 (0.07)	0.06	0.971	1	1	*DLD; LAMB1*	IGP69	–
9	rs4878639	3.51×10^{-08}	-0.20 (0.04)	0.26	0.953	1	1	*RECK*	IGP17	–
12	rs12828421	4.48×10^{-08}	-0.18 (0.03)	0.49	0.916	2	1	*PEX5*	IGP41	–
17	rs7224668	3.33×10^{-08}	0.17 (0.03)	0.48	0.945	2	1	*SLC38A10*	IGP31	–

nHits:number of SNPs with GW-significant or strongly suggestive association; nTraits:number of *N*-glycan traits associated with the region at GW-significant level, MAF: minor allele frequency, Mean RSq: average imputation quality (RSq) across meta-analysis populations

* effect size is for the minor allele in standard deviation units after adjustment for sex, age and first 3 principle components

+ description of the traits provided in Table 16

$ SNP effect is in the opposite direction to the most significant trait

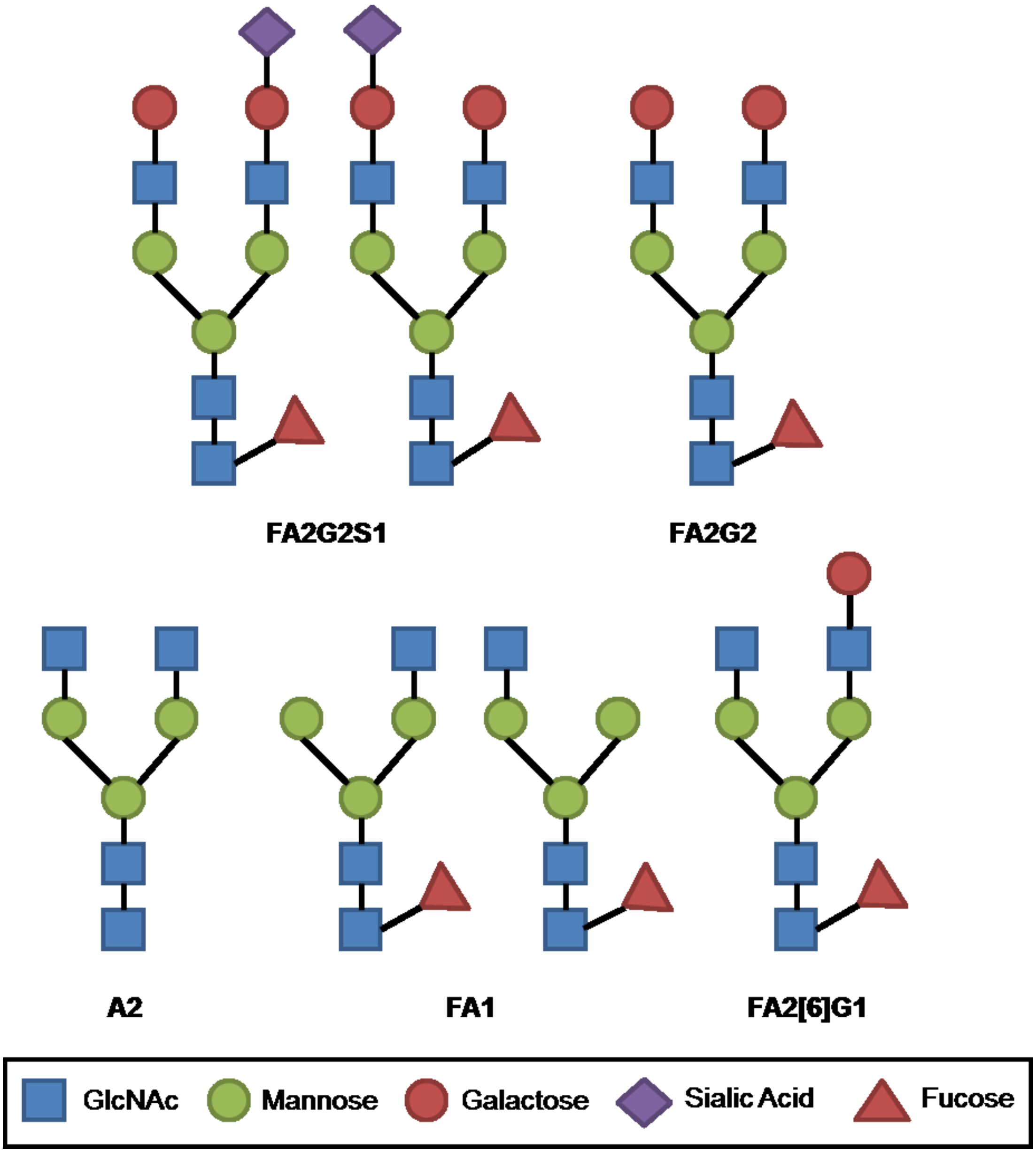


Figure 24: Structures for top associated *N*-glycan traits.
N-glycan structures for most significantly associated traits. These are shown only for traits that had one structure. For some structures, more than one configuration is possible so both have been shown. IGP17: FA2G2S1; IGP53: FA2G2; IGP2: A2; IGP41: FA1; IGP7: FA2[6]G1. GlcNAc: *N*-acetylglucosamine. F at the start of the abbreviation indicates a core fucose α1-6 linked to the inner GlcNAc; Ax, number of antenna (GlcNAc) on trimannosyl core; A2, biantennary with both GlcNAcs as β1-2 linked; B, bisecting GlcNAc linked β1-4 to β1-3 mannose; Gx, number (x) of β1-4 linked galactose on antenna; [6]G1 indicates that the galactose is on the antenna of the α1-6 mannose; Sx, number (x) of sialic acids linked to galactose.

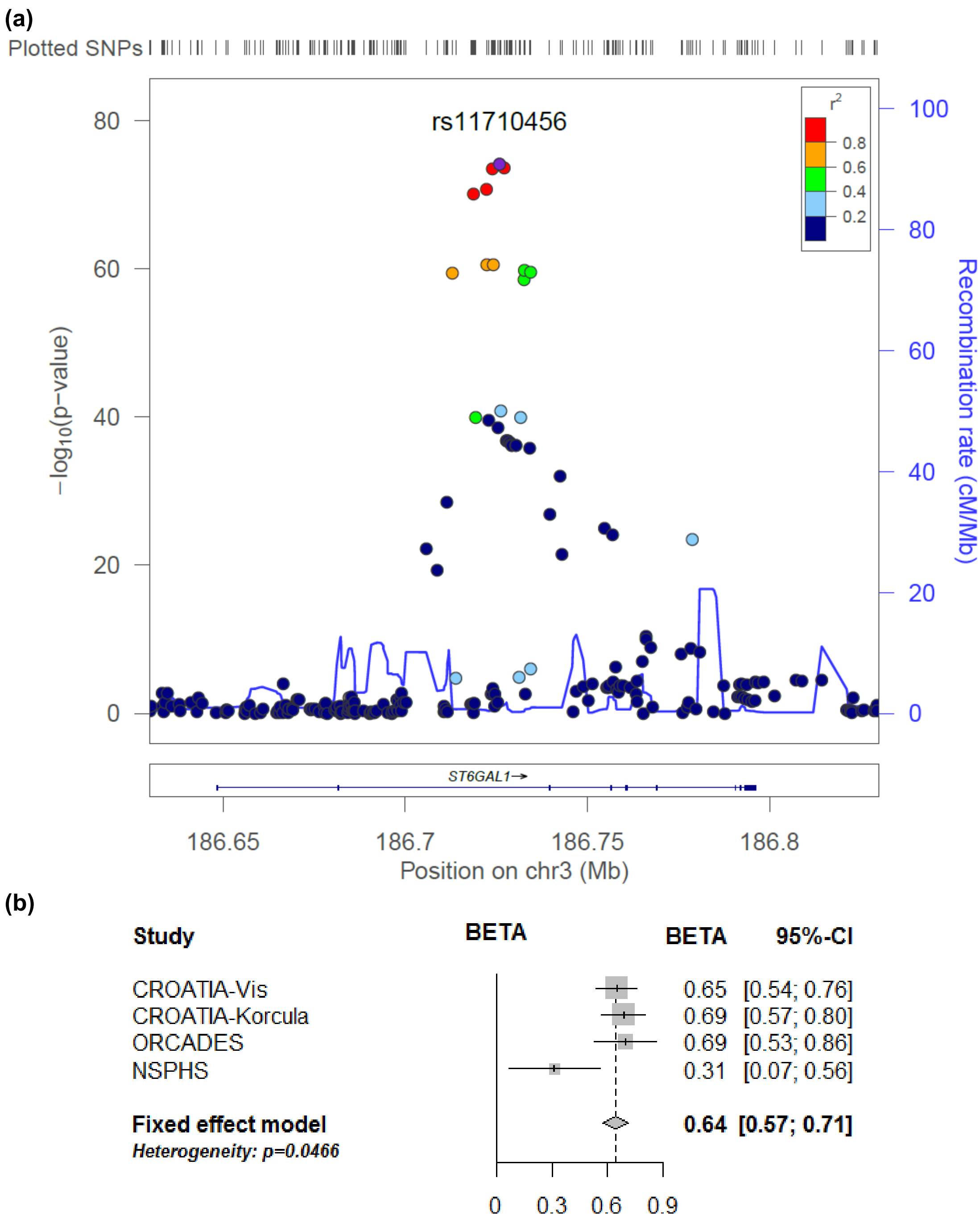


Figure 25: Significance (a) and Forest (b) plots for chromosome 3 region of the IGP29 meta-analysis.

(a) -Log_{10} of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

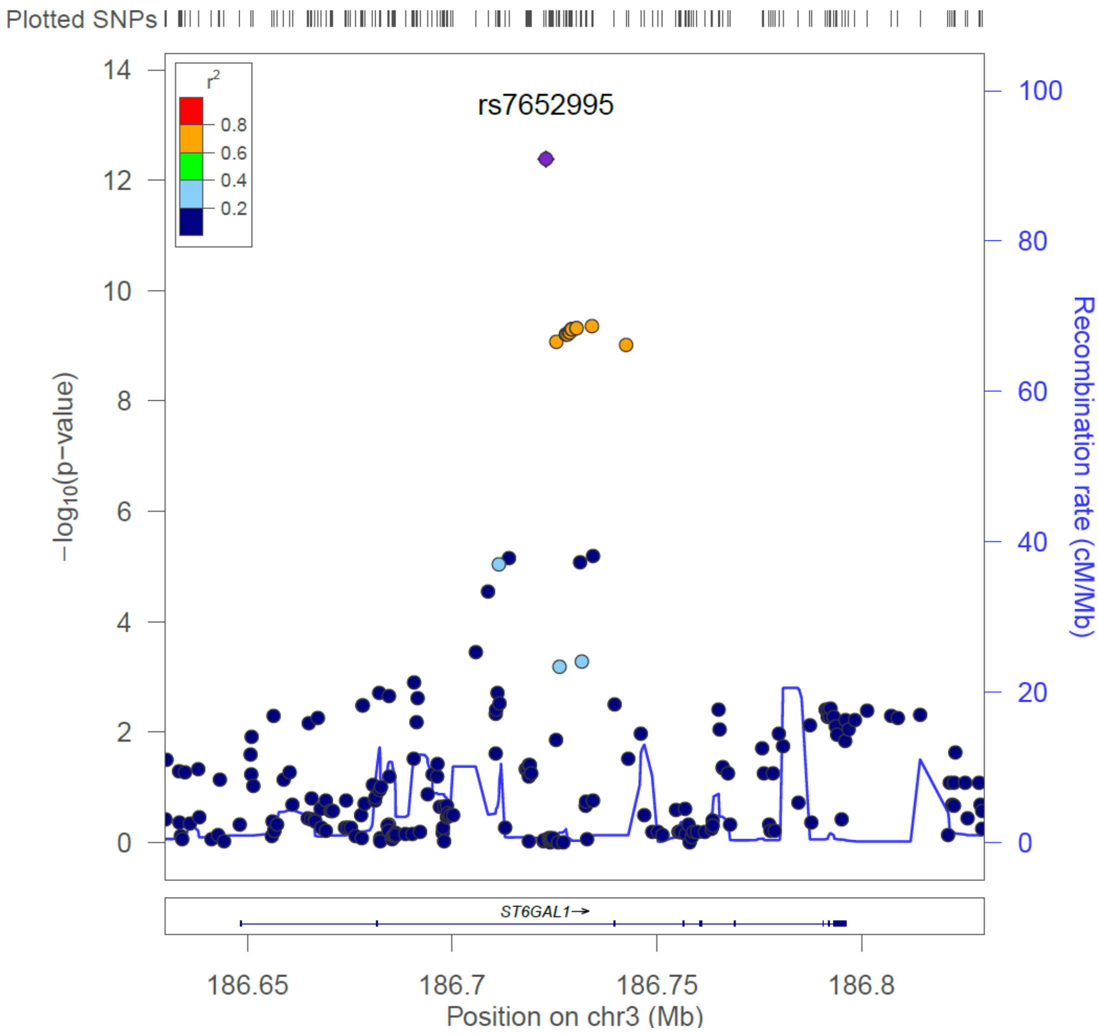


Figure 26: Significance plot for chromosome 3 region of the IGP29 meta-analysis after conditioning on rs11710456.

-Log$_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.

variance explained in this particular population. All variance explained are after adjusting the trait for age, sex and the first 3 principal components. After analysis conditioning on the top SNP (rs11710456) in this region, the SNP rs7652995 still reached genome-wide significance ($p = 4.15x10^{-13}$) (Figure 26). It explained an extra 0.2 - 6.1% of the trait variance on top of rs11710456 in these populations. After adjusting for this additional SNP, the association peak was completely removed. This suggests that there are several genetic factors underlying this association. Conditional analysis of all other significant and suggestive regions resulted in the complete removal of their respective association peaks.

Twenty-eight SNPs were significantly associated with 11 IgG glycosylation traits ($2.70x10^{-11} < p < 4.73x10^{-08}$) at a locus on chromosome 9 spanning over 60 kb (Figure 27). This region includes *UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 1* (*B4GALT1*, Entrez GeneID: 2683), which encodes one of the galactosyltransferase responsible for the addition of galactose to IgG glycans. The most significant trait associated in this region was IGP17 which describes the percentage of FA2G2S1 in the total fraction (Figure 24). The top SNP, rs12342831, explains 1.3, 2.1, 3.3 and 0.8% of the IGP17 trait variance in CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS.

A large (541 kb) region on chromosome 14 harbouring the *fucosyltranferase 8* (*FUT8*, Entrez GeneID: 2530) gene contained 167 SNPs showing significant associations with 12 IgG glycosylation traits reflecting fucosylation of IgG glycans (Figure 28). *FUT8* codes for an enzyme responsible for the addition of fucose to the core of an *N*-glycan. The strongest association ($P= 1.08x10^{-22}$) was observed with IGP59. This trait describes the percentage of fucosylation of agalactosylated structures. Although the top trait is not the same as was associated with total plasma *N*-glycans by GWAS (Chapter 3), that structure was also associated (IGP2). The top SNP, rs11847263, explains 2.0, 8.1, 4.0 & 7.7% of the IGP59 trait variance in CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS. This is fairly close to the percentage of trait variance explained by the same top SNP in the total plasma *N*-glycan GWAS (2.8, 9.2, 3.0 and 4.1%).

On chromosome 22, two loci were associated with IgG glycosylation. The first region spanned over 233 kb and contained several genes. This region contains 60 significant SNPs associated with 17 IgG glycosylation traits (Figure 29). Association was strongest between SNP rs909674 and IGP40, a trait which describes the incidence of bisecting GlcNAc in all fucosylated disialylated structures ($P= 9.66x10^{-25}$). Of the genes in this region, *mannosyl (beta-1,4-)-glycoprotein (beta-1,4)-N-acetylglucosaminyltransferase* (*MGAT3*, Entrez GeneID: 4248) encodes the enzyme responsible for the addition of bisecting GlcNAc to IgG

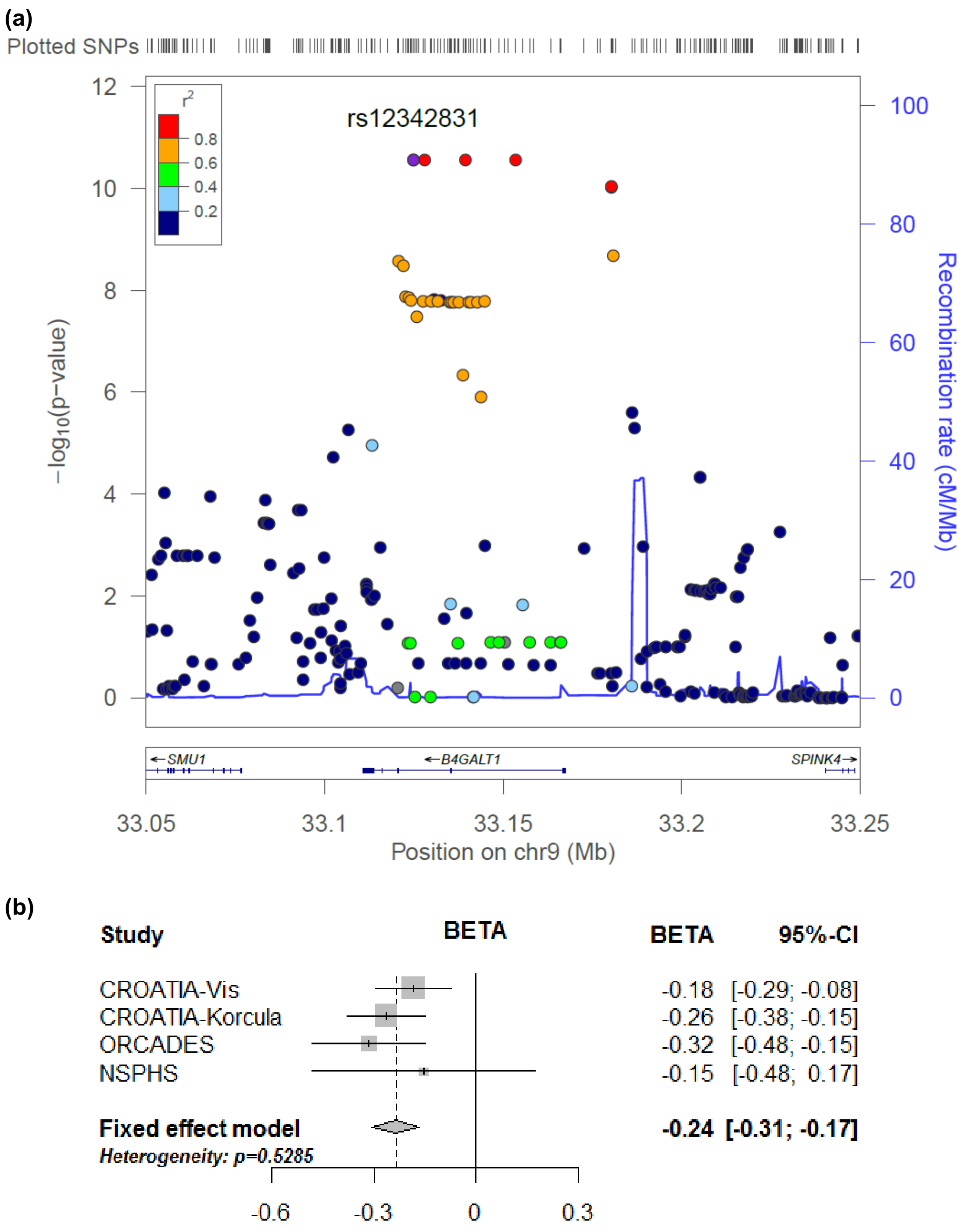


Figure 27: Significance (a) and Forest (b) plots for chromosome 9 region of the IGP17 meta-analysis.
(a) -Log$_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on "1000 Genomes Mar 2012 EUR".(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it's weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

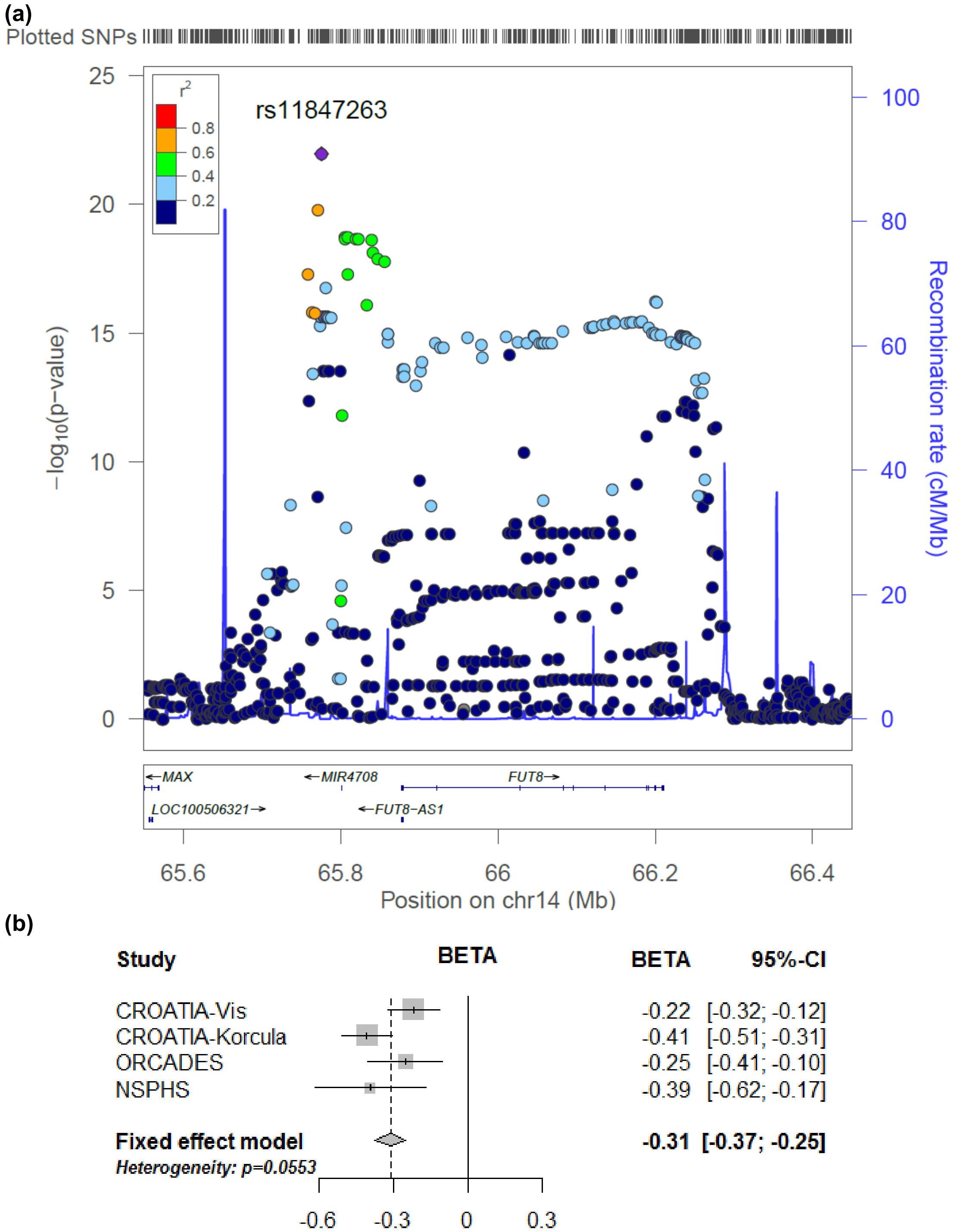


Figure 28: Significance (a) and Forest (b) plots for chromosome 14 region of the IGP59 meta-analysis.

(a) -Log$_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

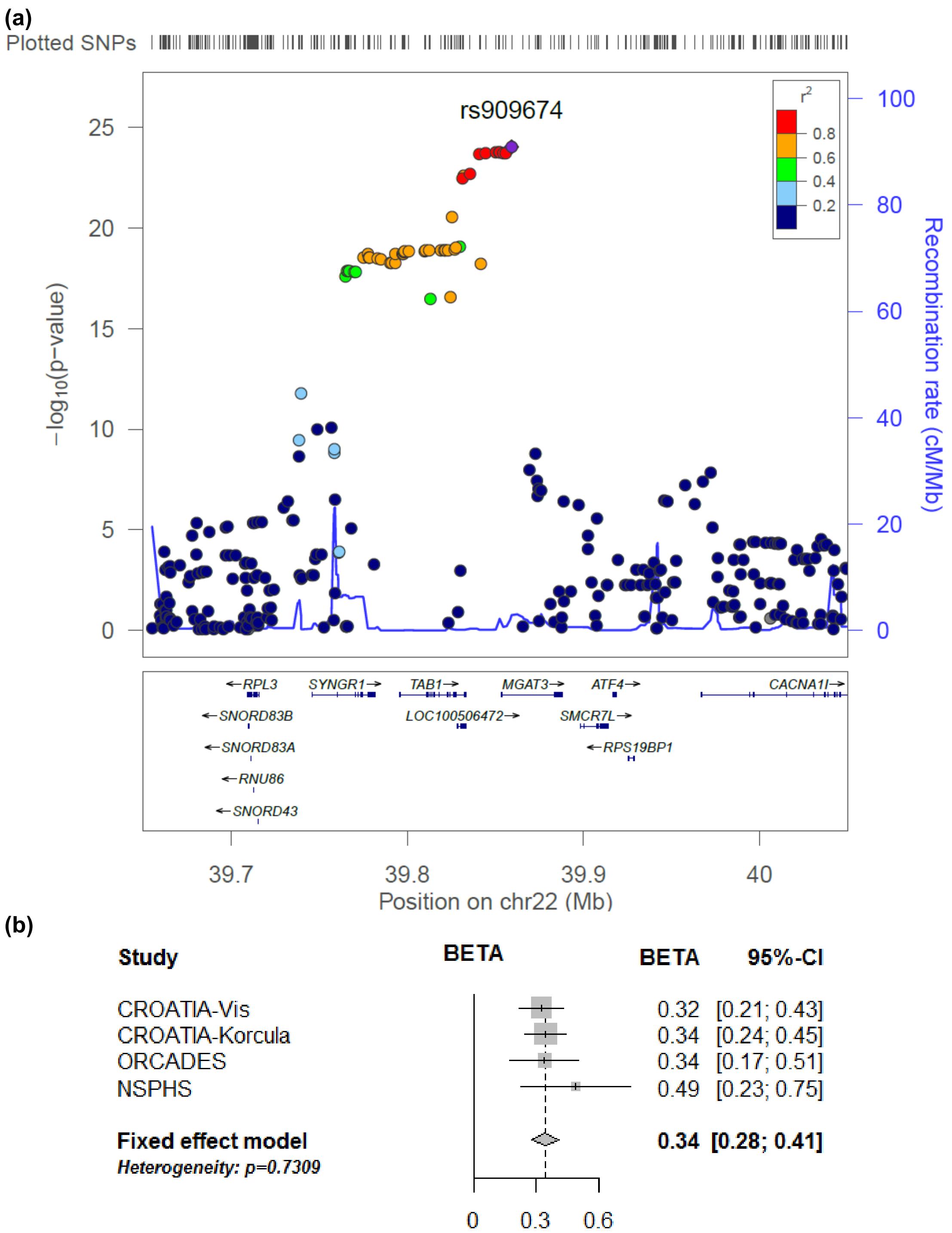


Figure 29: Significance (a) and Forest (b) plots for chromosome 22 region of the IGP40 meta-analysis.
(a) -Log_{10} of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

glycans, thus is the most biologically plausible candidate. The top SNP, rs909674, is located within an intron of *MGAT3* and explains 4.0, 4.9, 4.9 and 3.9 % of the IGP40 trait variance in CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS.

The glycosyltranferase genes at the four GWAS loci - *ST6GAL1*, *B4GALT1*, *FUT8*, and *MGAT3* – are responsible for adding sialic acid, galactose, fucose and bisecting GlcNAc to *N*-glycans and are associated with *N*-glycan structures containing these linkages that are present on IgG, thus demonstrating the proof of principle that GWAS was able to identify biologically relevant genes.

In addition to these four loci encoding known glycosylation enzymes, five novel associations showed genome-wide significance. A second region on chromosome 22 reached genome-wide significance which spanned 49 kb and contained the genes *SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily b, member 1* (*SMARCB1*, Entrez GeneID: 6598) and *derlin 3* (*DERL3*, Entrez GeneID: 91319) (Figure 30). The strongest association ($P=8.63x10^{-17}$) was observed between SNP rs2186369 and IGP72, the ratio of fucosylated non-bisecting GlcNAc structures and all structures with bisecting GlcNAc. rs2186369 is an intronic SNP within *SMARCB1* and explains 2.6-3.7% of the variance in IGP72 across the four populations analysed. Although *DERL3* is the most biologically plausible gene in the region as its protein product, derlin 3, plays a role in the degradation of misfolded glycoproteins in the ER [170], *SMARCB1* cannot be ruled out. Most of the strongly associated SNPs fall in a region of high LD encompassing *SMARCB1* and the protein product is a core component of a major transcriptional complex thereby also giving a strong biologically plausible role to this gene.

Chromosome 5 SNP rs17348299, located in a region containing *interleukin 6 signal transducer* (*IL6ST*, Entrez GeneID: 3572) and *ankyrin repeat domain 55* (*ANKRD55*, Entrez GeneID: 79722) was significantly associated with six IgG glycosylation traits. The most significantly associated trait was IGP53 ($P = 6.88x10^{-11}$) which measured the amount of FA2G2 in the neutral fraction (Figure 24, Figure 31). *IL6ST* is part of the cytokine receptor complex and its activation is dependent on the binding of these cytokines to their receptor. It is a signal transducer shared by many cytokines, including interleukin 6 (IL6), ciliary neurotrophic factor (CNTF), leukaemia inhibitory factor (LIF), and oncostatin M (OSM). Due to its role in immune function it is the most biologically relevant gene in this region. In addition, the large recombination spike towards the 3' end of *ANKRD55* seems to indicate that the top SNP is tagging an association around *IL6ST* rather than *ANKRD55*. The top SNP explains 0.8-2.6% of the variance in IGP53 across the study populations.

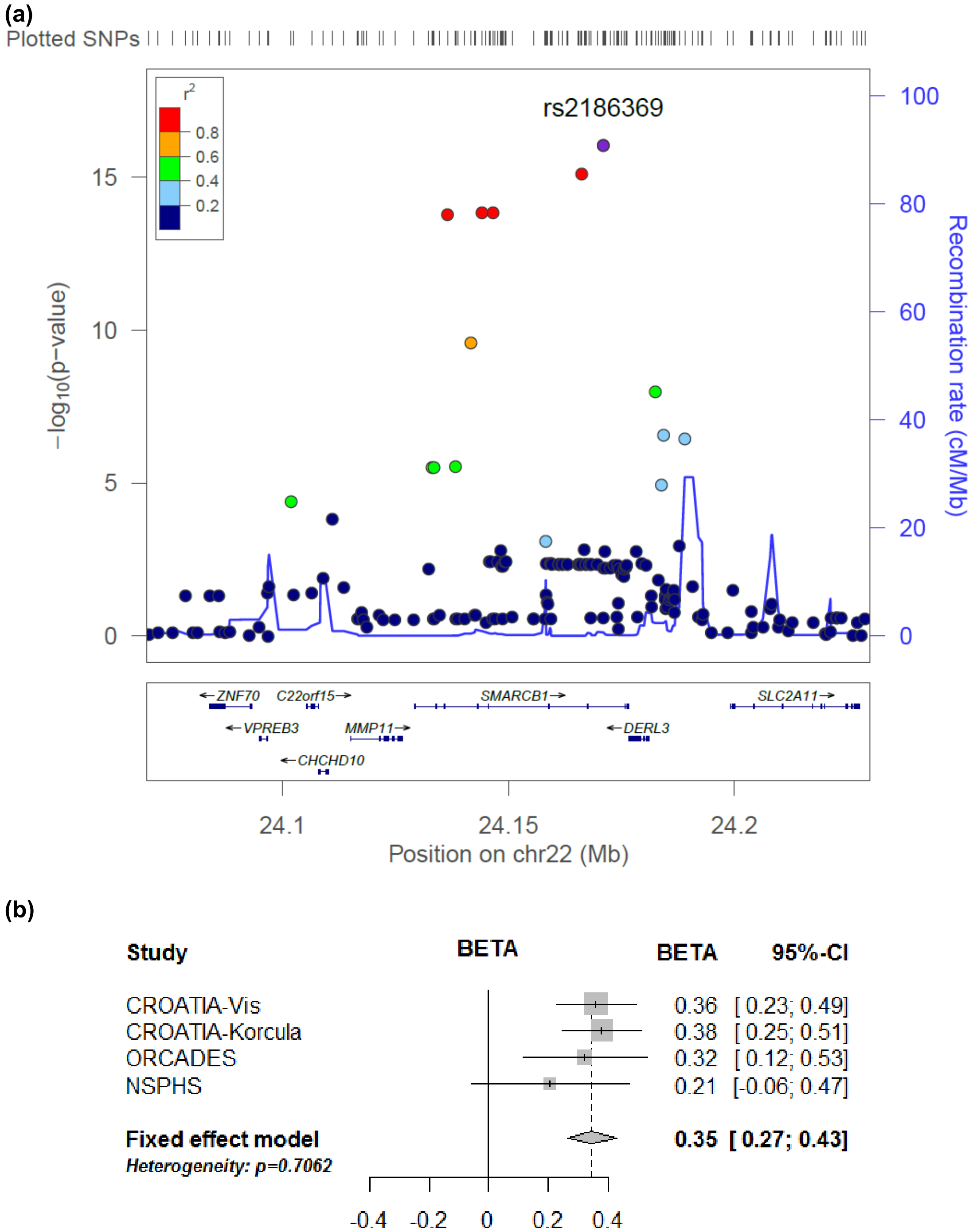
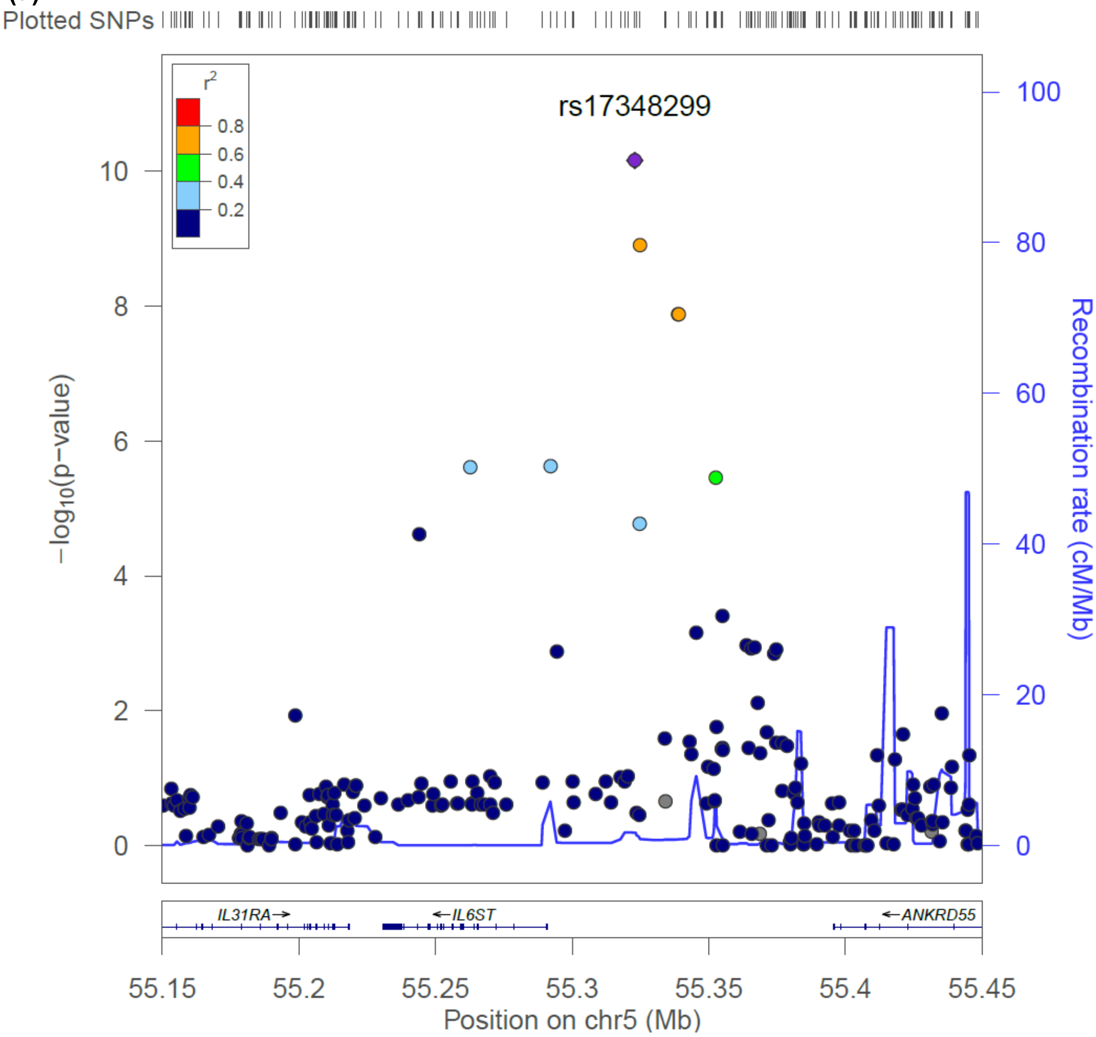


Figure 30: Significance (a) and Forest (b) plots for chromosome 22 region of the IGP72 meta-analysis.
(a) -Log_{10} of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

(a)



(b)

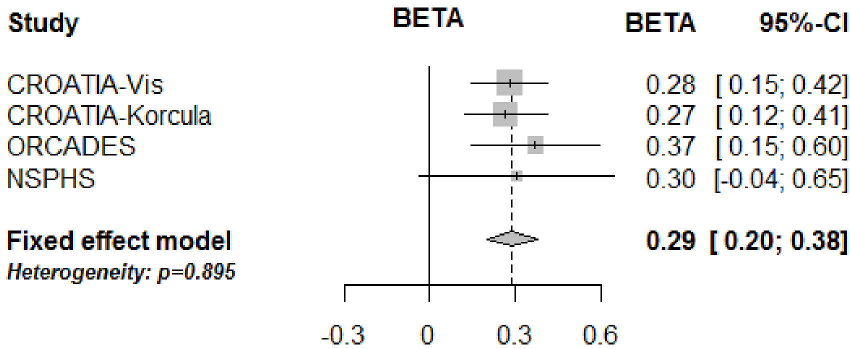


Figure 31: Significance (a) and Forest (b) plots for chromosome 5 region of the IGP53 meta-analysis.

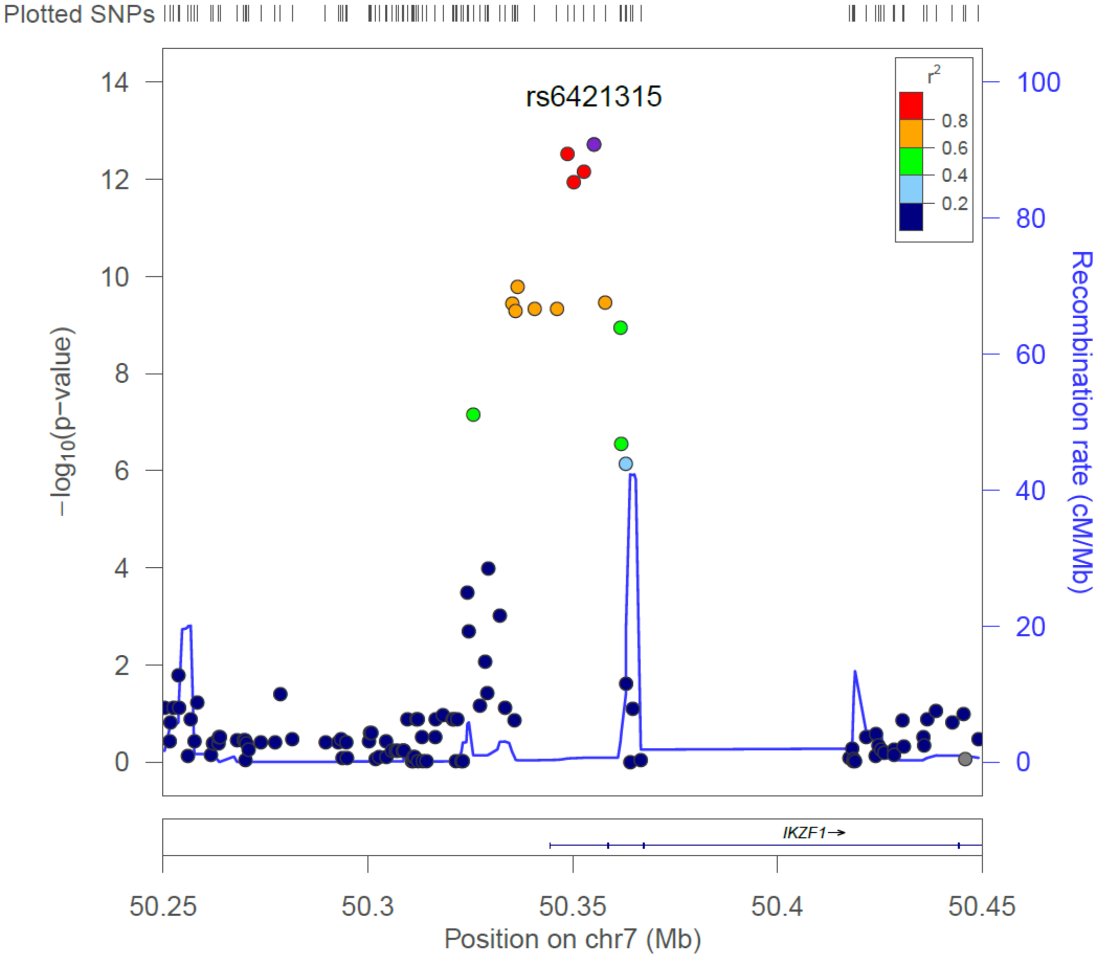
(a) -Log_{10} of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on "1000 Genomes Mar 2012 EUR".(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it's weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

Two regions on chromosome 7 showed genome-wide significant associations. The first, spanning 26kb contained 11 SNPs, and was associated with 13 IgG glycosylation traits (Figure 32). The strongest association ($P = 1.87 \times 10^{-13}$) was observed between SNP rs6421315 located in *IKAROS family zinc finger 1 (Ikaros)* (*IKZF1*, Entrez GeneID: 10320) and the percentage of fucosylation of agalactosylated structures without bisecting GlcNAc (IGP63). *IKZF1*'s encoded protein Ikaros is a DNA-binding protein which acts as a transcriptional regulator and is associated with chromatin remodelling. It is an important regulator of lymphocyte differentiation and has been shown to influence effector pathways through control of class switch recombination [171], thus representing a promising functional candidate [172]. The top SNP explains 1.1-3.6% of the variance in IGP63 across the study populations.

The second region on chromosome 7 contains *ATP-binding cassette, sub-family F, member 2* (*ABCF2*, Entrez GeneID: 10061) and *SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 3* (*SMARCD3*, Entrez GeneID: 6604). The best signal in this region was between SNP rs1122979 and IGP2 ($P= 2.10 \times 10^{-10}$) (Figure 33). IGP2 represents the percentage of A2 glycan in the total fraction (Figure 24) and rs1122979 explains 1.1, 1.1, 2.9, and 6.2% of the trait variance across CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS. The function of *ABCF2* is not well understood but it is known to be involved in molecular transport across extra- and intracellular membranes. *SMARCD3* is part of the ATP-dependent chromatin remodelling complex.

Finally, the chromosome 11 SNP rs4930561, located in a region containing the genes *suppressor of variegation 4-20 homolog 1* (*SUV420H1*, Entrez GeneID: 51111) and *choline kinase alpha* (*CHKA*, Entrez GeneID: 1119), was associated with percentage of FA1 in the neutral fraction (IGP41; $p = 8.88 \times 10^{-10}$) (Figure 24, Figure 34). This SNP explains 0.2, 2.9, 2.7 and 1.4% of the variance in IGP41 across CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS. *SUV420H1* encodes a histone-lysine N-methyltransferase which specifically trimethylates lysine 20 of histone H4 and could therefore affects activity of many different genes. It is thought to be involved in proviral silencing in somatic and germ line cells through epigenetic mechanisms [173]. *CHKA* has a key role in phospholipid biosynthesis and may contribute to tumour cell growth. This is the intial enzyme in the CDP-choline pathway for the biosynthesis of phosphatidylcholine. A recent paper from other collaborators within this project reported a number of strong associations between lipidomics and glycomics traits in human plasma [174], therefore an enzyme involved in phospholipid synthesis may also be a possible candidate for association.

(a)



(b)

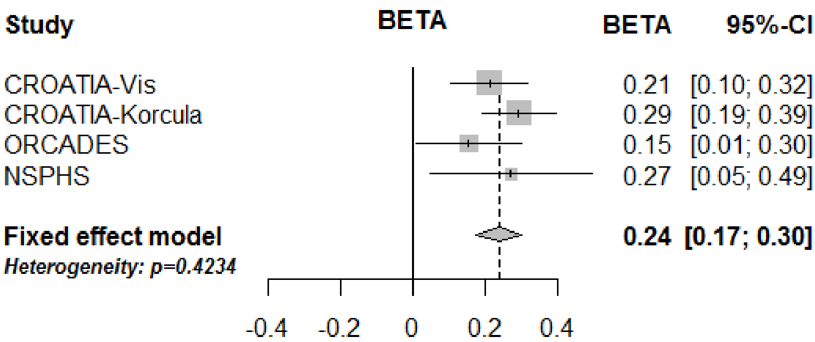


Figure 32: Significance (a) and Forest (b) plots for chromosome 7 region of the IGP63 meta-analysis.

(a) -Log$_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

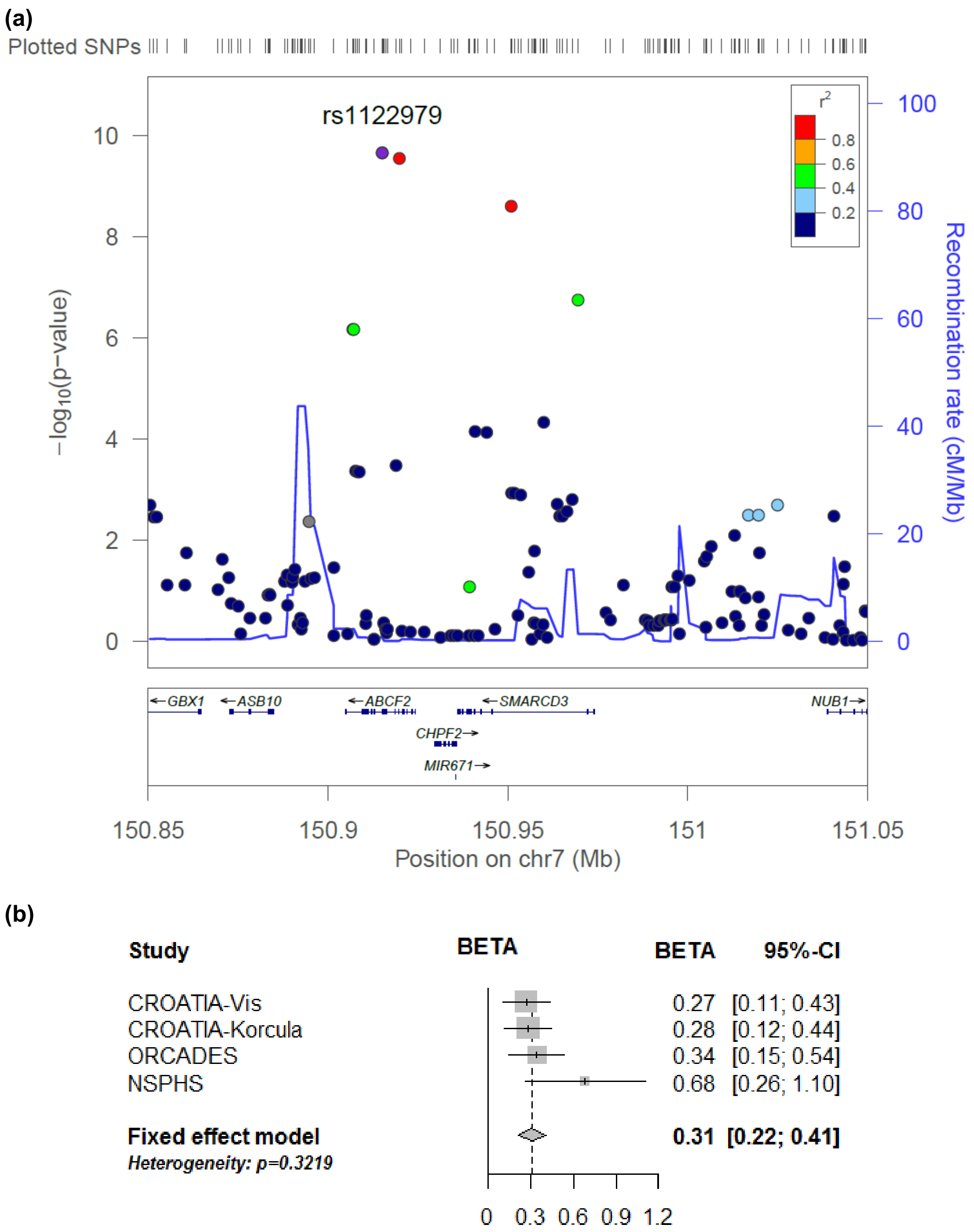


Figure 33: Significance (a) and Forest (b) plots for chromosome 7 region of the IGP2 meta-analysis.

(a) -Log$_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

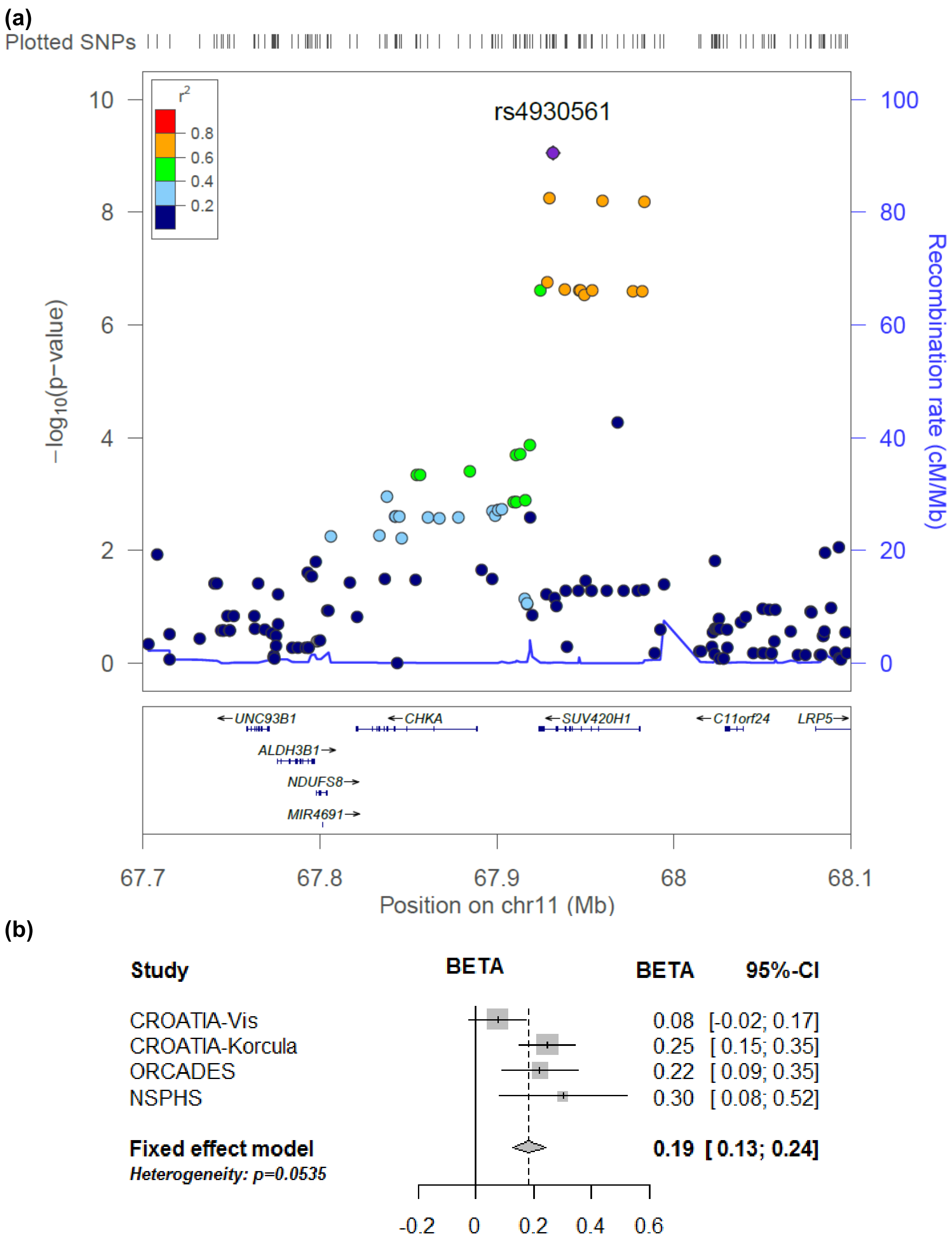


Figure 34: Significance (a) and Forest (b) plots for chromosome 11 region of the IGP41 meta-analysis.

(a) -Log$_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

Strongly suggestive associations were observed for several regions on chromosome 6 and single regions on chromosomes 7, 9, 12 and 17 (Figure 35 - Figure 40). Another signal on chromosome 6 was discarded due to a significant heterogeneity P-value (Figure 41). The most interesting of these is the suggestive association between rs404256 in the *BTB and CNC homology 1, basic leucine zipper transcription factor 2* (*BACH2*, Entrez GeneID: 60468) on chromosome 6 and IGP7, defined as the percentage of FA2[6]G1 in the total fraction ($p = 7.49x10^{-09}$) (Figure 24, Figure 36). *BACH2* is a B-cell specific transcription factor that can act as a suppressor or promoter of B-cell activation. It has been shown to orchestrate the transcriptional activation of B-cells, modify the cytotoxic effects of anticancer drugs and regulate IL-2 expression in umbilical cord blood CD4+ T cells [175]. The top SNP explains 2.0, 0.9, 0.9 and 2.3% of the trait variance in CROATIA-Vis, CROATIA-Korcula, ORCADES and NSPHS respectively.

5.3.2 Replication of GWAS Findings

Replication was sought for all genome-wide significant and strongly suggestive signals identified in the discovery analysis. The replication effort was undertaken by the Leiden Longevity Study (LLS) and was based on a different *N*-glycan quantitation method (MALDI-TOF-MS). While UPLC separates glycans according to structural similarities, MS groups them by mass. Furthermore, MS analysis focused on Fc glycans while UPLC measures both Fc and Fab glycans, thus all traits measured by the two methods could not be directly compared. Glycosylation patterns of IgG1 and IgG2 were investigated by analysis of tryptic glycopeptides, with six glycoforms per IgG subclass measured. The intensities of all glycoforms were related to the monogalactosylated, core-fucosylated biantennary species, providing five relative intensities registered per IgG subclass (Table 8). Structural diagrams for these glycans are contained in Figure 42. MS-measured traits from LLS were tested for association with the most significantly associated SNP in the gene regions from Table 7. A Bonferroni correction was applied based on the number of SNPs tested within each trait (e.g. For IGP3, 2 SNPs were tested, therefore 0.05/2 = 0.025, is the significance threshold for this trait). Not all associations were able to be tested because the equivalent structure was not measured in LLS. Replication was achieved for three regions, *B4GALT1* (FA2G2, $P= 5.35x10^{-08}$), *SMARCB1; DERL3* (FA2BG1, $P= 1.56x10^{-07}$; FA2BG2, $P= 1.06x10^{-03}$), and *MGAT3* (FA2BG1, $P= 1.62x10^{-10}$). Full results are presented in Table 9.

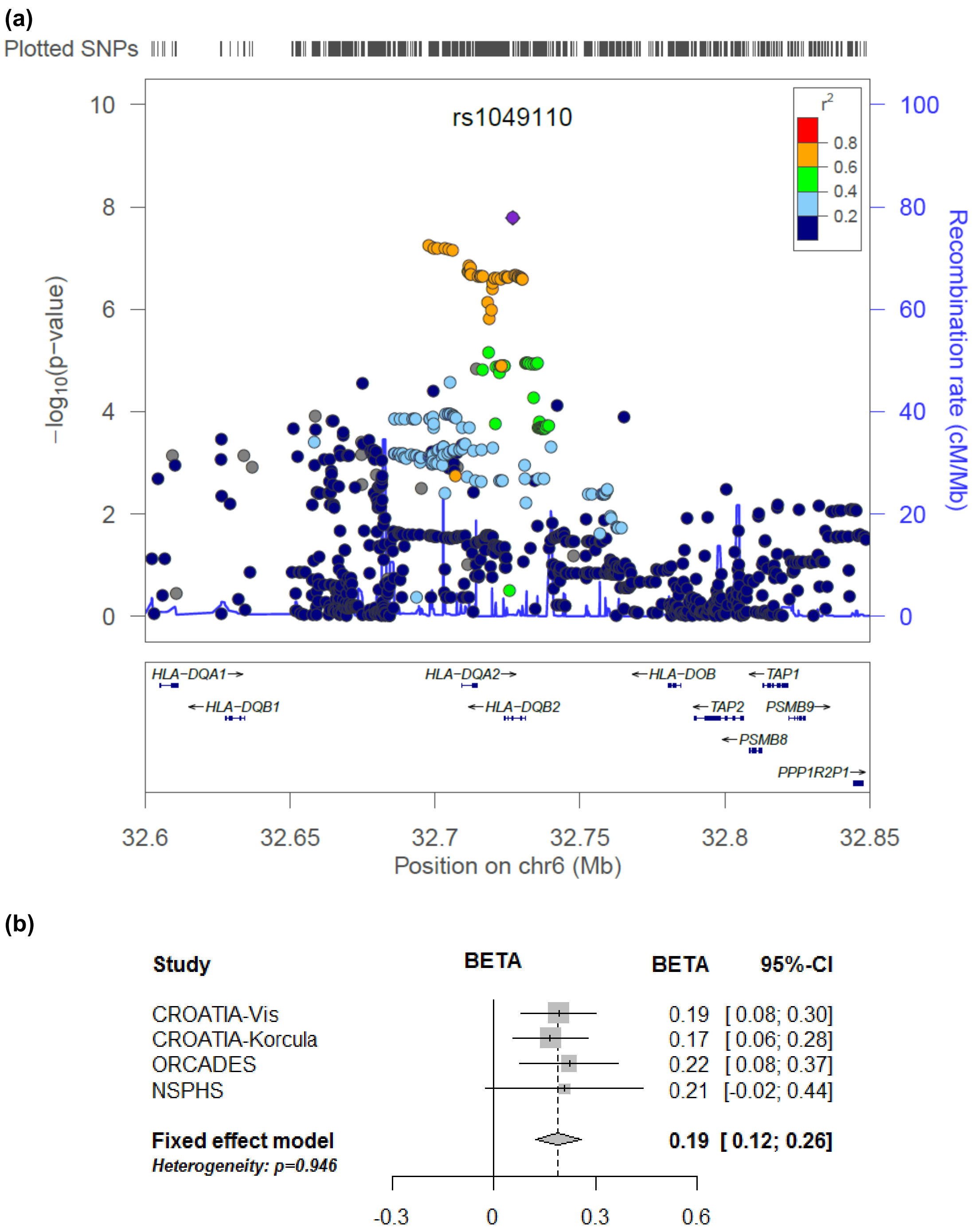
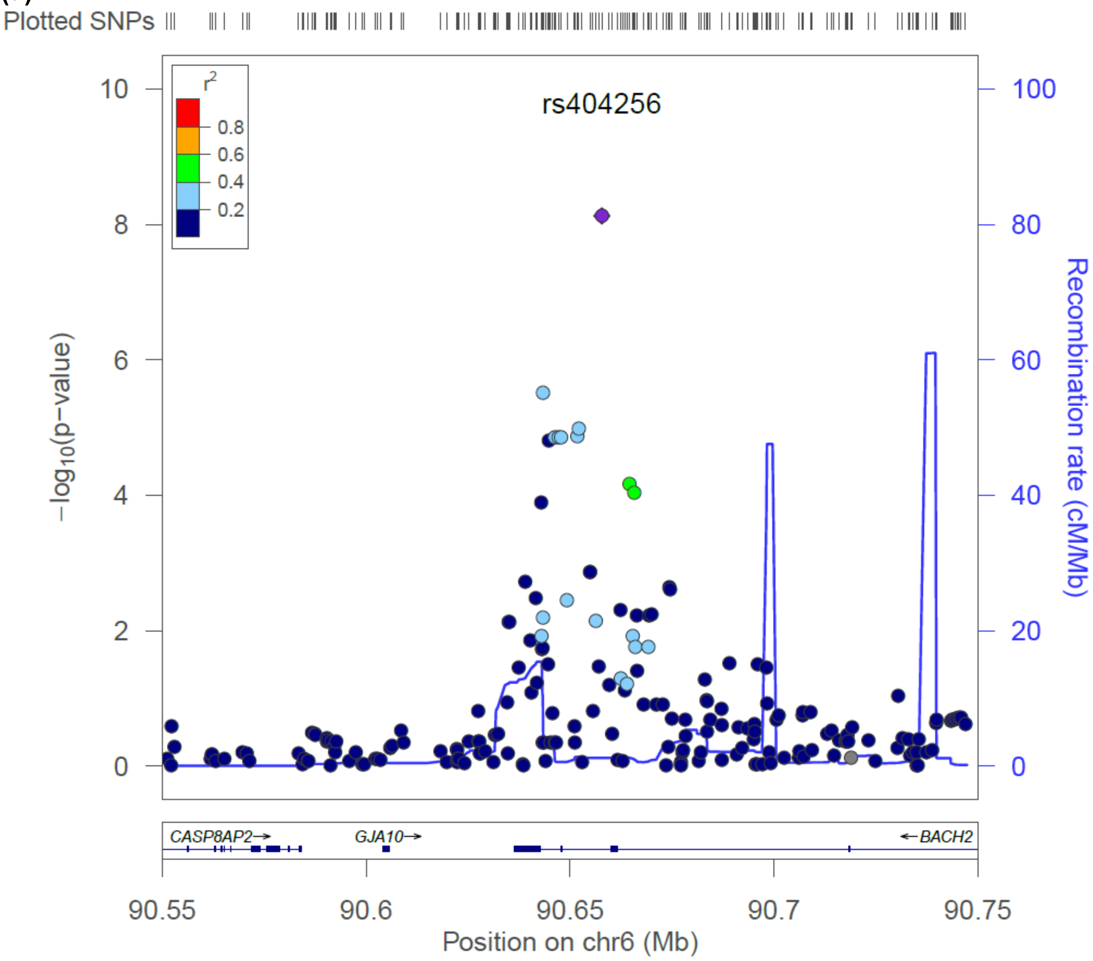


Figure 35: Significance (a) and Forest (b) plots for chromosome 6 region of the IGP42 meta-analysis.

(a) -Log$_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

(a)



(b)

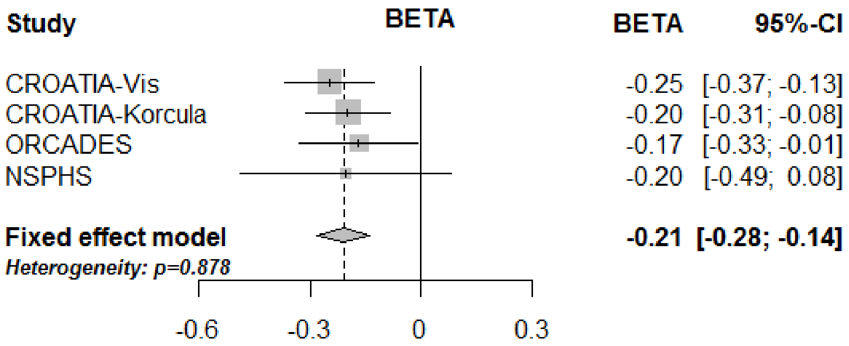


Figure 36: Significance (a) and Forest (b) plots for chromosome 6 region of the IGP7 meta-analysis.

(a) -Log$_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

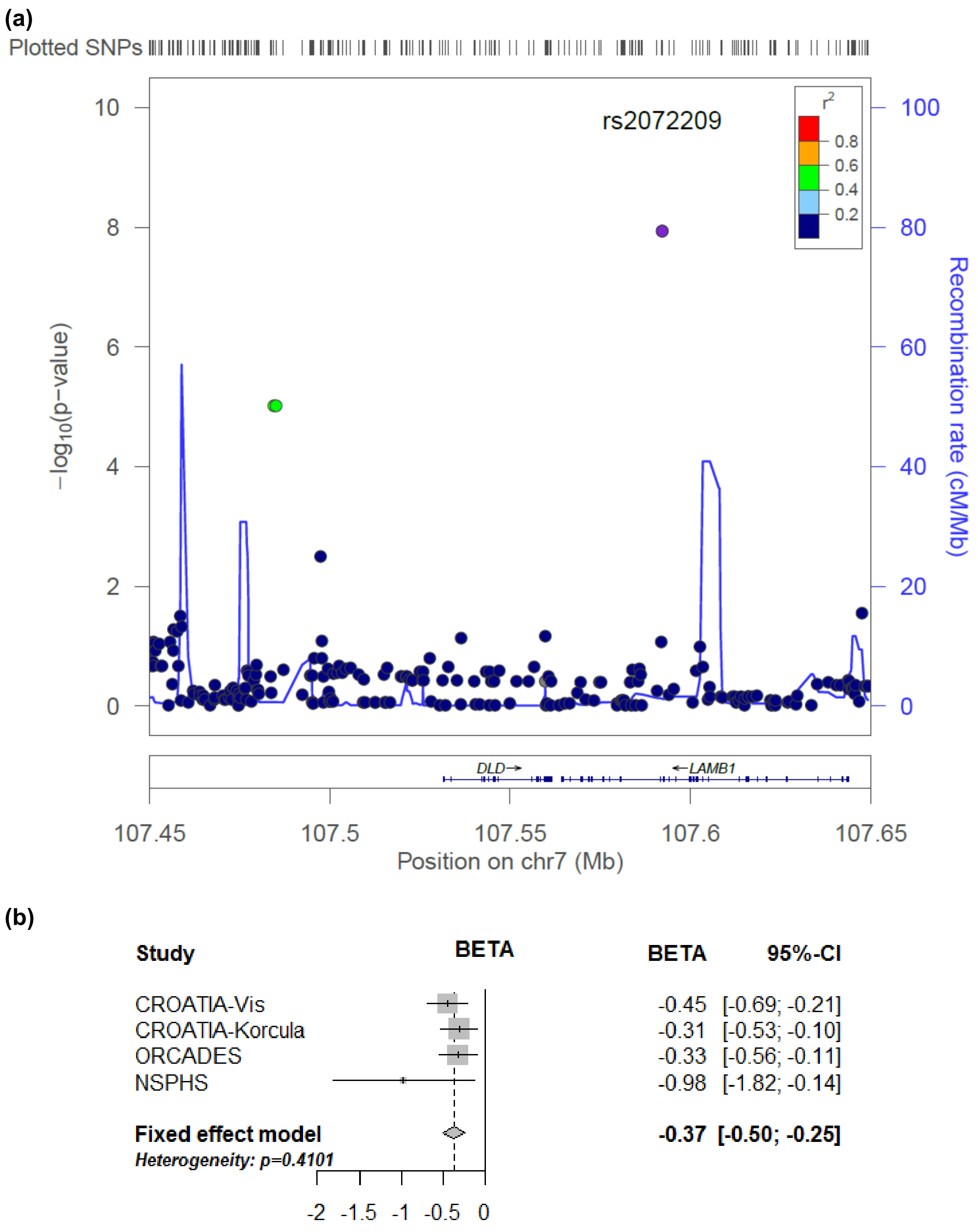


Figure 37: Significance (a) and Forest (b) plots for chromosome 7 region of the IGP69 meta-analysis.

(a) -$\log_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

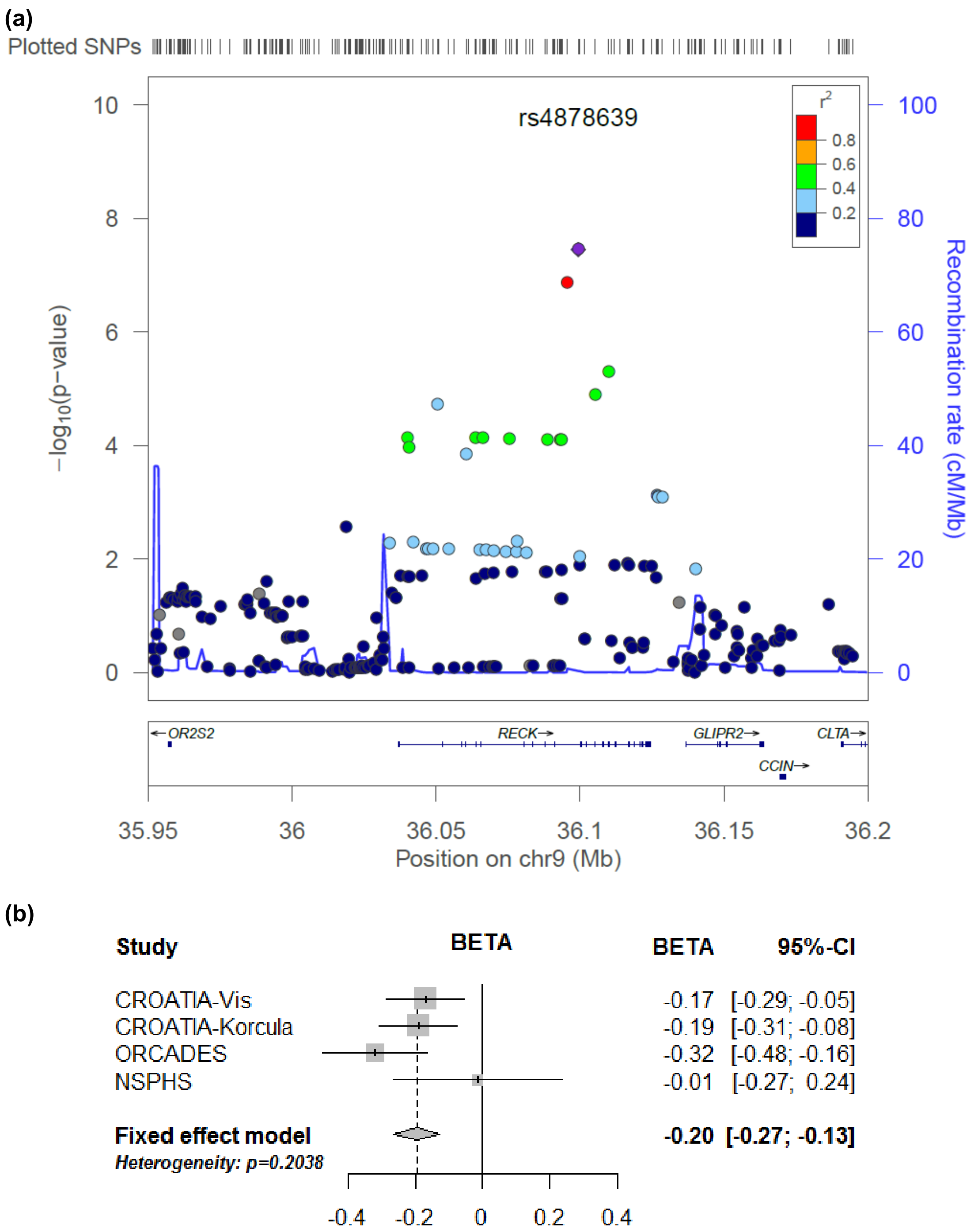


Figure 38: Significance (a) and Forest (b) plots for chromosome 9 region of the IGP17 meta-analysis.

(a) -Log_{10} of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

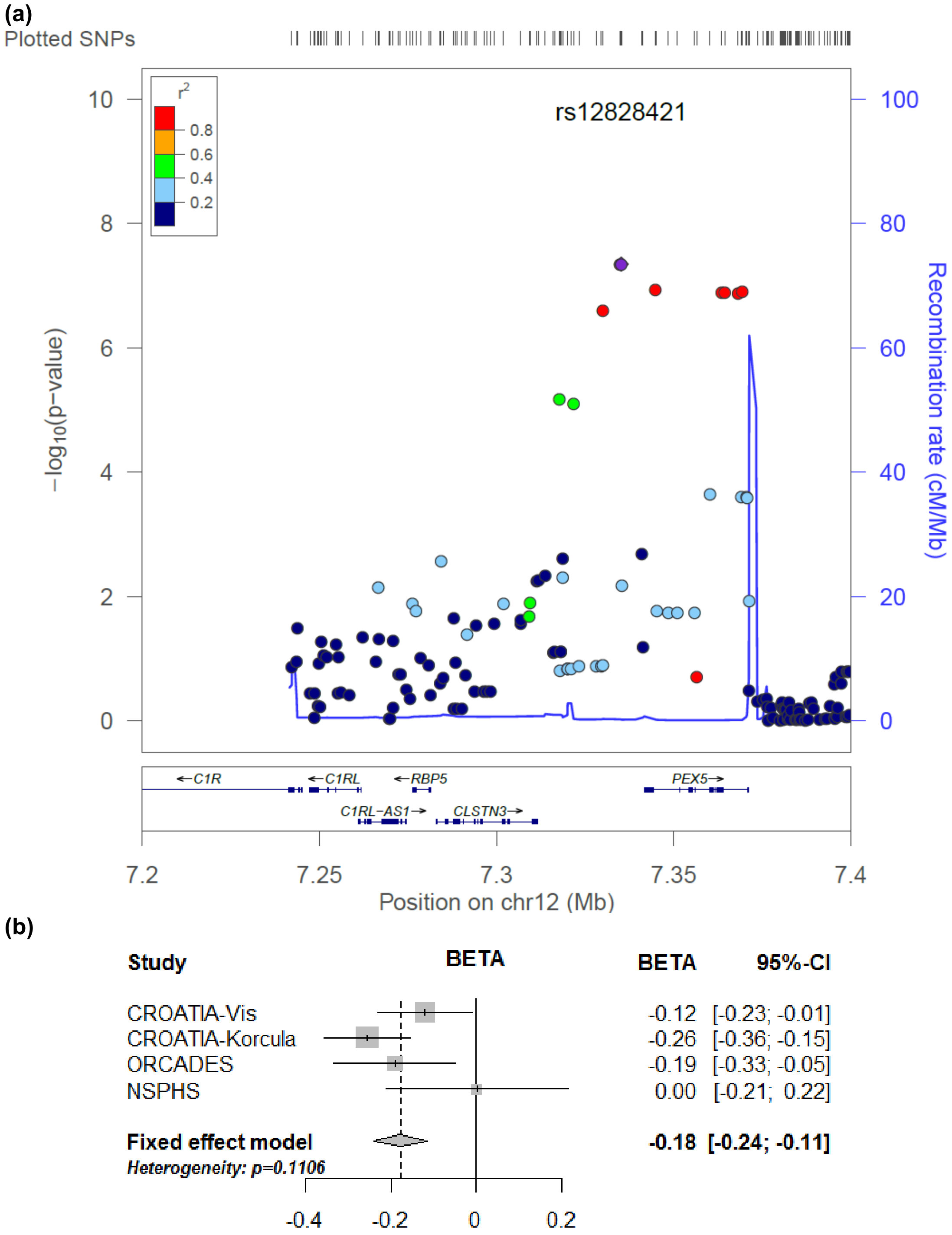


Figure 39: Significance (a) and Forest (b) plots for chromosome 12 region of the IGP41 meta-analysis.
(a) -Log_{10} of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

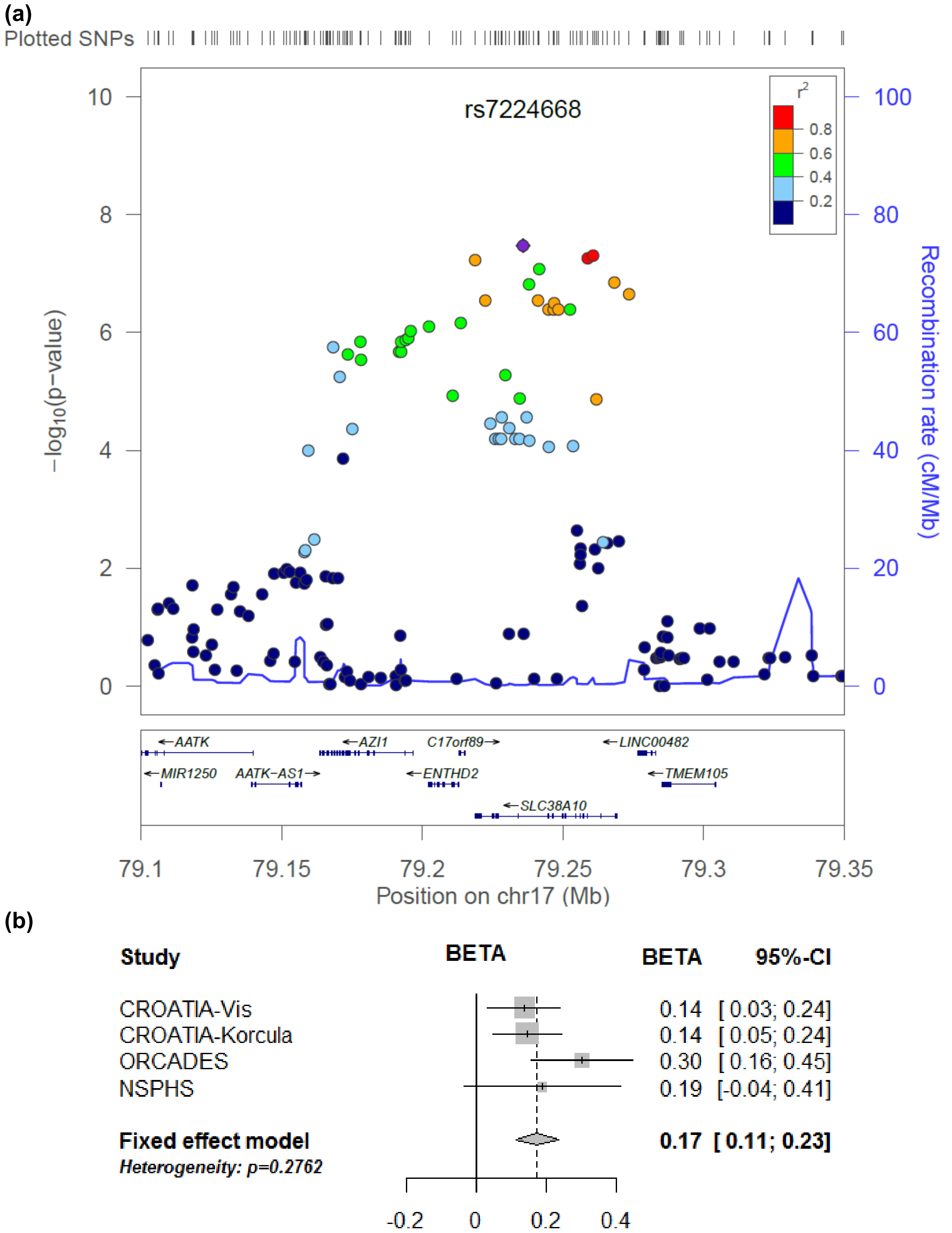


Figure 40: Significance (a) and Forest (b) plots for chromosome 17 region of the IGP31 meta-analysis.

(a) -$\log_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

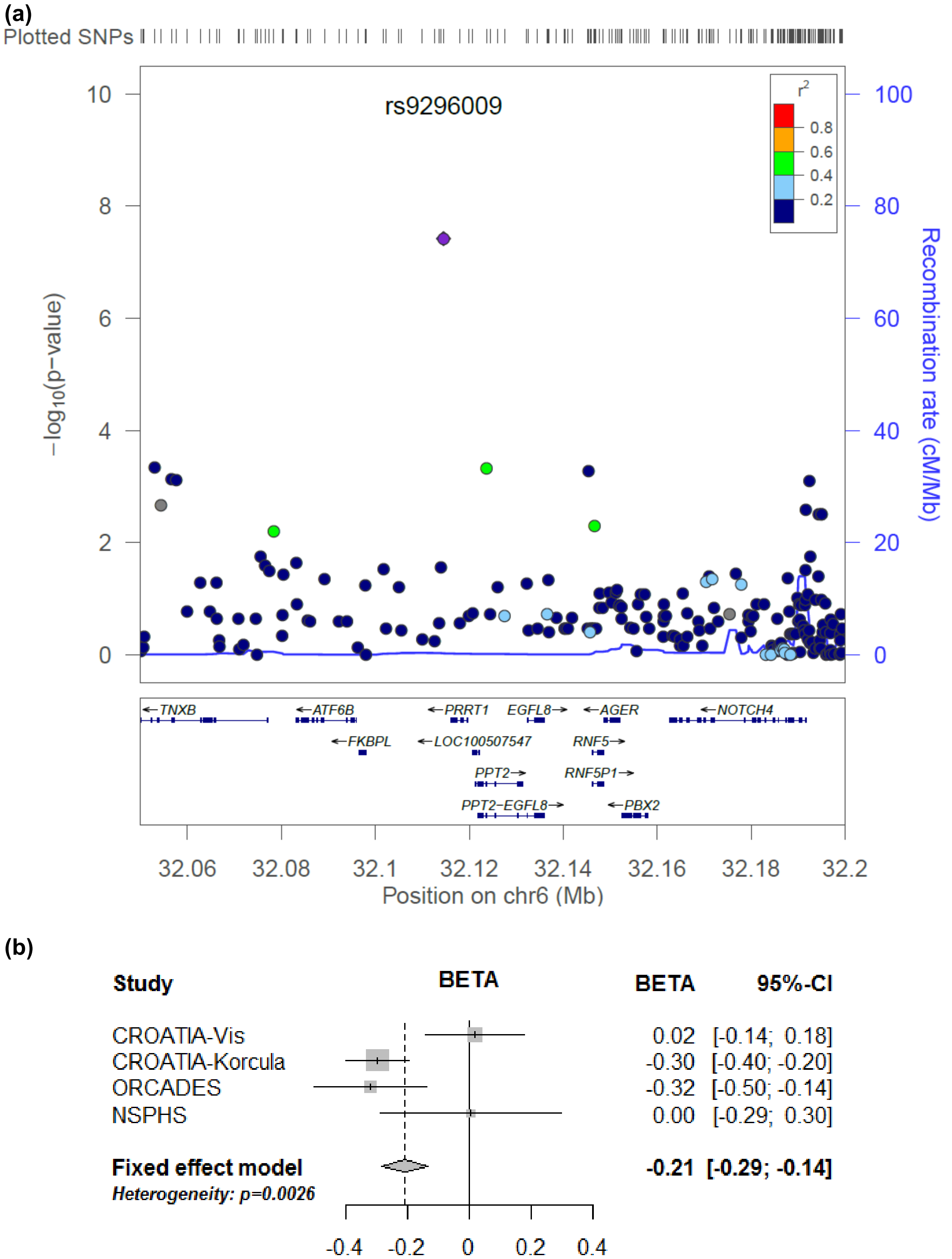


Figure 41: Significance (a) and Forest (b) plots for chromosome 6 region of the IGP23 meta-analysis.

(a) -Log$_{10}$ of the p-values are plotted against chromosome position. The most significant SNP is labelled with a purple diamond. Gene information and regional LD (r^2) are also shown based on “1000 Genomes Mar 2012 EUR”.(b)The estimate of effect size (BETA) and standard error for each population and the pool is shown, in which the size of the square for each individual cohort represents it’s weighting for the estimate of the pooled effect size. The effect size presented is the β-coefficient (BETA), which represents a change in IgG *N*-glycan level per copy of the minor allele in standard deviation units (after adjustment for age, sex and first 3 principal components).

Table 8: Description of *N*-glycan traits measured by MS and their descriptive statistics in LLS.

LLS MS IgG *N*-Glycan Trait	Formula	Median	IQR	Min	Max	Analogous UPLC IgG *N*-Glycan Trait
IgG1 FA2	log(FA2/FA2G1)	4.40	0.35	3.38	5.61	IGP3
IgG1 FA2B	log(FA2B/FA2G1)	3.75	0.30	2.71	4.68	IGP5
IgG1 FA2BG1	log(FA2BG1/FA2G1)	2.80	0.46	1.56	4.42	IGP9 + IGP10
IgG1 FA2G2	log(FA2G2/FA2G1)	3.05	0.32	2.07	4.31	IGP13
IgG1 FA2BG2	log(FA2BG2/FA2G1)	1.25	0.40	0.12	3.83	IGP14

IQR: trait interquartile range; Min: trait minimum; Max: trait maximum

Table 9: Replication results for IgG *N*-Glycan traits in LLS.

UPCL Trait	MS Trait	Gene Region	SNP Tested	P-Value	
				Discovery	Replication
IGP3	IgG1 FA2	*B4GALT1*	rs12342831	4.70x10^{-07}	3.95x10^{-02}
IGP3	IgG1 FA2	*IL6ST; ANKRD55*	rs17348299	2.39x10^{-09}	2.02x10^{-01}
IGP5	IgG1 FA2B	*ABCF2; SMARCD3*	rs1122979	1.89x10^{-09}	5.30x10^{-01}
IGP5	IgG1 FA2B	*IL6ST; ANKRD55*	rs17348299	2.42x10^{-06}	1.27x10^{-02}
IGP5	IgG1 FA2B	*IKZF1*	rs6421315	7.04x10^{-06}	3.90x10^{-01}
IGP5	IgG1 FA2B	*SYNGR; TAB1; MGAT3; CACNA1I*	rs909674	1.10x10^{-10}	3.12x10^{-08}
IGP9	IgG1 FA2BG1	*SMARCB1; DERL3*	rs2186369	3.00x10^{-13}	1.56x10^{-07}
IGP10				9.32x10^{-10}	
IGP9	IgG1 FA2BG1	*SYNGR1; TAB1; MGAT3; CACNA1I*	rs909674	2.80x10^{-09}	1.62x10^{-10}
IGP10				>1x10^{-05}	
IGP13	IgG1 FA2G2	*B4GALT1*	rs12342831	5.19x10^{-08}	5.35x10^{-08}
IGP13	IgG1 FA2G2	*IL6ST; ANKRD55*	rs17348299	1.27x10^{-10}	3.83x10^{-01}
IGP13	IgG1 FA2G2	*RECK*	rs4878639	5.67x10^{-06}	7.04x10^{-01}
IGP14	IgG1 FA2BG2	*ST6GAL1*	rs11710456	9.08x10^{-07}	9.79x10^{-01}
IGP14	IgG1 FA2BG2	*SMARCB1; DERL3*	rs2186369	3.40x10^{-08}	1.06x10^{-03}

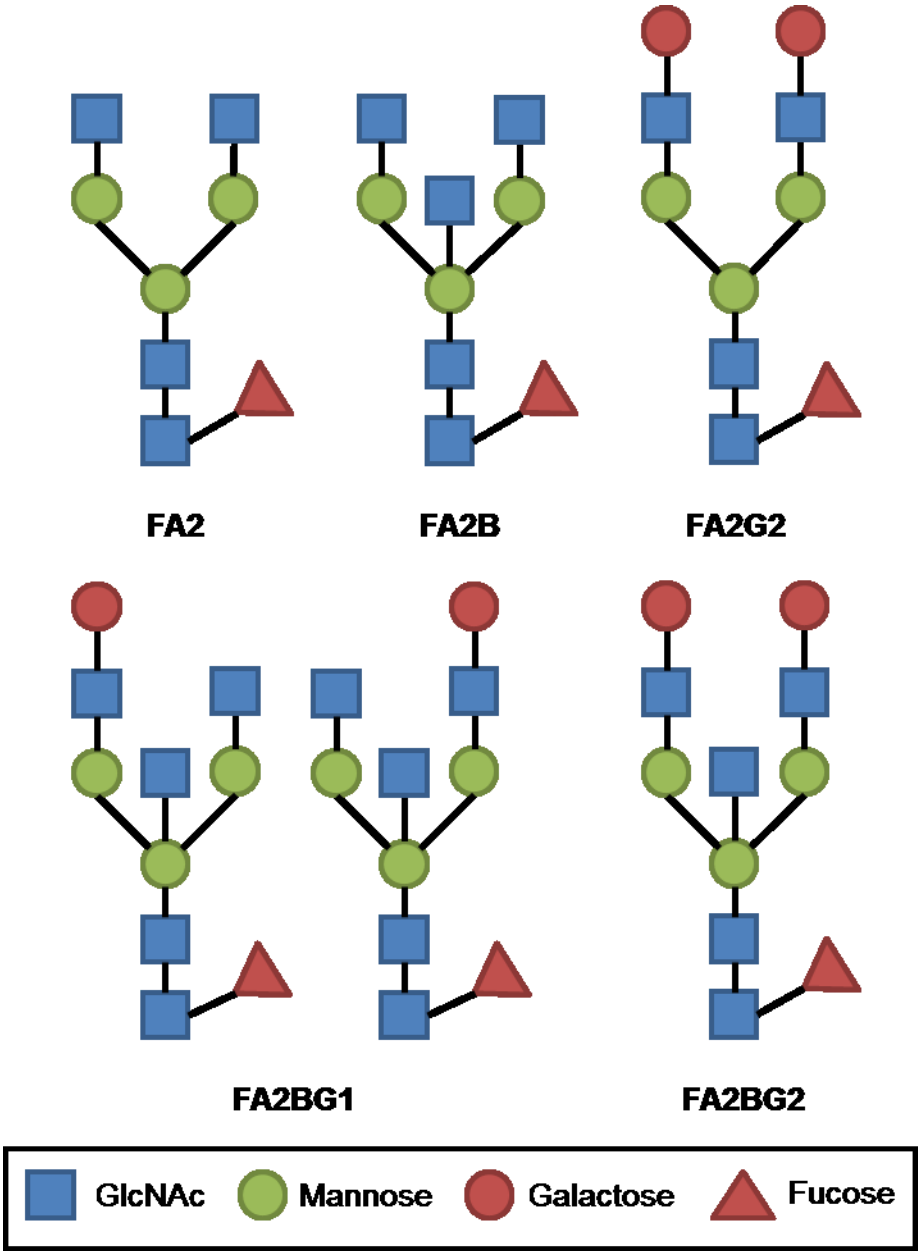


Figure 42: *N*-glycan structures available for replication in Leiden Longevity Study.
N-glycan structures available for replication in LLS as measured by MALDI-TOF-MS. GlcNAc: *N*-acetylglucosamine. F at the start of the abbreviation indicates a core fucose α1-6 linked to the inner GlcNAc; Ax, number of antenna (GlcNAc) on trimannosyl core; A2, biantennary with both GlcNAcs as β1-2 linked; B, bisecting GlcNAc linked β1-4 to β1-3 mannose; Gx, number (x) of β1-4 linked galactose on antenna.

5.3.3 Rare Variant Analysis

Rare variant burden tests were successfully run for all 13 IgG *N*-glycan traits which gave genome-wide significant or strongly suggestive P-values in the common variant GWAS (both IGP17 and IGP41 associated with two regions each). There were approximately 770 people with both genotype and phenotype information (depending on the phenotype) which is approximately 80 people less than available for the common variant HapMap2 GWAS.

No genes achieve the Bonferroni-corrected threshold for any trait or analysis. When looking only at the genes that achieved a P-value < $5x10^{-08}$ in the common variant GWAS, again, only *FUT8* achieved a p-value < 0.05, with the same single SNP with MAF < 5% (rs2229678, MAF= 0.031, P= $1.01x10^{-03}$) showing association. The P-value was moderately more significant than in the total plasma N-glycan rare variant analysis presented in Chapter 3, most likely due to a decrease in phenotypic noise since the glycans were isolated from one protein. Conditional analysis produced the same results as in Chapter 3.

5.3.4 Analysis of Pleiotropy within IgG *N*-Glycan Associated Genes

Many of the genes that were found in this GWAS have been associated with quantitative traits or disease. The NHGRI GWAS Catalog [7] was used to determine gene associations for all regions achieving a p-value < $5x10^{-08}$ in the discovery analysis and SNAP was used to calculated LD between the top disease associated SNP and the top SNP from the IgG *N*-glycan GWAS. Only studies achieving a P-value < $5x10^{-08}$ are reported unless the finding was replicated within the study or by another study.

Despite many of the same genes being associated with quantitative traits or diseases, the top SNPs tended to not be in high LD, therefore were unlikely to be tagging the same association signals (Table 10). Three associations did appear to be in high LD with the IgG *N*-glycan associated SNP, including an *ABCF2*; *SMARCD3* association with bone mineral density and *B4GALT1* association with serum urate concentrations. The urate paper also identified *HNF1A* which was associated with plasma *N*-glycans in Chapter 3.

Table 10: Analysis of pleiotropy between IgG *N*-glycan associated loci and quantitative trait or disease loci.

Gene Region	Top IgG *N*-glycan SNP	QT/Disease	Top QT or Disease SNP	P-Value	Reference	Ancestry	1000G (IgG)*		1000G (QT)**	
							R^2	D'	R^2	D'
ST6GAL1	rs11710456	Drug-induced liver injury (flucloxacillin)	rs10937275	$1x10^{-08}$	Daly et al., Nat Genet, 2009	European	0.017	1	-	-
		Type 2 diabetes	rs16861329	$3x10^{-08}$	Kooner et al., Nat Genet, 2011	South Asian	0	0.005	0.003	0.157
		Esophageal cancer (squamous cell)	rs2239612	$6x10^{-14}$	Wu et al., Nat Genet, 2012	Han Cinese	0.003	0.251	0.002	0.11
IL6ST; ANKRD55	rs17348299	Rheumatiod arthritis	rs6859219	$1x10^{-11}$	Stahl et al., Nat Genet, 2010	European	0.044	1	-	-
		Crohn's disease	rs10065637	$4x10^{-12}$	Jostins et al., Nature, 2012	European	0.044	1	-	-
		Triglycerides	rs9686661	$1x10^{-10}$	Teslovich et al., Nature, 2010	European	NA	NA	-	-
		Celiac disease and Rheumatiod arthritis	rs1020388	$3x10^{-07}$	Zhernakova et al., PLoS Genet, 2011	European	0.011	0.244	-	-
		Alzheimer's disease (cognitive decline)	rs4700060	$1x10^{-08}$	Sherva et al. Alzheimers Dement, 2013	European	0.001	0.034	-	-
		Urate levels (women)	rs456867	$3x10^{-06}$	Kottgen et al., Nat Genet, 2012	European	0.033	1		
IKZF1	rs6421315	Acute lymphoblastic leukemia (childhood)	rs11978267	$8x10^{-11}$	Trevino et al., Nat Genet, 2009	European	0.012	0.130	-	-
		Acute lymphoblastic leukemia (childhood)	rs4132601	$1x10^{-19}$	Papaemmanuil et al., Nat Genet, 2009	European	0.012	0.130	-	-
		Mean corpuscular volumne	rs12718597	$5x10^{-13}$	Ganesh et al., Nat Genet, 2009	European	0.019	0.161	-	-
		Systemic lupus erythematosus	rs4917014	$3x10^{-23}$	Han et al., Nat Genet, 2009	Han Chinese	0.053	0.277	0.097	0.4
		Crohn's disease	rs1456896	$1x10^{-08}$	Franke et al., Nat Genet, 2010	European	0	0.007	-	-

Gene Region	Top IgG *N*-glycan SNP	QT/Disease	Top QT or Disease SNP	P-Value	Reference	Ancestry	1000G (IgG)*		1000G (QT)**	
							R^2	D’	R^2	D’
IKZF1	rs6421315	Inflammatory bowel disease	rs1456896	$7x10^{-15}$	Jostins et al., Nature, 2012	European	0	0.007	-	-
		Red blood cell traits	rs12718598	$2x10^{-13}$	van der Harst et al., Nature, 2012	European	0.025	0.174	-	-
		Systemic lupus erythematosus	rs10276619	$6x10^{-06}$	Yang et al., Am J Hum Genet, 2012	Han Chinese	0	0.013	0.15	0.466
		Acute lymphoblastic leukemia (childhood)	rs6964969	$2x10^{-29}$	Xu et al., J Natl Cancer Inst, 2013	European/ African American / Hispanic	0.012	0.13	0.087	0.518
		HDL Cholesterol	rs4917014	$1x10^{-08}$	Willer et al., Nat Genet, 2013	European	0.053	0.277	-	-
ABCF2; SMARCD3	rs1122979	Bone Mineral Density	rs7812088	$7x10^{-09}$	Estrada et al., Nat Genet, 2012	European	1	1	-	-
B4GALT1	rs12342831	Urate levels	rs10813960	$4x10^{-07}$	Kottgen et al., Nat Genet, 2012	European	0.846	1	-	-
SYNGR1; TAB1; MGAT3; CACNA1I	rs909674	Inflammatory bowel disease	rs2413583	$4x10^{-33}$	Jostins et al., Nature, 2012	European	0.053	0.292	-	-
		Schizophrenia	rs9611198	$8x10^{-06}$	Irish Schizophrenia Genomics Consortium & the WTCC2 et al., Biol Psychiatry, 2012	European	0.157	0.696	-	-
HLA-DQB2	rs1049110	Kawasaki disease	rs2857151	$5x10^{-11}$	Onouchi et al., Nat Genet, 2012	Japanese	0.164	0.463	0.038	0.267
		Lymphoma (Follicular non-Hodgkin’s Lymphoma)	rs2621416	$2x10^{-09}$	Vijai et al., PLoS Genet, 2013	European	0.227	0.762	-	-
		Hepatitis B	rs7453920	$5x10^{-37}$	Hu et al., Nat Genet, 2013	Han Chinese	0.967	1	0.181	0.443
BACH2	rs404256	Type 1 diabetes	rs3757247	$1x10^{-06}$	Grant et al., Diabetes, 2008	European	0.042	0.204	-	-

Gene Region	Top IgG *N*-glycan SNP	QT/Disease	Top QT or Disease SNP	P-Value	Reference	Ancestry	1000G (IgG)*		1000G (QT)**	
							R^2	D'	R^2	D'
BACH2	rs404256	Type 1 diabetes	rs11755527	$5x10^{-12}$	Cooper et al., Nat Genet, 2008	European	0.031	0.179	-	-
		Type 1 diabetes	rs11755527	$5x10^{-08}$	Barrett et al., Nat Genet, 2009	European	0.031	0.179	-	-
		Celiac disease	rs10806425	$4x10^{-10}$	Dubois et al., Nat Genet, 2010	European	0.006	0.09	-	-
		Crohn's disease	rs1847472	$5x10^{-09}$	Franke et al., Nat Genet, 2010	European	0.009	0.124	-	-
		Type 1 diabetes autoantibodies	rs11755527	$3x10^{-08}$	Plagnol et al., PLoS Genet, 2011	European	0.031	0.179	-	-
		Muliple sclerosis	rs12212193	$4x10^{-08}$	Sawcer et al., Nature, 2011	European	0.027	0.166	-	-
		Graves' disease	rs370409	$2x10^{-06}$	Chu et al., Nat Genet, 2011	Chinese	0.009	0.166	0	0.021
		Vitiligo	rs3757247	$3x10^{-08}$	Jin et al., Nat Genet, 2012	European	0.042	0.204	-	-
		Systemic lupus erythematosus	rs12529935	$9x10^{-06}$	Yang et al., Am J Hum Genet, 2012	Han Chinese	0	0.047	0.005	0.207
DLD; LAMB1	rs2072209	Ulcerative colitis	rs4598195	$1x10^{-06}$	Silverberg et al., Nat Genet, 2009	European	0.115	1	-	-
		Ulcerative colitis	rs4598195	$8x10^{-08}$	McGovern et al., Nat Genet, 2010	European	0.115	1	-	-
		Ulcerative colitis	rs4380874	$2x10^{-26}$	Jostins et al., Nature, 2012	European	0.070	1	-	-
		Ulcerative colitis	rs886774	$3x10^{-08}$	Barrett et al., Nat Genet, 2009	European	0.067	1	-	-

Associations reported are from the NHGRI GWAS Catalog [7] (accessed 08/07/2014) and LD has been calculated using SNAP[104]. LD information is not available in SNAP for the HLA region so HapMap2 (release 22) data was used for HLA-DQB2. QT: quantitative trait

* Linkage disequilibrium from 1000 Genomes Pilot 1 CEU data (corresponding to ethnicity of the study populations for IgG *N*-glycan GWAS)

** Linkage disequilibrium from 1000 Genomes Pilot 1 data for the ethnic group most closely corresponding to ethnicity of the QT or disease study population (YRI or CHB/JPT)

5.4 Discussion

The results presented in this chapter further demonstrate that the recent developments in high-throughput glycomics and genomics now allow identification of genetic loci that control *N*-glycosylation using a GWAS approach. In Chapter 3 I reported the results of the first GWAS of the total plasma *N*-glycome as measured by HPLC. Although the study was of a comparable sample size (N~2000) to the IgG GWAS, it only identified six genome-wide significant and four strongly suggestive assocations [111,112] compared with nine genome-wide significant and six strongly suggestive associtions in this IgG *N*-glycan GWAS. It is possible that the power of the study presented in Chapter 3 was reduced because *N*-glycans in total plasma originate from different glycoproteins where they have different functions and undergo protein-specific or tissue-specific glycosylation. As well, individual protein *N*-glycan associations may be diluted and lost among the great many plasma *N*-glycan carrying proteins. In this study the largest percentage of variance explained by a single association was 16–18% whereas in the total *N*-glycan study this was 2–9%. Also, concentrations of individual glycoproteins in plasma vary in many physiological processes, introducing substantial noise to the quantitation of the total plasma *N*-glycome.

In this study both problems were avoided by isolating a single protein from plasma (IgG), which is produced by a single cell type (B lymphocytes), thus effectively excluding differential regulation of gene expression in different tissues, and the noise introduced by variation in plasma IgG concentration and by *N*-glycans on other plasma proteins. It was expected that this should increase the power of the study to detect genome-wide associations substantially. This study yielded more genome-wide association signals, which were also much more significant, in comparison to the total plasma *N*-glycome GWAS in the same cohorts (in fact, with a slightly reduced sample size). Fifteen loci were identified to be associated with IgG *N*-glycan traits with P-values < $5x10^{-08}$ and nine reached the multiple testing significance threshold of $2.27x10^{-09}$. During the replication effort in the LLS cohort using MS quantitation we replicated three of the eight loci that were able to be tested. We were unable to attempt to replicate associations for the remaining loci because those glycosylation structures were not measured. Failure to replicate many of the GWAS signals where the structure could be measured may be due to the different N-glycan measurement method used between the discovery cohorts (UPLC) and the replication study (MALDI-TOF-MS). The method used by the replication cohort was only able to quantify structures with core fucose and only from one subtype of IgG (IgG_1) therefore there were very few hits that could have replication attempted. Also, in some cases, the most highly associated *N*-

glycan trait could not be measured therefore one with a lesser signal was used. In the results which will be presented in Chapter 6, it was found that MALDI-TOF-MS produced the worst results of all N-glycan quantitation methods as compared by GWAS. In addition, the discovery cohorts were all population isolates, whereas the replication was a general population so it is possible that population-specific allele frequency differences reduced power to detect association, but as most SNPs were common, this is less likely.

The potential batch effects discussed in Chapter 3 are also present in the data analysed here but batch-corrected data only became available in the week prior to submission of this thesis so was not possible to include. Preliminary reports suggest that they have a minimal impact on GWAS meta-analysis p-values but may impact heritability estimates as discussed in Chapter 3.

Among the nine loci that reached genome-wide statistical significance, four involved genes encoding glycosyltransferases known to glycosylate IgG (*ST6GAL1*, *B4GALT1*, *FUT8*, *MGAT3*). The enzyme beta1,4-galactosyltransferase 1 is responsible for the addition of galactose to IgG glycans. Interestingly, variants in *B4GALT1* did not affect the main measures of IgG galactosylation, but instead differences in sialylation and the percentage of bisecting GlcNAc. These associations are still biologically plausible, because galactosylation is a prerequisite for sialylation, and enzymes which add galactose and bisecting GlcNAc compete for the same substrate [176].

Core-fucosylation of IgG has been intensively studied due to its role in antibody-dependent cell-mediated cytotoxicity (ADCC). ADCC is a process whereby effector cells of the immune system (natural killer cells, macrophages, neutrophils and eosinophils) bind to and kill target cells which have been bound by antibodies. This is one of the major pathways by which the immune system prevents infection but requires prior knowledge that the target cell is dangerous in order to have antibodies against it [50]. This mechanism is the basis of antibody-based therapeutics against tumours. Core-fucose is critically important to regulate this process, in fact IgGs without core fucose on the Fc glycan have been found to have ADCC activity enhanced by up to 100-fold [177]. Alpha-(1,6)-fucosyltransferase (fucosyltransferase 8) catalyses the transfer of fucose from GDP-fucose to N-linked type complex glycopeptides, and is encoded by the *FUT8* gene. In Chapter 3, SNPs located near this gene were found to influence overall levels of fucosylation in the total plasma *N*-glycome. This was also the case with IgG *N*-glycans, with the same top SNP explaining a similar amount of trait variance with similar structures, only isolated exclusively from IgG rather than from all plasma proteins. The directly measured IgG glycome traits most strongly associated with SNPs in the *FUT8* region consisted of A2, and, less strongly, A2G1 and A2G2. These associations are biologically plausible as these glycans serve as substrates for fucosyltransferase 8. Interestingly, SNPs located near the *IKZF1* gene influenced fucosylation of a specific subset of glycans, especially those without bisecting GlcNAc, and were also related to the ratio of fucosylated structures with and without bisecting GlcNAc. This suggests the *IKZF1* gene encoding Ikaros may be a potential indirect regulator of fucosylation in B-lymphocytes by promoting the addition of bisecting GlcNAc, which then inhibits fucosylation. This is difficult to confirm however as Ikaros is heavily involved throughout B-cell development, so any gene-level modifications to *IKZF1* will have implications for more than just IgG glycosylation.

Again, rare variant analyses yielded few results but suffers from the same power issues mentioned in Chapter 3. Further studies, with much larger samples sizes and more careful SNP inclusion criteria, may yield more promising results regarding the effect of rare variants on the genomic regulation of IgG *N*-glycans.

Nearly all genome-wide significant loci in our study have already been clearly demonstrated to be associated with autoimmune diseases, haematologic cancers, and some of them are also associated with chronic inflammation and/or neuropsychiatric disorders. Although the literature on those associations is extensive, I have looked only at those associations that were identified through GWAS (Table 10). The table implies abundant pleiotropy at the gene level between loci that control IgG *N*-glycosylation and loci that have been implicated in many human diseases. Autoimmune diseases (including SLE, RA, UC and over 80 others) are thought to be triggered by aggressive responses of the adaptive immune system to self antigens, thereby resulting in tissue damage and pathogenicity [178]. Among other mechanisms, IgG autoantibodies are responsible for the chronic inflammation and destruction of healthy tissues by cross-linking Fc receptors on innate immune effector cells [179]. Class and glycosylation of IgG are important for pathogenicity of autoantibodies in autoimmune diseases (reviewed in [180]). Removal of IgG glycans leads to the loss of the proinflammatory activity, suggesting that *in vivo* modulation of antibody glycosylation might be a strategy to interfere with autoimmune processes [179]. Indeed, the removal of IgG glycans by injections of EndoS *in vivo* interfered with autoantibody-mediated proinflammatory processes in a variety of autoimmune models [179]. Although the associated SNPs are not in high LD with the majority of loci associated with disease, causal disease variants that substantially dimish expression or alter protein structure may still have an impact on glycosylation. Also, this may mean that *N*-glycans may be good biomarkers of disease because although they may or may not be causal, they may still be altered in a disease state.

The results from this study suggest that IgG *N*-glycome composition is regulated through the interaction of genes directly involved in glycosylation and those that may have a higher-level regulatory function and that these loci may affect many different *N*-glycan structures. SNPs at several different loci in this GWAS showed genome-wide significant associations with the same or similar IgG *N*-glycosylation traits. For example, SNPs at loci on chromosomes 9 (*B4GALT1* region) and 3 (*ST6GAL1* region) both influenced the percentage of sialylation of galactosylated fucosylated structures (without bisecting GlcNAc) in the same direction. SNPs at these loci also influenced the ratio of fucosylated monosialylated structures (with and without bisecting GlcNAc) in the opposite direction. SNPs at the locus on chromosome 9 (*B4GALT1*), and two loci on chromosome 22 (*MGAT3* and *SMARCB1*; *DERL3* region) both influenced the ratio of fucosylated disialylated structures with and without bisecting GlcNAc. SNPs at loci on chromosome 7 (*IKZF1* region) and 14 (*FUT8* region) influenced an overlapping range of traits: percentage of A2 and A2G1 glycans, and, in the opposite direction, the percentage of fucosylation of agalactosylated structures.

Finally, I have demonstrated that findings from hypothesis-free GWAS, when targeted at a well-defined biological phenotype of likely relevance to human health and disease (such as *N*-glycans of a single plasma protein), illuminate new biological mechanisms. The unexpected pleiotropy of the implicated loci that linked them to diseases can change this study from hypothesis-free to hypothesis-driven [181], and allow the exploration of potential biomarkers using *N*-glycan traits for the prediction of a specific disease. This study offers many additional opportunities to investigate both the function of newly associated genes with no previous ties to glycosylation, as well as the investigation of further *N*-glycan biomarkers for diseases identified through gene-level pleiotropy.

5.5 Conclusions

New understanding of the genetic regulation of IgG *N*-glycan synthesis has been revealed by this study. Enzymes directly responsible for the addition of galactose, fucose and bisecting GlcNAc may not have primary responsibility for the final IgG *N*-glycan structures. For all three processes, genes that are not directly involved in glycosylation showed the most significant associations: *IL6ST*; *ANKRD55* for galactosylation; *IKZF1* for fucosylation; and *SMARCB1*; *DERL3* for the addition of bisecting GlcNAc. This study identified 9 loci that are likely to be part of a much larger genetic network that regulates the complex process of IgG

N-glycosylation and several further loci that show suggestive association with glycan traits and merit further study. Genetic variants in several of these genes were previously associated with a number of inflammatory and neoplastic diseases across ethnically diverse populations, all of which could benefit from earlier and more accurate diagnosis based on molecular biomarkers. Variations in individual SNPs have relatively small effects, but when several polymorphisms are combined in a complex pathway like *N*-glycosylation, the final product of the pathway - in this case IgG *N*-glycan - can be significantly different, with consequences for IgG function and possibly also disease susceptibility.

Chapter 6 - Comparative performance of four methods for high-throughput glycosylation analysis of immunoglobulin G in genetic and epidemiological research

6.1 Introduction

Rapid advances of technologies for high-throughput genome analysis in the past decade have enabled large-scale genome-wide association studies (GWAS). GWAS has become a reliable tool for identification of associations between genetic polymorphisms and various human diseases and quantitative traits [2]. Thousands of GWAS have been conducted in recent years, but these have not included the study of glycan traits until recently with the analyses discussed in Chapters 3 & 5 comprising three of the four published papers. The main reason was the absence of reliable tools for high-throughput quantitative analysis of glycans that could match the measurements of genomic, proteomic, lipidomic, metabolomic or other "omic" methods in their cost, precision and reproducibility. However, several promising high-throughput technologies for analysis of *N*-glycans have recently been developed [34,61,63,64,66,182,183]. Successful implementation of high-throughput analytical techniques for glycan analysis resulted in publication of four initial GWAS of the human glycome [111,112,184,185]. The final paper was looking for loci associated with carbohydrate deficient-transferrin so can only loosely be termed a "human glycome" GWAS.

In this Chapter, I have compared the results of ultra-performance liquid chromatography (UPLC) with fluorescence detection, multiplex capillary gel electrophoresis with laser induced fluorescence detection (xCGE-LIF), matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) and nano liquid chromatography electrospray mass spectrometry (LC-ESI-MS) as tools for mid-to-high-throughput glycomics and glycoproteomics. Colleagues in Zagreb, Leiden, and Magdeburg have analysed IgG *N*-glycans by all four methods in 1,201 individuals from the CROATIA-Vis and CROATIA-Korcula studies. Correlation analysis was undertaken, as well as GWAS, to identify the analytical method that shows the strongest potential to uncover biological mechanisms underlying protein *N*-glycosylation.

6.2 Methods

Participants from the CROATIA-Vis and CROATIA-Korcula studies were involved in this analysis. IgG was isolated from the plasma of 1821 individuals as described in Section 2.4.1 by colleagues from Genos (Zagreb, Croatia). Aliquots of IgG were sent to all participating laboratories for *N*-glycosylation analysis by UPLC, MALDI-TOF-MS, LC-ESI-MS or xCGE-LIF as described in Sections 2.4.2 – 2.4.4. UPLC measurements were performed by colleagues from Genos (Zagreb, Croatia), MS measurements by colleagues from Dr. Manfred Wuhrer's laboratory at the LUMC (Leiden, Netherlands), and xCGE-LIF measurements by colleagues from Dr. Erdmann Rapp's laboratory at MPI and glyXera (Magdaburg, Germany). Glycan analysis was successful for 1653 individuals (802 Vis, 851 Korcula) for UPLC, 1552 individuals (702 Vis, 850 Korcula) for MALDI-TOF-MS, 1595 individuals (708 Vis, 887 Korcula) for LC-ESI-MS, and 1440 individuals (610 Vis, 830 Korcula) for xCGE-LIF. A total of 1201 individuals were successfully measured by all four methods. Since not all structures could be measured by all four methods, a "minimal trait" dataset was defined which included 15 structures that were able to be directly measured or derived for all four analytical methods. A list of these glycan traits is found in Table 11 and diagrams of these structures are provided in Figure 43. Due to methodological differences, UPLC and xCGE-LIF gave values from total IgG for these structures, where as the MS-based methods gave results from both IgG1 and IgG2/IgG3 separately. Also, some structures that resulted in one peak from MS-based methods were found in two peaks using UPLC and xCGE-LIF.

Correlation coefficients were computed and compared for the same structure from the minimal dataset measure by different methods (see Section 2.5.7 for detailed methods). Not all individuals with glycan measurements had been successfully genotyped so the final sample size for comparative analysis was 1100 (445 Vis, 655 Korcula). GWAS was undertaken on directly genotyped SNP data using GenABEL. Each trait was adjusted for sex and age and the residuals transformed to ensure their normal distribution using quantile normalisation. Meta-analysis was performed using the inverse variance method implemented with the MetABEL package for R [73]. The threshold for a SNP reaching genome-wide significance was set at $p < 5x10^{-08}$. These methods are described in more detail in Section 2.5 and a table describing which samples contributed to which analysis is found in Appendix Table 22.

Table 11: Minimal trait dataset for IgG N-glycan method comparison.

Glycan Class	Glycan Trait	UPLC*	MALDI-TOF-MS*		nanoLC-ESI-MS*		xCGE-LIF*
			IgG1	IgG2 & IgG3	IgG1	IgG2 & IgG3	
Total IgG Glycans	FA2	IGP3	MS_IGP42	MS_IGP86	LC_IGP1	LC_IGP87	CGE_IGP14
	FA2B	IGP5	MS_IGP43	MS_IGP87	LC_IGP4	LC_IGP90	CGE_IGP17
	FA2G1	IGP7	MS_IGP46	MS_IGP89	LC_IGP2	LC_IGP88	CGE_IGP19
		IGP8					CGE_IGP20
	FA2BG1	IGP9	MS_IGP47	MS_IGP90	LC_IGP5	LC_IGP91	CGE_IGP21
		IGP10					CGE_IGP22
	FA2G2	IGP13	MS_IGP52	MS_IGP93	LC_IGP3	LC_IGP89	CGE_IGP24
	FA2BG2	IGP14	MS_IGP53	MS_IGP94	LC_IGP6	LC_IGP92	CGE_IGP25
	FA2G1S1	IGP15	MS_IGP50	MS_IGP92	LC_IGP7	LC_IGP93	CGE_IGP7
	FA2G2S1	IGP17	MS_IGP56	MS_IGP95	LC_IGP8	LC_IGP94	CGE_IGP11
Total IgG glycans – derived parameters	FGS/(FG+FGS)	IGP24	MS_IGP66	MS_IGP100	LC_IGP34	LC_IGP120	CGE_IGP26
	FGS/(F+FG+FGS)	IGP26	MS_IGP67	MS_IGP101	LC_IGP35	LC_IGP121	CGE_IGP28
	FG1S1/(FG1+FG1S1)	IGP28	MS_IGP68	MS_IGP102	LC_IGP36	LC_IGP122	CGE_IGP30
	FG2S1/(FG2+FG2S1+FG2S2)	IGP29	MS_IGP69	MS_IGP103	LC_IGP37	LC_IGP123	CGE_IGP32
Neutral IgG glycans – derived parameters	G0n	IGP55	MS_IGP13	MS_IGP78	LC_IGP58	LC_IGP144	CGE_IGP56
	G1n	IGP56	MS_IGP14	MS_IGP79	LC_IGP59	LC_IGP145	CGE_IGP57
	G2n	IGP57	MS_IGP15	MS_IGP80	LC_IGP60	LC_IGP146	CGE_IGP58

n= neutral; F at the start of the abbreviation indicates a core fucose α1-6 linked to the inner GlcNAc; Ax, number of antenna (GlcNAc) on trimannosyl core; A2, biantennary with both GlcNAcs as β1-2 linked; B, bisecting GlcNAc linked β1-4 to β1-3 mannose; Gx, number (x) of β1-4 linked galactose on antenna; F(x), number (x) of fucose linked α1-3 to antenna GlcNAc; Sx, number (x) of sialic acids linked to galactose.

*Glycan trait namings for specific methods correspond to those used in Appendix Table 16, Table 17, Table 20 and Table 21

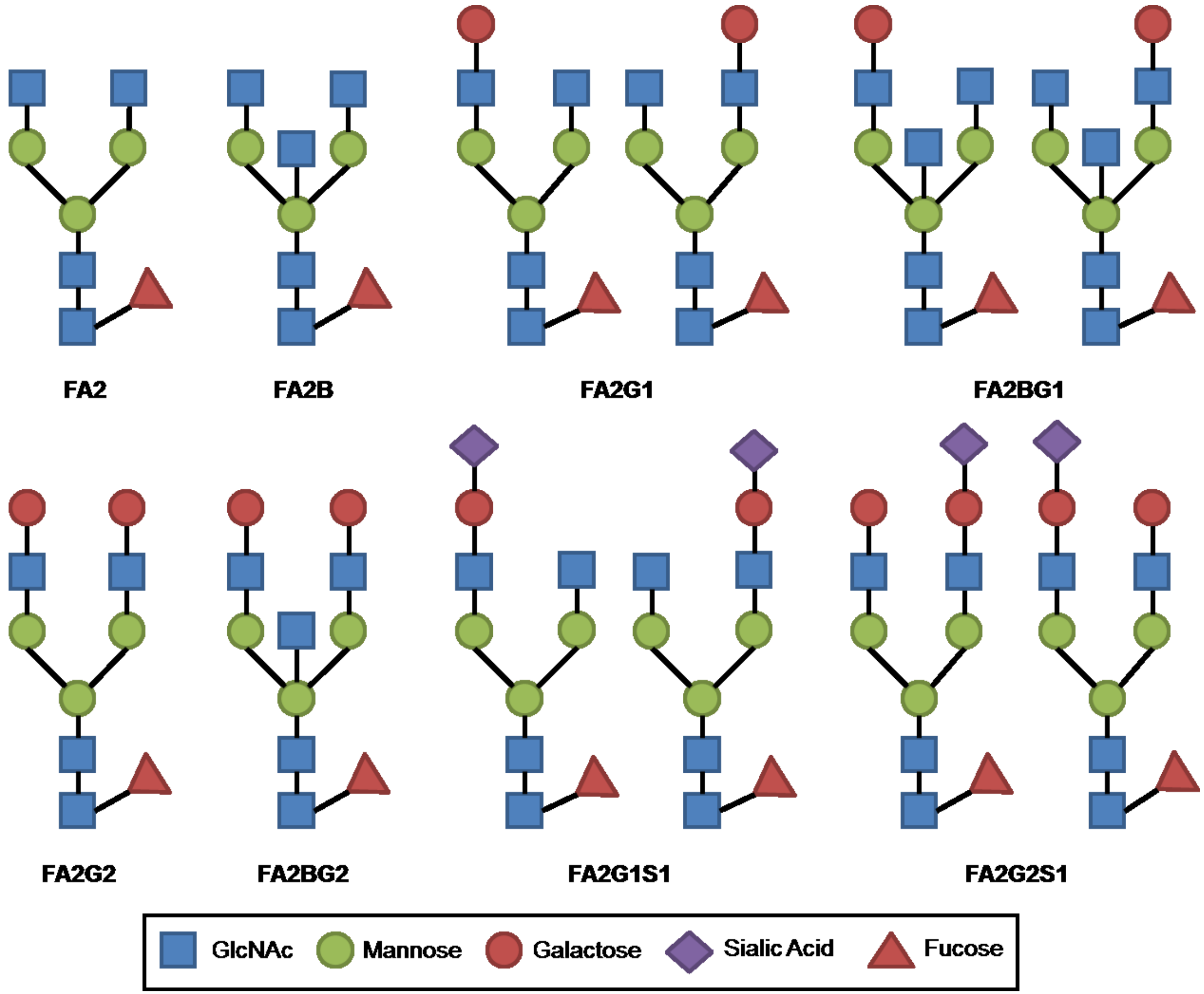


Figure 43: Structures for *N*-glycans from minimal trait dataset.
N-glycan structures traits in minimal trait dataset in Table 11. For some structures, more than one configuration is possible so both have been shown. GlcNAc: *N*-acetylglucosamine. F at the start of the abbreviation indicates a core fucose α1-6 linked to the inner GlcNAc; Ax, number of antenna (GlcNAc) on trimannosyl core; A2, biantennary with both GlcNAcs as β1-2 linked; B, bisecting GlcNAc linked β1-4 to β1-3 mannose; Gx, number (x) of β1-4 linked galactose on antenna; Sx, number (x) of sialic acids linked to galactose.

6.3 Results

IgG *N*-glycosylation profiling was performed for 1201 individuals using four different analytical approaches: UPLC, xCGE-LIF, MALDI-TOF-MS and LC-ESI-MS. An important difference between UPLC and xCGE-LIF, versus MS-based methods, on the other hand, is that UPLC and xCGE-LIF analyse IgG glycosylation at the level of released glycans (and therefore include glycans on both Fab and Fc parts of IgG), while MS-based methods included in this study analyse glycopeptides (therefore only capture the Fc region). Although in-depth analysis of released glycans may provide a detailed picture of the glycan structure, no information on the original glycan attachment site is provided with the methods used here. Such site-specific information can be obtained by the direct analysis of glycopeptides. Since different IgG subclasses have different amino acid sequences around the glycosylation site, by analysing glycans at the glycopeptide level MS-based methods are able to measure subclass-specific Fc glycosylation. However, unlike the MS-based methods used in this study, UPLC and xCGE-LIF provide branch-specific information i.e. separation between the 3-arm and 6-arm isomers of glycan species (e.g. FA2[3]G1 and FA2[6]G1, see Figure 43) due to a slightly higher retention of the 3-arm isomer. There are other factors that impact *N*-glycan quantitation due to methodological and technical differences between methods that were beyond the scope of this thesis. These are discussed in more detail in [83].

In addition to the directly measured glycan structures, a number of derived traits that represent common biologically meaningful features (e.g. galactosylation, fucosylation, etc.) shared among several measured glycans were calculated as described previously [61,90]. A full list of traits and a description of how they were calculated is available in Appendix Table 16, 12, 15 and 16. Due to the methodological differences, the information provided by the four used methods is similar, but not identical. To enable comparison of data measured by different methods, a shared "minimal" set of glycan features common to all four methods was defined (Table 11, Figure 43). Descriptive statistics for this minimal trait dataset is found in Table 12. Since the mean of the traits cannot be directly compared, the coefficient of variation (COV; standard deviation/mean) is provided which describes the variability of each measure.

Pearson correlation coefficients were calculated for each minimal dataset structure to obtain pairwise comparisons of all methods. These are presented in Appendix Table 26 - Table 39. Through this analysis I was able to identify a structure which had been incorrectly annotated by xCGE-LIF as it was not correlated with the same structure measured by any of the other methods. The correct peak containing this structure was identified and was subsequently used for all analyses presented here.

The *N*-glycan structures measured by MALDI-TOF-MS seemed to have a much higher COV than the other three methods which produced more similar results. This was also apparent through the lower correlation coefficients when comparing the same structure measured by the other three methods. However, even methods based on fluorescent dye quantification (UPLC and xCGE-LIF) had lower correlation coeffiecients for certain structures (for example: FG1S1/(FG1+FG1S1); Table 35). This indicates that in addition to different response factors in MS-based methods (which distort quantification), sample preparation and clean-up procedures (which can lead to selective loss or enrichment of some glycans) can also alter final results. Overall though, the correlation coefficients tended to be moderate to high (most >0.6), especially for directly measured structures.

At the moment there is no "gold standard" method to analyse protein glycosylation with absolute precision, therefore it is not possible to decide which of the methods we used most accurately reflects the real biological state. Aiming to evaluate the precision of the four methods, I performed GWAS on the minimal trait data set to compare results for the same structure across methods. Since glycome composition was shown to be under strong genetic influence as evidenced by the results of Chapters 3 and 5, it was believed that a GWAS approach would be a good tool to comparatively assess the power of detecting associations between SNPs and IgG *N*-glycans measured by each of the four methods. The aim was to look for consistant SNP associations across methods but it was also assumed that the most precise method would show the strongest associations due to reduced noise caused by experimental variability. In order to have an unbiased approach, GWAS was performed on the minimal trait dataset using only data from individuals whose glycosylation traits were successfully measured by all four methods (n=1100). The results are presented in Table 13. Genome-wide significant association with SNPs in two genomic loci were obtained using all four methods across six *N*-glycan structures. Both regions were associated with IgG *N*-glycans in the previous chapter and all structures that were significant here were also significant with the same genes in the previous chapter. It is only due to the lower sample size that some regions previously associated do not reach the genome-wide threshold here, for structures measured by UPLC. LC-ESI-MS analysis uncovered all six of these glycan traits, UPLC and xCGE-LIF found five, and four of the traits were observed with MALDI-TOF-MS. Glycan structures measured by MALDI-TOF-MS seemed to fare the worst in the

GWAS comparison, which also corresponded with lower correlation coefficients and higher COV.

Table 12: Descriptive statistics for IgG *N*-glycan minimal trait dataset for CROATIA-Vis (n=445) and CROATIA-Korcula (n=655).

Glycan Trait	Method	IgG Class	CROATIA-Vis			CROATIA-Korcula		
			Mean	SD	CV	Mean	SD	CV
FA2	UPLC	Total	26.23	7.27	0.277	25.18	6.78	0.263
	MALDI	IgG1	35.01	10.72	0.306	35.69	10.49	0.294
		IgG2&3	48.88	11.50	0.235	47.42	11.15	0.235
	LC-MS	IgG1	21.83	6.77	0.310	21.88	6.40	0.293
		IgG2&3	32.24	8.32	0.258	31.36	7.86	0.251
	xCGE	Total	26.27	7.64	0.291	25.74	7.11	0.276
FA2B	UPLC	Total	6.79	1.86	0.275	6.88	1.93	0.281
	MALDI	IgG1	5.54	1.92	0.347	5.83	2.37	0.407
		IgG2&3	5.69	1.93	0.339	6.00	2.16	0.361
	LC-MS	IgG1	8.04	2.54	0.316	8.04	2.73	0.340
		IgG2&3	8.49	2.40	0.282	8.59	2.50	0.292
	xCGE	Total	5.32	1.78	0.335	5.55	1.90	0.343
FA2G1*	UPLC	Total	20.34	1.96	0.096	20.13	1.79	0.089
			9.76	1.20	0.122	9.80	1.32	0.135
	MALDI	IgG1	39.46	5.98	0.152	38.59	6.37	0.165
		IgG2&3	33.15	6.78	0.204	33.30	6.72	0.202
	LC-MS	IgG1	29.66	2.63	0.089	29.14	2.75	0.094
		IgG2&3	26.64	2.88	0.108	26.34	2.90	0.110
	xCGE	Total	21.67	1.98	0.091	21.56	1.98	0.092
			10.60	1.34	0.127	10.67	1.51	0.142
FA2BG1*	UPLC	Total	5.86	1.08	0.185	5.78	1.07	0.185
			0.93	0.19	0.209	0.96	0.23	0.242
	MALDI	IgG1	5.92	1.98	0.334	6.00	2.03	0.338
		IgG2&3	2.51	1.08	0.431	2.72	1.12	0.411
	LC-MS	IgG1	11.02	2.20	0.200	10.20	2.12	0.208
		IgG2&3	5.17	1.21	0.234	5.33	1.21	0.227
	xCGE	Total	5.47	1.16	0.213	5.67	1.15	0.203
			0.59	0.13	0.224	0.62	0.14	0.227
FA2G2	UPLC	Total	13.80	4.20	0.304	13.90	4.10	0.295
	MALDI	IgG1	9.87	4.95	0.501	10.15	5.13	0.505
		IgG2&3	6.77	4.10	0.605	6.92	4.03	0.582
	LC-MS	IgG1	13.61	3.98	0.292	13.86	4.00	0.289
		IgG2&3	10.00	3.17	0.317	10.14	3.18	0.314
	xCGE	Total	15.40	4.62	0.300	15.31	4.55	0.297
FA2BG2	UPLC	Total	1.76	0.44	0.250	1.89	0.43	0.228
	MALDI	IgG1	0.49	0.30	0.609	0.46	0.29	0.625
		IgG2&3	0.23	0.16	0.672	0.26	0.18	0.701
	LC-MS	IgG1	1.85	0.63	0.343	1.73	0.56	0.324
		IgG2&3	1.00	0.41	0.412	1.04	0.42	0.401
	xCGE	Total	1.37	0.41	0.298	1.38	0.40	0.292
FA2G1S1	UPLC	Total	3.87	0.65	0.167	3.96	0.57	0.143
	MALDI	IgG1	1.75	0.93	0.532	1.27	0.71	0.559
		IgG2&3	1.20	0.47	0.392	1.51	0.54	0.356
	LC-MS	IgG1	2.11	0.41	0.195	2.27	0.41	0.180
		IgG2&3	5.92	1.03	0.175	6.43	1.06	0.166
	xCGE	Total	2.98	0.59	0.196	2.96	0.54	0.183

Glycan Trait	Method	IgG Class	CROATIA-Vis			CROATIA-Korcula		
			Mean	SD	CV	Mean	SD	CV
FA2G2S1	UPLC	Total	10.66	3.05	0.286	11.52	3.21	0.279
	MALDI	IgG1	1.96	1.08	0.551	2.01	1.13	0.565
		IgG2&3	1.57	1.22	0.779	1.87	1.30	0.692
	LC-MS	IgG1	11.89	3.89	0.327	12.88	4.13	0.321
		IgG2&3	10.54	3.92	0.372	10.78	3.93	0.364
	xCGE	Total	10.33	3.14	0.304	10.56	3.22	0.304
FGS/(FG + FGS)	UPLC	Total	24.68	2.87	0.116	25.90	2.89	0.112
	MALDI	IgG1	6.94	2.53	0.365	6.20	2.12	0.342
		IgG2&3	6.15	2.20	0.358	7.49	2.56	0.342
	LC-MS	IgG1	24.08	3.88	0.161	25.70	4.23	0.165
		IgG2&3	30.59	4.42	0.144	31.69	4.73	0.149
	xCGE	Total	21.57	2.86	0.132	21.90	2.93	0.134
FGS/(F + FG + FGS)	UPLC	Total	26.23	7.41	0.282	27.95	7.64	0.273
	MALDI	IgG1	4.23	1.89	0.446	3.75	1.68	0.449
		IgG2&3	3.02	1.78	0.590	3.72	1.92	0.517
	LC-MS	IgG1	17.63	4.58	0.260	18.85	4.70	0.249
		IgG2&3	19.24	5.20	0.270	20.17	5.14	0.255
	xCGE	Total	15.22	3.59	0.236	15.54	3.60	0.231
FG1S1/(FG1 + FG1S1)	UPLC	Total	11.42	1.88	0.164	11.71	1.59	0.135
	MALDI	IgG1	4.29	2.28	0.532	3.22	1.77	0.549
		IgG2&3	2.74	0.76	0.277	3.42	1.02	0.299
	LC-MS	IgG1	6.64	1.12	0.169	7.23	1.22	0.169
		IgG2&3	18.20	2.63	0.145	19.64	2.77	0.141
	xCGE	Total	8.44	1.47	0.174	8.41	1.37	0.163
FG2S1/(FG2 + FG2S1 + FG2S2)	UPLC	Total	43.79	3.32	0.076	45.48	3.17	0.070
	MALDI	IgG1	16.74	4.50	0.269	16.48	3.61	0.219
		IgG2&3	18.10	4.57	0.252	20.76	5.17	0.249
	LC-MS	IgG1	46.41	4.08	0.088	47.93	4.77	0.099
		IgG2&3	50.90	4.76	0.094	51.02	5.54	0.109
	xCGE	Total	40.21	3.09	0.077	40.84	3.05	0.075
G0n	UPLC	Total	38.35	8.91	0.232	37.65	8.40	0.223
	MALDI	IgG1	42.00	11.84	0.282	42.81	11.84	0.277
		IgG2&3	55.96	12.23	0.219	55.12	11.99	0.218
	LC-MS	IgG1	34.40	8.87	0.258	34.93	8.69	0.249
		IgG2&3	48.31	9.79	0.203	47.84	9.54	0.199
	xCGE	Total	36.14	9.19	0.254	35.89	8.78	0.245
G1n	UPLC	Total	43.25	3.69	0.085	43.46	3.36	0.077
	MALDI	IgG1	47.19	7.25	0.154	46.16	7.21	0.156
		IgG2&3	36.77	8.14	0.221	37.38	7.99	0.214
	LC-MS	IgG1	47.40	3.91	0.082	46.46	3.86	0.083
		IgG2&3	38.30	5.24	0.137	38.44	5.05	0.131
	xCGE	Total	44.30	3.64	0.082	44.60	3.41	0.076
G2n	UPLC	Total	18.39	5.99	0.326	18.89	5.96	0.315
	MALDI	IgG1	10.81	5.49	0.508	11.03	5.65	0.513
		IgG2&3	7.27	4.52	0.622	7.50	4.48	0.598
	LC-MS	IgG1	18.20	6.01	0.330	18.61	6.05	0.325
		IgG2&3	13.39	4.94	0.369	13.72	4.96	0.362
	xCGE	Total	19.56	6.42	0.328	19.51	6.39	0.327

SD: standard deviation, CV: coefficient of variation, MALDI: MALDI-TOF-MS, LC-MS: LC-ESI-MS, CGE: xCGE-LIF

* this structure is measured by two peaks by UPLC and xCGE-LIF but only one by MS-based methods

Table 13: Genome-wide significant ($P<5x10^{-08}$) associationswith IgG *N*-glycans measured by UPLC, MALDI-TOF-MS, LC-ESI-MS or xCGE-LIF.

Glycan Trait	Genes in Region	SNP with lowest P-value	Lowest P-value					
			UPLC	MALDI-TOF-MS		LC-ESI-MS		xCGE-LIF
				IgG1	IgG2&3	IgG1	IgG2&3	
FA2BG1*	*SMARCB1; DERL3*	rs9620326	**1.47x10^{-10}**	1.15x10^{-07}	1.70x10^{-06}	**1.63x10^{-08}**	**4.11x10^{-10}**	**1.11x10^{-10}**
			1.54x10^{-04}					7.46x10^{-06}
FA2G1S1	*ST6GAL1*	rs6764279	**2.80x10^{-22}**	0.2556	**4.36x10^{-10}**	**1.13x10^{-28}**	**1.15x10^{-27}**	**1.60x10^{-18}**
FGS/(FG+FGS)	*ST6GAL1*	rs6764279	**1.14x10^{-20}**	0.0154	**1.86x10^{-12}**	**4.87x10^{-12}**	**1.64x10^{-25}**	**4.83x10^{-18}**
FGS/(F+FG+FGS)	*ST6GAL1*	rs6764279	3.25x10^{-04}	0.1008	1.97x10^{-04}	1.21x10^{-05}	**1.44x10^{-09}**	3.82x10^{-07}
FG1S1/(FG1+FG1S1)	*ST6GAL1*	rs6764279	**1.50x10^{-22}**	0.3941	**9.60x10^{-21}**	**2.51x10^{-33}**	**1.31x10^{-40}**	**5.61x10^{-22}**
FG2S1/(FG2+FG2S1+FG2S2)	*ST6GAL1*	rs6764279	**1.54x10^{-36}**	**1.26x10^{-11}**	**3.49x10^{-23}**	**4.67x10^{-26}**	**1.37x10^{-32}**	**1.71x10^{-37}**

Bold text indicates that the p-value reaches genomewide significance ($P<5x10^{-08}$).

*This glycan structure is measured as two isomers with UPLC and xCGE-LIF but as only one mass in the MS methods

6.4 Discussion

In this Chapter, I have compared four different methods (UPLC, xCGE-LIF, MALDI-TOF-MS and LC-ESI-MS) for the quantitative analysis of IgG *N*-glycosylation by analysing the same 1100 IgG samples using all four methods. These four analytical methods comprise the majority of those that have been commonly used for glycosylation, but there is currently no “gold standard” method. Therefore, it was decided to use various statistical approaches to determine the relative accuracy of the four most widely used methods, namely correlations and GWAS.

GWAS has been successfully applied in Chapters 3 and 5 to identify genetic loci that are associated with the regulation of protein *N*-glycosylation [111,112,184,186]. For this study we decided to use GWAS to evaluate the consistency across methods and the precision of each method. Association analysis was performed separately on glycan data generated by the four methods under the assumption that any imprecision in measurement will decrease power to detect the biological association between SNPs and the measured *N*-glycans. Therefore the analytical method that is the most precise is expected to show the strongest association at a specific locus.

The results presented in Table 13 clearly show that all four methods generate glycan data of sufficiently high quality to be used to detect associations with genetic polymorphisms. In general, LC-ECI-MS tended to yield the most significant association, with the benefit of IgG class discrimination but, overall, all methods seemed to perform fairly well. In this study, not all previously reported genetic associations were detected but this was not unexpected since the number of individuals in this study was much lower. Indeed, for a GWAS of only 1100 individuals, the fact that any genetic associations were detected at all indicates that glycans are under strong genetic regulation.

This study clearly demonstrated that the relative quantification by both MALDI-TOF-MS and LC-ESI-MS are each very reliable, and that very strong genetic associations can be obtained with glycans measured by both methods, however LC-ESI-MS did perform better than MALDI-TOF-MS. Numeric values generated by mass spectrometry for different glycans or glycopeptides are not directly comparable since each molecular species has its own response factors in mass spectrometry [187], but this difference does not impact this study because the absolute numerical values were not used. This is evident from the detected genetic associations observed in this study. However, if derived traits (like fucosylation, galactosylation, sialylation, etc.) are calculated from MS data, their numerical values may not correspond to real biological situations because they would be distorted by different response factors for individual glycans/glycopeptides, and this is something that needs to be considered when interpreting MS-based data. Furthermore, there are various cost and throughput differences to take into account. These are summarised in Table 14 prepared by colleagues at Genos and also found in Huffman *et al.* [83]. All of this must be taken into consideration when designing a study based on what analyses are planned for the resulting data.

Each of the methods reveals some additional complementary information about the glycome, indicating that in some situations the combined analysis by different methods can yield additional useful information, which helps interpretation of complex biological systems.

6.5 Conclusions

It is increasingly recognised that variation in *N*-glycan structures are likely to play essential and ubiquitous roles in human physiology and pathophysiology. This recognition has led to glycomics being declared a research priority for the next decade [188], and it is expected that an increasing number of large clinical and population studies will include *N*-glycan analysis [20]. However, methods for high-throughput analysis have been developed only recently, and thorough evaluation and standardization of the analytical methods is needed before a significant amount of time, money and other resources should be invested in large-scale studies. In this study I have used several statistical methods as the evaluation criteria to compare four methods (UPLC, xCGE-LIF, MALDI-TOF-MS and LC-ESI-MS) that are currently being used to study protein *N*-glycosylation. All four methods delivered reliable quantitative data. A number of specific advantages and disadvantages of each method have been compiled (Table 14) in order to guide selection of the most appropriate and cost-effective approach for a given study.

Table 14: Comparison of four methods for high-throughput glycomics and glycoproteomic analysis.

CATEGORY	UPLC	xCGE-LIF	MALDI-TOF-MS	LC-ESI-MS
Acceptance/usage for glycomics	Widely used	Rarely used	Widely used	Moderately used
Throughput	Medium, approximately 50 samples per instrument per day	(Very) high, multiplexing with up to 96 capillaries enables analysis of thousands of samples	(Very) high, as measurement of a sample can be performed at a sub-minute time scale	Medium, approximately 100 samples per day per instrument
Required expertise	Medium	Medium	High	Very high
Resolution	High	High	Very high	Very high
Isomer separation	Good	Very good	None	Some
Quantification	Very good	Good	Medium	Good
Costs of equipment	€40–70,000	€100,000 for a 4-capillary instrument	€100–500,000	€200–500,000
Costs per sample in high throughput mode	Rather high costs, mainly due to low throughput and costs of consumables	Low costs per sample, due to low running costs and parallelization by multiplexing	Low costs per sample due to high throughput per instrument	Very high costs, mainly due to expensive equipment and low throughput per instrument
Main advantages for genetic and epidemiological studies	Reliable quantification, robustness	Less demanding in sample preparation, low costs, high robustness and high throughput, no sample carry over; reliable relative quantification, very sensitive	Low cost and high throughput, site specific glycosylation analysis, sensitive, enables structural elucidation via fragmentation experiments	Reliable quantification, site specific glycosylation analysis, sensitive, enables structural elucidation via fragmentation experiments
Main disadvantages for genetic and epidemiological studies	Inability to perform site specific glycosylation analysis, relatively low throughput and high cost	Inability to perform site specific glycosylation analysis, comparatively small database (to be enlarged)	Less reliable quantification, loss of sialic acids	Relatively high costs
Specific advantages for IgG glycosylation analysis	Differentiation of galactosylation on 3- and 6-arms, accurate quantification of IgG sialylation	Differentiation of galactosylation on 3- and 6-arms, accurate quantification of IgG sialylation	Differentiation of glycans on different IgG subclasses, analysis of only Fc glycans	Differentiation of glycans on different IgG subclasses, analysis of only Fc glycans, accurate quantification of IgG sialylation

Chapter 7 - Conclusion

The results presented here comprise the first GWAS of total plasma and IgG *N*-glycans. I have shown that plasma *N*-glycan concentrations are highly heritable and that the quantitation methods are accurate enough to enable GWAS. This was shown by the "positive control" associations of enzymes with known roles in glycosylation. In addition, associated loci with no previously known role in glycosylation provide new avenues for functional follow-up. Successful collaborations with colleagues here in Edinburgh provided insight into the role of *HNF1A* as a master regulator of *N*-glycan fucosylation and several other hits are currently under investigation both in Edinburgh and in Croatia. The *HNF1A* association also led to promising results identifying potential *N*-glycan biomarkers for MODY3 which are also being taken forward by colleagues in Croatia and the UK as part of a European FP7 grant (HighGlycans). Analysis of *N*-glycans attached to specific proteins, in this case IgG, illustrate an alternative approach, which led to this discovery of several other known glycosylation and novel genes. More loci and stronger associations were found by looking at *N*-glycans from a specific protein, rather than a pool. Finally, comparison of several different analytical methods for measuring *N*-glycans did not produce a clear winner from these analyses with all performing well, but information regarding other study-specific considerations have been outlined.

One line of future investigation would be laboratory-based follow-up of these genes to confirm and characterise their role in *N*-glycosylation. In Lauc *et al*. (2010) this proved very successful for *HNF1A* [112]. Current projects are now underway for several of the genes associated with IgG *N*-glycan levels. Dr. Chloe Stanton in our laboratory is pursuing the *IL6ST* and *IKZF1* associations. She is performing shRNA-mediated knockdown and TALEN/CRISPR-mediated knockout of *IL6ST* and *IKZF1* in lymphoblastoid cell lines to look at the effect on both the IgG *N*-glycan profile and the transcription levels of glycosylation-related genes. In addition, she is performing some pharmacological experiments looking at IL-6 signalling in the same cell lines. Dr. Vlatka Zoldos's laboratory in Zagreb, Croatia is investigating the *BACH2* association by looking at methylation patterns and expression differences of this transcription factor in conjunction with downstream differences in *N*-glycosylation.

A major finding was the gene-level pleiotropy observed for loci associated with *N*-glycans and other quantitative traits or diseases. The top SNPs located in or near *HNF1A* and *SLC39A8* were in LD with variants associated with many medically relevant traits, particularly cardiovascular and inflammation related phenotypes, including C-reactive protein, gamma-glutamyl transferase, HDL cholesterol, diastolic & systolic blood pressure, mean arterial pressure, hypertension, coronary heart disease and body mass index. Top SNPs from the IgG *N*-glycan GWAS appeared to be tagging the same regions associated with bone mineral density (*ABCF2*; *SMARCD3*) and serum urate concentration (*B4GALT1*). In addition, genes on or close to loci from the IgG *N*-glycan GWAS have been associated with many autoimmune related diseases but the association signals did not appear to be the same, i.e. the associated common variants are tagging different LD blocks than those of the glycan-associated SNPs. There is greater support for causality if the associated SNPs are in LD but whether these findings indicate a causal role for glycans, or simply highlight the multifaceted role of these genes will require further investigation beyond the scope of this project. There are specific methods for investigating causality within disease cohorts that additionally have the phenotype of interest measured (IgG *N*-glycans in this case), such as Mendelian randomization. This assesses causality under the assumption that the genetic variant is acting to cause disease directly through its effect on the risk factor. Due to the lack of disease cohorts with IgG *N*-glycans measured, this was not an option available within the scope of this PhD. Another consideration is that regardless of the LD structure, association with quantitative traits inform the likely function of the genes associated with diseases.

A mechanism for the causal role of *N*-glycans in disease has been proposed previously. A recent paper from Ohtsubo *et al*.[189] has implicated improper *N*-glycosylation in the development of T2D in the presence of a high fat diet. The authors showed in mouse models, that increased fatty acids in the diet led to decreased expression of *Foxa2* and *Hnf1a* transcription factors, in pancreatic beta cells due to their decreased nuclear localization. This in turn led to decreased beta cell expression of *Mgat4a*, a glycosyltransferase, and *Slc2a2* (also known as *Glut2*), the main glucose transporter in mice, leading to decreased glucose sensitivity. Following on the fact that *Mgat4a* knockout mice displayed T2D [190], further experiments showed that GnT-4a (the protein product of *Mgat4a*) was required for correct localisation of Glut-2 in the cell membrane, otherwise it was internalised into endosomes or lysosomes [189,191]. Similar results were found from experiments using human pancreatic cell lines as well as beta cells donated from both healthy controls and T2D patients. In humans, GLUT1 is the main glucose transporter, not GLUT2, but both were modified in a similar manner in these experiments. The authors then hypothesized that this may be the mechanism behind MODY3 as well but there do not appear to be any papers to date which confirm this.

Regardless of their pathogenic role, *N*-glycans provide new molecules for biomarker discovery. This was highlighted in the MODY3 work from Chapter 4 and was proven to be useful by the identification of four undocumented MODY3 cases in Thanabalasingham *et al*. [167]. Although currently UPLC methods may not be best suited for a clinical laboratory, the results from Chapter 6 show that different methodologies (such as MS) may be better able to be used at the translational stage. This work may also be taken forward to see if glycans structures could also be used to identify different *HNF1A* mutations by acting as a proxy for HNF1A function but this may require better sensitivity than was observed during the biomarker analysis. This may also explain why some of the MODY3 cases overlapped with T2D, T1D and non-diabetic controls for the biomarker in Thanabalasingham *et al*. [167].

Although many interesting finding have been presented here, these studies were performed in relatively small cohorts and have not yet been replicated by other groups. The next stage of the project will be to measure these *N*-glycan traits in other population cohorts. This is currently underway with a larger meta-analysis planned for autumn/winter 2014. In addition, expanding to case/control studies may help to elucidate some of the causality issues that were not able to be explored in the studies presented here. Measuring glycans in other large cohorts, such as Generation Scotland or UK Biobank, would provide the power to look at the glycans in relation to many other health-related aspects. These are both studies that have, or will have, medical record and prescription linkage and permission to recontact participants (only in a subset of Generation Scotland). As participants go on to develop disease they could be recontacted to obtain new biological samples. This would allow the analysis of samples before and after diagnosis which could help with biomarker discovery. One of the main limitations at this point is that commercial assays for the isolation of specific proteins are only available for IgG so these would need to be developed to look at disease-related glycosylated proteins. This is currently underway for a few proteins as part of a European FP7 grant (HighGlycans) but would need to be deemed commercially viable in order to proceed on a larger scale.

Rare variant analyses yielded very little in terms of identifying the “missing heritability” but this study was very under-powered so this was not an unexpected result. Looking at rare variants and/or structural variants in larger samples using the Exome Chip, sequencing or 1000 Genomes imputed data will also help to expand our knowledge of the genes and pathways involved in *N*-glycosylation.

This thesis describes the first steps in establishing the genetic contributions to the complex variation in protein *N*-glycosylation and future studies of the genes and pathways identified will expand the understanding of their impact on human health and disease.

Chapter 8 - References

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Chapter 9 - Appendix

9.1 Additional Methods

9.1.1 Isolation of Immunoglobulin G

Immunoglobulin G was isolated from plasma by affinity chromatography using 96-well protein G monolithic plates (BIA Separations, Ajdovščina, Slovenia). The protein G plate was first washed with 10 column volumes (CV) of ultrapure water and equilibrated with 10 CV of binding buffer (1× PBS, pH 7.4; Fisher Scientific, Pittsburgh, PA, USA). Plasma samples (50 µl) were diluted 10× with the binding buffer, applied to the plate and instantly washed five times with 5 CV of binding buffer to remove unbound proteins. IgGs were eluted from the protein G monoliths using 5 CV of 100 mM formic acid (FA; Fisher Scientific, Pittsburgh, PA, USA), pH 2.5. into a 96 deep well plate and immediately neutralized to pH 7.0 with 1 M ammonium bicarbonate (Fisher Scientific). After each sample application, the plate was regenerated with the following buffers: 10 CV of 10× PBS, followed by 10 CV of 0.1 M FA and afterwards 10 CV of 1× PBS to re-equilibrate the monoliths. Each step of the isolation was done under vacuum (approx. 60 mmHg pressure reduction while applying the samples, 500 mmHg during elution and washing steps) using a manual set-up consisting of a multichannel pipette, a vacuum manifold (Beckman Coulter, Brea, CA, USA) and a vacuum pump (Pall Life Sciences, Ann Arbor, MI, USA).

9.1.2 IgG *N*-Glycosylation by Hydrophilic Interaction Chromatography

9.1.2.1 Glycan release and labelling

Aliquots (1/5; 200 µl) of the protein G eluates were transferred to 96-well flat-bottomed microtitre plates, dried down in a vacuum concentrator and reconstituted by adding 2 µl of 5× sample buffer (125 µl of 0.5 M Tris (Sigma-Aldrich, St, Louis, MO, USA), pH 6.6, 200 µl of 10 % SDS (Sigma-Aldrich), and 675 µl of water), 7 µl of water, and 1 µl of 0.5 M dithiothreitol (DTT; Sigma-Aldrich) and incubating at 65°C for 15 min. Ultrapure water was used throughout. The samples were then alkylated by adding 1 µl of 100 mM iodoacetamide (IAA; Sigma-Aldrich) and incubated for 30 min in the dark at room temperature. Afterwards, the samples were immobilized in a gel block by adding 22.5 µl of 30 % (w/w) acrylamide/0.8 % (w/v) bis-acrylamide stock solution (37.5:1, Protogel; Sigma-Aldrich), 11.25 µl of 1.5 M Tris, pH 8.8, 1 µl of 10 % SDS (Invitrogen, Carlsbad, CA, USA). 1 µl of 10 % ammonium peroxodisulphate (APS; Sigma-Aldrich), and 1 µl of *N,N,N,N'*-tetramethyl-ethylenediamine (TEMED; Invitrogen). The gel blocks were transferred to a Whatman protein precipitation plate and washed with 1 ml of acetonitrile with shaking on a plate shaker for 10 min, followed by removal of the liquid on a vacuum manifold. The washing was repeated twice with 1 ml of 20 mM sodium bicarbonate ($NaHCO_3$; Sigma-Aldrich), pH 7.2, followed by 1 ml of acetonitrile (ACN; J.T.Baker, Phillipsburg, NJ, USA). *N*-glycans were released by adding 50 µl of 2.5 mU PNGase F (ProZyme, Leandro, CA, USA) in 20 mM $NaHCO_3$, pH 7.2, to reswell the gel pieces for 5 min, another 50 µl of 20 mM $NaHCO_3$, pH 7.2, was added and then the plates were sealed with adhesive film (USA Scientific, Ocala, FL, USA) and incubated over night at 37°C. The released *N*-glycans were collected into a 2-ml polypropylene 96-well plate (Waters, Milford, MA, USA) by washing the gel pieces with 3× 200 µl of water, 200 µl of ACN, 200 µl of water, and finally 200 µl of ACN. The released *N*-glycans were dried, redissolved in 20 µl of 1 % FA, incubated at room temperature for 40 min, and dried again. *N*-glycans were labelled with 5 µl of 2-AB labeling solution (55 mg of anthranilamide, 66 mg of sodium cyanoborohydride, 330 µl of glacial acetic acid, and 770 µl of dimethylsulfoxide (DMSO); all from Sigma-Aldrich), shaken for 5 min, incubated for 30 min at 65°C, shaken again for 5 min, and incubated for a further 90 min. Excess 2-AB was removed using solid-phase extraction with 1-cm square pieces of pre-washed, dried and folded into quarters Whatman 3MM chromatography paper placed into a Whatman protein precipitation plate (pre-washed with 200 µl of ACN followed by 200 µl of water). The 5 µl of 2-AB labelled IgG *N*-glycans were applied to the paper and left to dry and bind for 15 min. The excess 2-AB was washed off the paper by shaking with 1.6 ml of ACN for 15 min and then removing the ACN using a vacuum manifold; this step was repeated four times. The labelled *N*-glycans were eluted from the paper by shaking with 500 µl of water for 20 min and collected by vacuum into a 2-ml 96-well plate; this step was repeated two times. The eluted 2-AB IgG *N*-glycans were dried before resuspending in a known volume of water ready for analysis by UPLC-FLR.

9.1.2.2 Hydrophilic interaction chromatography

2-AB labelled IgG *N*-glycans were separated by hydrophilic interaction chromatography on a Waters Acquity UPLC instrument consisting of a quaternary solvent manager, sample manager and a FLR fluorescence detector set with excitation and emission wavelengths of 330 and 420 nm, respectively. The instrument was under the control of Empower 2 software, build 2145 (Waters). Labelled *N*-glycans were separated on a Waters BEH Glycan chromatography column, 100 x 2.1 mm i.d., 1.7 µm BEH particles, with 100 mM ammonium formate, pH 4.4, as solvent A and ACN as solvent B. A linear gradient of 75-62% ACN was used at flow rate of 0.4 ml/min in a 20 min analytical run. Samples were maintained at 5°C prior to injection, and the separation temperature was 60°C. The system was calibrated using an external standard of hydrolyzed and 2-AB labelled glucose oligomers from which the retention times for the individual glycans were converted to glucose units (GU). Data processing was performed using an automatic processing method with a traditional integration algorithm after which each chromatogram was manually corrected to maintain the same intervals of integration for all the samples. The chromatograms obtained were all separated in the same manner into 24 peaks and the amount of glycans in each peak was expressed as % of total integrated area. Additional structures could be derived from these 24 peaks to give a total of 77 structures. All structures and formulas are described in Appendix Table 16 .

9.1.3 IgG *N*-Glycosylation by Mass Spectrometry

9.1.3.1 Trypsin digestion and reverse-phase solid-phase extraction (RP-SPE)

Aliquots (1/20; 50 µl) of the protein G eluates were applied to 96-well polypropylene V-bottom microtitre plates. TPCK trypsin (Sigma-Aldrich) was first dissolved in ice-cold 20 mM acetic acid (Merck, Darmstadt, Germany) to a final concentration of 0.4 µg/µl after which it was further diluted to 0.02 µg/µl with ice-cold ultrapure water. To each sample 20 µl of the diluted trypsin was added followed by overnight incubation at 37°C.

For reverse-phase desalting and purification of glycopeptides, 5 mg of Chromabond C18ec beads (Marcherey-Nagel, Düren, Germany) were applied to each well of an OF1100 96-well polypropylene filter plate with a 10 µm polyethylene frit (Orochem Technologies Inc., Lombard, IL, USA). The RP stationary phase was activated with 3× 200 µl 80 % ACN containing 0.1 % trifluoroacetic acid (TFA; Fluka, Steinheim, Germany) and conditioned with 3× 200 µl 0.1 % TFA. The IgG digests were diluted 10× in 0.1 % TFA, loaded onto the C18 beads, and washed with 3× 200 µl 0.1 % TFA. The entire procedure was performed on a vacuum manifold (< 3 mmHg). IgG glycopeptides were eluted into a V-bottom microtitre plate by centrifugation at 500 rpm with 90 µl of 18 % ACN containing 0.1 % TFA. Eluates were dried by vacuum centrifugation, reconstituted in 20 µl MQ water and stored at -20ºC until analysis by MS.

9.1.3.2 MALDI-TOF-MS

Purified and desalted tryptic IgG glycopeptides (3 µl) were spotted onto MTP 384 polished steel target plates (Bruker Daltonics, Bremen, Germany) and allowed to dry at room temperature. Subsequently 1 µl of 5 mg/ml 4-chloro-α-cyanocinnamic acid (Cl-CCA; 95 % purity; Bionet Research, Camelford, Cornwall, UK) in 50 % ACN was applied on top of each sample and allowed to dry. Glycopeptides were analyzed on an UltrafleX II MALDI-

TOF/TOF mass spectrometer (Bruker Daltonics) operated in the negative-ion reflectron mode, since negative-ion mode has been found well-suited for the analysis of IgG glycopeptides and specifically for sialylated glycopeptides [84], while reflectron mode greatly improves the resolution and sensitivity of the analysis. Ions between m/z 1000 and 3800 were recorded. To allow homogeneous spot sampling a random walk laser movement with 50 laser shots per raster spot was applied and each IgG glycopeptide sum mass spectrum was generated by accumulation of 2000 laser shots. Mass spectra were internally calibrated using a list of known glycopeptides. Data processing and evaluation were performed with FlexAnalysis Software (Bruker Daltonics) and Microsoft Excel, respectively. Structural assignment of the detected glycoforms was performed on the basis of literature knowledge of IgG *N*-glycosylation [44,85-89]. The data were baseline subtracted and the intensities of a defined set of 27 glycopeptides (16 glycoforms for IgG1 and 11 for IgG2&3) were automatically defined for each spectrum as described before [90].

In Caucasian populations, IgG2 and IgG3 have identical peptide moieties ($E_{293}EQFNSTFR_{301}$) of their tryptic Fc glycopeptides and were, therefore, not distinguished by the profiling method [91]. Relative intensities of IgG Fc glycopeptides were obtained by integrating and summing four isotopic peaks followed by normalization to the total subclass specific glycopeptide intensities, as described previously [90]. Additional structures could be derived from these directly measured values to give a total of 103 structures. All structures and formulas are described in Appendix Table 17. The list of the assigned IgG1, IgG2&3 and IgG4 glycopeptides as well as the charge states corresponding m/z values is given in Appendix Table 18.

9.1.3.3 Reverse phase nano-LC-sheath-flow-ESI-MS (LC-ESI-MS)

Purified and desalted tryptic IgG glycopeptides were also analysed on an Ultimate 3000 HPLC system (Dionex Corporation, Sunnyvale, CA, USA), consisting of a degasser unit, binary loading pump, dual binary gradient pump, autosampler maintained at 5°C and fitted with a 10µl PEEK sample loop, and two column oven compartments set at 30°C. To protect the trap and analytical column for particulates, samples were centrifuged at 4000 rpm for 5 min and passed through a 2 µm pore size stainless steel frit mounted between the autosampler transfer tubing and the trap column. Samples (250-5000 nl) were applied to a Dionex Acclaim PepMap100 C18 (5 mm x 300 µm i.d.) SPE trap column conditioned with 0.1 % TFA (mobile phase A) for 1 min at 25 µl/min. After sample loading the trap column was switched in-line with the gradient and Ascentis Express C18 nano-LC column (50 mm x 75 µm i.d., 2.7 µm HALO fused core particles; Supelco, Bellefonte, USA) for 8 min while sample elution took place. This was followed by an off-line cleaning of the trap column with three full loop injections containing 5 µl 5 % isopropanol (IPA) + 0.1 % FA and 5 µl 50 % IPA + 0.1 % FA. On-column separation was achieved at 900 nl/min using the following gradient of mobile phase A and 95 % ACN (Biosolve BV, Valkenswaard, the Netherlands; mobile phase B): 0 min 3 % B, 2 min 5 % B, 5 min 20 % B, 6 min 30 % B, 8 min 30 % B, 9 min 0 % B, and 14 min 0 % B. The separation was coupled to a quadrupole-TOF-MS (micrOTOF-Q; Bruker Daltonics, Bremen, Germany) equipped with a standard ESI source (Bruker Daltonics) and a sheath-flow ESI sprayer (capillary electrophoresis ESI-MS sprayer; Agilent Technologies, Santa Clara, USA). The column outlet tubing (20 µm i.d., 360 µm o.d.) was directly applied as sprayer needle. A 2 µl/min sheath-flow of 50 % IPA, 20 % propionic acid (PA) and 30 % ultrapure water was applied by one of the binary gradient pumps to reduce the TFA gas phase ion pairing and assist with ESI spray formation. A nitrogen stream was applied as dry gas at 4 l/min with a nebulizer pressure of 0.4 bars to improve mobile phase evaporation. Glycan decay during ion transfer was reduced by applying 2 and 4 eV quadrupole ion energy and collision energy, respectively. Scan spectra were recorded from m/z 300 to 2000 with 2 averaged scans at a frequency of 1 Hz. Per sample the total analysis time was 16 min. The software used to operate the Ultimate 3000 HPLC system and the Bruker micrOTOF-Q were Chromeleon Client version 6.8 and micrOTOF control version 2.3, respectively.

Each LC-MS dataset was calibrated internally using a list of known glycopeptides, exported to the open mzXML format by Bruker DataAnalysis 4.0 in batch mode [92] and aligned to a master dataset of a typical sample (containing many of the (glyco)peptide species shared between multiple samples) using msalign2 [93] and a simple warping script in AWK [94]. From each dataset a list of 402 pre-defined features defined as peak maximum in an within mass window of + m/z 0.04 and a retention time window of +10 [95] , were extracted using the in-house developed "Xtractor2D" software and merged to a complete data matrix as described previously [65]. As input, Xtractor2D takes a dataset in the mzXML format aligned to the master dataset and a reference list with pre-defined features with *m/z* windows and retention times in seconds. The theoretical m/z values used to identify the glycopeptide features are calculated, and the retention times on the chromatographic time scale of the master dataset are used for the alignment. Due to the use of TFA as ion pairing reagent, all glycopeptides belonging to the same IgG subclass have approximately the same retention time, regardless of the number of N-acetylneuraminic acid residues. The software and ancillary scripts are freely available at www.ms-utils.org/Xtractor2D. The complete sample-data matrix was finally evaluated using Microsoft Excel.

Structural assignment of the detected glycoforms was performed on the basis of literature knowledge of IgG *N*-glycosylation [44,85-89]. Relative intensities of 20 IgG1, 20 IgG2/3 and 10 IgG4 glycopeptide species were obtained by integrating and summing the first three isotopic peaks of both doubly and triply charged glycopeptide species followed by background correction and normalization to the total IgG subclass specific glycopeptide intensities. The list of the assigned IgG1, IgG2&3 and IgG4 glycopeptides as well as the charge states corresponding m/z values is given in Appendix Table 19 as well as in [65]. Non-fucosylated IgG4 species were not included in this list, because of spectral overlap with isomeric IgG1 species. These IgG4 species are not expected to influence the IgG1 glycopeptide abundance levels, since they elute after the IgG1 glycopeptides. There is also spectral overlap between several IgG2&3 and IgG4 glycopeptides, but since IgG4 elutes before IgG2&3 and is present at a much lower abundace, this is not expected to be a problem for the analysis of either of the glycopeptides. Additional structures could be derived from these directly measured species to give a total of 205 structures. All structures and formulas are described in Appendix Table 20.

9.1.4 IgG *N*-Glycosylation by Multiplex Capillary Gel Electrophoresis with Laser-Induced Fluorescence (xCGE-LIF)

9.1.4.1 Glycan release and labeling

Approximately 10 µg of the protein G monolithic plate IgG eluates were redissolved in 3 µl 1× PBS (Sigma-Aldrich) and dispensed into a 96-well microtitre plate (Greiner Bio-One, Solingen, Germany). IgG samples were denatured with the addition of 4 µl of 0.5 % (w/v) SDS (AppliChem, Darmstadt, Germany) in 1× PBS and by incubation at 60°C for 10 min. Subsequently, the remaining SDS was neutralized by adding 2 µl 4 % (v/v) IGEPAL (Sigma-Aldrich) in 1× PBS. IgG *N*-glycans were released by adding 0.1 U PNGase F (BioReagent ≥ 95 %, Sigma-Aldrich) in 1 µl 1× PBS. The 96-well microtitre plate was sealed with adhesive tape and the final sample volume of 10 µL was incubated for 3 hours at 37°C. After *N*-glycan release samples were dried in a vacuum centrifuge and stored until labeling at -80°C.

Dried samples were redissolved by adding 2 µl of 1× PBS, 2 µl of 20 mM aminopyrene-1,3,6-trisulfonic acid (APTS; Darmstadt, Sigma-Aldrich) in 3.6 M citric acid monohydrate (CAaq; Merck-Millipore, Germany) and 2 µl of 0.2 M 2-picoline-borane (2-PB; Sigma-Aldrich) solution in DMSO (Sigma-Aldrich). Ultrapure water was used throughout. The 96-well microtitre plate was sealed using adhesive tape followed by shaking for 2 min at 900 rpm. Labeling was performed at 37°C for 16 h. To stop the reaction, 100 µl 80 % ACN (LC-

MS Grade ≥ 99.5 %, Sigma-Aldrich) was added and the plate was shaken for 2 min at 500 rpm. Post derivatization sample clean-up was performed by HILIC-solid phase extraction (SPE). To remove free APTS, reducing agent and other impurities, 200 µl of 100 mg/ml BioGel P10 (Bio-Rad, Munich, Germany) suspension in water/EtOH/ACN (70:20:10 %, v/v) was applied to AcroPrep 96-well GHP Filter Plates (Pall Corporation, Dreieich, Germany). Solvent was removed by application of vacuum using a vacuum manifold (Merck-Millipore, Germany). All wells were prewashed with 5× 200 µl water, followed by equilibration with 3× 200 µl 80 % ACN. The samples were applied to the wells of the GHP Filter Plate and shaken for 5 min at 500 rpm to enhance glycan binding. The plate was subsequently washed 5× with 200 µl 80 % ACN containing 100 mM triethylamine (TEA; Sigma-Aldrich) adjusted to pH 8.5 with acetic acid (Sigma-Aldrich), followed by washing 3× 200 µl 80 % ACN. After addition of solvent, each washing step was followed by incubation for 2 min and removal of solvent by vacuum. For elution 1× 100 µl (swelling of BioGel) and 2× 200 µl of water were applied to each well followed by 5 min incubation at 500 rpm. The eluates were removed by vacuum and collected in a 96-well storage plate (Thermo Scientific, Germany). The combined eluates were either analysed immediately by xCGE-LIF or stored at -20°C until required.

9.1.4.2 xCGE-LIF

For xCGE-LIF measurement, 1 µl of *N*-glycan eluate was mixed with 1 µl GeneScan 500 LIZ Size Standard (Life Technologies, Darmstadt, Germany; 1:50 dilution in Hi-Di Formamide) and 9 µl Hi-Di Formamide (Life Technologies). The mixture was transferred to a MicroAmp Optical 384-well Reaction Plate (Life Technologies), sealed with a 384-well plate septa (Life Technologies) and centrifuged at 1000 rpm for 1 min to avoid air bubbles at the bottom of the wells. The xCGE-LIF measurement was performed in a 3130xl Genetic Analyzer, equipped with a 50 cm 16-capillary array filled with POP-7 polymer (all from Life Technologies). After electrokinetic sample injection, samples were analysed with a running voltage of 15 kV. Data were collected for 45 min. Raw data files were converted to .xml file format using DataFileConverter (Life Technologies) and subsequently analysed using the MATLAB (The Mathworks, Inc., Natick, MA, USA) based glycan analysis tools glyXtool and glyXalign. GlyXtool was used for structural identification by patented migration time normalization to an internal standard and *N*-glycan database driven peak annotation [96]. The data comparison was performed by glyXalign [97]. Additional structures could be derived from to give a total of 92 structures. All structures and formulas are described in Appendix Table 21.

9.2 Additional Tables

Table 15: Total Plasma *N*-Glycan Features by HPLC for GWAS.

Trait Code	Glycan Structure*	Trait Description / Formula
GP1	A2	Relative percentage of specific peak area/total peak area from HILIC profile
GP2	A2B, A1G1, FA2	
GP3	M5, FA2B, A2[6]G1, A2[6]BG1	
GP4	A2[3]G1, A2[3]BG1, M4A1G1, FA2G1, FA2BG1, A1G1S1, M6D1, D2	
GP5	M6D3, A2G1S1, A2G2, A2BG2	
GP6	FA2G1S1, FA2BG1S1, M4A1G1S1, FA2G2, A2BG1S1	
GP7	FA2BG2, M7D3, A2G2S1, M7D1	
GP8	A2BG2S1, M5A1G1S1, FA2G2S1, A3G3, FA2BG2S1	
GP9	A2F1G2S1, M8D2, D3, A2G2S2, M8D1,D3	
GP10	A2BG2S2, A3BG3S1, FA2G2S2	
GP11	FA2BG2S2, M9	
GP12	A2F1G2S2, A3G3S2, A3BG3S2	
GP13	A3G3F1S2, FA3G3S2, FA3BG3S2, A3G3S3	
GP14	A3F1G3S3, FA3F1G3S3, A4G4S2, A4G4S3, A4F1G4S2, A4G4S3	
GP15	A4G4S4, A4F1G4S3	
GP16	A4G4S4, A4BG4S4, FA4G4S4, A4F1G4S4, A4G4LacS4, A4F2G4S4, FA4F1G4S4	
DG1	A2	Relative percentage of specific peak area/total peak area from HILIC profile after sialidase treatment
DG2	A2B, A1G1, FA2	
DG3	M5, FA2B, A2[6]G1, A2[6]BG1	
DG4	M4A1G1, A2[3]G1, A2[3]BG1, FA2BG1,FA2[3]G1	
DG5	M6D1, D2, M6D3, A2G2, A2BG2	
DG6	FA2G2, M5A1G1, FA2BG2	
DG7	M7D3, A2F1G2, M7D1	
DG8	A3G3, A2F2G2, FA3G3, M8D2, D3,M8D1,D3	
DG9	FA3BG3, A3F1G3	
DG10	M9, FA3F1G3	
DG11	A4G4, A4BG4, A3F2G3, FA4G4	
DG12	A4F1G4	
DG13	A4G4Lac, A4F2G4, FA4F1G4	
MonoS	% monosialylated	Relative percentage of specific peak area/total peak area from WAX analysis
DiS	% disialylated	
TriS	% trisialylated	
TetraS	% tetrasialylated	

Trait Code	Glycan Structure*	Trait Description / Formula
C-FUC	Core fucosylated glycans	(DG6/(DG5+DG6))*100
A-FUC	Antennary fucosylated glycans	(DG7/(DG5+DG7))*100
A2	Biantennary nongalactosylated glycans	(GP1+DG1)/2
BA	Biantennary glycans	DG1+DG2+DG3+DG4+DG5+DG6+DG7
BAMS	Monosialylated biantennary glycans	((GP7+GP8)/(DG5+DG6+DG7))*100
BADS	Disialylated biantennary glycans	((GP9+GP10+GP11)/(DG5+DG6+DG7))*100
TRIA	Triantennary glycans	DG8+DG9+DG10
TA	Tetra-antennary glycans	DG11+DG12+DG13
G0	Nongalactosylated glycans	DG1+DG2
G1	Monogalactosylated glycans	DG3+DG4
G2	Digalactosylated glycans	DG5+DG6+DG7
G3	Trigalactosylated glycans	GP12+GP13+GP14
G4	Tetragalactosylated glycans	GP15+GP16

* Structures for GP and DG traits taken from Knezevic et al.[36] . All *N*-glycans have two core GlcNAcs; F at the start of the abbreviation indicates a core fucose α1-6 linked to the inner GlcNAc; Mx, number (x) of mannose on core GlcNAcs; D1 indicates that the α1-2 mannose is on the Manα1-6Manα1-6 arm, D2 on the Manα1-3Manα1-6 arm, D3 on the Manα1-3 arm of M6 and on the Manα1-2Manα1-3 arm of M7 and M8; Ax, number of antenna (GlcNAc) on trimannosyl core; A2, biantennary with both GlcNAcs as β1-2 linked; A3, triantennary with a GlcNAc linked β1-2 to both mannose and the third GlcNAc linked β1-4 to the α1-3 linked mannose; A4, GlcNAcs linked as A3 with additional GlcNAc β1-6 linked to α1-6 mannose; B, bisecting GlcNAc linked β1-4 to β1-3 mannose; Gx, number (x) of β1-4 linked galactose on antenna; [3]G1 and [6]G1 indicates that the galactose is on the antenna of the α1-3 or α1-6 mannose; F(x), number (x) of fucose linked α1-3 to antenna GlcNAc; Lac(x), number (x) of lactosamine (Galβ1-4GlcNAc) extensions; Sx, number (x) of sialic acids linked to galactose. If there is no linkage number, all forms were present.

Table 16: IgG *N*-Glycan Features by UPLC for GWAS.

Trait Code	Glycan Trait	Trait Description	Formula
IGP1	GP1	% FA1 glycan in total IgG glycans	GP1 / GP* 100
IGP2	GP2	% A2 glycan in total IgG glycans	GP2 / GP* 100
IGP3	GP4	% FA2 glycan in total IgG glycans	GP4 / GP* 100
IGP4	GP5	% M5 glycan in total IgG glycans	GP5 / GP* 100
IGP5	GP6	% FA2B glycan in total IgG glycans	GP6 / GP* 100
IGP6	GP7	% A2G1 glycan in total IgG glycans	GP7 / GP* 100
IGP7	GP8	% FA2[6]G1 glycan in total IgG glycans	GP8 / GP* 100
IGP8	GP9	% FA2[3]G1 glycan in total IgG glycans	GP9 / GP* 100
IGP9	GP10	% FA2[6]BG1 glycan in total IgG glycans	GP10 / GP* 100
IGP10	GP11	% FA2[3]BG1 glycan in total IgG glycans	GP11 / GP* 100
IGP11	GP12	% A2G2 glycan in total IgG glycans	GP12 / GP* 100
IGP12	GP13	% A2BG2 glycan in total IgG glycans	GP13 / GP* 100
IGP13	GP14	% FA2G2 glycan in total IgG glycans	GP14 / GP* 100
IGP14	GP15	% FA2BG2 glycan in total IgG glycans	GP15 / GP* 100
IGP15	GP16	% FA2G1S1 glycan in total IgG glycans	GP16 / GP * 100
IGP16	GP17	% A2G2S1 glycan in total IgG glycans	GP17/ GP * 100
IGP17	GP18	% FA2G2S1 glycan in total IgG glycans	GP18 / GP * 100
IGP18	GP19	% FA2BG2S1 glycan in total IgG glycans	GP19 / GP * 100
IGP19	GP20	Structure not determined	GP20 / GP * 100
IGP20	GP21	% A2G2S2 glycan in total IgG glycans	GP21 / GP * 100
IGP21	GP22	% A2BG2S2 glycan in total IgG glycans	GP22 / GP * 100
IGP22	GP23	% FA2G2S2 glycan in total IgG glycans	GP23 / GP * 100
IGP23	GP24	% FA2BG2S2 glycan in total IgG glycans	GP24 / GP * 100

Trait Code	Glycan Trait	Trait Description	Formula
IGP24	FGS/(FG+FGS)	% sialylation of fucosylated galactosylated structures without bisecting GlcNAc in total IgG glycans	SUM(GP16 + GP18 + GP23) / SUM(GP16 + GP18 + GP23 + GP8 + GP9 + GP14)* 100
IGP25	FBGS/(FBG+FBGS)	% sialylation of fucosylated galactosylated structures with bisecting GlcNAc in total IgG glycans	SUM(GP19 + GP24) / SUM(GP19 + GP24 + GP10 + GP11 + GP15)* 100
IGP26	FGS/(F+FG+FGS)	% sialylation of all fucosylated structures without bisecting GlcNAc in total IgG glycans	SUM(GP16 + GP18 + GP23) / SUM(GP16 + GP18 + GP23 + GP4 + GP8 + GP9 + GP14)* 100
IGP27	FBGS/(FB+FBG+FBGS)	% sialylation of all fucosylated structures with bisecting GlcNAc in total IgG glycans	SUM(GP19 + GP24) / SUM(GP19 + GP24 + GP6 + GP10 + GP11 + GP15)* 100
IGP28	FG1S1/(FG1+FG1S1)	% monosialylation of fucosylated monogalactosylated structures in total IgG glycans	GP16 / SUM(GP16 + GP8 + GP9)* 100
IGP29	FG2S1/(FG2+FG2S1+FG2S2)	% monosialylation of fucosylated digalactosylated structures in total IgG glycans	GP18 / SUM(GP18 + GP14 + GP23)* 100
IGP30	FG2S2/(FG2+FG2S1+FG2S2)	% disialylation of fucosylated digalactosylated structures in total IgG glycans	GP23 / SUM(GP23 + GP14 + GP18)* 100
IGP31	FBG2S1/(FBG2+FBG2S1+FBG2S2)	% monosialylation of fucosylated digalactosylated structures with bisecting GlcNAc in total IgG glycans	GP19 / SUM(GP19 + GP15 + GP24)* 100
IGP32	FBG2S2/(FBG2+FBG2S1+FBG2S2)	% disialylation of fucosylated digalactosylated structures with bisecting GlcNAc in total IgG glycans	GP24 / SUM(GP24 + GP15 + GP19)* 100
IGP33	$F^{total}S1/F^{total}S2$	Ratio of all fucosylated (+/- bisecting GlyNAc) monosyalilated and disialylated structures in total IgG glycans	SUM(GP16 + GP18 + GP19) / SUM(GP23 + GP24)
IGP34	FS1/FS2	Ratio of fucosylated (without bisecting GlcNAc) monosialylated and disialylated structures in total IgG glycans	SUM(GP16 + GP18) / GP23
IGP35	FBS1/FBS2	Ratio of fucosylated (with bisecting GlcNAc) monosialylated and disialylated structures in total IgG glycans	GP19 / GP24
IGP36	FBS^{total}/FS^{total}	Ratio of all fucosylated sialylated structures with and without bisecting GlcNAc	SUM(GP19 + GP24) / SUM(GP16 + GP18 + GP23)

Trait Code	Glycan Trait	Trait Description	Formula
IGP37	FBS1/FS1	Ratio of fucosylated monosialylated structures with and without bisecting GlcNAc	GP19 / SUM(GP16 + GP18)
IGP38	FBS1/(FS1+FBS1)	The incidence of bisecting GlcNAc in all fucosylated monosialylated structures in total IgG glycans	GP19 / SUM(GP16 + GP18 + GP19)
IGP39	FBS2/FS2	Ratio of fucosylated disialylated structures with and without bisecting GlcNAc	GP24 / GP23
IGP40	FBS2/(FS2+FBS2)	The incidence of bisecting GlcNAc in all fucosylated disialylated structures in total IgG glycans	GP24 / SUM(GP23 + GP24)
IGP41	$GP1^n$	% FA1 glycan in total neutral IgG glycans (GP^n)	GP1 / GP^n* 100
IGP42	$GP2^n$	% A2 glycan in total neutral IgG glycans (GP^n)	GP2 / GP^n* 100
IGP43	$GP4^n$	% FA2 glycan in total neutral IgG glycans (GP^n)	GP4 / GP^n* 100
IGP44	$GP5^n$	% M5 glycan in total neutral IgG glycans (GP^n)	GP5 / GP^n* 100
IGP45	$GP6^n$	% FA2B glycan in total neutral IgG glycans (GP^n)	GP6 / GP^n* 100
IGP46	$GP7^n$	% A2G1 glycan in total Ineutral IgG glycans (GP^n)	GP7 / GP^n* 100
IGP47	$GP8^n$	% FA2[6]G1 glycan in total neutral IgG glycans (GP^n)	GP8 / GP^n* 100
IGP48	$GP9^n$	% FA2[3]G1 glycan in total neutral IgG glycans (GP^n)	GP9 / GP^n* 100
IGP49	$GP10^n$	% FA2[6]BG1 glycan in total neutral IgG glycans (GP^n)	GP10 / GP^n* 100
IGP50	$GP11^n$	% FA2[3]BG1 glycan in total neutral IgG glycans (GP^n)	GP11 / GP^n* 100
IGP51	$GP12^n$	% A2G2 glycan in total neutral IgG glycans (GP^n)	GP12 / GP^n* 100
IGP52	$GP13^n$	% A2BG2 glycan in total neutral IgG glycans (GP^n)	GP13 / GP^n* 100
IGP53	$GP14^n$	% FA2G2 glycan in total neutral IgG glycans (GP^n)	GP14 / GP^n* 100
IGP54	$GP15^n$	% FA2BG2 glycan in total neutral IgG glycans (GP^n)	GP15 / GP^n* 100
IGP55	$G0^n$	% agalactosylated structures in total neutral IgG glycans	SUM($GP1^n$: $GP6^n$)
IGP56	$G1^n$	% monogalactosylated structures in total neutral IgG glycans	SUM($GP7^n$: $GP11^n$)

Trait Code	Glycan Trait	Trait Description	Formula
IGP57	$G2^n$	% digalactosylated structures in total neutral IgG glycans	SUM($GP12^n$: $GP15^n$)
IGP58	$F^{n\ total}$	% all fucosylated (+/- bisecting GlcNAc) structures in total neutral IgG glycans	SUM($GP1^n$+ $GP4^n$+ $GP5^n$+ $GP6^n$+ $GP8^n$+ $GP9^n$+ $GP10^n$+ $GP11^n$+ $GP14^n$+ $GP15^n$)
IGP59	$FG0^{n\ total}/G0^n$	% fucosylation of agalactosylated structures	SUM($GP1^n$+ $GP4^n$+ $GP5^n$+ $GP6^n$) / $G0^n$ * 100
IGP60	$FG1^{n\ total}/G1^n$	% fucosylation of monogalactosylated structures	SUM($GP8^n$+ $GP9^n$+ $GP10^n$+ $GP11^n$) / $G1^n$ * 100
IGP61	$FG2^{n\ total}$ /$G2^n$	% fucosylation of digalactosylated structures	SUM($GP14^n$+ GP15) / $G2^n$ * 100
IGP62	F^n	% fucosylated (without bisecting GlcNAc) structures in total neutral IgG glycans	SUM($GP1^n$+ $GP4^n$+ $GP5^n$+ $GP8^n$+ $GP9^n$+ $GP14^n$)
IGP63	$FG0^n/G0^n$	% fucosylation (without bisecting GlcNAc) of agalactosylated structures	SUM($GP1^n$+ $GP4^n$+ $GP5^n$) / $G0^n$ * 100
IGP64	$FG1^n/G1^n$	% fucosylation (without bisecting GlcNAc) of monogalactosylated structures	SUM($GP8^n$+ $GP9^n$) / $G1^n$ * 100
IGP65	$FG2^n/G2^n$	% fucosylation (without bisecting GlcNAc) of digalactosylated structures	$GP14^n$/ $G2^n$ * 100
IGP66	FB^n	% fucosylated (with bisecting GlcNAc) structures in total neutral IgG glycans	SUM($GP6^n$ + $GP10^n$ + $GP11^n$ + $GP15^n$)
IGP67	$FBG0^n/G0^n$	% fucosylation (with bisecting GlcNAc) of agalactosylated structures	$GP6^n$/ $G0^n$ * 100
IGP68	$FBG1^n/G1^n$	% fucosylation (with bisecting GlcNAc) of monogalactosylated structures	SUM($GP10^n$ + $GP11^n$) / $G1^n$ * 100
IGP69	$FBG2^n/G2^n$	% fucosylation (with bisecting GlcNAc) of digalactosylated structures	GP15) / $G2^n$ * 100
IGP70	FB^n/F^n	Ratio of fucosylated structures with and without bisecting GlcNAc	FB^n/ F^n * 100
IGP71	$FB^n/F^{n\ total}$	The incidence of bisecting GlcNAc in all fucosylated structures in total neutral IgG glycans	FB^n/ $F^{n\ total}$ * 100
IGP72	$F^n/(B^n + FB^n)$	Ratio of fucosylated non-bisecting GlcNAc structures and all structures with bisecting GlcNAc	F^n/($GP13^n$ + FB^n)

Trait Code	Glycan Trait	Trait Description	Formula
IGP73	$B^n/(F^n + FB^n)$	Ratio of structures with bisecting GlcNAc and all fucosylated structures (+/- bisecting GlcNAc)	$GP13^n/ (F^n + FB^n) * 100$
IGP74	$FBG2^n/FG2^n$	Ratio of fucosylated digalactosylated structures with and without bisecting GlcNAc	$GP15^n/GP14^n$
IGP75	$FBG2^n/(FG2^n + FBG2^n)$	The incidence of bisecting GlcNAc in all fucosylated digalactosylated structures in total neutral IgG glycans	$GP15^n/(GP14^n + GP15^n) * 100$
IGP76	$FG2^n/(BG2^n + FBG2^n)$	Ratio of fucosylated digalactosylated non-bisecting GlcNAc structures and all digalactosylated structures with bisecting GlcNAc	$GP14^n/(GP13^n + GP15^n)$
IGP77	$BG2^n/(FG2^n + FBG2^n)$	Ratio of digalactosylated structures with bisecting GlcNAc and all fucosylated digalactosylated structures (+/- bisecting GlcNAc)	$GP15^n/(GP14^n + GP15^n) * 100$

^{n}= neutral; GP = sum(GP1:GP24); GP^n = sum($GP1^n$:$GP15^n$); F at the start of the abbreviation indicates a core fucose α1-6 linked to the inner GlcNAc; Mx, number (x) of mannose on core GlcNAcs; Ax, number of antenna (GlcNAc) on trimannosyl core; A2, biantennary with both GlcNAcs as β1-2 linked; B, bisecting GlcNAc linked β1-4 to β1-3 mannose; Gx, number (x) of β1-4 linked galactose on antenna; [3]G1 and [6]G1 indicates that the galactose is on the antenna of the α1-3 or α1-6 mannose; F(x), number (x) of fucose linked α1-3 to antenna GlcNAc; Sx, number (x) of sialic acids linked to galactose.

Table 17: IgG *N*-Glycan Features by MALDI-TOF-MS for GWAS.

Trait Code	Glycan Trait	Trait Description	Formula
MS_IGP1	IgG1 G0n	% G0 glycan in neutral IgG1 glycans	
MS_IGP2	IgG1 G0Fn	% G0F glycan in neutral IgG1 glycans	
MS_IGP3	IgG1 G0FNn	% G0FN glycan in neutral IgG1 glycans	
MS_IGP4	IgG1 G0Nn	% G0N glycan in neutral IgG1 glycans	
MS_IGP5	IgG1 G1n	% G1 glycan in neutral IgG1 glycans	
MS_IGP6	IgG1 G1Fn	% G1F glycan in neutral IgG1 glycans	
MS_IGP7	IgG1 G1FNn	% G1FN glycan in neutral IgG1 glycans	
MS_IGP8	IgG1 G1Nn	% G1N glycan in neutral IgG1 glycans	
MS_IGP9	IgG1 G2n	% G2glycan in neutral IgG1 glycans	
MS_IGP10	IgG1 G2Fn	% G2F glycan in neutral IgG1 glycans	
MS_IGP11	IgG1 G2FNn	% G2FN glycan in neutral IgG1 glycans	
MS_IGP12	IgG1 G2Nn	% G2N glycan in neutral IgG1 glycans	
MS_IGP13	IgG1 G0n	% agalactosylated structures in neutral IgG1 glycans	SUM(G0n+G0Fn+G0FNn+G0Nn)
MS_IGP14	IgG1 G1n	% monogalactosylated structures in neutral IgG1 glycans	SUM(G1n+G1Fn+G1FNn+G1Nn)
MS_IGP15	IgG1 G2n	% digalactosylated structures in neutral IgG1 glycans	SUM(G2n+G2Fn+G2FNn+G2Nn)
MS_IGP16	IgG1 Fn total	% all fucosylated (+/- bisecting GlcNAc) structures in neutral IgG1 glycans	SUM(G0Fn+G0FNn+G1Fn+G1FNn+G2Fn+G2FNn)
MS_IGP17	IgG1 FG0n total/G0n	% fucosylation of agalactosylated structures	SUM(G0Fn+G0FNn)/G0n*100
MS_IGP18	IgG1 FG1n total/G1n	% fucosylation of monogalactosylated structures	SUM(G1Fn+G1FNn)/G1n*100
MS_IGP19	IgG1 FG2n total/G2n	% fucosylation of digalactosylated structures	SUM(G2Fn+G2FNn)/G2n*100
MS_IGP20	IgG1 Fn	% fucosylated (without bisecting GlcNAc) structures in neutral glycan fraction	SUM(G0Fn+G1Fn+G2Fn)
MS_IGP21	IgG1 FG0n/G0n	% fucosylation (without bisecting GlcNAc) of agalactosylated structures	G0Fn/G0n*100

Trait Code	Glycan Trait	Trait Description	Formula
MS_IGP22	IgG1 FG1n/G1n	% fucosylation (without bisecting GlcNAc) of monogalactosylated structures	G1Fn/G1n*100
MS_IGP23	IgG1 FG2n/G2n	% fucosylation (without bisecting GlcNAc) of digalactosylated structures	G2Fn/G2n*100
MS_IGP24	IgG1 FBn	% fucosylated (with bisecting GlcNAc) structures in neutral glycan fraction	SUM(G0FNn+G1FNn+G2FNn)
MS_IGP25	IgG1 FBG0n/G0n	% fucosylation (with bisecting GlcNAc) of agalactosylated structures	G0FNn/G0n*100
MS_IGP26	IgG1 FBG1n/G1n	% fucosylation (with bisecting GlcNAc) of monogalactosylated structures	G1FNn/G1n*100
MS_IGP27	IgG1 FBG2n/G2n	% fucosylation (with bisecting GlcNAc) of digalactosylated structures	G2FNn/G2n*100
MS_IGP28	IgG1 Bn total	The incidence of bisecting GlcNAc (+/- core Fuc) in neutral glycan fraction	SUM(G0Nn+G1Nn+G2Nn+G0FNn+G1FNn+G2FNn)
MS_IGP29	IgG1 BG0n total/G0n	The incidence of bisecting GlcNAc (+/- core Fuc) in agalactosylated structures	SUM(G0Nn+G0FNn)/G0n
MS_IGP30	IgG1 BG1n total/G1n	The incidence of bisecting GlcNAc (+/- core Fuc) in monogalactosylated structures	SUM(G1Nn+G1FNn)/G1n
MS_IGP31	IgG1 BG2n total/G2n	The incidence of bisecting GlcNAc (+/- core Fuc) in digalactosylated structures	SUM(G2Nn+G2FNn)/G2n
MS_IGP32	IgG1 Bn	The incidence of bisecting GlcNAc (without core Fuc) in neutral glycan fraction	SUM(G0Nn+G1Nn+G2Nn)
MS_IGP33	IgG1 BG0n/G0n	The incidence of bisecting GlcNAc (without core Fuc) in agalactosylated structures	G0Nn/G0n
MS_IGP34	IgG1 BG1n/G1n	The incidence of bisecting GlcNAc (without core Fuc) in monogalactosylated structures	G1Nn/G1n
MS_IGP35	IgG1 BG2n/G2n	The incidence of bisecting GlcNAc (without core Fuc) in digalactosylated structures	G2Nn/G2n
MS_IGP36	IgG1 FBn/Fn total	The incidence of bisecting GlcNAc in all fucosylated structures in neutral glycan fraction	FBn/Fn total*100
MS_IGP37	IgG1 FBn/Fn	Ratio of fucosylated structures with and without bisecting GlcNAc	FBn/Fn*100

Trait Code	Glycan Trait	Trait Description	Formula
MS_IGP38	IgG1 FBn/Bn total	% fucosylation in all structures with bisecting GlcNAc in neutral glycan fraction	FBn/Bn total*100
MS_IGP39	IgG1 Fn/Bn total	Ratio of fucosylated non-bisecting GlcNAc structures and all structures with bisecting GlcNAc	Fn/Bn total
MS_IGP40	IgG1 Bn/Fn total ‰	Ratio of structures with bisecting GlcNAc and all fucosylated structures (+/- bisecting GlcNAc)	Bn/Fn total*1000
MS_IGP41	IgG1 G0	% G0 glycan in total IgG1 glycans	
MS_IGP42	IgG1 G0F	% G0F glycan in total IgG1 glycans	
MS_IGP43	IgG1 G0FN	% G0FN glycan in total IgG1 glycans	
MS_IGP44	IgG1 G0N	% G0N glycan in total IgG1 glycans	
MS_IGP45	IgG1 G1	% G1 glycan in total IgG1 glycans	
MS_IGP46	IgG1 G1F	% G1F glycan in total IgG1 glycans	
MS_IGP47	IgG1 G1FN	% G1FN glycan in total IgG1 glycans	
MS_IGP48	IgG1 G1N	% G1N glycan in total IgG1 glycans	
MS_IGP49	IgG1 G1S*	% G1S glycan in total IgG1 glycans	
MS_IGP50	IgG1 G1FS	% G1FS glycan in total IgG1 glycans	
MS_IGP51	IgG1 G2	% G2 glycan in total IgG1 glycans	
MS_IGP52	IgG1 G2F	% G2F glycan in total IgG1 glycans	
MS_IGP53	IgG1 G2FN	% G2FN glycan in total IgG1 glycans	
MS_IGP54	IgG1 G2N	% G2N glycan in total IgG1 glycans	
MS_IGP55	IgG1 G2S	% G2S glycan in total IgG1 glycans	
MS_IGP56	IgG1 G2FS	% G2FS glycan in total IgG1 glycans	
MS_IGP57	IgG1 Gal	% IgG1 galactosylation	(G1+G1F+G1FN+G1N+G1S+G1FS)*0.5 +G2+G2F+G2FN+G2N+G2S+G2FS

Trait Code	Glycan Trait	Trait Description	Formula
MS_IGP58	IgG1 Bis GlcNAc	The incidence of bisecting GlcNAc of IgG1	SUM(G0N+G1N+G2N+G0FN+G1FN+G2FN)
MS_IGP59	IgG1 Core F	% IgG1 core fucosylation	SUM(G0F+G0FN+G1F+G1FN+G1FS+G2F+G2FN+G2FS)
MS_IGP60	IgG1 Sial	% IgG1 sialylation	SUM(G1S+G1FS+G2S+G2FS)
MS_IGP61	IgG1 Sial/Gal	% sialylation of all IgG1 galactosylated glycans	Sial/Gal
MS_IGP62	IgG1 GS/(G+GS)	% sialylation of afucosylated galactosylated structures without bisecting GlcNAc in total IgG1 glycans	SUM(G1S+G2S)/SUM(G1+G1S+G2+G2S)*100
MS_IGP63	IgG1 GS/(G0+G+GS)	% sialylation of all afucosylated structures without bisecting GlcNAc in total IgG1 glycans	SUM(G1S+G2S)/SUM(G0+G1+G1S+G2+G2S)*100
MS_IGP64	IgG1 G1S1/(G1+G1S1)	% monosialylation of afucosylated monogalactosylated (without bisecting GlcNAc) structures in total IgG1 glycans	G1S/SUM(G1+G1S)*100
MS_IGP65	IgG1 G2S1/(G2+G2S1)	% monosialylation of afucosylated digalactosylated (without bisecting GlcNAc) structures in total IgG1 glycans	G2S/SUM(G2+G2S)*100
MS_IGP66	IgG1 FGS/(FG+FGS)	% sialylation of fucosylated galactosylated structures without bisecting GlcNAc in total IgG1 glycans	SUM(G1FS+G2FS)/SUM(G1F+G1FS+G2F+G2FS)*100
MS_IGP67	IgG1 FGS/(F+FG+FGS)	% sialylation of all fucosylated structures without bisecting GlcNAc in total IgG1 glycans	SUM(G1FS+G2FS)/SUM(G0F+G1F+G1FS+G2F+G2FS)*100
MS_IGP68	IgG1 FG1S1/(FG1+FG1S1)	% monosialylation of fucosylated monogalactosylated (without bisecting GlcNAc) structures in total IgG1 glycans	G1FS/SUM(G1F+G1FS)*100
MS_IGP69	IgG1 FG2S1/(FG2+FG2S1)	% monosialylation of fucosylated digalactosylated (without bisecting GlcNAc) structures in total IgG1 glycans	G2FS/SUM(G2F+G2FS)*100
MS_IGP70	IgG2 G0n	% G0 glycan in neutral IgG2 glycans	
MS_IGP71	IgG2 G0Fn	% G0F glycan in neutral IgG2 glycans	
MS_IGP72	IgG2 G0FNn	% G0FN glycan in neutral IgG2 glycans	
MS_IGP73	IgG2 G0Nn	% G0N glycan in neutral IgG2 glycans	
MS_IGP74	IgG2 G1Fn	% G1F glycan in neutral IgG2 glycans	

Trait Code	Glycan Trait	Trait Description	Formula
MS_IGP75	IgG2 G1FNn	% G1FN glycan in neutral IgG2 glycans	
MS_IGP76	IgG2 G2Fn	% G2F glycan in neutral IgG2 glycans	
MS_IGP77	IgG2 G2FNn	% G2FN glycan in neutral IgG2 glycans	
MS_IGP78	IgG2 G0n	% agalactosylated structures in neutral IgG2 glycans	SUM(G0n+G0Fn+G0FNn+G0Nn)
MS_IGP79	IgG2 G1n	% monogalactosylated structures in neutral IgG2 glycans	SUM(G1Fn+G1FNn)
MS_IGP80	IgG2 G2n	% digalactosylated structures in neutral IgG2 glycans	SUM(G2Fn+G2FNn)
MS_IGP81	IgG2 Bn	The incidence of bisecting GlcNAc (without core Fuc) in neutral IgG2 glycan fraction	G0Nn
MS_IGP82	IgG2 BG0n/G0n	The incidence of bisecting GlcNAc (without core Fuc) in agalactosylated IgG2 structures	G0Nn/G0n
MS_IGP83	IgG2 Bn total	The incidence of bisecting GlcNAc (+/- core Fuc) in neutral IgG2 glycan fraction	SUM(G0Nn+G0FNn+G1FNn+G2FNn)
MS_IGP84	IgG2 BG0n total/G0n	The incidence of bisecting GlcNAc (+/- core Fuc) in agalactosylated IgG2 structures	SUM(G0Nn+G0FNn)/G0n
MS_IGP85	IgG2 G0	% G0 glycan in total IgG2 glycans	
MS_IGP86	IgG2 G0F	% G0F glycan in total IgG2 glycans	
MS_IGP87	IgG2 G0FN	% G0FN glycan in total IgG2 glycans	
MS_IGP88	IgG2 G0N	% G0N glycan in total IgG2 glycans	
MS_IGP89	IgG2 G1F	% G1F glycan in total IgG2 glycans	
MS_IGP90	IgG2 G1FN	% G1FN glycan in total IgG2 glycans	
MS_IGP91	IgG2 G1S	% G1S glycan in total IgG2 glycans	
MS_IGP92	IgG2 G1FS	% G1FSglycan in total IgG2 glycans	
MS_IGP93	IgG2 G2F	% G2F glycan in total IgG2 glycans	
MS_IGP94	IgG2 G2FN	% G2FN glycan in total IgG2 glycans	
MS_IGP95	IgG2 G2FS	% G2FS glycan in total IgG2 glycans	

Trait Code	Glycan Trait	Trait Description	Formula
MS_IGP96	IgG2 Gal	% IgG2 galactosylation	(G1F+G1FN+G1S+G1FS)*0.5+ G2F+G2FN+G2FS
MS_IGP97	IgG2 Bis GlcNAc	The incidence of bisecting GlcNAc of IgG2	SUM(G0N+G0FN+G1FN+G2FN)
MS_IGP98	IgG2 Sial	% IgG2 sialylation	SUM(G1S+G1FS+G2FS)
MS_IGP99	IgG2 Sial/Gal	% sialylation of all IgG2 galactosylated glycans	Sial/Gal
MS_IGP100	IgG2 FGS/(FG+FGS)	% sialylation of fucosylated galactosylated structures without bisecting GlcNAc in total IgG2 glycans	SUM(G1FS+G2FS)/SUM(G1F+ G1FS+G2F+G2FS)*100
MS_IGP101	IgG2 FGS/(F+FG+ FGS)	% sialylation of all fucosylated structures without bisecting GlcNAc in total IgG2 glycans	SUM(G1FS+G2FS)/SUM(G0F+ G1F+G1FS+G2F+G2FS)*100
MS_IGP102	IgG2 FG1S1/(FG1 +FG1S1)	% of monosialylation of fucosylated monogalactosylated structures in total IgG2 glycans	G1FS/SUM(G1F+G1FS)*100
MS_IGP103	IgG2 FG2S1/(FG2 +FG2S1)	% monosialylation of fucosylated digalactosylated structures in total IgG2 glycans	G2FS/SUM(G2F+G2FS)*100

n= neutral; F at the start of the abbreviation indicates a core fucose α1-6 linked to the inner GlcNAc; Mx, number (x) of mannose on core GlcNAcs; Ax, number of antenna (GlcNAc) on trimannosyl core; A2, biantennary with both GlcNAcs as β1-2 linked; B, bisecting GlcNAc linked β1-4 to β1-3 mannose; Gx, number (x) of β1-4 linked galactose on antenna; [3]G1 and [6]G1 indicates that the galactose is on the antenna of the α1-3 or α1-6 mannose; F(x), number (x) of fucose linked α1-3 to antenna GlcNAc; Sx, number (x) of sialic acids linked to galactose.

Table 18: Calculated m/z values of tryptic IgG Fc glycopeptides detected by MALDI-TOF-MS.

Glycan Species[c]	IgG1 P01857[a] $E_{293}EQYNSTYR_{301}$[b] $[M-H]^-$	IgG2&3 P01859[a] $E_{293}EQFNSTFR_{301}$[b] $[M-H]^-$	IgG4 P01861[a] $E_{293}EQFNSTYR_{301}$[b] $[M-H]^-$
no glycan	1189.512	1157.5222	1173.5171
G0F	2632,0460[d1]	2600.0561	2616,0509[e1]
G1F	2794,0988[d2]	2762.1089	2778,1037[e2]
G2F	2956.1516	2924.1617	2940.1565
G0FN	2835,1253[d3]	2803.1354	2819,1305[e3]
G1FN	2997,1781[d4]	2965.1882	2981,1833[e4]
G2FN	3159.2309	3127.241	3143.2361
G1FS1	3085,1942[d5]	3053.2043	3069,1991[e5]
G2FS1	3247.247	3215.2571	3231.2519
G0	2485.988	2453.9981	2469.9932
G1	2648.0408	2616,0509[e1]	2632,046[d1]
G2	2810.0936	2778,1037[e2]	2794,0988[d2]
G0N	2689.0673	2657.0774	2673.0725
G1N	2851.1201	2819,1305[e3]	2835,1253[d3]
G2N	3013.1729	2981,1833[e4]	2997,1781[d4]
G1S1	2939.1362	2907.1463	2923.1414
G2S1	3101.189	3069,1991[e5]	3085,1942[d5]

[a] SwissProt entry number.
[b] Tryptic IgG glycopeptide sequence.
[c] Glycan structural features are given in terms of number of galactoses (G0, G1, G2), fucose (F), bisecting N-acetylglucosamine (N), and N-acetylneuraminic acid (S).
[d1 – d5] isomeric glycopeptide species of IgG1 and IgG4.
[e1 – e5] isomeric glycopeptide species of IgG2 and IgG4.

Table 19: Calculated m/z values of tryptic IgG Fc glycopeptides detected by nano-LC-ESI-MS.

Glycan Species[c]	IgG1 P01857[a] $E_{293}EQYNSTYR_{301}$[b]		IgG2&3 P01859[a] $E_{293}EQFNSTFR_{301}$[b]		IgG4 P01861[a] $E_{293}EQFNSTYR_{301}$[b]	
	$[M+2H]^{2+}$	$[M+3H]^{3+}$	$[M+2H]^{2+}$	$[M+3H]^{3+}$	$[M+2H]^{2+}$	$[M+3H]^{3+}$
No glycan	595.260	397.176	579.265	386.513	587.263	391.844
G0F	1317.527	878.687 [d1]	1301.532	868.024	1309.529	873.356 [e1]
G1F	1398.553	932.705 [d2]	1382.558	922.042	1390.556	927.373 [e2]
G2F	1479.58	986.722	1463.585	976.059	1471.582	981.391
G0FN	1419.067	946.380 [d3]	1403.072	935.717	1411.069	941.049 [e3]
G1FN	1500.093	1000.398 [d4]	1484.098	989.735	1492.096	995.066 [e4]
G2FN	1581.119	1054.416	1565.125	1043.752	1573.122	1049.084
G1FS	1544.101	1029.737 [d5]	1528.106	1019.073	1536.104	1024.405 [e5]
G2FS	1625.127	1083.754	1609.133	1073.091	1617.13	1078.423
G1FNS	1645.641	1097.430	1629.646	1086.767	1637.643	1092.098
G2FNS	1726.667	1151.447	1710.672	1140.784	1718.67	1146.116
G0	1244.498	830.001	1228.503	819.338	1236.501	824.67
G1	1325.524	884.019	1309.529	873.356 [e1]	1317.527	878.687 [d1]
G2	1406.551	938.036	1390.556	927.373 [e2]	1398.553	932.705 [d2]
G0N	1346.038	897.694	1330.043	887.031	1338.04	892.363
G1N	1427.064	951.712	1411.069	941.049 [e3]	1419.067	946.380 [d3]
G2N	1508.090	1005.730	1492.096	995.066 [e4]	1500.093	1000.398 [d4]
G1S	1471.072	981.051	1455.077	970.387	1463.075	975.719
G2S	1552.098	1035.068	1536.104	1024.405 [e5]	1544.101	1029.737 [d5]
G1NS	1572.612	1048.744	1556.617	1038.081	1564.614	1043.412
G2NS	1653.638	1102.761	1637.643	1092.098	1645.641	1097.430[d6]

[a] SwissProt entry number.
[b] Tryptic IgG glycopeptide sequence.
[c] Glycan structural features are given in terms of number of galactoses (G0, G1, G2), fucose (F), bisecting N-acetylglucosamine (N), and N-acetylneuraminic acid (S).
[d1 – d5] isomeric glycopeptide species of IgG1 and IgG4.
[e1 – e5] isomeric glycopeptide species of IgG2 and IgG4.

Table 20: IgG *N*-Glycan Features by nano-LC-ESI-MS for GWAS.

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP1	IgG1 G0F	% G0F glycan in total IgG1 glycans	
LC_IGP2	IgG1 G1F	% G1F glycan in total IgG1 glycans	
LC_IGP3	IgG1 G2F	% G2F glycan in total IgG1 glycans	
LC_IGP4	IgG1 G0FN	% G0FN glycan in total IgG1 glycans	
LC_IGP5	IgG1 G1FN	% G1FN glycan in total IgG1 glycans	
LC_IGP6	IgG1 G2FN	% G2FN glycan in total IgG1 glycans	
LC_IGP7	IgG1 G1FS1	% G1FS1 glycan in total IgG1 glycans	
LC_IGP8	IgG1 G2FS1	% G2FS1 glycan in total IgG1 glycans	
LC_IGP9	IgG1 G1FNS1	% G1FNS1 glycan in total IgG1 glycans	
LC_IGP10	IgG1 G2FNS1	% G2FNS1 glycan in total IgG1 glycans	
LC_IGP11	IgG1 G0	% G0 glycan in total IgG1 glycans	
LC_IGP12	IgG1 G1	% G1 glycan in total IgG1 glycans	
LC_IGP13	IgG1 G2	% G2 glycan in total IgG1 glycans	
LC_IGP14	IgG1 G0N	% G0N glycan in total IgG1 glycans	
LC_IGP15	IgG1 G1N	% G1N glycan in total IgG1 glycans	
LC_IGP16	IgG1 G2N	% G2N glycan in total IgG1 glycans	
LC_IGP17	IgG1 G1S1	% G1S1 glycan in total IgG1 glycans	
LC_IGP18	IgG1 G2S1	% G2S1 glycan in total IgG1 glycans	
LC_IGP19	IgG1 G1NS1	% G1NS1 glycan in total IgG1 glycans	
LC_IGP20	IgG1 G2NS1	% G2NS1 glycan in total IgG1 glycans	
LC_IGP21	IgG1 Fucosylation	% IgG1 core fucosylation	SUM(G0F+G1F+G2F+G0FN+ G1FN+G2FN+G1FS1+G2FS1+ G1FNS1+G2FNS1)

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP22	IgG1 Bisecting_GlcNAc	The incidence of bisecting GlcNAc of IgG1	SUM(G0FN+G1FN+G2FN+G1FNS1+G2FNS1+G0N+G1N+G2N+G1NS1+G2NS1)
LC_IGP23	IgG1 Galactosylation	% IgG1 galactosylation	SUM(G1F+G1FN+G1FS1+G1FNS1+G1+G1N+G1S1+G1NS1)*0.5+SUM(G2F+G2FN+G2FS1+G2FNS1+G2+G2N+G2S1+G2NS1)
LC_IGP24	IgG1 Sialylation	The percentage of IgG1 sialylation	SUM(G1FS1+G2FS1+G1FNS1+G2FNS1+G1S1+G2S1+G1NS1+G2NS1)
LC_IGP25	IgG1 SA per Gal	The number of sialic acid moieties on galactose moieties in total IgG1 glycans	IgG1 Sialylation/IgG1 Galactosylation
LC_IGP26	IgG1 GS1/(G+GS1)	% monosialylation of afucosylated galactosylated structures without bisecting GlcNAc in total IgG1 glycans	SUM(G1S1+G2S1)/SUM(G1+G1S1+G2+G2S1)*100
LC_IGP27	IgG1 GS1/(G0+G+GS1)	% monosialylation of all afucosylated structures without bisecting GlcNAc in total IgG1 glycans	SUM(G1S1+G2S1)/SUM(G0+G1+G1S1+G2+G2S1)*100
LC_IGP28	IgG1 G1S1/(G1+G1S1)	% monosialylation of afucosylated monogalactosylated (without bisecting GlcNAc) structures in total IgG1 glycans	G1S1/SUM(G1+G1S1)*100
LC_IGP29	IgG1 G2S1/(G2+G2S1)	% monosialylation of afucosylated digalactosylated (without bisecting GlcNAc) structures in total IgG1 glycans	G2S1/SUM(G2+G2S1)*100
LC_IGP30	IgG1 BGS1/(BG+BGS1)	% monosialylation of afucosylated galactosylated structures with bisecting GlcNAc in total IgG1 glycans	SUM(G1NS1+G2NS1)/SUM(G1N+G1NS1+G2N+G2NS1)*100
LC_IGP31	IgG1 BGS1/(BG0+BG+BGS1)	% monosialylation of all afucosylated structures with bisecting GlcNAc in total IgG1 glycans	SUM(G1NS1+G2NS1)/SUM(G0N+G1N+G1NS1+G2N+G2NS1)*100
LC_IGP32	IgG1 BG1S1/(BG1+BG1S1)	% monosialylation of afucosylated monogalactosylated (with bisecting GlcNAc) structures in total IgG1 glycans	G1NS1/SUM(G1N+G1NS1)*100
LC_IGP33	IgG1 BG2S1/(BG2+BG2S1)	% monosialylation of afucosylated digalactosylated (with bisecting GlcNAc) structures in total IgG1 glycans	G2NS1/SUM(G2N+G2NS1)*100

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP34	IgG1 FGS1/(FG+FGS1)	% monosialylation of fucosylated galactosylated structures without bisecting GlcNAc in total IgG1 glycans	SUM(G1FS1+G2FS1)/SUM(G1F+G1FS1+G2F+G2FS1)*100
LC_IGP35	IgG1 FGS1/(F+FG+FGS1)	% monosialylation of all fucosylated structures without bisecting GlcNAc in total IgG1 glycans	SUM(G1FS1+G2FS1)/SUM(G0F+G1F+G1FS1+G2F+G2FS1)*100
LC_IGP36	IgG1 FG1S1/(FG1+FG1S1)	% monosialylation of fucosylated monogalactosylated (without bisecting GlcNAc) structures in total IgG1 glycans	G1FS1/SUM(G1F+G1FS1)*100
LC_IGP37	IgG1 FG2S1/(FG2+FG2S1)	% monosialylation of fucosylated digalactosylated (without bisecting GlcNAc) structures in total IgG1 glycans	G2FS1/SUM(G2F+G2FS1)*100
LC_IGP38	IgG1 FBGS1/(FBG+FBGS1)	% monosialylation of fucosylated galactosylated structures with bisecting GlcNAc in total IgG1 glycans	SUM(G1FNS1+G2FNS1)/SUM(G1FN+G1FNS1+G2FN+G2FNS1)*100
LC_IGP39	IgG1 FBGS1/(FB+FBG+FBGS1)	% monosialylation of all fucosylated structures with bisecting GlcNAc in total IgG1 glycans	SUM(G1FNS1+G2FNS1)/SUM(G0FN+G1FN+G1FS1+G2FN+G2FS1)*100
LC_IGP40	IgG1 FBG1S1/(FBG1+FBG1S1)	% monosialylation of fucosylated monogalactosylated (with bisecting GlcNAc) structures in total IgG1 glycans	G1FNS1/SUM(G1FN+G1FNS1)*100
LC_IGP41	IgG1 FBG2S1/(FBG2+FBG2S1)	% monosialylation of fucosylated digalactosylated (with bisecting GlcNAc) structures in total IgG1 glycans	G2FNS1/SUM(G2FN+G2FNS1)*100
LC_IGP42	IgG1 BS1/S1	Ratio of afucosylated monosialylated structures with and without bisecting GlcNAc in total IgG1 glycans	SUM(G1NS1+G2NS1)/SUM(G1S1+G2S1)
LC_IGP43	IgG1 FBS1/FS1	Ratio of fucosylated monosialylated structures with and without bisecting GlcNAc in total IgG1 glycans	SUM(G1FNS1+G2FNS1)/SUM(G1FS1+G2FS1)
LC_IGP44	IgG1 BS1/(S1+BS1)	The incidence of bisecting GlcNAc in all afucosylated monosialylated structures in total IgG1 glycans	SUM(G1NS1+G2NS1)/SUM(G1S1+G1NS1+G2S1+G2NS1)

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP45	IgG1 FBS1/(FS1+FBS1)	The incidence of bisecting GlcNAc in all fucosylated monosialylated structures in total IgG1 glycans	SUM(G1FNS1+G2FNS1)/SUM(G1FS1+G1FNS1+G2FS1+G2FNS1)
LC_IGP46	IgG1 G0Fn	% G0F glycan in neutral IgG1 glycans	
LC_IGP47	IgG1 G1Fn	% G1F glycan in neutral IgG1 glycans	
LC_IGP48	IgG1 G2Fn	% G2F glycan in neutral IgG1 glycans	
LC_IGP49	IgG1 G0FNn	% G0FN glycan in neutral IgG1 glycans	
LC_IGP50	IgG1 G1FNn	% G1FN glycan in neutral IgG1 glycans	
LC_IGP51	IgG1 G2FNn	% G2FN glycan in neutral IgG1 glycans	
LC_IGP52	IgG1 G0n	% G0 glycan in neutral IgG1 glycans	
LC_IGP53	IgG1 G1n	% G1 glycan in neutral IgG1 glycans	
LC_IGP54	IgG1 G2n	% G2 glycan in neutral IgG1 glycans	
LC_IGP55	IgG1 G0Nn	% G0N glycan in neutral IgG1 glycans	
LC_IGP56	IgG1 G1Nn	% G1N glycan in neutral IgG1 glycans	
LC_IGP57	IgG1 G2Nn	% G2N glycan in neutral IgG1 glycans	
LC_IGP58	IgG1 G0n	% agalactosylated structures in neutral IgG1 glycan fraction	SUM(G0n+G0Fn+G0FNn+G0Nn)
LC_IGP59	IgG1 G1n	% monogalactosylated structures in neutral IgG1 glycan fraction	SUM(G1n+G1Fn+G1FNn+G1Nn)
LC_IGP60	IgG1 G2n	% digalactosylated structures in neutral IgG1 glycan fraction	SUM(G2n+G2Fn+G2FNn+G2Nn)
LC_IGP61	IgG1 Fn total	% all fucosylated (+/- bisecting GlcNAc) structures in neutral IgG1 glycan fraction	SUM(G0Fn+G0FNn+G1Fn+G1FNn+G2Fn+G2FNn)
LC_IGP62	IgG1 FG0n total/G0n	% fucosylation of agalactosylated structures in neutral IgG1 glycan fraction	SUM(G0Fn+G0FNn)/G0n*100
LC_IGP63	IgG1 FG1n total/G1n	% fucosylation of monogalactosylated structures in neutral IgG1 glycan fraction	SUM(G1Fn+G1FNn)/G1n*100
LC_IGP64	IgG1 FG2n total/G2n	% fucosylation of digalactosylated structures in neutral IgG1 glycan fraction	SUM(G2Fn+G2FNn)/G2n*100

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP65	IgG1 Fn	% fucosylated (without bisecting GlcNAc) structures i in neutral IgG1 glycan fraction	SUM(G0Fn+G1Fn+G2Fn)
LC_IGP66	IgG2 FG0n/G0n	% fucosylation (without bisecting GlcNAc) of agalactosylated structures in neutral IgG1 glycan fraction	G0Fn/G0n*100
LC_IGP67	IgG2 FG1n/G1n	% fucosylation (without bisecting GlcNAc) of monogalactosylated structures in neutral IgG1 glycan fraction	G1Fn/G1n*100
LC_IGP68	IgG2 FG2n/G2n	% fucosylation (without bisecting GlcNAc) of digalactosylated structures in neutral IgG1 glycan fraction	G2Fn/G2n*100
LC_IGP69	IgG2 FBn	% fucosylated (with bisecting GlcNAc) structures in neutral IgG1 glycan fraction	SUM(G0FNn+G1FNn+G2FNn)
LC_IGP70	IgG2 FBG0n/G0n	% fucosylation (with bisecting GlcNAc) of agalactosylated structures in neutral IgG1 glycan fraction	G0FNn/G0n*100
LC_IGP71	IgG2 FBG1n/G1n	% fucosylation (with bisecting GlcNAc) of monogalactosylated structures in neutral IgG1 glycan fraction	G1FNn/G1n*100
LC_IGP72	IgG2 FBG2n/G2n	% fucosylation (with bisecting GlcNAc) of digalactosylated structures in neutral IgG1 glycan fraction	G2FNn/G2n*100
LC_IGP73	IgG1 Bn total	The incidence of bisecting GlcNAc (+/- core Fuc) in neutral IgG1 glycan fraction	SUM(G0Nn+G1Nn+G2Nn+G0 FNn+G1FNn+G2FNn)
LC_IGP74	IgG1 BG0n total/G0n	The incidence of bisecting GlcNAc (+/- core Fuc) in agalactosylated structures in neutral IgG1 glycan fraction	SUM(G0Nn+G0FNn)/G0n*100
LC_IGP75	IgG1 BG1n total/G1n	The incidence of bisecting GlcNAc (+/- core Fuc) in monogalactosylated structures in neutral IgG1 glycan fraction	SUM(G1Nn+G1FNn)/G1n*100
LC_IGP76	IgG1 BG2n total/G2n	The incidence of bisecting GlcNAc (+/- core Fuc) in digalactosylated structures in neutral IgG1 glycan fraction	SUM(G2Nn+G2FNn)/G2n*100
LC_IGP77	IgG1 Bn	The incidence of bisecting GlcNAc (without core Fuc) in neutral IgG1 glycan fraction	SUM(G0Nn+G1Nn+G2Nn)

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP78	IgG1 BG0n/G0n	The incidence of bisecting GlcNAc (without core Fuc) in agalactosylated structures in neutral IgG1 glycan fraction	G0Nn/G0n*100
LC_IGP79	IgG1 BG1n/G1n	The incidence of bisecting GlcNAc (without core Fuc) in monogalactosylated structures in neutral IgG1 glycan fraction	G1Nn/G1n*100
LC_IGP80	IgG1 BG2n/G2n	The incidence of bisecting GlcNAc (without core Fuc) in digalactosylated structures in neutral IgG1 glycan fraction	G2Nn/G2n*100
LC_IGP81	IgG1 Fn/Bn	Ratio of fucosylated structures without bisecting GlcNAc and afucosylated structures with bisecting GlcNAc in neutral IgG1 glycan fraction	Fn/Bn
LC_IGP82	IgG1 FBn/Fn	Ratio of fucosylated structures with and without bisecting GlcNAc in neutral IgG1 glycan fraction	FBn/Fn
LC_IGP83	IgG1 FBn/Fn total	The incidence of bisecting GlcNAc in all fucosylated structures in neutral IgG1 glycan fraction	FBn/Fn total*100
LC_IGP84	IgG1 FBn/Bn total	% fucosylation in all structures with bisecting GlcNAc in neutral IgG1 glycan fraction	FBn/Bn total*100
LC_IGP85	IgG1 Fn/Bn total	Ratio of fucosylated non-bisecting GlcNAc structures and all structures with bisecting GlcNAc in neutral IgG1 glycans fraction	Fn/Bn total
LC_IGP86	IgG1 Bn/Fn total ‰	Ratio of structures with bisecting GlcNAc and all fucosylated structures (+/- bisecting GlcNAc) in neutral IgG1 glycan fraction	Bn/Fn total*1000
LC_IGP87	IgG2 G0F	The percentage of G0F glycan in total IgG2 glycans	
LC_IGP88	IgG2 G1F	The percentage of G1F glycan in total IgG2 glycans	
LC_IGP89	IgG2 G2F	The percentage of G2F glycan in total IgG2 glycans	
LC_IGP90	IgG2 G0FN	The percentage of G0FN glycan in total IgG2 glycans	
LC_IGP91	IgG2 G1FN	The percentage of G1FN glycan in total IgG2 glycans	

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP92	IgG2 G2FN	The percentage of G2FN glycan in total IgG2 glycans	
LC_IGP93	IgG2 G1FS1	The percentage of G1FS1 glycan in total IgG2 glycans	
LC_IGP94	IgG2 G2FS1	The percentage of G2FS1 glycan in total IgG2 glycans	
LC_IGP95	IgG2 G1FNS1	The percentage of G1FNS1 glycan in total IgG2 glycans	
LC_IGP96	IgG2 G2FNS1	The percentage of G2FNS1 glycan in total IgG2 glycans	
LC_IGP97	IgG2 G0	The percentage of G0 glycan in total IgG2 glycans	
LC_IGP98	IgG2 G1	The percentage of G1 glycan in total IgG2 glycans	
LC_IGP99	IgG2 G2	The percentage of G2 glycan in total IgG2 glycans	
LC_IGP100	IgG2 G0N	The percentage of G0N glycan in total IgG2 glycans	
LC_IGP101	IgG2 G1N	The percentage of G1N glycan in total IgG2 glycans	
LC_IGP102	IgG2 G2N	The percentage of G2N glycan in total IgG2 glycans	
LC_IGP103	IgG2 G1S1	The percentage of G1S1 glycan in total IgG2 glycans	
LC_IGP104	IgG2 G2S1	The percentage of G2S1 glycan in total IgG2 glycans	
LC_IGP105	IgG2 G1NS1	The percentage of G1NS1 glycan in total IgG2 glycans	
LC_IGP106	IgG2 G2NS1	The percentage of G2NS1 glycan in total IgG2 glycans	
LC_IGP107	IgG2 Fucosylation	The percentage of IgG2 core fucosylation	SUM(G0F+G1F+G2F+G0FN+G1FN+G2FN+G1FS1+G2FS1+G1FNS1+G2FNS1)
LC_IGP108	IgG2 Bisecting GlcNAc	The incidence of bisecting GlcNAc of IgG2	SUM(G0FN+G1FN+G2FN+G1FNS1+G2FNS1+G0N+G1N+G2N+G1NS1+G2NS1)
LC_IGP109	IgG2 Galactosylation	The percentage of IgG2 galactosylation	SUM(G1F+G1FN+G1FS1+G1FNS1+G1+G1N+G1S1+G1NS1)*0.5+SUM(G2F+G2FN+G2FS1+G2FNS1+G2+G2N+G2S1+G2NS1)
LC_IGP110	IgG2 Sialylation	The percentage of IgG2 sialylation	SUM(G1FS1+G2FS1+G1FNS1+G2FNS1+G1S1+G2S1+G1NS1+G2NS1)
LC_IGP111	IgG2 SA per Gal	The number of sialic acid moieties on galactose moieties in total IgG2 glycans	IgG2 Sialylation/IgG2 Galactosylation

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP112	IgG2 GS1/(G+GS1)	The percentage of monosialylation of afucosylated galactosylated structures without bisecting GlcNAc in total IgG2 glycans	SUM(G1S1+G2S1)/SUM(G1+G1S1+G2+G2S1)*100
LC_IGP113	IgG2 GS1/(G0+G+GS1)	The percentage of monosialylation of all afucosylated structures without bisecting GlcNAc in total IgG2 glycans	SUM(G1S1+G2S1)/SUM(G0+G1+G1S1+G2+G2S1)*100
LC_IGP114	IgG2 G1S1/(G1+G1S1)	The percentage of monosialylation of afucosylated monogalactosylated (without bisecting GlcNAc) structures in total IgG2 glycans	G1S1/SUM(G1+G1S1)*100
LC_IGP115	IgG2 G2S1/(G2+G2S1)	The percentage of monosialylation of afucosylated digalactosylated (without bisecting GlcNAc) structures in total IgG2 glycans	G2S1/SUM(G2+G2S1)*100
LC_IGP116	IgG2 BGS1/(BG+BGS1)	The percentage of monosialylation of afucosylated galactosylated structures with bisecting GlcNAc in total IgG2 glycans	SUM(G1NS1+G2NS1)/SUM(G1N+G1NS1+G2N+G2NS1)*100
LC_IGP117	IgG2 BGS1/(BG0+BG+BGS1)	The percentage of monosialylation of all afucosylated structures with bisecting GlcNAc in total IgG2 glycans	SUM(G1NS1+G2NS1)/SUM(G0N+G1N+G1NS1+G2N+G2NS1)*100
LC_IGP118	IgG2 BG1S1/(BG1+BG1S1)	The percentage of monosialylation of afucosylated monogalactosylated (with bisecting GlcNAc) structures in total IgG2 glycans	G1NS1/SUM(G1N+G1NS1)*100
LC_IGP119	IgG2 BG2S1/(BG2+BG2S1)	The percentage of monosialylation of afucosylated digalactosylated (with bisecting GlcNAc) structures in total IgG2 glycans	G2NS1/SUM(G2N+G2NS1)*100
LC_IGP120	IgG2 FGS1/(FG+FGS1)	The percentage of monosialylation of fucosylated galactosylated structures without bisecting GlcNAc in total IgG2 glycans	SUM(G1FS1+G2FS1)/SUM(G1F+G1FS1+G2F+G2FS1)*100

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP121	IgG2 FGS1/(F+FG+FGS1)	The percentage of monosialylation of all fucosylated structures without bisecting GlcNAc in total IgG2 glycans	SUM(G1FS1+G2FS1)/SUM(G0F+G1F+G1FS1+G2F+G2FS1)*100
LC_IGP122	IgG2 FG1S1/(FG1+FG1S1)	The percentage of monosialylation of fucosylated monogalactosylated (without bisecting GlcNAc) structures in total IgG2 glycans	G1FS1/SUM(G1F+G1FS1)*100
LC_IGP123	IgG2 FG2S1/(FG2+FG2S1)	The percentage of monosialylation of fucosylated digalactosylated (without bisecting GlcNAc) structures in total IgG2 glycans	G2FS1/SUM(G2F+G2FS1)*100
LC_IGP124	IgG2 FBGS1/(FBG+FBGS1)	The percentage of monosialylation of fucosylated galactosylated structures with bisecting GlcNAc in total IgG2 glycans	SUM(G1FNS1+G2FNS1)/SUM(G1FN+G1FNS1+G2FN+G2FNS1)*100
LC_IGP125	IgG2 FBGS1/(FB+FBG+FBGS1)	The percentage of monosialylation of all fucosylated structures with bisecting GlcNAc in total IgG2 glycans	SUM(G1FNS1+G2FNS1)/SUM(G0FN+G1FN+G1FS1+G2FN+G2FS1)*100
LC_IGP126	IgG2 FBG1S1/(FBG1+FBG1S1)	The percentage of monosialylation of fucosylated monogalactosylated (with bisecting GlcNAc) structures in total IgG2 glycans	G1FNS1/SUM(G1FN+G1FNS1)*100
LC_IGP127	IgG2 FBG2S1/(FBG2+FBG2S1)	The percentage of monosialylation of fucosylated digalactosylated (with bisecting GlcNAc) structures in total IgG2 glycans	G2FNS1/SUM(G2FN+G2FNS1)*100
LC_IGP128	IgG2 BS1/S1	Ratio of afucosylated monosialylated structures with and without bisecting GlcNAc in total IgG2 glycans	SUM(G1NS1+G2NS1)/SUM(G1S1+G2S1)
LC_IGP129	IgG2 FBS1/FS1	Ratio of fucosylated monosialylated structures with and without bisecting GlcNAc in total IgG2 glycans	SUM(G1FNS1+G2FNS1)/SUM(G1FS1+G2FS1)
LC_IGP130	IgG2 BS1/(S1+BS1)	The incidence of bisecting GlcNAc in all afucosylated monosialylated structures in total IgG2 glycans	SUM(G1NS1+G2NS1)/SUM(G1S1+G1NS1+G2S1+G2NS1)

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP131	IgG2 FBS1/(FS1+FBS1)	The incidence of bisecting GlcNAc in all fucosylated monosialylated structures in total IgG2 glycans	SUM(G1FNS1+G2FNS1)/SUM(G1FS1+G1FNS1+G2FS1+G2FNS1)
LC_IGP132	IgG2 G0Fn	The percentage of G0F glycan in neutral IgG2 glycans	
LC_IGP133	IgG2 G1Fn	The percentage of G1F glycan in neutral IgG2 glycans	
LC_IGP134	IgG2 G2Fn	The percentage of G2F glycan in neutral IgG2 glycans	
LC_IGP135	IgG2 G0FNn	The percentage of G0FN glycan in neutral IgG2 glycans	
LC_IGP136	IgG2 G1FNn	The percentage of G1FN glycan in neutral IgG2 glycans	
LC_IGP137	IgG2 G2FNn	The percentage of G2FN glycan in neutral IgG2 glycans	
LC_IGP138	IgG2 G0n	The percentage of G0 glycan in neutral IgG2 glycans	
LC_IGP139	IgG2 G1n	The percentage of G1 glycan in neutral IgG2 glycans	
LC_IGP140	IgG2 G2n	The percentage of G2 glycan in neutral IgG2 glycans	
LC_IGP141	IgG2 G0Nn	The percentage of G0N glycan in neutral IgG2 glycans	
LC_IGP142	IgG2 G1Nn	The percentage of G1N glycan in neutral IgG2 glycans	
LC_IGP143	IgG2 G2Nn	The percentage of G2N glycan in neutral IgG2 glycans	
LC_IGP144	IgG2 G0n	The percentage of agalactosylated structures in neutral IgG2 glycan fraction	SUM(G0n+G0Fn+G0FNn+G0Nn)
LC_IGP145	IgG2 G1n	The percentage of monogalactosylated structures in neutral IgG2 glycan fraction	SUM(G1n+G1Fn+G1FNn+G1Nn)
LC_IGP146	IgG2 G2n	The percentage of digalactosylated structures in neutral IgG2 glycan fraction	SUM(G2n+G2Fn+G2FNn+G2Nn)
LC_IGP147	IgG2 Fn total	The percentage of all fucosylated (+/- bisecting GlcNAc) structures in neutral IgG2 glycan fraction	SUM(G0Fn+G0FNn+G1Fn+G1FNn+G2Fn+G2FNn)
LC_IGP148	IgG2 FG0n total/G0n	The percentage of fucosylation of agalactosylated structures in neutral IgG2 glycan fraction	SUM(G0Fn+G0FNn)/G0n*100

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP149	IgG2 FG1n total/G1n	The percentage of fucosylation of monogalactosylated structures in neutral IgG2 glycan fraction	SUM(G1Fn+G1FNn)/G1n*100
LC_IGP150	IgG2 FG2n total/G2n	The percentage of fucosylation of digalactosylated structures in neutral IgG2 glycan fraction	SUM(G2Fn+G2FNn)/G2n*100
LC_IGP151	IgG2 Fn	The percentage of fucosylated (without bisecting GlcNAc) structures in neutral IgG2 glycan fraction	SUM(G0Fn+G1Fn+G2Fn)
LC_IGP152	IgG2 FG0n/G0n	The percentage of fucosylation (without bisecting GlcNAc) of agalactosylated structures in neutral IgG2 glycan fraction	G0Fn/G0n*100
LC_IGP153	IgG2 FG1n/G1n	The percentage of fucosylation (without bisecting GlcNAc) of monogalactosylated structures in neutral IgG2 glycan fraction	G1Fn/G1n*100
LC_IGP154	IgG2 FG2n/G2n	The percentage of fucosylation (without bisecting GlcNAc) of digalactosylated structures in neutral IgG2 glycan fraction	G2Fn/G2n*100
LC_IGP155	IgG2 FBn	The percentage of fucosylated (with bisecting GlcNAc) structures in neutral IgG2 glycan fraction	SUM(G0FNn+G1FNn+G2FNn)
LC_IGP156	IgG2 FBG0n/G0n	The percentage of fucosylation (with bisecting GlcNAc) of agalactosylated structures in neutral IgG2 glycan fraction	G0FNn/G0n*100
LC_IGP157	IgG2 FBG1n/G1n	The percentage of fucosylation (with bisecting GlcNAc) of monogalactosylated structures in neutral IgG2 glycan fraction	G1FNn/G1n*100
LC_IGP158	IgG2 FBG2n/G2n	The percentage of fucosylation (with bisecting GlcNAc) of digalactosylated structures in neutral IgG2 glycan fraction	G2FNn/G2n*100
LC_IGP159	IgG2 Bn total	The incidence of bisecting GlcNAc (+/- core Fuc) in neutral IgG2 glycan fraction	SUM(G0Nn+G1Nn+G2Nn+G0FNn+G1FNn+G2FNn)

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP160	IgG2 BG0n total/G0n	The incidence of bisecting GlcNAc (+/- core Fuc) in agalactosylated structures in neutral IgG2 glycan fraction	SUM(G0Nn+G0FNn)/G0n*100
LC_IGP161	IgG2 BG1n total/G1n	The incidence of bisecting GlcNAc (+/- core Fuc) in monogalactosylated structures in neutral IgG2 glycan fraction	SUM(G1Nn+G1FNn)/G1n*100
LC_IGP162	IgG2 BG2n total/G2n	The incidence of bisecting GlcNAc (+/- core Fuc) in digalactosylated structures in neutral IgG2 glycan fraction	SUM(G2Nn+G2FNn)/G2n*100
LC_IGP163	IgG2 Bn	The incidence of bisecting GlcNAc (without core Fuc) in neutral IgG2 glycan fraction	SUM(G0Nn+G1Nn+G2Nn)
LC_IGP164	IgG2 BG0n/G0n	The incidence of bisecting GlcNAc (without core Fuc) in agalactosylated structures in neutral IgG2 glycan fraction	G0Nn/G0n*100
LC_IGP165	IgG2 BG1n/G1n	The incidence of bisecting GlcNAc (without core Fuc) in monogalactosylated structures in neutral IgG2 glycan fraction	G1Nn/G1n*100
LC_IGP166	IgG2 BG2n/G2n	The incidence of bisecting GlcNAc (without core Fuc) in digalactosylated structures in neutral IgG2 glycan fraction	G2Nn/G2n*100
LC_IGP167	IgG2 Fn/Bn	Ratio of fucosylated structures without bisecting GlcNAc and afucosylated structures with bisecting GlcNAc in neutral IgG2 glycan fraction	Fn/Bn
LC_IGP168	IgG2 FBn/Fn	Ratio of fucosylated structures with and without bisecting GlcNAc in neutral IgG2 glycan fraction	FBn/Fn
LC_IGP169	IgG2 FBn/Fn total	The incidence of bisecting GlcNAc in all fucosylated structures in neutral IgG2 glycan fraction	FBn/Fn total*100
LC_IGP170	IgG2 FBn/Bn total	The percentage of fucosylation in all structures with bisecting GlcNAc in neutral IgG2 glycan fraction	FBn/Bn total*100
LC_IGP171	IgG2 Fn/Bn total	Ratio of fucosylated non-bisecting GlcNAc structures and all structures with bisecting GlcNAc in neutral IgG2 glycans fraction	Fn/Bn total

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP172	IgG2 Bn/Fn total ‰	Ratio of structures with bisecting GlcNAc and all fucosylated structures (+/- bisecting GlcNAc) in neutral IgG2 glycan fraction	Bn/Fn total*1000
LC_IGP173	IgG4 G0F	The percentage of G0F glycan in total IgG4 glycans	
LC_IGP174	IgG4 G1F	The percentage of G1F glycan in total IgG4 glycans	
LC_IGP175	IgG4 G2F	The percentage of G2F glycan in total IgG4 glycans	
LC_IGP176	IgG4 G0FN	The percentage of G0FN glycan in total IgG4 glycans	
LC_IGP177	IgG4 G1FN	The percentage of G1FN glycan in total IgG4 glycans	
LC_IGP178	IgG4 G2FN	The percentage of G2FN glycan in total IgG4 glycans	
LC_IGP179	IgG4 G1FS1	The percentage of G1FS1 glycan in total IgG4 glycans	
LC_IGP180	IgG4 G2FS1	The percentage of G2FS1 glycan in total IgG4 glycans	
LC_IGP181	IgG4 G1FNS1	The percentage of G1FNS1 glycan in total IgG4 glycans	
LC_IGP182	IgG4 G2FNS1	The percentage of G2FNS1 glycan in total IgG4 glycans	
LC_IGP183	IgG4 Bisecting GlcNAc	The incidence of bisecting GlcNAc of IgG4	SUM(G0FN+G1FN+G2FN)
LC_IGP184	IgG4 Galactosylation	The percentage of IgG4 galactosylation	SUM(G1F+G1FN+G1FS1+G1FNS1)*0.5+SUM(G2F+G2FN+G2FS1+G2FNS1)
LC_IGP185	IgG4 Sialylation	The percentage of IgG4 sialylation	SUM(G1FS1+G2FS1+G1FNS1+G2FNS1)
LC_IGP186	IgG4 SA per Gal	The number of sialic acid moieties on galactose moieties in total IgG4 glycans	IgG4 Sialylation/IgG4 Galactosylation
LC_IGP187	IgG4 FGS1/(FG+FGS1)	The percentage of monosialylation of fucosylated galactosylated structures without bisecting GlcNAc in total IgG4 glycans	SUM(G1FS1+G2FS1)/SUM(G1F+G1FS1+G2F+G2FS1)*100
LC_IGP188	IgG4 FGS1/(F+FG+FGS1)	The percentage of monosialylation of all fucosylated structures without bisecting GlcNAc in total IgG4 glycans	SUM(G1FS1+G2FS1)/SUM(G0F+G1F+G1FS1+G2F+G2FS1)*100

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP189	IgG4 FG1S1/(FG1+FG1S1)	The percentage of monosialylation of fucosylated monogalactosylated (without bisecting GlcNAc) structures in total IgG4 glycans	G1FS1/SUM(G1F+G1FS1)*100
LC_IGP190	IgG4 FG2S1/(FG2+FG2S1)	The percentage of monosialylation of fucosylated digalactosylated (without bisecting GlcNAc) structures in total IgG4 glycans	G2FS1/SUM(G2F+G2FS1)*100
LC_IGP191	IgG4 FBGS1/(FBG+FBGS1)	The percentage of monosialylation of fucosylated galactosylated structures with bisecting GlcNAc in total IgG4 glycans	SUM(G1FNS1+G2FNS1)/SUM(G1FN+G1FNS1+G2FN+G2FNS1)*100
LC_IGP192	IgG4 FBGS1/(FB+FBG+FBGS1)	The percentage of monosialylation of all fucosylated structures with bisecting GlcNAc in total IgG4 glycans	SUM(G1FNS1+G2FNS1)/SUM(G0FN+G1FN+G1FNS1+G2FN+G2FNS1)*100
LC_IGP193	IgG4 FBG1S1/(FBG1+FBG1S1)	The percentage of monosialylation of fucosylated monogalactosylated (with bisecting GlcNAc) structures in total IgG4 glycans	G1FNS1/SUM(G1FN+G1FNS1)*100
LC_IGP194	IgG4 FBG2S1/(FBG2+FBG2S1)	The percentage of monosialylation of fucosylated digalactosylated (with bisecting GlcNAc) structures in total IgG4 glycans	G2FNS1/SUM(G2FN+G2FNS1)*100
LC_IGP195	IgG4 FBS1/FS1	Ratio of fucosylated monosialylated structures with and without bisecting GlcNAc in total IgG4 glycans	SUM(G1FNS1+G2FNS1)/SUM(G1FS1+G2FS1)
LC_IGP196	IgG4 FBS1/(FS1+FBS1)	The incidence of bisecting GlcNAc in all fucosylated monosialylated structures in total IgG4 glycans	SUM(G1FNS1+G2FNS1)/SUM(G1FS1+G1FNS1+G2FS1+G2FNS1)
LC_IGP197	IgG4 G0Fn	The percentage of G0F glycan in neutral IgG4 glycans	
LC_IGP198	IgG4 G1Fn	The percentage of G1F glycan in neutral IgG4 glycans	
LC_IGP199	IgG4 G2Fn	The percentage of G2F glycan in neutral IgG4 glycans	
LC_IGP200	IgG4 G0FNn	The percentage of G0FN glycan in neutral IgG4 glycans	

Trait Code	Glycan Trait	Trait Description	Formula
LC_IGP201	IgG4 G1FNn	The percentage of G1FN glycan in neutral IgG4 glycans	
LC_IGP202	IgG4 G2FNn	The percentage of G2FN glycan in neutral IgG4 glycans	
LC_IGP203	IgG4 G0n	The percentage of agalactosylated structures in neutral IgG4 glycan fraction	SUM(G0F+G0FN)
LC_IGP204	IgG4 G1n	The percentage of monogalactosylated structures in neutral IgG4 glycan fraction	SUM(G1F+G1FN)
LC_IGP205	IgG4 G2n	The percentage of digalactosylated structures in neutral IgG4 glycan fraction	SUM(G2F+G2FN)

n= neutral; F at the start of the abbreviation indicates a core fucose α1-6 linked to the inner GlcNAc; Mx, number (x) of mannose on core GlcNAcs; Ax, number of antenna (GlcNAc) on trimannosyl core; A2, biantennary with both GlcNAcs as β1-2 linked; B, bisecting GlcNAc linked β1-4 to β1-3 mannose; Gx, number (x) of β1-4 linked galactose on antenna; [3]G1 and [6]G1 indicates that the galactose is on the antenna of the α1-3 or α1-6 mannose; F(x), number (x) of fucose linked α1-3 to antenna GlcNAc; Sx, number (x) of sialic acids linked to galactose.

Table 21: IgG *N*-Glycan Features by xCGE-LIF for GWAS.

Trait Code	Glycan Trait	Trait Description	Formula
CGE_IGP1	P1	% A2G2S2 glycan in total IgG glycans	P1 /Ptotal*100
CGE_IGP2	P2	% A2G2S2 glycan in total IgG glycans	P2 /Ptotal*100
CGE_IGP3	P3	% A2BG2S2 glycan in total IgG glycans	P2 /Ptotal*100
CGE_IGP4	P4	% FA2G2S2 glycan in total IgG glycans	P4 /Ptotal*100
CGE_IGP5	P5	% FA2BG2S2 glycan in total IgG glycans	P5 /Ptotal*100
CGE_IGP6	P6	% A2G1S1[3] glycan in total IgG glycans	P6 /Ptotal*100
CGE_IGP7	P7	% FA2G1S1[3] glycan in total IgG glycans	P7 /Ptotal*100
CGE_IGP8	P8	% A2G2S1[3] glycan in total IgG glycans	P8 /Ptotal*100
CGE_IGP9	P9	% A2BG2S1 glycan in total IgG glycans	P9 /Ptotal*100
CGE_IGP10	P10	% A2BG2S1 glycan in total IgG glycans	P10 /Ptotal*100
CGE_IGP11	P11	% FA2G2S1 glycan in total IgG glycans	P11 /Ptotal*100
CGE_IGP12	P12	% FA2BG2S1 glycan in total IgG glycans	P12 /Ptotal*100
CGE_IGP13	P13	% A2B glycan in total IgG glycans	P13 /Ptotal*100
CGE_IGP14	P14	% FA2 glycan in total IgG glycans	P14 /Ptotal*100
CGE_IGP15	P15	% A2[6]G1 glycan in total IgG glycans	P15 /Ptotal*100
CGE_IGP16	P16	% A2[3]G1 glycan in total IgG glycans	P16 /Ptotal*100
CGE_IGP17	P17	% FA2B glycan in total IgG glycans	P17/Ptotal*100
CGE_IGP18	P18	% A2BG1 glycan in total IgG glycans	P18 /Ptotal*100
CGE_IGP19	P19	% FA2[6]G1 glycan in total IgG glycans	P19 /Ptotal*100
CGE_IGP20	P20	% FA2[3]G1 glycan in total IgG glycans	P20 /Ptotal*100
CGE_IGP21	P21	% FA2[6]BG1 glycan in total IgG glycans	P21 /Ptotal*100
CGE_IGP22	P22	% FA2[3]BG1 glycan in total IgG glycans	P22 /Ptotal*100
CGE_IGP23	P23	% A2BG2 glycan in total IgG glycans	P23 /Ptotal*100

Trait Code	Glycan Trait	Trait Description	Formula
CGE_IGP24	P24	% FA2G2 glycan in total IgG glycans	P24 /Ptotal*100
CGE_IGP25	P25	% FA2BG2 glycan in total IgG glycans	P25 /Ptotal*100
CGE_IGP26	FGS/(FG+FGS)	% sialylation of fucosylated galactosylated structures without bisecting GlcNAc in total IgG glycans	SUM(P4+P7+P11)/SUM(P4+P7 +P11+P19+P20+P24)*100
CGE_IGP27	FBGS/(FBG+F BGS)	% sialylation of fucosylated galactosylated structures with bisecting GlcNAc in total IgG glycans	SUM(P5+P12)/SUM(P5+P12+P2 1+P22+P25)*100
CGE_IGP28	FGS/(F+FG+FG S)	% sialylation of all fucosylated structures without bisecting GlcNAc in total IgG glycans	SUM(P4+P7+P11)/SUM(P4+P7 +P11+P14+P19+P20+P24)*100
CGE_IGP29	FBGS/(FB+FB G+FBGS)	% sialylation of all fucosylated structures with bisecting GlcNAc in total IgG glycans	SUM(P5+P12)/SUM(P5+P12+P1 7+P21+P22+P25)*100
CGE_IGP30	FG1S1/(FG1+F G1S1)	% monosialylation of fucosylated monogalactosylated structures without bisecting GlcNAc in total IgG glycans	P7/SUM(P7+P19+P20)*100
CGE_IGP31	FG2S1/(FG2+F G2S1+FG2S2)	% monosialylation of fucosylated digalactosylated structures without bisecting GlcNAc in total IgG glycans	P11/SUM(P24+P11+P4)*100
CGE_IGP32	FG2S2/(FG2+F G2S1+FG2S2)	% disialylation of fucosylated digalactosylated structures without bisecting GlcNAc in total IgG glycans	P4/SUM(P24+P11+P4)*100
CGE_IGP33	FBG2S1/(FBG2 +FBG2S1+FBG 2S2)	% monosialylation of fucosylated digalactosylated structures with bisecting GlcNAc in total IgG glycans	P12/SUM(P25+P12+P5)*100
CGE_IGP34	FBG2S2/(FBG2 +FBG2S1+FBG 2S2)	% disialylation of fucosylated digalactosylated structures with bisecting GlcNAc in total IgG glycans	P5/SUM(P25+P12+P5)*100
CGE_IGP35	FtotalS1/FtotalS 2	Ratio of all fucosylated monosialylated and disialylated structures (+/- bisecting GlyNAc) in total IgG glycans	SUM(P7+P11+P12)/SUM(P4+P5)
CGE_IGP36	FS1/FS2	Ratio of fucosylated monosialylated and disialylated structures (without bisecting GlcNAc) in total IgG glycans	SUM(P11+P7)/P4

Trait Code	Glycan Trait	Trait Description	Formula
CGE_IGP37	FBS1/FBS2	Ratio of fucosylated monosialylated and disialylated structures (with bisecting GlcNAc) in total IgG glycans	P12/P5
CGE_IGP38	FBStotal/FStotal	Ratio of all fucosylated sialylated structures with and without bisecting GlcNAc in total IgG glycans	SUM(P5+P12)/SUM(P4+P7+P11)
CGE_IGP39	FBS1/FS1	Ratio of fucosylated monosialylated structures with and without bisecting GlcNAc in total IgG glycans	P12/SUM(P7+P11)
CGE_IGP40	FBS1/(FS1+FBS1)	The incidence of bisecting GlcNAc in all fucosylated monosialylated structures in total IgG glycans in total IgG glycans	P12/SUM(P7+P11+P12)*100
CGE_IGP41	FBS2/FS2	Ratio of fucosylated disialylated structures with and without bisecting GlcNAc in total IgG glycans	P5/P4
CGE_IGP42	FBS2/(FS2+FBS2)	The incidence of bisecting GlcNAc in all fucosylated disialylated structures in total IgG glycans	P5/SUM(P5+P4)*100
CGE_IGP43	P13n	% A2B glycan in total neutral IgG glycans (Pn)	P13n/Pntotal*100
CGE_IGP44	P14n	% FA2 glycan in total neutral IgG glycans (Pn)	P14n/Pntotal*100
CGE_IGP45	P15n	% A2[6]G1 glycan in total neutral IgG glycans (Pn)	P15n/Pntotal*100
CGE_IGP46	P16n	% A2[3]G1 glycan in total neutral IgG glycans (Pn)	P16n/Pntotal*100
CGE_IGP47	P17n	% FA2B glycan in total neutral IgG glycans (Pn)	P17n/Pntotal*100
CGE_IGP48	P18n	% A2BG1 glycan in total neutral IgG glycans (Pn)	P18n/Pntotal*100
CGE_IGP49	P19n	% FA2[6]G1 glycan in total neutral IgG glycans (Pn)	P19n/Pntotal*100
CGE_IGP50	P20n	% FA2[3]G1 glycan in total neutral IgG glycans (Pn)	P20n/Pntotal*100
CGE_IGP51	P21n	% FA2[6]BG1 glycan in total neutral IgG glycans (Pn)	P21n/Pntotal*100
CGE_IGP52	P22n	% FA2[3]BG1 glycan in total neutral IgG glycans (Pn)	P22n/Pntotal*100
CGE_IGP53	P23n	% A2BG2 glycan in total neutral IgG glycans (Pn)	P23n/Pntotal*100

Trait Code	Glycan Trait	Trait Description	Formula
CGE_IGP54	P24n	% FA2G2 glycan in total neutral IgG glycans (Pn)	P24n/Pntotal*100
CGE_IGP55	P25n	% FA2BG2 glycan in total neutral IgG glycans (Pn)	P25n/Pntotal*100
CGE_IGP56	G0n	% agalactosylated structures in total neutral IgG glycans	SUM(P13n+P14n+P17n)
CGE_IGP57	G1n	% monogalactosylated structures in total neutral IgG glycans	SUM(P15n+P16n+P18n+P19n+P20n+P21n+P22n)
CGE_IGP58	G2n	% digalactosylated structures in total neutral IgG glycans	SUM(P23n+P24n+P25n)
CGE_IGP59	Fn total	% all fucosylated structures (+/- bisecting GlcNAc) in total neutral IgG glycans	SUM(P14n+P17n+P19n+P20n+P21n+P22n+P24n+P25n)
CGE_IGP60	FG0n total/G0n	% fucosylation of agalactosylated structures in total neutral IgG glycans	SUM(P14n+P17n)/G0n*100
CGE_IGP61	FG1n total/G1n	% fucosylation of monogalactosylated structures in total neutral IgG glycans	SUM(P19n+P20n+P21n+P22n)/ G1n*100
CGE_IGP62	FG2n total /G2n	% fucosylation of digalactosylated structures in total neutral IgG glycans	SUM(P24n+P25n)/G2n*100
CGE_IGP63	Fn	% fucosylated structures (without bisecting GlcNAc) in total neutral IgG glycans	SUM(P14n+P19n+P20n+P24n)
CGE_IGP64	FG0n/G0n	% fucosylation of agalactosylated structures (without bisecting GlcNAc) in total neutral IgG glycans	P14n/G0n*100
CGE_IGP65	FG1n/G1n	% fucosylation of monogalactosylated structures (without bisecting GlcNAc) in total neutral IgG glycans	SUM(P19n+P20n)/G1n*100
CGE_IGP66	FG2n/G2n	% fucosylation of digalactosylated structures (without bisecting GlcNAc) in total neutral IgG glycans	P24n/G2n*100
CGE_IGP67	FBn	% fucosylated structures (with bisecting GlcNAc) in total neutral IgG glycans	SUM(P17n+P21n+P22n+P25n)
CGE_IGP68	FBG0n/G0n	% fucosylation of agalactosylated structures (with bisecting GlcNAc) in total neutral IgG glycans	P17n/G0n*100

Trait Code	Glycan Trait	Trait Description	Formula
CGE_IGP69	FBG1n/G1n	% fucosylation of monogalactosylated structures (with bisecting GlcNAc) in total neutral IgG glycans	SUM(P21n+P22n)/G1n*100
CGE_IGP70	FBG2n/G2n	% fucosylation of digalactosylated structures (with bisecting GlcNAc) in total neutral IgG glycans	P25n/G2n*100
CGE_IGP71	Bn	The incidence of bisecting GlcNAc (without core Fuc) in total neutral IgG glycans	SUM(P13n+P18n+P23n)
CGE_IGP72	BG0n/G0n	The incidence of bisecting GlcNAc (without core Fuc) in agalactosylated structures in total neutral IgG glycans	P13n/G0n*100
CGE_IGP73	BG1n/G1n	The incidence of bisecting GlcNAc (without core Fuc) in monogalactosylated structures in total neutral IgG glycans	P18n/G1n*100
CGE_IGP74	BG2n/G2n	The incidence of bisecting GlcNAc (without core Fuc) in digalactosylated structures in total neutral IgG glycans	P23n/G2n*100
CGE_IGP75	Bn total	The incidence of bisecting GlcNAc (+/- core Fuc) in total neutral IgG glycans	SUM(P13n+P17n+P18n+P21n+P22n+P23n+P25n)
CGE_IGP76	BG0n total/G0n	The incidence of bisecting GlcNAc (+/- core Fuc) in agalactosylated structures in total neutral IgG glycans	SUM(P13n+P17n)/G0n*100
CGE_IGP77	BG1n total/G1n	The incidence of bisecting GlcNAc (+/- core Fuc) in monogalactosylated structures in total neutral IgG glycans	SUM(P18n+P21n+P22n)/G1n*100
CGE_IGP78	BG2n total /G2n	The incidence of bisecting GlcNAc (+/- core Fuc) in digalactosylated structures in total neutral IgG glycans	SUM(P23n+P25n)/G2n*100
CGE_IGP79	Fn/Bn	Ratio of fucosylated structures without bisecting GlcNAc and afucosylated structures with bisecting GlcNAc in neutral IgG1 glycan fraction	Fn/Bn
CGE_IGP80	Fn/Bn total	Ratio of fucosylated non-bisecting GlcNAc structures and all structures with bisecting GlcNAc in total neutral IgG glycans	Fn/Bn total

Trait Code	Glycan Trait	Trait Description	Formula
CGE_IGP81	FBn/Fn	Ratio of fucosylated structures with and without bisecting GlcNAc in total neutral IgG glycans	FBn/Fn
CGE_IGP82	Bn/Fn total	Ratio of structures with bisecting GlcNAc and all fucosylated structures (+/- bisecting GlcNAc) in total neutral IgG glycans	Bn/Fn total*1000
CGE_IGP83	FBn/Fn total	The incidence of bisecting GlcNAc in all fucosylated structures in total neutral IgG glycans	FBn/Fn total*100
CGE_IGP84	FBn/Bn total	% fucosylation in all structures with bisecting GlcNAc in neutral IgG1 glycan fraction	FBn/Bn total*100
CGE_IGP85	FBG0n/FG0n	Ratio of fucosylated agalactosylated structures with and without bisecting GlcNAc in total neutral IgG glycans	P17n/P14n
CGE_IGP86	FBG0n /(FG0n + FBG0n)	The incidence of bisecting GlcNAc in all fucosylated agalactosylated structures in total neutral IgG glycans	P17n/SUM(P14n+P17n)*100
CGE_IGP87	FBG1n/FG1n	Ratio of fucosylated monogalactosylated structures with and without bisecting GlcNAc in total neutral IgG glycans	SUM(P21n+P22n)/SUM(P19n+P20n)
CGE_IGP88	FBG1n /(FG1n + FBG1n)	The incidence of bisecting GlcNAc in all fucosylated monogalactosylated structures in total neutral IgG glycans	SUM(P21n+P22n)/SUM(P19n+P20n+P21n+P22n)*100
CGE_IGP89	FBG2n/FG2n	Ratio of fucosylated digalactosylated structures with and without bisecting GlcNAc in total neutral IgG glycans	P25n/P24n
CGE_IGP90	FBG2n /(FG2n + FBG2n)	The incidence of bisecting GlcNAc in all fucosylated digalactosylated structures in total neutral IgG glycans	P25n/SUM(P24n+P25n)*100
CGE_IGP91	BG1n/G1n	Ratio of afucosylated monogalactosylated structures with and without bisecting GlcNAc in total neutral IgG glycans	P18n/SUM(P15n+P16n)

Trait Code	Glycan Trait	Trait Description	Formula
CGE_IGP92	BG1n /(G1n + BG1n)	The incidence of bisecting GlcNAc in all afucosylated monogalactosylated structures in total neutral IgG glycans	P18n/SUM(P15n+P16n+P18n)*100

Ptotal = SUM(P1:P25), Pntotal = SUM(P13n:P25n); n= neutral; F at the start of the abbreviation indicates a core fucose α1-6 linked to the inner GlcNAc; Mx, number (x) of mannose on core GlcNAcs; Ax, number of antenna (GlcNAc) on trimannosyl core; A2, biantennary with both GlcNAcs as β1-2 linked; B, bisecting GlcNAc linked β1-4 to β1-3 mannose; Gx, number (x) of β1-4 linked galactose on antenna; [3]G1 and [6]G1 indicates that the galactose is on the antenna of the α1-3 or α1-6 mannose; F(x), number (x) of fucose linked α1-3 to antenna GlcNAc; Sx, number (x) of sialic acids linked to galactose.

Table 22: Overview of samples and methods used for all *N*-glycan analyses presented in this thesis.

	Total *N*-Glycan GWAS			MODY3 Biomarker Study	IgG *N*-Glycan GWAS		IgG *N*-Glycan Method Comparison
Genotype Data Used	Genotype	HapMap2	Exome Chip	NA	HapMap2	Exome Chip	Genotype
Cohorts Involved in Discovery (N)	Vis (900) Korcula (896) ORCADES (886) NSPHS (652)	Vis (894) Korcula (896) ORCADES (886) NSPHS (652)	Korcula (791)	MODY3 cases from Edinburgh (14) and Oxford (19) T2D cases from Oxford(41) Non-diabetic controls from ORCADES (59)	Vis (802) Korcula (851) ORCADES (415) NSPHS (179)	Korcula (855)	Vis (445) Korcula (655)
Cohort(s) Involved in Replication (N)	NA			NA	LLS (1848)	NA	NA
***N*-Glycan Method**	HPLC			HPLC	UPLC (discovery) MALDI-TOF-MS (replication)	UPLC	UPLC MALDI-TOF-MS LC-ESI-MS xCGE-LIF
Publication Status	PLoS Genet (2010) [112] Hum Mol Genet (2011) [111]	Thesis Chapter 3	Thesis Chapter 3	Thesis Chapter 4*	PLoS Genet (2013) [184] Thesis Chapter 5	Thesis Chapter 5	Mol Cell Proteomics (2014) [83] Thesis Chapter 6

*further analysis was undertaken in another centre by another investigator using more samples and this was published in Diabetes (2013) [167].

Table 23: Testing for effect size differences between men and women for significant total *N*-glycan SNPs.

Gene	Trait	SNP	Major, minor allele (MAF)	Females only		Males only		P-value
				Beta*	SE	Beta*	SE	
FUT6	GP14	rs3760776	G,A (0.13)	-0.293	0.052	-0.342	0.058	0.53
FUT6	DG7	rs3760776	G,A (0.13)	-0.314	0.051	-0.425	0.059	0.16
FUT6	DG9	rs3760776	G,A (0.13)	-0.427	0.052	-0.445	0.058	0.82
FUT6	DG12	rs3760776	G,A (0.13)	-0.375	0.051	-0.298	0.058	0.32
FUT6	A-FUC	rs3760776	G,A (0.13)	-0.305	0.051	-0.408	0.059	0.18
FUT8	GP1	rs7159888	G,A (0.45)	0.249	0.034	0.260	0.040	0.83
FUT8	GP10	rs10483776	A,G (0.21)	-0.282	0.042	-0.215	0.049	0.30
FUT8	DG1	rs11621121	A,G (0.43)	0.281	0.034	0.248	0.041	0.53
FUT8	DG6	rs10483776	A,G (0.21)	-0.228	0.042	-0.150	0.049	0.23
FUT8	DG10	rs10483776	A,G (0.21)	-0.158	0.043	-0.191	0.048	0.61
FUT8	C-FUC	rs10483776	A,G (0.21)	-0.203	0.042	-0.150	0.049	0.42
FUT8	A2	rs7159888	G,A (0.45)	0.248	0.034	0.280	0.041	0.55
HNF1A	GP13	rs735396	A,G (0.40)	0.169	0.035	0.179	0.040	0.85
HNF1A	GP15	rs735396	A,G (0.40)	0.140	0.035	0.149	0.040	0.87
HNF1A	DG7	rs735396	A,G (0.39)	-0.169	0.035	-0.206	0.041	0.49
HNF1A	DG9	rs7953249	A,G (0.47)	-0.153	0.034	-0.207	0.039	0.30
HNF1A	DG11	rs735396	A,G (0.39)	0.157	0.035	0.163	0.040	0.91
HNF1A	A-FUC	rs735396	A,G (0.40)	-0.146	0.034	-0.187	0.041	0.44
MGAT5	DG11	rs1257220	G,A (0.26)	0.220	0.037	0.146	0.045	0.20
MGAT5	TA	rs1257220	G,A (0.26)	0.221	0.037	0.136	0.045	0.14
B3GAT1	DG13	rs7928758	A,C (0.12)	-0.271	0.053	-0.169	0.061	0.20
SLC9A9	TetraS	rs4839604	G,A (0.23)	0.203	0.041	0.253	0.046	0.42

MAF: minor allele frequency; SE: standard error of beta
*for minor allele, z-score units for trait adjusted for age and principal components

Table 24: SNP associations with P-value<1E-07 in total plasma *N*-glycans GWAS analysed by HPLC.

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
GP1	rs3094093	6	30787607	T	0.10	0.76	0.247	0.044	1.69E-08
GP1	rs1256519	14	64806077	G	0.44	0.89	-0.178	0.027	8.78E-11
GP1	rs7159888	14	64828395	G	0.55	0.99	-0.248	0.026	5.12E-21
GP1	rs12431963	14	64829447	C	0.92	0.93	-0.340	0.050	8.82E-12
GP1	rs1256540	14	64833822	C	0.42	1.00	0.217	0.026	2.52E-16
GP1	rs4902383	14	64834326	C	0.19	0.94	0.255	0.033	2.95E-14
GP1	rs1269068	14	64837086	C	0.58	1.00	-0.217	0.026	2.28E-16
GP1	rs1760978	14	64840800	G	0.43	0.98	0.257	0.027	3.29E-22
GP1	rs10144975	14	64843735	C	0.80	0.98	-0.259	0.032	6.40E-16
GP1	rs17102587	14	64844230	C	0.20	0.98	0.263	0.032	2.69E-16
GP1	rs8017974	14	64844940	C	0.20	0.99	0.264	0.032	1.97E-16
GP1	rs11847263	14	64845448	G	0.39	0.99	0.289	0.027	1.12E-26
GP1	rs10132229	14	64847313	G	0.10	1.00	0.308	0.043	6.54E-13
GP1	rs4902386	14	64848043	C	0.80	0.99	-0.263	0.032	1.85E-16
GP1	rs10147958	14	64848586	C	0.10	1.00	0.308	0.043	6.36E-13
GP1	rs8019473	14	64848881	G	0.80	0.99	-0.263	0.032	1.80E-16
GP1	rs10138662	14	64849235	G	0.20	1.00	0.264	0.032	1.71E-16
GP1	rs10134589	14	64850987	T	0.20	0.94	0.268	0.033	8.11E-16
GP1	rs7151212	14	64851375	C	0.80	1.00	-0.264	0.032	1.59E-16
GP1	rs11158587	14	64852465	G	0.80	1.00	-0.264	0.032	1.56E-16
GP1	rs8019767	14	64852538	G	0.80	1.00	-0.264	0.032	1.55E-16
GP1	rs6573598	14	64852772	C	0.20	1.00	0.264	0.032	1.52E-16
GP1	rs6573599	14	64852880	C	0.80	1.00	-0.264	0.032	1.44E-16
GP1	rs10144503	14	64853862	G	0.90	1.00	-0.309	0.043	5.15E-13
GP1	rs6573602	14	64854363	C	0.20	1.00	0.264	0.032	1.38E-16
GP1	rs17102598	14	64854613	G	0.80	1.00	-0.264	0.032	1.36E-16
GP1	rs12436299	14	64854947	G	0.90	1.00	-0.309	0.043	4.92E-13
GP1	rs6573604	14	64857694	C	0.20	1.00	0.264	0.032	1.33E-16
GP1	rs9635250	14	64869101	T	0.10	1.00	0.310	0.043	4.51E-13
GP1	rs12881755	14	64871564	G	0.66	0.96	-0.197	0.029	5.30E-12
GP1	rs747541	14	64875163	C	0.44	0.97	0.230	0.027	8.93E-18
GP1	rs1954052	14	64875462	T	0.43	0.99	0.230	0.027	8.07E-18
GP1	rs12436465	14	64876630	C	0.73	0.98	-0.170	0.030	1.34E-08
GP1	rs12886005	14	64879000	C	0.44	0.87	0.222	0.028	3.72E-15
GP1	rs12886168	14	64879039	C	0.44	0.98	0.230	0.027	8.00E-18
GP1	rs11623920	14	64889067	C	0.57	1.00	-0.230	0.027	6.80E-18
GP1	rs11621121	14	64892246	C	0.43	1.00	0.229	0.027	6.91E-18
GP1	rs10148907	14	64903125	C	0.70	0.98	-0.270	0.029	3.11E-20
GP1	rs4902393	14	64909267	C	0.57	0.99	-0.227	0.027	2.55E-17
GP1	rs11621604	14	64910527	G	0.58	0.98	-0.220	0.027	3.33E-16
GP1	rs12882269	14	64916897	G	0.58	0.98	-0.217	0.027	7.93E-16
GP1	rs11158591	14	64925515	C	0.42	0.98	0.214	0.027	1.49E-15
GP1	rs11158592	14	64929721	G	0.48	0.99	0.219	0.026	4.08E-17
GP1	rs11158593	14	64929737	G	0.49	0.99	0.219	0.026	3.26E-17
GP1	rs10138570	14	64929791	G	0.51	0.99	-0.219	0.026	3.32E-17
GP1	rs10138671	14	64929845	G	0.59	0.99	-0.146	0.026	3.22E-08
GP1	rs4587890	14	64933537	T	0.41	0.99	0.146	0.026	3.29E-08
GP1	rs2411823	14	64934819	C	0.41	0.99	0.146	0.026	3.38E-08
GP1	rs17246007	14	64935424	C	0.08	0.99	0.277	0.049	1.57E-08
GP1	rs11844747	14	64939881	C	0.08	0.99	0.277	0.049	1.51E-08
GP1	rs17246035	14	64943883	G	0.08	1.00	0.278	0.049	1.30E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
GP1	rs2411822	14	64948148	G	0.49	1.00	-0.198	0.026	2.73E-14
GP1	rs1953416	14	64948560	C	0.51	1.00	0.198	0.026	2.39E-14
GP1	rs1953417	14	64948662	C	0.92	1.00	-0.279	0.049	1.25E-08
GP1	rs883081	14	64950374	C	0.51	1.00	0.198	0.026	2.24E-14
GP1	rs883082	14	64950693	G	0.49	1.00	-0.198	0.026	2.54E-14
GP1	rs7145574	14	64954155	C	0.92	1.00	-0.279	0.049	1.25E-08
GP1	rs867972	14	64965514	C	0.50	0.97	-0.199	0.026	3.76E-14
GP1	rs11851576	14	64970036	C	0.55	0.99	-0.175	0.026	3.61E-11
GP1	rs12879971	14	64971357	G	0.51	0.99	0.201	0.026	1.12E-14
GP1	rs12892058	14	64973194	C	0.49	0.99	-0.203	0.026	6.55E-15
GP1	rs10483776	14	64984620	G	0.21	1.00	0.204	0.033	4.88E-10
GP1	rs17826580	14	64985015	C	0.08	1.00	0.280	0.049	1.07E-08
GP1	rs2184602	14	64985425	G	0.08	1.00	0.280	0.049	1.07E-08
GP1	rs2152375	14	64985531	C	0.08	1.00	0.280	0.049	1.07E-08
GP1	rs12589698	14	64990188	G	0.50	0.98	0.208	0.026	2.16E-15
GP1	rs4899179	14	64996501	G	0.50	0.99	-0.208	0.026	1.79E-15
GP1	rs2184603	14	65000423	C	0.50	0.99	-0.208	0.026	1.72E-15
GP1	rs11850847	14	65003551	C	0.92	1.00	-0.280	0.049	1.06E-08
GP1	rs12434585	14	65008121	G	0.08	1.00	0.280	0.049	1.06E-08
GP1	rs3825640	14	65030957	C	0.50	1.00	0.208	0.026	1.30E-15
GP1	rs11627084	14	65048589	G	0.50	1.00	-0.207	0.026	1.57E-15
GP1	rs10483780	14	65049923	C	0.51	1.00	-0.207	0.026	2.22E-15
GP1	rs2149841	14	65080072	C	0.50	0.99	0.207	0.026	1.69E-15
GP1	rs7153679	14	65082707	G	0.08	1.00	0.282	0.049	8.72E-09
GP1	rs11621680	14	65084434	G	0.51	1.00	-0.205	0.026	4.29E-15
GP1	rs11851013	14	65085965	G	0.08	1.00	0.282	0.049	8.68E-09
GP1	rs11623662	14	65090945	G	0.61	0.99	-0.157	0.027	3.89E-09
GP1	rs11851772	14	65091800	C	0.92	1.00	-0.282	0.049	8.56E-09
GP1	rs9972106	14	65092884	T	0.61	0.99	-0.157	0.027	4.00E-09
GP1	rs11158601	14	65095116	G	0.50	1.00	-0.204	0.026	4.32E-15
GP1	rs7146742	14	65102687	G	0.41	0.99	0.188	0.027	2.29E-12
GP1	rs1958561	14	65106514	G	0.50	1.00	-0.204	0.026	3.75E-15
GP1	rs12887134	14	65115296	C	0.50	1.00	-0.205	0.026	3.03E-15
GP1	rs7155541	14	65115995	C	0.50	1.00	-0.205	0.026	3.00E-15
GP1	rs6573615	14	65116287	G	0.39	0.99	0.157	0.027	4.27E-09
GP1	rs7160780	14	65122466	G	0.39	1.00	0.160	0.027	1.89E-09
GP1	rs7161123	14	65122654	G	0.50	1.00	0.208	0.026	1.21E-15
GP1	rs2411356	14	65122914	G	0.39	1.00	0.160	0.027	1.86E-09
GP1	rs12433827	14	65125363	G	0.92	1.00	-0.281	0.049	9.77E-09
GP1	rs4581615	14	65125696	C	0.50	1.00	0.208	0.026	1.21E-15
GP1	rs8005309	14	65126261	T	0.92	1.00	-0.281	0.049	9.80E-09
GP1	rs17753508	14	65127205	G	0.21	1.00	0.206	0.033	4.06E-10
GP1	rs3783709	14	65128417	T	0.50	1.00	0.208	0.026	1.21E-15
GP1	rs12889002	14	65133335	C	0.50	1.00	0.208	0.026	1.21E-15
GP1	rs743085	14	65137886	G	0.50	1.00	-0.208	0.026	1.21E-15
GP1	rs17826724	14	65138073	C	0.08	1.00	0.280	0.049	1.15E-08
GP1	rs11849252	14	65139522	G	0.92	1.00	-0.280	0.049	1.16E-08
GP1	rs7140341	14	65140170	C	0.33	1.00	0.152	0.028	4.87E-08
GP1	rs11158603	14	65141793	C	0.33	1.00	0.152	0.028	4.87E-08
GP1	rs17826736	14	65151955	C	0.08	1.00	0.280	0.049	1.21E-08
GP1	rs2073294	14	65152246	C	0.92	1.00	-0.280	0.049	1.21E-08
GP1	rs8012278	14	65152326	G	0.50	1.00	-0.211	0.026	4.51E-16
GP1	rs8019762	14	65156931	G	0.67	1.00	-0.153	0.028	4.67E-08
GP1	rs2268956	14	65159898	G	0.33	1.00	0.153	0.028	4.66E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
GP1	rs11849862	14	65167778	G	0.08	1.00	0.279	0.049	1.25E-08
GP1	rs10873191	14	65180381	C	0.67	1.00	-0.153	0.028	4.59E-08
GP1	rs7144345	14	65181594	C	0.67	1.00	-0.153	0.028	4.44E-08
GP1	rs2268957	14	65182986	C	0.92	1.00	-0.279	0.049	1.30E-08
GP1	rs12890902	14	65186375	T	0.50	1.00	0.211	0.026	3.65E-16
GP1	rs2300865	14	65189768	C	0.50	1.00	-0.211	0.026	3.60E-16
GP1	rs7144971	14	65190403	G	0.33	1.00	0.153	0.028	4.36E-08
GP1	rs10143206	14	65190428	C	0.33	1.00	0.153	0.028	4.41E-08
GP1	rs11627184	14	65191196	C	0.50	1.00	0.211	0.026	3.61E-16
GP1	rs12435908	14	65191221	C	0.92	1.00	-0.279	0.049	1.30E-08
GP1	rs11627185	14	65191245	G	0.50	1.00	-0.211	0.026	3.61E-16
GP1	rs1998035	14	65195983	G	0.08	1.00	0.279	0.049	1.30E-08
GP1	rs2268958	14	65197991	T	0.08	1.00	0.279	0.049	1.30E-08
GP1	rs7142651	14	65202474	C	0.50	1.00	0.211	0.026	5.21E-16
GP1	rs1998036	14	65207952	C	0.50	1.00	-0.210	0.026	5.38E-16
GP1	rs2268959	14	65215071	C	0.79	1.00	-0.208	0.033	2.05E-10
GP1	rs2268960	14	65215253	G	0.07	0.98	0.298	0.051	6.06E-09
GP1	rs2268961	14	65216518	C	0.50	1.00	-0.210	0.026	5.55E-16
GP1	rs2268962	14	65217026	G	0.50	1.00	-0.210	0.026	5.57E-16
GP1	rs2300871	14	65217447	C	0.08	1.00	0.279	0.049	1.30E-08
GP1	rs2300872	14	65217514	G	0.08	1.00	0.278	0.049	1.51E-08
GP1	rs2064694	14	65217999	G	0.50	1.00	0.207	0.026	1.39E-15
GP1	rs12588838	14	65232391	G	0.50	1.00	0.207	0.026	1.46E-15
GP1	rs8019491	14	65237863	G	0.08	1.00	0.278	0.049	1.59E-08
GP1	rs11628765	14	65238202	C	0.50	1.00	-0.207	0.026	1.53E-15
GP1	rs2411351	14	65241294	C	0.50	1.00	-0.207	0.026	1.64E-15
GP1	rs11846546	14	65246146	G	0.14	0.99	0.208	0.037	2.01E-08
GP1	rs8018278	14	65249841	G	0.50	1.00	-0.207	0.026	1.61E-15
GP1	rs11627067	14	65252706	G	0.50	1.00	-0.207	0.026	1.57E-15
GP1	rs4143898	14	65258635	T	0.43	0.99	0.190	0.026	7.63E-13
GP1	rs11622829	14	65261535	T	0.49	1.00	0.206	0.026	2.43E-15
GP1	rs11624104	14	65265890	G	0.51	1.00	-0.205	0.026	2.77E-15
GP1	rs1535173	14	65268892	C	0.49	1.00	0.206	0.026	1.94E-15
GP1	rs3742597	14	65269930	G	0.28	1.00	0.266	0.030	2.28E-19
GP1	rs927004	14	65270664	C	0.51	1.00	-0.206	0.026	1.89E-15
GP1	rs1950557	14	65271510	C	0.72	1.00	-0.267	0.030	2.02E-19
GP1	rs8010876	14	65276729	G	0.51	1.00	-0.207	0.026	1.66E-15
GP1	rs1054218	14	65278943	C	0.39	1.00	0.216	0.027	7.65E-16
GP1	rs761830	14	65282739	G	0.39	1.00	0.216	0.027	7.57E-16
GP1	rs10483785	14	65289270	G	0.49	1.00	0.211	0.026	4.15E-16
GP1	rs6573624	14	65296638	G	0.50	0.98	0.214	0.026	2.89E-16
GP1	rs2411405	14	65301839	G	0.53	0.98	-0.222	0.026	2.46E-17
GP1	rs743084	14	65302355	C	0.53	0.97	-0.223	0.026	2.68E-17
GP1	rs11625362	14	65302622	G	0.47	0.98	0.222	0.026	2.43E-17
GP1	rs4080329	14	65303243	C	0.63	0.97	-0.235	0.027	6.73E-18
GP1	rs11627605	14	65304066	G	0.47	0.98	0.223	0.026	2.39E-17
GP1	rs11627578	14	65304201	C	0.47	0.98	0.223	0.026	2.38E-17
GP1	rs11628840	14	65305395	G	0.53	0.98	-0.223	0.026	2.39E-17
GP1	rs1003401	14	65307473	G	0.38	0.98	0.233	0.027	6.66E-18
GP1	rs4902416	14	65307843	C	0.53	0.98	-0.222	0.026	2.48E-17
GP1	rs1984855	14	65309010	C	0.62	0.97	-0.233	0.027	6.61E-18
GP1	rs730807	14	65309043	C	0.47	0.97	0.223	0.026	2.44E-17
GP1	rs2411404	14	65309154	C	0.47	0.97	0.223	0.026	2.43E-17
GP1	rs1075566	14	65309210	C	0.47	0.97	0.223	0.026	2.42E-17

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
GP1	rs7157449	14	65309890	G	0.53	0.97	-0.223	0.026	2.43E-17
GP1	rs6573625	14	65310387	C	0.63	0.97	-0.235	0.027	7.52E-18
GP1	rs6573626	14	65310448	C	0.53	0.97	-0.223	0.026	2.57E-17
GP1	rs7158556	14	65310482	T	0.37	0.97	0.235	0.027	7.33E-18
GP1	rs12894466	14	65310520	G	0.47	0.97	0.223	0.026	2.55E-17
GP1	rs11625882	14	65314952	G	0.47	0.97	0.223	0.026	2.66E-17
GP1	rs2236067	14	65317765	G	0.62	0.97	-0.233	0.027	7.08E-18
GP1	rs968540	14	65318817	G	0.63	0.97	-0.236	0.027	6.05E-18
GP1	rs7142165	14	65319985	G	0.53	0.97	-0.224	0.026	2.19E-17
GP1	rs7143026	14	65320709	G	0.39	0.95	0.227	0.027	1.04E-16
GP1	rs6573627	14	65322079	C	0.52	0.97	-0.217	0.026	2.01E-16
GP1	rs4400971	14	65324331	C	0.42	0.98	0.193	0.027	3.70E-13
GP1	rs7151846	14	65325534	C	0.51	0.98	-0.213	0.026	4.41E-16
GP1	rs4073416	14	65329147	C	0.42	0.98	0.193	0.027	3.76E-13
GP1	rs4073415	14	65329283	G	0.51	0.98	-0.213	0.026	4.58E-16
GP1	rs11850120	14	65330132	C	0.41	0.97	0.194	0.027	4.75E-13
GP1	rs8018379	14	65331690	C	0.57	0.95	-0.204	0.027	4.63E-14
GP1	rs8007846	14	65332716	G	0.47	0.98	0.145	0.026	4.86E-08
GP1	rs8006608	14	65336577	G	0.96	0.81	-0.410	0.074	2.73E-08
GP1	rs10140750	14	65339625	G	0.12	0.78	-0.250	0.043	4.52E-09
GP1	rs3924222	14	65343491	C	0.41	0.80	-0.180	0.029	8.88E-10
GP1	rs10149325	14	65347120	G	0.41	0.79	-0.180	0.029	8.16E-10
GP4	rs1984769	1	159824353	G	0.77	0.48	0.237	0.043	2.54E-08
GP5	rs13107325	4	103407732	C	0.92	0.90	-0.284	0.048	4.73E-09
GP7	rs1820248	16	70597106	G	0.29	0.95	0.155	0.029	8.36E-08
GP7	rs3213423	16	70600326	G	0.75	1.00	-0.190	0.030	1.60E-10
GP7	rs1424241	16	70636408	G	0.79	0.99	-0.173	0.032	4.76E-08
GP7	rs217181	16	70671503	C	0.81	0.92	0.198	0.033	2.72E-09
GP10	rs1794265	6	32782715	C	0.96	0.69	0.341	0.063	7.48E-08
GP10	rs12207186	6	162234911	T	0.06	0.85	-0.303	0.057	9.66E-08
GP10	rs17102601	14	64859324	C	0.18	0.97	-0.188	0.035	8.02E-08
GP10	rs12436465	14	64876630	C	0.73	0.98	0.201	0.030	1.94E-11
GP10	rs10148907	14	64903125	C	0.70	0.98	0.171	0.029	5.17E-09
GP10	rs7150448	14	64941255	C	0.35	1.00	-0.167	0.027	1.22E-09
GP10	rs8013442	14	64941614	G	0.66	1.00	0.172	0.028	4.02E-10
GP10	rs7147536	14	64944451	C	0.36	1.00	-0.167	0.027	6.95E-10
GP10	rs7145500	14	64953965	G	0.35	1.00	-0.164	0.027	1.91E-09
GP10	rs7145759	14	64954290	C	0.35	1.00	-0.165	0.027	1.81E-09
GP10	rs7151561	14	64960356	C	0.65	0.99	0.165	0.027	1.66E-09
GP10	rs2210805	14	64962477	C	0.35	0.99	-0.166	0.027	1.62E-09
GP10	rs2184601	14	64967121	T	0.34	0.99	-0.166	0.027	1.49E-09
GP10	rs11851576	14	64970036	C	0.55	0.99	0.154	0.026	5.10E-09
GP10	rs7157109	14	64970186	C	0.34	0.99	-0.167	0.028	1.34E-09
GP10	rs1999725	14	64973990	G	0.35	0.98	-0.173	0.027	2.77E-10
GP10	rs11158595	14	64976122	G	0.67	0.98	0.178	0.028	2.07E-10
GP10	rs11844682	14	64980597	C	0.67	0.98	0.178	0.028	2.05E-10
GP10	rs10483776	14	64984620	G	0.21	1.00	-0.246	0.033	6.16E-14
GP10	rs1953418	14	64984979	G	0.33	0.98	-0.178	0.028	2.00E-10
GP10	rs12885842	14	64988405	C	0.34	0.98	-0.175	0.028	2.27E-10
GP10	rs7140695	14	64998885	C	0.67	0.99	0.178	0.028	1.91E-10
GP10	rs8010726	14	65002350	G	0.33	0.99	-0.173	0.028	5.71E-10
GP10	rs1889731	14	65012464	C	0.68	1.00	0.177	0.028	2.08E-10
GP10	rs1959144	14	65015804	G	0.68	1.00	0.177	0.028	2.21E-10
GP10	rs2411820	14	65016497	C	0.33	1.00	-0.172	0.028	6.23E-10

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
GP10	rs4902399	14	65026650	G	0.68	1.00	0.177	0.028	2.16E-10
GP10	rs8011224	14	65039423	T	0.33	1.00	-0.172	0.028	6.09E-10
GP10	rs2898818	14	65042337	C	0.68	1.00	0.177	0.028	2.08E-10
GP10	rs7141536	14	65057065	T	0.33	1.00	-0.173	0.028	5.76E-10
GP10	rs1953415	14	65057787	G	0.68	1.00	0.178	0.028	1.98E-10
GP10	rs12147233	14	65064702	C	0.90	0.63	0.310	0.055	1.73E-08
GP10	rs10144979	14	65067391	G	0.33	1.00	-0.173	0.028	5.57E-10
GP10	rs1113962	14	65075551	C	0.33	1.00	-0.173	0.028	5.53E-10
GP10	rs7147636	14	65080937	C	0.67	0.96	0.166	0.028	4.18E-09
GP10	rs2411815	14	65089824	T	0.68	1.00	0.179	0.028	1.60E-10
GP10	rs2898814	14	65093714	C	0.67	1.00	0.174	0.028	4.45E-10
GP10	rs3783711	14	65098199	G	0.68	1.00	0.179	0.028	1.53E-10
GP10	rs3825639	14	65098258	C	0.68	1.00	0.179	0.028	1.53E-10
GP10	rs12433597	14	65098600	C	0.68	1.00	0.179	0.028	1.54E-10
GP10	rs9323461	14	65101158	C	0.68	1.00	0.179	0.028	1.55E-10
GP10	rs7147002	14	65102299	C	0.68	1.00	0.179	0.028	1.56E-10
GP10	rs7146742	14	65102687	G	0.41	0.99	-0.154	0.027	9.35E-09
GP10	rs7158153	14	65104339	C	0.32	1.00	-0.179	0.028	1.59E-10
GP10	rs2183277	14	65105182	C	0.68	1.00	0.179	0.028	1.60E-10
GP10	rs10142283	14	65113882	G	0.33	1.00	-0.174	0.028	4.70E-10
GP10	rs8007497	14	65114229	C	0.68	1.00	0.179	0.028	1.63E-10
GP10	rs6573616	14	65116569	G	0.69	0.95	0.183	0.029	2.15E-10
GP10	rs4902404	14	65116775	C	0.68	1.00	0.179	0.028	1.67E-10
GP10	rs10152007	14	65117187	T	0.68	1.00	0.178	0.028	1.95E-10
GP10	rs7146993	14	65118625	C	0.32	1.00	-0.178	0.028	1.96E-10
GP10	rs17753508	14	65127205	G	0.21	1.00	-0.246	0.033	7.19E-14
GP10	rs12587057	14	65136128	C	0.32	1.00	-0.178	0.028	2.06E-10
GP10	rs7140341	14	65140170	C	0.33	1.00	-0.178	0.028	1.73E-10
GP10	rs11158603	14	65141793	C	0.33	1.00	-0.178	0.028	1.73E-10
GP10	rs2092914	14	65148868	C	0.34	0.99	-0.178	0.028	9.37E-11
GP10	rs8019762	14	65156931	G	0.67	1.00	0.178	0.028	1.73E-10
GP10	rs2268956	14	65159898	G	0.33	1.00	-0.178	0.028	1.73E-10
GP10	rs11158605	14	65177673	T	0.34	0.99	-0.178	0.028	9.67E-11
GP10	rs10873191	14	65180381	C	0.67	1.00	0.178	0.028	1.74E-10
GP10	rs11158607	14	65180550	G	0.66	0.99	0.178	0.027	9.79E-11
GP10	rs7144345	14	65181594	C	0.67	1.00	0.178	0.028	1.75E-10
GP10	rs7144971	14	65190403	G	0.33	1.00	-0.178	0.028	1.77E-10
GP10	rs10143206	14	65190428	C	0.33	1.00	-0.178	0.028	1.73E-10
GP10	rs2268959	14	65215071	C	0.79	1.00	0.245	0.033	7.10E-14
GP10	rs1956010	14	65220843	G	0.35	0.99	-0.183	0.027	2.01E-11
GP10	rs1121885	14	65226667	G	0.67	1.00	0.181	0.028	8.43E-11
GP10	rs4143898	14	65258635	T	0.43	0.99	-0.161	0.026	1.18E-09
GP10	rs3742597	14	65269930	G	0.28	1.00	-0.172	0.030	5.72E-09
GP10	rs1950557	14	65271510	C	0.72	1.00	0.172	0.030	5.70E-09
GP10	rs1054218	14	65278943	C	0.39	1.00	-0.144	0.027	7.08E-08
GP10	rs761830	14	65282739	G	0.39	1.00	-0.144	0.027	7.07E-08
GP10	rs4080329	14	65303243	C	0.63	0.97	0.150	0.027	3.78E-08
GP10	rs1003401	14	65307473	G	0.38	0.98	-0.154	0.027	1.35E-08
GP10	rs1984855	14	65309010	C	0.62	0.97	0.154	0.027	1.35E-08
GP10	rs6573625	14	65310387	C	0.63	0.97	0.150	0.027	3.61E-08
GP10	rs7158556	14	65310482	T	0.37	0.97	-0.150	0.027	3.63E-08
GP10	rs2236067	14	65317765	G	0.62	0.97	0.154	0.027	1.26E-08
GP10	rs968540	14	65318817	G	0.63	0.97	0.151	0.027	3.33E-08
GP10	rs7143026	14	65320709	G	0.39	0.95	-0.152	0.027	2.32E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
GP10	rs4400971	14	65324331	C	0.42	0.98	-0.158	0.027	2.81E-09
GP10	rs4073416	14	65329147	C	0.42	0.98	-0.157	0.027	2.85E-09
GP10	rs11850120	14	65330132	C	0.41	0.97	-0.153	0.027	1.00E-08
GP13	rs7953249	12	119888107	G	0.47	1.00	0.146	0.026	2.70E-08
GP13	rs7979473	12	119904643	G	0.55	0.94	-0.159	0.027	3.72E-09
GP13	rs7979478	12	119904646	G	0.55	0.94	-0.159	0.027	3.67E-09
GP13	rs1183910	12	119905190	G	0.60	0.94	-0.147	0.027	7.57E-08
GP13	rs2393791	12	119908339	C	0.45	0.94	0.159	0.027	3.51E-09
GP13	rs2393775	12	119908957	G	0.45	0.94	0.159	0.027	3.46E-09
GP13	rs7310409	12	119909244	G	0.55	0.94	-0.159	0.027	3.47E-09
GP13	rs1169300	12	119915608	G	0.63	1.00	-0.154	0.027	1.46E-08
GP13	rs2259820	12	119919725	C	0.63	1.00	-0.154	0.027	1.67E-08
GP13	rs2464196	12	119919810	G	0.63	1.00	-0.153	0.027	2.11E-08
GP13	rs2464195	12	119919858	G	0.60	1.00	-0.167	0.027	4.55E-10
GP13	rs2259816	12	119919970	G	0.60	1.00	-0.167	0.027	4.52E-10
GP13	rs1169303	12	119920759	C	0.51	1.00	0.142	0.026	4.72E-08
GP13	rs1169306	12	119922694	C	0.60	0.97	-0.172	0.027	2.18E-10
GP13	rs735396	12	119923227	C	0.40	1.00	0.169	0.027	2.72E-10
GP13	rs1169310	12	119923816	G	0.60	1.00	-0.169	0.027	2.72E-10
GP13	rs1169312	12	119925844	G	0.60	1.00	-0.169	0.027	2.70E-10
GP13	rs1169313	12	119927053	C	0.40	1.00	0.170	0.027	2.66E-10
GP13	rs2257764	12	119930829	T	0.37	1.00	0.155	0.027	1.35E-08
GP13	rs2258287	12	119938696	C	0.61	0.98	-0.150	0.027	3.30E-08
GP13	rs1182933	12	119939005	C	0.63	0.98	-0.156	0.027	1.28E-08
GP13	rs3213545	12	119955720	G	0.64	0.87	-0.156	0.029	8.11E-08
GP13	rs217181	16	70671503	C	0.81	0.92	-0.182	0.034	6.25E-08
GP13	rs3760775	19	5792356	G	0.92	0.79	-0.431	0.052	2.31E-16
GP14	rs8101385	19	5789595	C	0.88	0.91	0.368	0.042	2.49E-18
GP14	rs3760776	19	5790746	G	0.88	0.93	0.367	0.042	1.89E-18
GP14	rs3760775	19	5792356	G	0.92	0.79	0.517	0.053	6.88E-23
GP15	rs7979473	12	119904643	G	0.55	0.94	-0.148	0.027	4.03E-08
GP15	rs7979478	12	119904646	G	0.55	0.94	-0.148	0.027	3.99E-08
GP15	rs2393791	12	119908339	C	0.45	0.94	0.148	0.027	3.92E-08
GP15	rs2393775	12	119908957	G	0.45	0.94	0.148	0.027	3.93E-08
GP15	rs7310409	12	119909244	G	0.55	0.94	-0.148	0.027	3.96E-08
GP15	rs2464195	12	119919858	G	0.60	1.00	-0.146	0.027	4.60E-08
GP15	rs2259816	12	119919970	G	0.60	1.00	-0.146	0.027	4.56E-08
GP15	rs1169306	12	119922694	C	0.60	0.97	-0.151	0.027	2.61E-08
GP15	rs735396	12	119923227	C	0.40	1.00	0.148	0.027	3.09E-08
GP15	rs1169310	12	119923816	G	0.60	1.00	-0.148	0.027	3.09E-08
GP15	rs1169312	12	119925844	G	0.60	1.00	-0.148	0.027	3.11E-08
GP15	rs1169313	12	119927053	C	0.40	1.00	0.148	0.027	3.12E-08
GP16	rs9344613	6	87210387	C	0.15	0.91	0.196	0.037	9.31E-08
DG1	rs1256519	14	64806077	G	0.44	0.90	-0.192	0.028	3.93E-12
DG1	rs7159888	14	64828395	G	0.55	0.99	-0.262	0.027	5.71E-23
DG1	rs12431963	14	64829447	C	0.92	0.93	-0.386	0.050	8.09E-15
DG1	rs1256540	14	64833822	C	0.42	1.00	0.237	0.027	3.47E-19
DG1	rs4902383	14	64834326	C	0.19	0.94	0.283	0.034	4.25E-17
DG1	rs1269068	14	64837086	C	0.58	1.00	-0.237	0.026	3.72E-19
DG1	rs10135194	14	64840731	C	0.94	0.87	-0.359	0.059	9.29E-10
DG1	rs1760978	14	64840800	G	0.43	0.98	0.282	0.027	3.88E-26
DG1	rs10144975	14	64843735	C	0.80	0.98	-0.291	0.032	1.75E-19
DG1	rs17102587	14	64844230	C	0.20	0.98	0.294	0.032	1.01E-19
DG1	rs8017974	14	64844940	C	0.20	0.99	0.293	0.032	1.06E-19

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
DG1	rs11847263	14	64845448	G	0.39	0.99	0.314	0.027	7.57E-31
DG1	rs10132229	14	64847313	G	0.10	1.00	0.349	0.043	3.55E-16
DG1	rs4902386	14	64848043	C	0.80	0.99	-0.292	0.032	1.09E-19
DG1	rs10147958	14	64848586	C	0.10	1.00	0.349	0.043	3.41E-16
DG1	rs8019473	14	64848881	G	0.80	0.99	-0.292	0.032	1.05E-19
DG1	rs10138662	14	64849235	G	0.20	1.00	0.292	0.032	9.89E-20
DG1	rs10134589	14	64850987	T	0.20	0.94	0.300	0.033	2.52E-19
DG1	rs7151212	14	64851375	C	0.80	1.00	-0.293	0.032	9.07E-20
DG1	rs11158587	14	64852465	G	0.80	1.00	-0.293	0.032	8.91E-20
DG1	rs8019767	14	64852538	G	0.80	1.00	-0.293	0.032	8.81E-20
DG1	rs6573598	14	64852772	C	0.20	1.00	0.293	0.032	8.63E-20
DG1	rs6573599	14	64852880	C	0.80	1.00	-0.293	0.032	8.08E-20
DG1	rs10144503	14	64853862	G	0.90	1.00	-0.351	0.043	2.51E-16
DG1	rs6573602	14	64854363	C	0.20	1.00	0.293	0.032	7.66E-20
DG1	rs17102598	14	64854613	G	0.80	1.00	-0.293	0.032	7.58E-20
DG1	rs12436299	14	64854947	G	0.90	1.00	-0.351	0.043	2.34E-16
DG1	rs6573604	14	64857694	C	0.20	1.00	0.293	0.032	7.38E-20
DG1	rs9635250	14	64869101	T	0.10	1.00	0.352	0.043	2.14E-16
DG1	rs12881755	14	64871564	G	0.66	0.96	-0.224	0.029	4.60E-15
DG1	rs747541	14	64875163	C	0.44	0.97	0.271	0.027	5.06E-24
DG1	rs1954052	14	64875462	T	0.43	0.99	0.273	0.027	2.28E-24
DG1	rs12436465	14	64876630	C	0.73	0.98	-0.210	0.030	3.04E-12
DG1	rs12886005	14	64879000	C	0.44	0.87	0.273	0.028	6.34E-22
DG1	rs12886168	14	64879039	C	0.44	0.98	0.271	0.027	4.60E-24
DG1	rs11623920	14	64889067	C	0.57	1.00	-0.273	0.027	1.99E-24
DG1	rs11621121	14	64892246	C	0.43	1.00	0.272	0.027	2.03E-24
DG1	rs10148907	14	64903125	C	0.70	0.98	-0.312	0.029	2.43E-26
DG1	rs4902393	14	64909267	C	0.57	0.98	-0.271	0.027	7.47E-24
DG1	rs11621604	14	64910527	G	0.58	0.98	-0.265	0.027	1.15E-22
DG1	rs12882269	14	64916897	G	0.58	0.98	-0.262	0.027	3.14E-22
DG1	rs11845794	14	64917871	C	0.92	0.98	-0.275	0.049	1.59E-08
DG1	rs11850160	14	64917876	C	0.08	0.98	0.275	0.049	1.62E-08
DG1	rs11850163	14	64917898	T	0.92	0.98	-0.275	0.049	1.63E-08
DG1	rs10083421	14	64920911	C	0.08	0.98	0.275	0.049	1.63E-08
DG1	rs10083525	14	64921309	C	0.08	0.98	0.275	0.049	1.65E-08
DG1	rs17826448	14	64921770	G	0.92	0.99	-0.274	0.049	1.67E-08
DG1	rs17826466	14	64921923	G	0.92	0.99	-0.274	0.049	1.68E-08
DG1	rs10083488	14	64923099	C	0.08	0.99	0.274	0.049	1.69E-08
DG1	rs12433416	14	64923928	G	0.92	0.99	-0.274	0.049	1.70E-08
DG1	rs12433423	14	64923990	C	0.08	0.99	0.274	0.049	1.71E-08
DG1	rs8017202	14	64924711	G	0.08	0.99	0.274	0.049	1.71E-08
DG1	rs11158591	14	64925515	C	0.42	0.98	0.259	0.027	7.07E-22
DG1	rs11158592	14	64929721	G	0.48	0.99	0.253	0.026	3.52E-22
DG1	rs11158593	14	64929737	G	0.49	0.99	0.253	0.026	2.82E-22
DG1	rs10138570	14	64929791	G	0.51	0.99	-0.253	0.026	2.91E-22
DG1	rs10138671	14	64929845	G	0.59	0.99	-0.176	0.027	2.83E-11
DG1	rs4587890	14	64933537	T	0.41	0.99	0.176	0.027	2.90E-11
DG1	rs2411823	14	64934819	C	0.41	0.99	0.176	0.027	2.98E-11
DG1	rs17246007	14	64935424	C	0.08	0.99	0.290	0.049	3.26E-09
DG1	rs11844747	14	64939881	C	0.08	0.99	0.290	0.049	3.18E-09
DG1	rs17246035	14	64943883	G	0.08	1.00	0.292	0.049	2.52E-09
DG1	rs7147536	14	64944451	C	0.36	1.00	0.148	0.027	5.66E-08
DG1	rs2411822	14	64948148	G	0.49	1.00	-0.233	0.026	4.89E-19
DG1	rs1953416	14	64948560	C	0.51	1.00	0.233	0.026	4.63E-19

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
DG1	rs1953417	14	64948662	C	0.92	1.00	-0.292	0.049	2.42E-09
DG1	rs883081	14	64950374	C	0.51	1.00	0.233	0.026	4.41E-19
DG1	rs883082	14	64950693	G	0.49	1.00	-0.233	0.026	4.65E-19
DG1	rs7145500	14	64953965	G	0.35	1.00	0.151	0.027	4.05E-08
DG1	rs7145574	14	64954155	C	0.92	1.00	-0.292	0.049	2.42E-09
DG1	rs7145759	14	64954290	C	0.35	1.00	0.152	0.028	3.51E-08
DG1	rs7151561	14	64960356	C	0.65	0.99	-0.153	0.028	2.98E-08
DG1	rs2210805	14	64962477	C	0.35	0.99	0.153	0.028	2.84E-08
DG1	rs867972	14	64965514	C	0.50	0.97	-0.235	0.026	4.72E-19
DG1	rs2184601	14	64967121	T	0.35	0.99	0.154	0.028	2.42E-08
DG1	rs11851576	14	64970036	C	0.55	0.99	-0.203	0.027	1.88E-14
DG1	rs7157109	14	64970186	C	0.35	0.99	0.155	0.028	1.94E-08
DG1	rs12879971	14	64971357	G	0.51	0.99	0.236	0.026	1.91E-19
DG1	rs12892058	14	64973194	C	0.49	0.99	-0.238	0.026	1.23E-19
DG1	rs1999725	14	64973990	G	0.35	0.98	0.157	0.028	1.28E-08
DG1	rs11158595	14	64976122	G	0.67	0.98	-0.170	0.028	1.51E-09
DG1	rs11844682	14	64980597	C	0.67	0.98	-0.170	0.028	1.43E-09
DG1	rs10483776	14	64984620	G	0.21	1.00	0.249	0.033	3.65E-14
DG1	rs1953418	14	64984979	G	0.33	0.98	0.170	0.028	1.30E-09
DG1	rs17826580	14	64985015	C	0.08	1.00	0.294	0.049	2.01E-09
DG1	rs2184602	14	64985425	G	0.08	1.00	0.294	0.049	2.01E-09
DG1	rs2152375	14	64985531	C	0.08	1.00	0.294	0.049	2.01E-09
DG1	rs12885842	14	64988405	C	0.34	0.98	0.167	0.028	1.67E-09
DG1	rs12589698	14	64990188	G	0.50	0.98	0.242	0.026	2.97E-20
DG1	rs4899179	14	64996501	G	0.50	0.99	-0.243	0.026	2.37E-20
DG1	rs7140695	14	64998885	C	0.67	0.99	-0.172	0.028	8.39E-10
DG1	rs2184603	14	65000423	C	0.50	0.99	-0.243	0.026	2.28E-20
DG1	rs8010726	14	65002350	G	0.33	0.99	0.172	0.028	8.86E-10
DG1	rs11850847	14	65003551	C	0.92	1.00	-0.294	0.049	2.00E-09
DG1	rs12434585	14	65008121	G	0.08	1.00	0.294	0.049	2.00E-09
DG1	rs1889731	14	65012464	C	0.67	1.00	-0.173	0.028	6.89E-10
DG1	rs1959144	14	65015804	G	0.67	1.00	-0.173	0.028	6.98E-10
DG1	rs2411820	14	65016497	C	0.33	1.00	0.172	0.028	7.36E-10
DG1	rs4902399	14	65026650	G	0.67	1.00	-0.173	0.028	6.65E-10
DG1	rs3825640	14	65030957	C	0.50	1.00	0.242	0.026	2.03E-20
DG1	rs8011224	14	65039423	T	0.33	1.00	0.172	0.028	7.58E-10
DG1	rs2898818	14	65042337	C	0.67	1.00	-0.173	0.028	6.94E-10
DG1	rs11627084	14	65048589	G	0.50	1.00	-0.242	0.026	2.25E-20
DG1	rs10483780	14	65049923	C	0.51	1.00	-0.242	0.026	2.37E-20
DG1	rs7141536	14	65057065	T	0.33	1.00	0.172	0.028	8.20E-10
DG1	rs1953415	14	65057787	G	0.67	1.00	-0.173	0.028	7.46E-10
DG1	rs12147233	14	65064702	C	0.90	0.63	-0.297	0.055	7.41E-08
DG1	rs10144979	14	65067391	G	0.33	1.00	0.172	0.028	8.85E-10
DG1	rs1113962	14	65075551	C	0.33	1.00	0.171	0.028	9.01E-10
DG1	rs2149841	14	65080072	C	0.50	0.99	0.241	0.026	2.68E-20
DG1	rs7153679	14	65082707	G	0.08	1.00	0.296	0.049	1.61E-09
DG1	rs11621680	14	65084434	G	0.51	1.00	-0.240	0.026	4.82E-20
DG1	rs11851013	14	65085965	G	0.08	1.00	0.296	0.049	1.60E-09
DG1	rs2411815	14	65089824	T	0.68	1.00	-0.170	0.028	1.35E-09
DG1	rs11623662	14	65090945	G	0.61	0.99	-0.187	0.027	2.60E-12
DG1	rs11851772	14	65091800	C	0.92	1.00	-0.296	0.049	1.58E-09
DG1	rs9972106	14	65092884	T	0.61	0.99	-0.187	0.027	2.67E-12
DG1	rs2898814	14	65093714	C	0.67	1.00	-0.168	0.028	2.04E-09
DG1	rs11158601	14	65095116	G	0.51	1.00	-0.239	0.026	6.71E-20

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
DG1	rs3783711	14	65098199	G	0.68	1.00	-0.169	0.028	1.86E-09
DG1	rs3825639	14	65098258	C	0.68	1.00	-0.169	0.028	1.79E-09
DG1	rs12433597	14	65098600	C	0.68	1.00	-0.169	0.028	1.78E-09
DG1	rs9323461	14	65101158	C	0.68	1.00	-0.169	0.028	1.74E-09
DG1	rs7147002	14	65102299	C	0.68	1.00	-0.169	0.028	1.71E-09
DG1	rs7146742	14	65102687	G	0.41	0.99	0.218	0.027	5.75E-16
DG1	rs7158153	14	65104339	C	0.32	1.00	0.169	0.028	1.64E-09
DG1	rs2183277	14	65105182	C	0.68	1.00	-0.169	0.028	1.63E-09
DG1	rs1958561	14	65106514	G	0.51	1.00	-0.239	0.026	5.87E-20
DG1	rs1958560	14	65106548	G	0.41	1.00	0.159	0.027	2.11E-09
DG1	rs10142283	14	65113882	G	0.33	1.00	0.169	0.028	1.72E-09
DG1	rs8007497	14	65114229	C	0.68	1.00	-0.170	0.028	1.51E-09
DG1	rs12887134	14	65115296	C	0.50	1.00	-0.239	0.026	5.21E-20
DG1	rs7155541	14	65115995	C	0.50	1.00	-0.239	0.026	5.16E-20
DG1	rs6573615	14	65116287	G	0.39	0.99	0.187	0.027	2.92E-12
DG1	rs6573616	14	65116569	G	0.69	0.95	-0.174	0.029	1.88E-09
DG1	rs4902404	14	65116775	C	0.68	1.00	-0.170	0.028	1.45E-09
DG1	rs10152007	14	65117187	T	0.68	1.00	-0.174	0.028	6.21E-10
DG1	rs7146993	14	65118625	C	0.32	1.00	0.174	0.028	6.16E-10
DG1	rs1958559	14	65121808	C	0.41	1.00	0.162	0.026	8.72E-10
DG1	rs7160780	14	65122466	G	0.39	1.00	0.190	0.027	1.16E-12
DG1	rs7161123	14	65122654	G	0.50	1.00	0.242	0.026	1.85E-20
DG1	rs2411356	14	65122914	G	0.39	1.00	0.190	0.027	1.14E-12
DG1	rs12433827	14	65125363	G	0.92	1.00	-0.295	0.049	1.82E-09
DG1	rs4581615	14	65125696	C	0.50	1.00	0.242	0.026	1.85E-20
DG1	rs8005309	14	65126261	T	0.92	1.00	-0.295	0.049	1.83E-09
DG1	rs17753508	14	65127205	G	0.21	1.00	0.251	0.033	2.76E-14
DG1	rs3783709	14	65128417	T	0.50	1.00	0.242	0.026	1.85E-20
DG1	rs12889002	14	65133335	C	0.50	1.00	0.242	0.026	1.85E-20
DG1	rs12587057	14	65136128	C	0.33	1.00	0.174	0.028	5.87E-10
DG1	rs2064695	14	65136841	G	0.59	1.00	-0.162	0.026	8.40E-10
DG1	rs743085	14	65137886	G	0.50	1.00	-0.242	0.026	1.86E-20
DG1	rs17826724	14	65138073	C	0.08	1.00	0.293	0.049	2.27E-09
DG1	rs11849252	14	65139522	G	0.92	1.00	-0.293	0.049	2.30E-09
DG1	rs7140341	14	65140170	C	0.33	1.00	0.176	0.028	3.53E-10
DG1	rs11158603	14	65141793	C	0.33	1.00	0.176	0.028	3.55E-10
DG1	rs17826736	14	65151955	C	0.08	1.00	0.293	0.049	2.43E-09
DG1	rs2073294	14	65152246	C	0.92	1.00	-0.292	0.049	2.44E-09
DG1	rs8012278	14	65152326	G	0.50	1.00	-0.243	0.026	1.12E-20
DG1	rs8019762	14	65156931	G	0.67	1.00	-0.175	0.028	3.70E-10
DG1	rs2268955	14	65159762	T	0.41	1.00	0.165	0.026	5.00E-10
DG1	rs2268956	14	65159898	G	0.33	1.00	0.175	0.028	3.72E-10
DG1	rs11849862	14	65167778	G	0.08	1.00	0.292	0.049	2.56E-09
DG1	rs10873191	14	65180381	C	0.67	1.00	-0.175	0.028	3.83E-10
DG1	rs7144345	14	65181594	C	0.67	1.00	-0.175	0.028	3.80E-10
DG1	rs2268957	14	65182986	C	0.92	1.00	-0.292	0.049	2.73E-09
DG1	rs12890902	14	65186375	T	0.50	1.00	0.243	0.026	1.18E-20
DG1	rs2300865	14	65189768	C	0.50	1.00	-0.243	0.026	1.19E-20
DG1	rs7144971	14	65190403	G	0.33	1.00	0.175	0.028	3.92E-10
DG1	rs10143206	14	65190428	C	0.33	1.00	0.175	0.028	3.97E-10
DG1	rs11627184	14	65191196	C	0.50	1.00	0.243	0.026	1.21E-20
DG1	rs12435908	14	65191221	C	0.92	1.00	-0.292	0.049	2.73E-09
DG1	rs11627185	14	65191245	G	0.50	1.00	-0.243	0.026	1.21E-20
DG1	rs1998035	14	65195983	G	0.08	1.00	0.292	0.049	2.74E-09

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
DG1	rs2268958	14	65197991	T	0.08	1.00	0.292	0.049	2.74E-09
DG1	rs7142651	14	65202474	C	0.50	1.00	0.242	0.026	1.82E-20
DG1	rs1998036	14	65207952	C	0.50	1.00	-0.242	0.026	1.90E-20
DG1	rs2268959	14	65215071	C	0.79	1.00	-0.250	0.033	2.62E-14
DG1	rs2268960	14	65215253	G	0.07	0.98	0.311	0.051	1.19E-09
DG1	rs2268961	14	65216518	C	0.50	1.00	-0.242	0.026	2.03E-20
DG1	rs2268962	14	65217026	G	0.50	1.00	-0.242	0.026	2.05E-20
DG1	rs2300871	14	65217447	C	0.08	1.00	0.292	0.049	2.76E-09
DG1	rs2300872	14	65217514	G	0.08	1.00	0.291	0.049	3.06E-09
DG1	rs2064694	14	65217999	G	0.50	1.00	0.239	0.026	5.72E-20
DG1	rs1121885	14	65226667	G	0.67	1.00	-0.170	0.028	1.18E-09
DG1	rs12588838	14	65232391	G	0.50	1.00	0.238	0.026	6.11E-20
DG1	rs8019491	14	65237863	G	0.08	1.00	0.291	0.049	3.22E-09
DG1	rs11628765	14	65238202	C	0.50	1.00	-0.238	0.026	6.57E-20
DG1	rs2411351	14	65241294	C	0.50	1.00	-0.238	0.026	7.22E-20
DG1	rs11846546	14	65246146	G	0.14	0.99	0.231	0.037	5.64E-10
DG1	rs8018278	14	65249841	G	0.50	1.00	-0.238	0.026	7.15E-20
DG1	rs11627067	14	65252706	G	0.50	1.00	-0.238	0.026	7.08E-20
DG1	rs4143898	14	65258635	T	0.43	0.99	0.215	0.027	6.45E-16
DG1	rs11622829	14	65261535	T	0.49	1.00	0.237	0.026	1.04E-19
DG1	rs11624104	14	65265890	G	0.51	1.00	-0.235	0.026	2.11E-19
DG1	rs1535173	14	65268892	C	0.49	1.00	0.235	0.026	2.22E-19
DG1	rs3742597	14	65269930	G	0.28	1.00	0.302	0.030	2.47E-24
DG1	rs927004	14	65270664	C	0.51	1.00	-0.235	0.026	2.20E-19
DG1	rs1950557	14	65271510	C	0.72	1.00	-0.303	0.030	2.09E-24
DG1	rs8010876	14	65276729	G	0.51	1.00	-0.236	0.026	1.90E-19
DG1	rs1054218	14	65278943	C	0.40	1.00	0.239	0.027	5.97E-19
DG1	rs761830	14	65282739	G	0.40	1.00	0.239	0.027	5.87E-19
DG1	rs10483785	14	65289270	G	0.49	1.00	0.239	0.026	3.71E-20
DG1	rs6573624	14	65296638	G	0.49	0.98	0.243	0.026	2.24E-20
DG1	rs2411405	14	65301839	G	0.53	0.98	-0.251	0.026	1.60E-21
DG1	rs743084	14	65302355	C	0.53	0.97	-0.253	0.026	1.11E-21
DG1	rs11625362	14	65302622	G	0.47	0.98	0.251	0.026	1.56E-21
DG1	rs4080329	14	65303243	C	0.63	0.98	-0.259	0.027	2.48E-21
DG1	rs11627605	14	65304066	G	0.47	0.98	0.251	0.026	1.51E-21
DG1	rs11627578	14	65304201	C	0.47	0.98	0.252	0.026	1.50E-21
DG1	rs11628840	14	65305395	G	0.53	0.98	-0.252	0.026	1.50E-21
DG1	rs1003401	14	65307473	G	0.38	0.98	0.256	0.027	3.71E-21
DG1	rs4902416	14	65307843	C	0.53	0.98	-0.251	0.026	1.57E-21
DG1	rs1984855	14	65309010	C	0.62	0.98	-0.256	0.027	3.66E-21
DG1	rs730807	14	65309043	C	0.47	0.98	0.252	0.026	1.53E-21
DG1	rs2411404	14	65309154	C	0.47	0.97	0.252	0.026	1.51E-21
DG1	rs1075566	14	65309210	C	0.47	0.97	0.252	0.026	1.50E-21
DG1	rs7157449	14	65309890	G	0.53	0.97	-0.252	0.026	1.50E-21
DG1	rs6573625	14	65310387	C	0.63	0.97	-0.259	0.027	2.53E-21
DG1	rs6573626	14	65310448	C	0.53	0.97	-0.252	0.026	1.51E-21
DG1	rs7158556	14	65310482	T	0.37	0.97	0.260	0.027	2.45E-21
DG1	rs12894466	14	65310520	G	0.47	0.97	0.252	0.026	1.49E-21
DG1	rs11625882	14	65314952	G	0.47	0.97	0.252	0.026	1.51E-21
DG1	rs2236067	14	65317765	G	0.62	0.97	-0.257	0.027	3.53E-21
DG1	rs968540	14	65318817	G	0.63	0.97	-0.261	0.027	1.89E-21
DG1	rs7142165	14	65319985	G	0.53	0.97	-0.253	0.026	1.26E-21
DG1	rs7143026	14	65320709	G	0.39	0.95	0.250	0.027	7.20E-20
DG1	rs6573627	14	65322079	C	0.52	0.97	-0.245	0.026	1.93E-20

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
DG1	rs4400971	14	65324331	C	0.42	0.98	0.215	0.027	6.79E-16
DG1	rs7151846	14	65325534	C	0.52	0.98	-0.240	0.026	7.00E-20
DG1	rs4073416	14	65329147	C	0.42	0.98	0.215	0.027	6.96E-16
DG1	rs4073415	14	65329283	G	0.52	0.98	-0.240	0.026	7.13E-20
DG1	rs11850120	14	65330132	C	0.41	0.97	0.217	0.027	5.49E-16
DG1	rs8018379	14	65331690	C	0.57	0.95	-0.247	0.027	1.03E-19
DG1	rs8007846	14	65332716	G	0.47	0.98	0.199	0.027	8.20E-14
DG1	rs8006608	14	65336577	G	0.96	0.81	-0.403	0.075	7.15E-08
DG1	rs4078408	14	65342587	G	0.29	0.85	-0.173	0.031	2.72E-08
DG1	rs3924222	14	65343491	C	0.41	0.79	-0.210	0.029	8.10E-13
DG1	rs10149325	14	65347120	G	0.41	0.79	-0.211	0.029	7.57E-13
DG1	rs10149555	14	65347410	G	0.56	0.98	-0.152	0.026	6.08E-09
DG1	rs12878546	14	65348273	C	0.56	0.97	-0.153	0.026	5.78E-09
DG1	rs8009488	14	65349289	C	0.56	0.96	-0.153	0.026	6.50E-09
DG3	rs2592781	2	23039477	G	0.45	1.00	-0.144	0.026	3.74E-08
DG3	rs2681019	2	23041009	C	0.45	0.99	-0.144	0.026	3.73E-08
DG3	rs2681005	2	23046536	C	0.45	0.99	-0.145	0.026	3.75E-08
DG3	rs2681008	2	23047436	G	0.45	0.98	-0.145	0.026	3.77E-08
DG3	rs2272406	2	27745527	T	0.22	0.96	-0.170	0.032	8.72E-08
DG3	rs13023094	2	27764210	C	0.22	0.97	-0.170	0.032	7.35E-08
DG3	rs13030973	2	27782301	C	0.22	0.99	-0.173	0.031	3.22E-08
DG3	rs6727388	2	27786091	G	0.22	0.99	-0.173	0.031	3.18E-08
DG3	rs4616435	2	27787146	C	0.78	0.99	0.173	0.031	3.13E-08
DG3	rs6727215	2	27788235	G	0.78	0.99	0.173	0.031	3.09E-08
DG3	rs13023194	2	27820764	C	0.20	0.92	-0.196	0.033	3.64E-09
DG3	rs13030345	2	27856678	G	0.81	0.87	0.210	0.035	2.66E-09
DG3	rs2305929	2	27967415	G	0.19	0.98	-0.192	0.033	6.27E-09
DG6	rs12436465	14	64876630	C	0.73	0.98	0.171	0.030	1.12E-08
DG6	rs7150448	14	64941255	C	0.35	1.00	-0.149	0.027	5.45E-08
DG6	rs8013442	14	64941614	G	0.66	1.00	0.154	0.027	2.14E-08
DG6	rs7147536	14	64944451	C	0.36	1.00	-0.149	0.027	4.01E-08
DG6	rs7145500	14	64953965	G	0.35	1.00	-0.147	0.027	7.51E-08
DG6	rs7145759	14	64954290	C	0.35	1.00	-0.147	0.027	7.84E-08
DG6	rs7151561	14	64960356	C	0.65	0.99	0.147	0.027	7.75E-08
DG6	rs2210805	14	64962477	C	0.35	0.99	-0.147	0.027	7.74E-08
DG6	rs2184601	14	64967121	T	0.35	0.99	-0.147	0.027	7.74E-08
DG6	rs7157109	14	64970186	C	0.35	0.99	-0.148	0.027	7.68E-08
DG6	rs1999725	14	64973990	G	0.35	0.98	-0.152	0.027	3.14E-08
DG6	rs11158595	14	64976122	G	0.67	0.98	0.152	0.028	5.21E-08
DG6	rs11844682	14	64980597	C	0.67	0.98	0.152	0.028	5.29E-08
DG6	rs10483776	14	64984620	G	0.21	1.00	-0.202	0.033	7.05E-10
DG6	rs1953418	14	64984979	G	0.33	0.98	-0.152	0.028	5.43E-08
DG6	rs12885842	14	64988405	C	0.34	0.98	-0.148	0.028	8.75E-08
DG6	rs7140695	14	64998885	C	0.67	0.99	0.151	0.028	6.15E-08
DG6	rs1889731	14	65012464	C	0.67	1.00	0.150	0.028	7.47E-08
DG6	rs1959144	14	65015804	G	0.67	1.00	0.150	0.028	8.01E-08
DG6	rs4902399	14	65026650	G	0.67	1.00	0.150	0.028	7.81E-08
DG6	rs2898818	14	65042337	C	0.67	1.00	0.150	0.028	7.60E-08
DG6	rs1953415	14	65057787	G	0.67	1.00	0.150	0.028	7.32E-08
DG6	rs2411815	14	65089824	T	0.68	1.00	0.151	0.028	6.25E-08
DG6	rs3783711	14	65098199	G	0.68	1.00	0.151	0.028	6.04E-08
DG6	rs3825639	14	65098258	C	0.68	1.00	0.151	0.028	6.07E-08
DG6	rs12433597	14	65098600	C	0.68	1.00	0.151	0.028	6.09E-08
DG6	rs9323461	14	65101158	C	0.68	1.00	0.151	0.028	6.12E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
DG6	rs7147002	14	65102299	C	0.68	1.00	0.151	0.028	6.16E-08
DG6	rs7158153	14	65104339	C	0.32	1.00	-0.151	0.028	6.23E-08
DG6	rs2183277	14	65105182	C	0.68	1.00	0.151	0.028	6.25E-08
DG6	rs8007497	14	65114229	C	0.68	1.00	0.151	0.028	6.35E-08
DG6	rs6573616	14	65116569	G	0.69	0.95	0.155	0.029	7.77E-08
DG6	rs4902404	14	65116775	C	0.68	1.00	0.151	0.028	6.45E-08
DG6	rs10152007	14	65117187	T	0.68	1.00	0.150	0.028	7.55E-08
DG6	rs7146993	14	65118625	C	0.32	1.00	-0.150	0.028	7.58E-08
DG6	rs17753508	14	65127205	G	0.21	1.00	-0.201	0.033	7.97E-10
DG6	rs12587057	14	65136128	C	0.33	1.00	-0.150	0.028	7.85E-08
DG6	rs7140341	14	65140170	C	0.33	1.00	-0.153	0.028	4.11E-08
DG6	rs11158603	14	65141793	C	0.33	1.00	-0.153	0.028	4.05E-08
DG6	rs2092914	14	65148868	C	0.34	0.99	-0.147	0.027	9.00E-08
DG6	rs8019762	14	65156931	G	0.67	1.00	0.154	0.028	3.43E-08
DG6	rs2268956	14	65159898	G	0.33	1.00	-0.154	0.028	3.36E-08
DG6	rs11158605	14	65177673	T	0.34	0.99	-0.148	0.027	7.64E-08
DG6	rs10873191	14	65180381	C	0.67	1.00	0.154	0.028	3.05E-08
DG6	rs11158607	14	65180550	G	0.66	0.99	0.148	0.027	7.17E-08
DG6	rs7144345	14	65181594	C	0.67	1.00	0.154	0.028	2.89E-08
DG6	rs7144971	14	65190403	G	0.33	1.00	-0.155	0.028	2.64E-08
DG6	rs10143206	14	65190428	C	0.33	1.00	-0.155	0.028	2.59E-08
DG6	rs2268959	14	65215071	C	0.79	1.00	0.207	0.033	2.22E-10
DG6	rs1956010	14	65220843	G	0.35	0.99	-0.152	0.027	2.48E-08
DG6	rs1121885	14	65226667	G	0.67	1.00	0.158	0.028	1.37E-08
DG7	rs2649999	12	119864927	C	0.59	0.84	0.180	0.029	4.33E-10
DG7	rs2650000	12	119873345	C	0.57	1.00	0.164	0.027	5.90E-10
DG7	rs7953249	12	119888107	G	0.47	1.00	-0.177	0.026	1.43E-11
DG7	rs2251468	12	119889509	C	0.43	0.99	-0.166	0.027	3.60E-10
DG7	rs10774579	12	119889593	C	0.44	0.99	0.150	0.026	9.70E-09
DG7	rs1169288	12	119901033	C	0.40	0.95	-0.183	0.027	1.49E-11
DG7	rs2244608	12	119901371	G	0.40	0.95	-0.184	0.027	1.48E-11
DG7	rs1169286	12	119903439	C	0.49	0.94	-0.150	0.027	1.65E-08
DG7	rs7979473	12	119904643	G	0.55	0.94	0.197	0.027	2.81E-13
DG7	rs7979478	12	119904646	G	0.55	0.94	0.197	0.027	2.78E-13
DG7	rs1183910	12	119905190	G	0.60	0.94	0.188	0.027	7.27E-12
DG7	rs11065385	12	119907769	G	0.61	0.88	0.188	0.028	4.35E-11
DG7	rs2393791	12	119908339	C	0.45	0.94	-0.197	0.027	2.70E-13
DG7	rs2393775	12	119908957	G	0.44	0.94	-0.197	0.027	2.64E-13
DG7	rs7310409	12	119909244	G	0.56	0.94	0.198	0.027	2.63E-13
DG7	rs1169300	12	119915608	G	0.63	1.00	0.184	0.027	1.56E-11
DG7	rs2259820	12	119919725	C	0.63	1.00	0.183	0.027	1.78E-11
DG7	rs2464196	12	119919810	G	0.63	1.00	0.182	0.027	2.25E-11
DG7	rs2464195	12	119919858	G	0.61	1.00	0.186	0.027	4.01E-12
DG7	rs2259816	12	119919970	G	0.61	1.00	0.186	0.027	3.97E-12
DG7	rs1169306	12	119922694	C	0.60	0.97	0.190	0.027	2.52E-12
DG7	rs735396	12	119923227	C	0.39	1.00	-0.188	0.027	2.48E-12
DG7	rs1169310	12	119923816	G	0.61	1.00	0.188	0.027	2.47E-12
DG7	rs1169312	12	119925844	G	0.61	1.00	0.188	0.027	2.44E-12
DG7	rs1169313	12	119927053	C	0.39	1.00	-0.188	0.027	2.38E-12
DG7	rs2257764	12	119930829	T	0.37	1.00	-0.185	0.027	1.29E-11
DG7	rs2258287	12	119938696	C	0.61	0.98	0.170	0.027	3.92E-10
DG7	rs1182933	12	119939005	C	0.63	0.98	0.187	0.027	9.17E-12
DG7	rs3213545	12	119955720	G	0.64	0.87	0.204	0.029	2.60E-12
DG7	rs8101385	19	5789595	C	0.88	0.91	0.408	0.042	2.58E-22

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
DG7	rs3760776	19	5790746	G	0.88	0.93	0.403	0.042	3.84E-22
DG7	rs3760775	19	5792356	G	0.92	0.79	0.632	0.052	1.75E-33
DG7	rs874232	19	5794609	C	0.41	0.85	-0.171	0.028	1.14E-09
DG8	rs7979473	12	119904643	G	0.55	0.94	-0.145	0.027	7.89E-08
DG8	rs7979478	12	119904646	G	0.55	0.94	-0.145	0.027	7.81E-08
DG8	rs2393791	12	119908339	C	0.45	0.94	0.145	0.027	7.57E-08
DG8	rs2393775	12	119908957	G	0.44	0.94	0.146	0.027	7.34E-08
DG8	rs7310409	12	119909244	G	0.56	0.94	-0.146	0.027	7.29E-08
DG8	rs2464195	12	119919858	G	0.61	1.00	-0.148	0.027	4.02E-08
DG8	rs2259816	12	119919970	G	0.61	1.00	-0.148	0.027	3.99E-08
DG8	rs1169306	12	119922694	C	0.60	0.97	-0.152	0.027	2.37E-08
DG8	rs735396	12	119923227	C	0.39	1.00	0.150	0.027	2.52E-08
DG8	rs1169310	12	119923816	G	0.61	1.00	-0.150	0.027	2.52E-08
DG8	rs1169312	12	119925844	G	0.61	1.00	-0.150	0.027	2.50E-08
DG8	rs1169313	12	119927053	C	0.39	1.00	0.150	0.027	2.45E-08
DG8	rs217181	16	70671503	C	0.81	0.92	-0.200	0.034	3.36E-09
DG8	rs8101385	19	5789595	C	0.88	0.91	-0.243	0.042	8.54E-09
DG8	rs3760776	19	5790746	G	0.88	0.93	-0.240	0.042	1.03E-08
DG8	rs3760775	19	5792356	G	0.92	0.79	-0.447	0.053	1.87E-17
DG9	rs2649999	12	119864927	C	0.59	0.84	0.173	0.029	2.22E-09
DG9	rs2650000	12	119873345	C	0.57	1.00	0.157	0.027	3.83E-09
DG9	rs7953249	12	119888107	G	0.47	1.00	-0.175	0.026	2.99E-11
DG9	rs2251468	12	119889509	C	0.43	0.99	-0.161	0.027	1.72E-09
DG9	rs10774579	12	119889593	C	0.44	0.99	0.146	0.026	3.06E-08
DG9	rs1169288	12	119901033	C	0.40	0.95	-0.177	0.027	9.91E-11
DG9	rs2244608	12	119901371	G	0.40	0.95	-0.177	0.027	1.01E-10
DG9	rs7979473	12	119904643	G	0.55	0.94	0.193	0.027	1.01E-12
DG9	rs7979478	12	119904646	G	0.55	0.94	0.193	0.027	9.99E-13
DG9	rs1183910	12	119905190	G	0.60	0.94	0.180	0.028	6.73E-11
DG9	rs11065385	12	119907769	G	0.61	0.88	0.181	0.029	2.88E-10
DG9	rs2393791	12	119908339	C	0.45	0.94	-0.194	0.027	9.65E-13
DG9	rs2393775	12	119908957	G	0.44	0.94	-0.193	0.027	1.03E-12
DG9	rs7310409	12	119909244	G	0.56	0.94	0.193	0.027	1.06E-12
DG9	rs1169300	12	119915608	G	0.63	1.00	0.161	0.027	4.15E-09
DG9	rs2259820	12	119919725	C	0.63	1.00	0.160	0.027	4.71E-09
DG9	rs2464196	12	119919810	G	0.63	1.00	0.160	0.027	5.78E-09
DG9	rs2464195	12	119919858	G	0.61	1.00	0.170	0.027	3.02E-10
DG9	rs2259816	12	119919970	G	0.61	1.00	0.170	0.027	3.02E-10
DG9	rs1169306	12	119922694	C	0.60	0.97	0.173	0.027	2.52E-10
DG9	rs735396	12	119923227	C	0.39	1.00	-0.170	0.027	2.81E-10
DG9	rs1169310	12	119923816	G	0.61	1.00	0.170	0.027	2.80E-10
DG9	rs1169312	12	119925844	G	0.61	1.00	0.170	0.027	2.78E-10
DG9	rs1169313	12	119927053	C	0.39	1.00	-0.171	0.027	2.70E-10
DG9	rs2257764	12	119930829	T	0.37	1.00	-0.160	0.027	5.07E-09
DG9	rs2258287	12	119938696	C	0.61	0.98	0.147	0.027	7.12E-08
DG9	rs1182933	12	119939005	C	0.63	0.98	0.163	0.028	3.96E-09
DG9	rs3213545	12	119955720	G	0.64	0.87	0.177	0.029	1.42E-09
DG9	rs778805	19	5783209	G	0.66	0.93	0.150	0.028	9.93E-08
DG9	rs8101385	19	5789595	C	0.88	0.91	0.486	0.042	1.51E-30
DG9	rs3760776	19	5790746	G	0.88	0.93	0.480	0.042	2.71E-30
DG9	rs3760775	19	5792356	G	0.92	0.79	0.744	0.053	2.92E-45
DG9	rs874232	19	5794609	C	0.41	0.85	-0.176	0.028	4.60E-10
DG10	rs10148907	14	64903125	C	0.70	0.98	0.159	0.029	5.74E-08
DG10	rs10483776	14	64984620	G	0.21	1.00	-0.192	0.033	5.11E-09

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
DG10	rs17753508	14	65127205	G	0.21	1.00	-0.191	0.033	6.53E-09
DG10	rs2268959	14	65215071	C	0.79	1.00	0.187	0.033	1.26E-08
DG11	rs1257189	2	134718008	C	0.73	0.88	-0.167	0.031	5.48E-08
DG11	rs2593704	2	134721747	C	0.75	0.90	-0.193	0.031	7.55E-10
DG11	rs1257196	2	134722302	G	0.27	0.89	0.167	0.031	5.55E-08
DG11	rs1257197	2	134724206	G	0.73	0.87	-0.193	0.031	6.54E-10
DG11	rs2442046	2	134730548	C	0.74	0.98	-0.184	0.030	6.09E-10
DG11	rs2460382	2	134730586	G	0.26	0.98	0.184	0.030	6.13E-10
DG11	rs2460383	2	134730596	C	0.74	0.98	-0.183	0.030	6.19E-10
DG11	rs1257220	2	134731817	G	0.74	0.99	-0.183	0.030	6.56E-10
DG11	rs1257221	2	134733088	C	0.71	0.88	-0.181	0.030	2.00E-09
DG11	rs7953249	12	119888107	G	0.47	1.00	0.140	0.026	7.67E-08
DG11	rs7979473	12	119904643	G	0.55	0.94	-0.154	0.027	1.01E-08
DG11	rs7979478	12	119904646	G	0.55	0.94	-0.154	0.027	9.98E-09
DG11	rs2393791	12	119908339	C	0.45	0.94	0.154	0.027	9.56E-09
DG11	rs2393775	12	119908957	G	0.44	0.94	0.154	0.027	9.24E-09
DG11	rs7310409	12	119909244	G	0.56	0.94	-0.154	0.027	9.16E-09
DG11	rs2464195	12	119919858	G	0.61	1.00	-0.155	0.027	6.95E-09
DG11	rs2259816	12	119919970	G	0.61	1.00	-0.155	0.027	6.89E-09
DG11	rs1169306	12	119922694	C	0.60	0.97	-0.158	0.027	4.85E-09
DG11	rs1169307	12	119922765	C	0.62	1.00	0.143	0.027	8.37E-08
DG11	rs735396	12	119923227	C	0.39	1.00	0.157	0.027	4.19E-09
DG11	rs1169310	12	119923816	G	0.61	1.00	-0.157	0.027	4.18E-09
DG11	rs1169312	12	119925844	G	0.61	1.00	-0.157	0.027	4.15E-09
DG11	rs1169313	12	119927053	C	0.39	1.00	0.157	0.027	4.09E-09
DG11	rs217181	16	70671503	C	0.81	0.92	-0.184	0.034	4.64E-08
DG11	rs3760775	19	5792356	G	0.92	0.79	-0.327	0.052	4.28E-10
DG12	rs8101385	19	5789595	C	0.88	0.91	0.379	0.042	2.12E-19
DG12	rs3760776	19	5790746	G	0.88	0.93	0.375	0.042	3.14E-19
DG12	rs3760775	19	5792356	G	0.92	0.79	0.615	0.053	1.11E-31
DG13	rs11223780	11	133766360	G	0.11	0.92	-0.238	0.044	4.86E-08
DG13	rs7948031	11	133774301	C	0.12	0.93	-0.233	0.042	3.93E-08
MonoS	rs217181	16	70671503	C	0.81	0.92	0.187	0.034	2.71E-08
TriS	rs217181	16	70671503	C	0.81	0.92	-0.248	0.033	1.25E-13
TetraS	rs1372288	3	144384227	C	0.25	1.00	0.214	0.030	9.54E-13
TetraS	rs920570	3	144403114	C	0.24	0.98	0.216	0.030	1.08E-12
TetraS	rs6785254	3	144408513	G	0.76	0.98	-0.216	0.030	9.35E-13
TetraS	rs990739	3	144409455	G	0.76	0.98	-0.217	0.030	9.13E-13
TetraS	rs9842703	3	144417383	G	0.24	0.97	0.224	0.030	1.58E-13
TetraS	rs894175	3	144419283	C	0.31	0.96	0.191	0.028	1.09E-11
TetraS	rs6775385	3	144421193	G	0.24	0.97	0.224	0.030	1.43E-13
TetraS	rs4553947	3	144421904	T	0.24	0.97	0.224	0.030	1.42E-13
TetraS	rs9879103	3	144422465	C	0.76	0.97	-0.224	0.030	1.42E-13
TetraS	rs9829667	3	144426857	G	0.76	0.97	-0.225	0.030	1.25E-13
TetraS	rs985247	3	144432690	C	0.77	0.98	-0.229	0.031	1.31E-13
TetraS	rs10470450	3	144435495	C	0.77	0.98	-0.229	0.031	1.23E-13
TetraS	rs17470684	3	144438749	C	0.87	0.62	-0.282	0.046	8.97E-10
TetraS	rs7631070	3	144439114	G	0.77	0.99	-0.224	0.031	3.08E-13
TetraS	rs4839604	3	144442963	C	0.77	1.00	-0.223	0.031	3.49E-13
TetraS	rs13317029	3	144443913	G	0.23	0.99	0.224	0.031	3.44E-13
TetraS	rs4602353	3	144445234	G	0.77	0.99	-0.225	0.031	3.35E-13
TetraS	rs4307732	11	125750165	G	0.88	0.84	-0.229	0.043	9.40E-08
C-FUC	rs10483776	14	64984620	G	0.21	1.00	-0.190	0.033	6.12E-09
C-FUC	rs17753508	14	65127205	G	0.21	1.00	-0.189	0.033	7.20E-09

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
C-FUC	rs2268959	14	65215071	C	0.79	1.00	0.195	0.033	2.37E-09
A-FUC	rs2649999	12	119864927	C	0.59	0.84	0.170	0.029	3.40E-09
A-FUC	rs2650000	12	119873345	C	0.57	1.00	0.153	0.027	8.40E-09
A-FUC	rs7953249	12	119888107	G	0.47	1.00	-0.166	0.026	2.46E-10
A-FUC	rs2251468	12	119889509	C	0.43	0.99	-0.155	0.027	5.72E-09
A-FUC	rs1169288	12	119901033	C	0.40	0.95	-0.169	0.027	5.74E-10
A-FUC	rs2244608	12	119901371	G	0.40	0.95	-0.169	0.027	5.80E-10
A-FUC	rs7979473	12	119904643	G	0.55	0.94	0.183	0.027	1.29E-11
A-FUC	rs7979478	12	119904646	G	0.55	0.94	0.183	0.027	1.29E-11
A-FUC	rs1183910	12	119905190	G	0.60	0.94	0.172	0.027	3.66E-10
A-FUC	rs11065385	12	119907769	G	0.61	0.88	0.169	0.029	2.94E-09
A-FUC	rs2393791	12	119908339	C	0.45	0.94	-0.183	0.027	1.28E-11
A-FUC	rs2393775	12	119908957	G	0.44	0.94	-0.183	0.027	1.29E-11
A-FUC	rs7310409	12	119909244	G	0.56	0.94	0.183	0.027	1.31E-11
A-FUC	rs1169300	12	119915608	G	0.63	1.00	0.160	0.027	4.50E-09
A-FUC	rs2259820	12	119919725	C	0.63	1.00	0.159	0.027	5.34E-09
A-FUC	rs2464196	12	119919810	G	0.63	1.00	0.158	0.027	7.11E-09
A-FUC	rs2464195	12	119919858	G	0.61	1.00	0.166	0.027	5.94E-10
A-FUC	rs2259816	12	119919970	G	0.61	1.00	0.166	0.027	5.89E-10
A-FUC	rs1169306	12	119922694	C	0.60	0.97	0.170	0.027	3.82E-10
A-FUC	rs735396	12	119923227	C	0.39	1.00	-0.169	0.027	3.44E-10
A-FUC	rs1169310	12	119923816	G	0.61	1.00	0.169	0.027	3.43E-10
A-FUC	rs1169312	12	119925844	G	0.61	1.00	0.169	0.027	3.41E-10
A-FUC	rs1169313	12	119927053	C	0.39	1.00	-0.169	0.027	3.36E-10
A-FUC	rs2257764	12	119930829	T	0.37	1.00	-0.161	0.027	4.04E-09
A-FUC	rs2258287	12	119938696	C	0.61	0.98	0.146	0.027	7.10E-08
A-FUC	rs1182933	12	119939005	C	0.63	0.98	0.162	0.027	3.49E-09
A-FUC	rs3213545	12	119955720	G	0.64	0.87	0.174	0.029	2.27E-09
A-FUC	rs8101385	19	5789595	C	0.88	0.91	0.398	0.042	2.95E-21
A-FUC	rs3760776	19	5790746	G	0.88	0.93	0.393	0.042	4.73E-21
A-FUC	rs3760775	19	5792356	G	0.92	0.79	0.593	0.052	1.34E-29
A-FUC	rs874232	19	5794609	C	0.41	0.85	-0.180	0.028	1.72E-10
A2	rs3094093	6	30787607	T	0.10	0.75	0.240	0.044	5.70E-08
A2	rs1270077	14	64776511	G	0.30	0.92	0.160	0.030	7.96E-08
A2	rs1256519	14	64806077	G	0.44	0.89	-0.192	0.028	4.51E-12
A2	rs7159888	14	64828395	G	0.55	0.99	-0.261	0.027	1.15E-22
A2	rs12431963	14	64829447	C	0.92	0.93	-0.376	0.050	6.44E-14
A2	rs1256540	14	64833822	C	0.42	1.00	0.235	0.027	1.34E-18
A2	rs4902383	14	64834326	C	0.19	0.94	0.280	0.034	1.27E-16
A2	rs1269068	14	64837086	C	0.58	1.00	-0.235	0.027	1.32E-18
A2	rs10135194	14	64840731	C	0.94	0.87	-0.341	0.059	7.17E-09
A2	rs1760978	14	64840800	G	0.43	0.98	0.277	0.027	5.86E-25
A2	rs10144975	14	64843735	C	0.80	0.98	-0.286	0.032	1.05E-18
A2	rs17102587	14	64844230	C	0.20	0.98	0.289	0.033	5.95E-19
A2	rs8017974	14	64844940	C	0.20	0.99	0.288	0.032	6.07E-19
A2	rs11847263	14	64845448	G	0.39	0.99	0.310	0.027	8.86E-30
A2	rs10132229	14	64847313	G	0.10	1.00	0.341	0.043	2.70E-15
A2	rs4902386	14	64848043	C	0.80	0.99	-0.287	0.032	6.19E-19
A2	rs10147958	14	64848586	C	0.10	1.00	0.341	0.043	2.61E-15
A2	rs8019473	14	64848881	G	0.80	0.99	-0.287	0.032	6.02E-19
A2	rs10138662	14	64849235	G	0.20	1.00	0.288	0.032	5.68E-19
A2	rs10134589	14	64850987	T	0.20	0.94	0.294	0.034	2.46E-18
A2	rs7151212	14	64851375	C	0.80	1.00	-0.288	0.032	5.24E-19
A2	rs11158587	14	64852465	G	0.80	1.00	-0.288	0.032	5.15E-19

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
A2	rs8019767	14	64852538	G	0.80	1.00	-0.288	0.032	5.10E-19
A2	rs6573598	14	64852772	C	0.20	1.00	0.288	0.032	5.01E-19
A2	rs6573599	14	64852880	C	0.80	1.00	-0.288	0.032	4.71E-19
A2	rs10144503	14	64853862	G	0.90	1.00	-0.343	0.043	1.95E-15
A2	rs6573602	14	64854363	C	0.20	1.00	0.288	0.032	4.48E-19
A2	rs17102598	14	64854613	G	0.80	1.00	-0.288	0.032	4.44E-19
A2	rs12436299	14	64854947	G	0.90	1.00	-0.343	0.043	1.82E-15
A2	rs6573604	14	64857694	C	0.20	1.00	0.288	0.032	4.34E-19
A2	rs9635250	14	64869101	T	0.10	1.00	0.344	0.043	1.66E-15
A2	rs12881755	14	64871564	G	0.66	0.96	-0.217	0.029	4.47E-14
A2	rs747541	14	64875163	C	0.44	0.97	0.257	0.027	1.73E-21
A2	rs1954052	14	64875462	T	0.43	0.99	0.258	0.027	1.29E-21
A2	rs12436465	14	64876630	C	0.73	0.98	-0.192	0.030	1.92E-10
A2	rs12886005	14	64879000	C	0.44	0.87	0.254	0.029	6.06E-19
A2	rs12886168	14	64879039	C	0.44	0.98	0.257	0.027	1.55E-21
A2	rs11623920	14	64889067	C	0.57	1.00	-0.257	0.027	1.10E-21
A2	rs11621121	14	64892246	C	0.43	1.00	0.257	0.027	1.12E-21
A2	rs10148907	14	64903125	C	0.70	0.98	-0.300	0.030	3.67E-24
A2	rs4902393	14	64909267	C	0.57	0.98	-0.254	0.027	5.57E-21
A2	rs11621604	14	64910527	G	0.58	0.98	-0.247	0.027	1.16E-19
A2	rs12882269	14	64916897	G	0.58	0.98	-0.243	0.027	3.31E-19
A2	rs11845794	14	64917871	C	0.92	0.98	-0.277	0.049	1.47E-08
A2	rs11850160	14	64917876	C	0.08	0.98	0.277	0.049	1.49E-08
A2	rs11850163	14	64917898	T	0.92	0.98	-0.277	0.049	1.49E-08
A2	rs10083421	14	64920911	C	0.08	0.98	0.277	0.049	1.49E-08
A2	rs10083525	14	64921309	C	0.08	0.98	0.277	0.049	1.51E-08
A2	rs17826448	14	64921770	G	0.92	0.99	-0.277	0.049	1.53E-08
A2	rs17826466	14	64921923	G	0.92	0.99	-0.277	0.049	1.54E-08
A2	rs10083488	14	64923099	C	0.08	0.99	0.277	0.049	1.54E-08
A2	rs12433416	14	64923928	G	0.92	0.99	-0.277	0.049	1.55E-08
A2	rs12433423	14	64923990	C	0.08	0.99	0.276	0.049	1.56E-08
A2	rs8017202	14	64924711	G	0.08	0.99	0.276	0.049	1.56E-08
A2	rs11158591	14	64925515	C	0.42	0.98	0.241	0.027	7.24E-19
A2	rs11158592	14	64929721	G	0.48	0.99	0.240	0.026	7.53E-20
A2	rs11158593	14	64929737	G	0.49	0.99	0.241	0.026	5.02E-20
A2	rs10138570	14	64929791	G	0.51	0.99	-0.241	0.026	5.14E-20
A2	rs10138671	14	64929845	G	0.59	0.99	-0.162	0.027	1.38E-09
A2	rs4587890	14	64933537	T	0.41	0.99	0.162	0.027	1.42E-09
A2	rs2411823	14	64934819	C	0.41	0.99	0.161	0.027	1.46E-09
A2	rs17246007	14	64935424	C	0.08	0.99	0.296	0.049	1.97E-09
A2	rs11844747	14	64939881	C	0.08	0.99	0.296	0.049	1.89E-09
A2	rs17246035	14	64943883	G	0.08	1.00	0.297	0.049	1.53E-09
A2	rs2411822	14	64948148	G	0.49	1.00	-0.219	0.026	7.97E-17
A2	rs1953416	14	64948560	C	0.51	1.00	0.219	0.026	6.27E-17
A2	rs1953417	14	64948662	C	0.92	1.00	-0.298	0.049	1.46E-09
A2	rs883081	14	64950374	C	0.51	1.00	0.220	0.026	5.89E-17
A2	rs883082	14	64950693	G	0.49	1.00	-0.219	0.026	7.44E-17
A2	rs7145574	14	64954155	C	0.92	1.00	-0.298	0.049	1.45E-09
A2	rs867972	14	64965514	C	0.50	0.97	-0.221	0.027	7.15E-17
A2	rs11851576	14	64970036	C	0.55	0.99	-0.194	0.027	3.34E-13
A2	rs12879971	14	64971357	G	0.51	0.99	0.222	0.026	3.19E-17
A2	rs12892058	14	64973194	C	0.49	0.99	-0.224	0.026	1.81E-17
A2	rs11158595	14	64976122	G	0.67	0.98	-0.159	0.028	1.96E-08
A2	rs11844682	14	64980597	C	0.67	0.98	-0.159	0.028	1.86E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
A2	rs10483776	14	64984620	G	0.21	1.00	0.228	0.033	5.81E-12
A2	rs1953418	14	64984979	G	0.33	0.98	0.159	0.028	1.69E-08
A2	rs17826580	14	64985015	C	0.08	1.00	0.299	0.049	1.20E-09
A2	rs2184602	14	64985425	G	0.08	1.00	0.299	0.049	1.20E-09
A2	rs2152375	14	64985531	C	0.08	1.00	0.299	0.049	1.20E-09
A2	rs12885842	14	64988405	C	0.34	0.98	0.156	0.028	2.48E-08
A2	rs12589698	14	64990188	G	0.50	0.98	0.229	0.026	4.74E-18
A2	rs4899179	14	64996501	G	0.50	0.99	-0.228	0.026	4.77E-18
A2	rs7140695	14	64998885	C	0.67	0.99	-0.161	0.028	1.15E-08
A2	rs2184603	14	65000423	C	0.50	0.99	-0.228	0.026	4.59E-18
A2	rs8010726	14	65002350	G	0.33	0.99	0.161	0.028	1.07E-08
A2	rs11850847	14	65003551	C	0.92	1.00	-0.299	0.049	1.19E-09
A2	rs12434585	14	65008121	G	0.08	1.00	0.299	0.049	1.19E-09
A2	rs1889731	14	65012464	C	0.67	1.00	-0.162	0.028	9.63E-09
A2	rs1959144	14	65015804	G	0.67	1.00	-0.162	0.028	9.77E-09
A2	rs2411820	14	65016497	C	0.33	1.00	0.162	0.028	9.02E-09
A2	rs4902399	14	65026650	G	0.67	1.00	-0.162	0.028	9.30E-09
A2	rs3825640	14	65030957	C	0.50	1.00	0.229	0.026	3.34E-18
A2	rs8011224	14	65039423	T	0.33	1.00	0.162	0.028	9.33E-09
A2	rs2898818	14	65042337	C	0.67	1.00	-0.162	0.028	9.77E-09
A2	rs11627084	14	65048589	G	0.50	1.00	-0.228	0.026	4.55E-18
A2	rs10483780	14	65049923	C	0.51	1.00	-0.229	0.026	3.18E-18
A2	rs7141536	14	65057065	T	0.33	1.00	0.161	0.028	1.02E-08
A2	rs1953415	14	65057787	G	0.68	1.00	-0.161	0.028	1.06E-08
A2	rs10144979	14	65067391	G	0.33	1.00	0.161	0.028	1.11E-08
A2	rs1113962	14	65075551	C	0.33	1.00	0.161	0.028	1.13E-08
A2	rs2149841	14	65080072	C	0.50	0.99	0.228	0.026	4.53E-18
A2	rs7153679	14	65082707	G	0.08	1.00	0.301	0.049	9.43E-10
A2	rs11621680	14	65084434	G	0.51	1.00	-0.227	0.026	6.89E-18
A2	rs11851013	14	65085965	G	0.08	1.00	0.301	0.049	9.37E-10
A2	rs2411815	14	65089824	T	0.68	1.00	-0.159	0.028	1.99E-08
A2	rs11623662	14	65090945	G	0.61	0.99	-0.172	0.027	1.83E-10
A2	rs11851772	14	65091800	C	0.92	1.00	-0.302	0.049	9.22E-10
A2	rs9972106	14	65092884	T	0.61	0.99	-0.171	0.027	1.89E-10
A2	rs2898814	14	65093714	C	0.67	1.00	-0.157	0.028	2.65E-08
A2	rs11158601	14	65095116	G	0.50	1.00	-0.224	0.026	1.48E-17
A2	rs3783711	14	65098199	G	0.68	1.00	-0.157	0.028	2.77E-08
A2	rs3825639	14	65098258	C	0.68	1.00	-0.157	0.028	2.67E-08
A2	rs12433597	14	65098600	C	0.68	1.00	-0.157	0.028	2.65E-08
A2	rs9323461	14	65101158	C	0.68	1.00	-0.157	0.028	2.59E-08
A2	rs7147002	14	65102299	C	0.68	1.00	-0.157	0.028	2.54E-08
A2	rs7146742	14	65102687	G	0.41	0.99	0.209	0.027	1.17E-14
A2	rs7158153	14	65104339	C	0.32	1.00	0.157	0.028	2.44E-08
A2	rs2183277	14	65105182	C	0.68	1.00	-0.158	0.028	2.42E-08
A2	rs1958561	14	65106514	G	0.50	1.00	-0.224	0.026	1.27E-17
A2	rs1958560	14	65106548	G	0.41	1.00	0.144	0.027	7.34E-08
A2	rs10142283	14	65113882	G	0.33	1.00	0.158	0.028	2.22E-08
A2	rs8007497	14	65114229	C	0.68	1.00	-0.158	0.028	2.24E-08
A2	rs12887134	14	65115296	C	0.50	1.00	-0.226	0.026	9.12E-18
A2	rs7155541	14	65115995	C	0.50	1.00	-0.226	0.026	9.02E-18
A2	rs6573615	14	65116287	G	0.39	0.99	0.171	0.027	2.05E-10
A2	rs6573616	14	65116569	G	0.69	0.95	-0.163	0.029	2.25E-08
A2	rs4902404	14	65116775	C	0.68	1.00	-0.158	0.028	2.14E-08
A2	rs10152007	14	65117187	T	0.68	1.00	-0.162	0.028	9.10E-09

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
A2	rs7146993	14	65118625	C	0.32	1.00	0.162	0.028	9.02E-09
A2	rs1958559	14	65121808	C	0.41	1.00	0.148	0.027	2.98E-08
A2	rs7160780	14	65122466	G	0.39	1.00	0.175	0.027	8.10E-11
A2	rs7161123	14	65122654	G	0.50	1.00	0.228	0.026	3.63E-18
A2	rs2411356	14	65122914	G	0.39	1.00	0.175	0.027	7.97E-11
A2	rs12433827	14	65125363	G	0.92	1.00	-0.300	0.049	1.07E-09
A2	rs4581615	14	65125696	C	0.50	1.00	0.228	0.026	3.63E-18
A2	rs8005309	14	65126261	T	0.92	1.00	-0.300	0.049	1.08E-09
A2	rs17753508	14	65127205	G	0.21	1.00	0.229	0.033	4.63E-12
A2	rs3783709	14	65128417	T	0.50	1.00	0.228	0.026	3.64E-18
A2	rs12889002	14	65133335	C	0.50	1.00	0.228	0.026	3.64E-18
A2	rs12587057	14	65136128	C	0.33	1.00	0.162	0.028	8.58E-09
A2	rs2064695	14	65136841	G	0.59	1.00	-0.148	0.027	2.86E-08
A2	rs743085	14	65137886	G	0.50	1.00	-0.228	0.026	3.64E-18
A2	rs17826724	14	65138073	C	0.08	1.00	0.299	0.049	1.31E-09
A2	rs11849252	14	65139522	G	0.92	1.00	-0.299	0.049	1.33E-09
A2	rs7140341	14	65140170	C	0.33	1.00	0.165	0.028	4.46E-09
A2	rs11158603	14	65141793	C	0.33	1.00	0.165	0.028	4.48E-09
A2	rs17826736	14	65151955	C	0.08	1.00	0.299	0.049	1.39E-09
A2	rs2073294	14	65152246	C	0.92	1.00	-0.299	0.049	1.40E-09
A2	rs8012278	14	65152326	G	0.50	1.00	-0.230	0.026	1.63E-18
A2	rs8019762	14	65156931	G	0.67	1.00	-0.165	0.028	4.48E-09
A2	rs2268955	14	65159762	T	0.41	1.00	0.151	0.027	1.42E-08
A2	rs2268956	14	65159898	G	0.33	1.00	0.165	0.028	4.49E-09
A2	rs11849862	14	65167778	G	0.08	1.00	0.298	0.049	1.46E-09
A2	rs10873191	14	65180381	C	0.67	1.00	-0.165	0.028	4.53E-09
A2	rs7144345	14	65181594	C	0.67	1.00	-0.165	0.028	4.43E-09
A2	rs2268957	14	65182986	C	0.92	1.00	-0.298	0.049	1.54E-09
A2	rs12890902	14	65186375	T	0.50	1.00	0.231	0.026	1.50E-18
A2	rs2300865	14	65189768	C	0.50	1.00	-0.230	0.026	1.49E-18
A2	rs7144971	14	65190403	G	0.33	1.00	0.165	0.028	4.46E-09
A2	rs10143206	14	65190428	C	0.33	1.00	0.165	0.028	4.52E-09
A2	rs11627184	14	65191196	C	0.50	1.00	0.230	0.026	1.51E-18
A2	rs12435908	14	65191221	C	0.92	1.00	-0.298	0.049	1.55E-09
A2	rs11627185	14	65191245	G	0.50	1.00	-0.230	0.026	1.52E-18
A2	rs1998035	14	65195983	G	0.08	1.00	0.298	0.049	1.55E-09
A2	rs2268958	14	65197991	T	0.08	1.00	0.298	0.049	1.55E-09
A2	rs7142651	14	65202474	C	0.50	1.00	0.229	0.026	2.35E-18
A2	rs1998036	14	65207952	C	0.50	1.00	-0.229	0.026	2.46E-18
A2	rs2268959	14	65215071	C	0.79	1.00	-0.231	0.033	3.10E-12
A2	rs2268960	14	65215253	G	0.07	0.98	0.318	0.051	6.34E-10
A2	rs2268961	14	65216518	C	0.50	1.00	-0.229	0.026	2.63E-18
A2	rs2268962	14	65217026	G	0.50	1.00	-0.229	0.026	2.65E-18
A2	rs2300871	14	65217447	C	0.08	1.00	0.298	0.049	1.56E-09
A2	rs2300872	14	65217514	G	0.08	1.00	0.297	0.049	1.77E-09
A2	rs2064694	14	65217999	G	0.50	1.00	0.226	0.026	7.66E-18
A2	rs1121885	14	65226667	G	0.67	1.00	-0.160	0.028	1.46E-08
A2	rs12588838	14	65232391	G	0.50	1.00	0.225	0.026	8.17E-18
A2	rs8019491	14	65237863	G	0.08	1.00	0.297	0.049	1.87E-09
A2	rs11628765	14	65238202	C	0.50	1.00	-0.225	0.026	8.74E-18
A2	rs2411351	14	65241294	C	0.50	1.00	-0.225	0.026	9.57E-18
A2	rs11846546	14	65246146	G	0.14	0.99	0.225	0.038	2.00E-09
A2	rs8018278	14	65249841	G	0.50	1.00	-0.225	0.026	9.43E-18
A2	rs11627067	14	65252706	G	0.50	1.00	-0.225	0.026	9.28E-18

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
A2	rs4143898	14	65258635	T	0.43	0.99	0.206	0.027	1.20E-14
A2	rs11622829	14	65261535	T	0.49	1.00	0.224	0.026	1.49E-17
A2	rs11624104	14	65265890	G	0.51	1.00	-0.223	0.026	2.23E-17
A2	rs1535173	14	65268892	C	0.49	1.00	0.223	0.026	1.88E-17
A2	rs3742597	14	65269930	G	0.28	1.00	0.291	0.030	2.50E-22
A2	rs927004	14	65270664	C	0.51	1.00	-0.223	0.026	1.84E-17
A2	rs1950557	14	65271510	C	0.72	1.00	-0.291	0.030	2.14E-22
A2	rs8010876	14	65276729	G	0.51	1.00	-0.224	0.026	1.59E-17
A2	rs1054218	14	65278943	C	0.40	1.00	0.232	0.027	9.20E-18
A2	rs761830	14	65282739	G	0.40	1.00	0.232	0.027	9.06E-18
A2	rs10483785	14	65289270	G	0.49	1.00	0.228	0.026	3.02E-18
A2	rs6573624	14	65296638	G	0.49	0.98	0.231	0.026	1.95E-18
A2	rs2411405	14	65301839	G	0.53	0.98	-0.239	0.027	2.21E-19
A2	rs743084	14	65302355	C	0.53	0.97	-0.240	0.027	1.89E-19
A2	rs11625362	14	65302622	G	0.47	0.98	0.239	0.027	2.16E-19
A2	rs4080329	14	65303243	C	0.63	0.97	-0.251	0.027	7.39E-20
A2	rs11627605	14	65304066	G	0.47	0.98	0.239	0.027	2.11E-19
A2	rs11627578	14	65304201	C	0.47	0.98	0.239	0.027	2.09E-19
A2	rs11628840	14	65305395	G	0.53	0.98	-0.239	0.027	2.10E-19
A2	rs1003401	14	65307473	G	0.38	0.98	0.247	0.027	1.64E-19
A2	rs4902416	14	65307843	C	0.53	0.98	-0.239	0.027	2.19E-19
A2	rs1984855	14	65309010	C	0.62	0.97	-0.247	0.027	1.62E-19
A2	rs730807	14	65309043	C	0.47	0.98	0.239	0.027	2.15E-19
A2	rs2411404	14	65309154	C	0.47	0.97	0.239	0.027	2.13E-19
A2	rs1075566	14	65309210	C	0.47	0.97	0.239	0.027	2.11E-19
A2	rs7157449	14	65309890	G	0.53	0.97	-0.239	0.027	2.11E-19
A2	rs6573625	14	65310387	C	0.63	0.97	-0.251	0.028	7.94E-20
A2	rs6573626	14	65310448	C	0.53	0.97	-0.239	0.027	2.17E-19
A2	rs7158556	14	65310482	T	0.37	0.97	0.251	0.028	7.71E-20
A2	rs12894466	14	65310520	G	0.47	0.97	0.239	0.027	2.14E-19
A2	rs11625882	14	65314952	G	0.47	0.97	0.239	0.027	2.20E-19
A2	rs2236067	14	65317765	G	0.62	0.97	-0.247	0.027	1.67E-19
A2	rs968540	14	65318817	G	0.63	0.97	-0.252	0.028	6.33E-20
A2	rs7142165	14	65319985	G	0.53	0.97	-0.240	0.027	1.82E-19
A2	rs7143026	14	65320709	G	0.39	0.95	0.241	0.028	1.90E-18
A2	rs6573627	14	65322079	C	0.52	0.97	-0.232	0.027	2.71E-18
A2	rs4400971	14	65324331	C	0.42	0.98	0.206	0.027	1.60E-14
A2	rs7151846	14	65325534	C	0.51	0.98	-0.228	0.026	7.69E-18
A2	rs4073416	14	65329147	C	0.42	0.98	0.205	0.027	1.63E-14
A2	rs4073415	14	65329283	G	0.51	0.98	-0.228	0.026	7.92E-18
A2	rs11850120	14	65330132	C	0.41	0.97	0.209	0.027	9.77E-15
A2	rs8018379	14	65331690	C	0.57	0.95	-0.230	0.027	4.14E-17
A2	rs8007846	14	65332716	G	0.47	0.98	0.176	0.027	5.48E-11
A2	rs8006608	14	65336577	G	0.96	0.81	-0.426	0.075	1.36E-08
A2	rs3924222	14	65343491	C	0.41	0.79	-0.199	0.030	1.75E-11
A2	rs10149325	14	65347120	G	0.41	0.79	-0.199	0.030	1.56E-11
A2	rs10149555	14	65347410	G	0.56	0.98	-0.145	0.026	3.38E-08
A2	rs12878546	14	65348273	C	0.56	0.97	-0.147	0.027	3.16E-08
A2	rs8009488	14	65349289	C	0.56	0.96	-0.147	0.027	3.51E-08
BA	rs217181	16	70671503	C	0.81	0.92	0.220	0.034	5.82E-11
BAMS	rs1820248	16	70597106	G	0.29	0.95	0.187	0.029	1.53E-10
BAMS	rs3213423	16	70600326	G	0.75	1.00	-0.203	0.030	1.35E-11
BAMS	rs152828	16	70681387	C	0.90	0.99	-0.231	0.042	3.99E-08
BAMS	rs150617	16	70696897	C	0.89	0.95	-0.230	0.042	5.57E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
BAMS	rs30433	16	70702905	C	0.90	0.90	-0.250	0.045	2.14E-08
TRIA	rs217181	16	70671503	C	0.81	0.92	-0.225	0.034	2.47E-11
TA	rs1257189	2	134718008	C	0.73	0.88	-0.176	0.031	7.77E-09
TA	rs2593704	2	134721747	C	0.75	0.90	-0.194	0.031	4.84E-10
TA	rs1257196	2	134722302	G	0.27	0.89	0.176	0.030	7.69E-09
TA	rs1257197	2	134724206	G	0.73	0.87	-0.196	0.031	2.44E-10
TA	rs2442046	2	134730548	C	0.74	0.98	-0.187	0.029	1.79E-10
TA	rs2460382	2	134730586	G	0.26	0.98	0.187	0.029	1.80E-10
TA	rs2460383	2	134730596	C	0.74	0.98	-0.187	0.029	1.81E-10
TA	rs1257220	2	134731817	G	0.74	0.99	-0.187	0.029	1.87E-10
TA	rs1257221	2	134733088	C	0.71	0.88	-0.191	0.030	1.82E-10
G3	rs2878404	16	70602687	C	0.32	0.99	0.153	0.028	2.62E-08
G3	rs1465457	16	70603769	C	0.68	0.99	-0.154	0.028	2.36E-08
G3	rs217181	16	70671503	C	0.81	0.92	-0.257	0.034	2.49E-14
G3	rs2023929	16	70794457	G	0.88	0.99	-0.216	0.040	5.21E-08

Chr= chromosome; Position= position (build 36); EA= effect allele; EAF= effect allele frequency; RSq= average imputation quality (RSq) across meta-analysis populations; SE= standard error of beta

*effect expressed in standard deviation units after adjustment for sex, age and the first 3 principal components

Table 25: SNP associations with P-value<1E-07 in IgG *N*-glycans GWAS analysed by UPLC.

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP1	rs1894204	11	67686247	C	0.59	0.88	0.179	0.033	4.28E-08
IGP1	rs10896298	11	67688035	C	0.51	1.00	0.171	0.030	1.31E-08
IGP1	rs4930561	11	67688337	G	0.51	1.00	0.171	0.030	1.30E-08
IGP1	rs7931502	11	67716183	C	0.59	0.89	0.178	0.032	4.47E-08
IGP1	rs4930564	11	67739857	G	0.41	0.86	-0.181	0.033	4.45E-08
IGP2	rs1049110	6	32834781	C	0.35	0.98	0.185	0.034	4.44E-08
IGP2	rs7782210	7	50319291	G	0.38	0.98	-0.187	0.032	4.12E-09
IGP2	rs6583437	7	50320813	G	0.64	0.98	0.193	0.032	1.56E-09
IGP2	rs7789913	7	50323241	C	0.62	1.00	0.185	0.032	4.23E-09
IGP2	rs6421315	7	50325753	C	0.37	0.95	-0.190	0.032	4.25E-09
IGP2	rs1122979	7	150546004	G	0.88	0.91	0.313	0.049	2.10E-10
IGP2	rs7812088	7	150550762	G	0.87	0.98	0.298	0.047	2.72E-10
IGP2	rs7781265	7	150581873	G	0.88	0.92	0.299	0.050	2.40E-09
IGP2	rs1256519	14	64806077	G	0.44	0.89	-0.191	0.033	4.31E-09
IGP2	rs7159888	14	64828395	G	0.55	0.99	-0.251	0.031	1.22E-15
IGP2	rs12431963	14	64829447	C	0.92	0.92	-0.406	0.059	6.08E-12
IGP2	rs1256540	14	64833822	C	0.43	1.00	0.251	0.031	1.16E-15
IGP2	rs4902383	14	64834326	C	0.19	0.94	0.261	0.040	6.39E-11
IGP2	rs1269068	14	64837086	C	0.57	1.00	-0.251	0.031	1.25E-15
IGP2	rs10135194	14	64840731	C	0.94	0.84	-0.417	0.071	3.87E-09
IGP2	rs1760978	14	64840800	G	0.43	0.98	0.280	0.031	5.17E-19
IGP2	rs10144975	14	64843735	C	0.80	0.98	-0.275	0.038	7.11E-13
IGP2	rs17102587	14	64844230	C	0.20	0.97	0.283	0.039	2.22E-13
IGP2	rs8017974	14	64844940	C	0.20	0.99	0.284	0.038	1.29E-13
IGP2	rs11847263	14	64845448	G	0.39	0.98	0.291	0.032	7.93E-20
IGP2	rs10132229	14	64847313	G	0.10	1.00	0.373	0.051	2.69E-13
IGP2	rs4902386	14	64848043	C	0.81	0.99	-0.284	0.038	1.16E-13
IGP2	rs10147958	14	64848586	C	0.10	1.00	0.373	0.051	2.66E-13
IGP2	rs8019473	14	64848881	G	0.81	0.99	-0.284	0.038	1.14E-13
IGP2	rs10138662	14	64849235	G	0.19	0.99	0.284	0.038	1.10E-13
IGP2	rs10134589	14	64850987	T	0.19	0.94	0.306	0.040	1.10E-14
IGP2	rs7151212	14	64851375	C	0.81	0.99	-0.284	0.038	1.05E-13
IGP2	rs11158587	14	64852465	G	0.81	0.99	-0.285	0.038	1.03E-13
IGP2	rs8019767	14	64852538	G	0.81	1.00	-0.285	0.038	1.02E-13
IGP2	rs6573598	14	64852772	C	0.19	1.00	0.285	0.038	1.01E-13
IGP2	rs6573599	14	64852880	C	0.81	1.00	-0.285	0.038	9.79E-14
IGP2	rs10144503	14	64853862	G	0.90	1.00	-0.374	0.051	2.43E-13
IGP2	rs6573602	14	64854363	C	0.19	1.00	0.285	0.038	9.51E-14
IGP2	rs17102598	14	64854613	G	0.81	1.00	-0.285	0.038	9.44E-14
IGP2	rs12436299	14	64854947	G	0.90	1.00	-0.374	0.051	2.39E-13
IGP2	rs6573604	14	64857694	C	0.19	1.00	0.285	0.038	9.26E-14
IGP2	rs9635250	14	64869101	T	0.10	1.00	0.374	0.051	2.33E-13
IGP2	rs12881755	14	64871564	G	0.65	0.96	-0.240	0.033	8.12E-13
IGP2	rs747541	14	64875163	C	0.45	0.98	0.274	0.032	6.21E-18
IGP2	rs1954052	14	64875462	T	0.44	0.99	0.274	0.032	5.35E-18
IGP2	rs12436465	14	64876630	C	0.72	0.98	-0.202	0.035	1.05E-08
IGP2	rs12886005	14	64879000	C	0.45	0.87	0.279	0.034	1.32E-16
IGP2	rs12886168	14	64879039	C	0.45	0.98	0.274	0.032	6.16E-18
IGP2	rs11623920	14	64889067	C	0.56	1.00	-0.274	0.032	5.30E-18
IGP2	rs11621121	14	64892246	C	0.44	1.00	0.274	0.032	5.36E-18
IGP2	rs10148907	14	64903125	C	0.69	0.98	-0.274	0.034	1.80E-15
IGP2	rs4902393	14	64909267	C	0.56	0.99	-0.274	0.032	7.42E-18

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP2	rs11621604	14	64910527	G	0.56	0.98	-0.271	0.032	2.07E-17
IGP2	rs12882269	14	64916897	G	0.56	0.97	-0.270	0.032	3.30E-17
IGP2	rs11158591	14	64925515	C	0.44	0.97	0.268	0.032	4.29E-17
IGP2	rs11158592	14	64929721	G	0.50	0.99	0.248	0.031	9.38E-16
IGP2	rs11158593	14	64929737	G	0.50	0.99	0.250	0.031	4.68E-16
IGP2	rs10138570	14	64929791	G	0.50	0.99	-0.250	0.031	4.73E-16
IGP2	rs10138671	14	64929845	G	0.58	0.99	-0.173	0.031	3.18E-08
IGP2	rs4587890	14	64933537	T	0.42	0.99	0.173	0.031	3.22E-08
IGP2	rs2411823	14	64934819	C	0.42	0.99	0.173	0.031	3.27E-08
IGP2	rs2411822	14	64948148	G	0.48	1.00	-0.233	0.031	3.88E-14
IGP2	rs1953416	14	64948560	C	0.53	1.00	0.236	0.031	2.12E-14
IGP2	rs883081	14	64950374	C	0.53	1.00	0.236	0.031	2.20E-14
IGP2	rs883082	14	64950693	G	0.48	1.00	-0.233	0.031	4.07E-14
IGP2	rs867972	14	64965514	C	0.48	0.97	-0.237	0.031	3.30E-14
IGP2	rs11851576	14	64970036	C	0.54	0.99	-0.203	0.031	7.89E-11
IGP2	rs12879971	14	64971357	G	0.52	0.99	0.236	0.031	2.63E-14
IGP2	rs12892058	14	64973194	C	0.47	0.99	-0.239	0.031	1.19E-14
IGP2	rs10483776	14	64984620	G	0.22	1.00	0.218	0.038	1.41E-08
IGP2	rs12589698	14	64990188	G	0.52	0.98	0.244	0.031	3.92E-15
IGP2	rs4899179	14	64996501	G	0.49	0.99	-0.242	0.031	6.33E-15
IGP2	rs2184603	14	65000423	C	0.49	0.99	-0.242	0.031	6.21E-15
IGP2	rs3825640	14	65030957	C	0.51	0.99	0.244	0.031	3.21E-15
IGP2	rs11627084	14	65048589	G	0.49	1.00	-0.241	0.031	5.89E-15
IGP2	rs10483780	14	65049923	C	0.50	0.99	-0.237	0.031	1.97E-14
IGP2	rs2149841	14	65080072	C	0.51	0.99	0.244	0.031	3.13E-15
IGP2	rs11621680	14	65084434	G	0.50	0.99	-0.237	0.031	1.87E-14
IGP2	rs11623662	14	65090945	G	0.60	0.99	-0.180	0.032	1.24E-08
IGP2	rs9972106	14	65092884	T	0.60	0.99	-0.180	0.032	1.22E-08
IGP2	rs11158601	14	65095116	G	0.49	1.00	-0.241	0.031	5.75E-15
IGP2	rs7146742	14	65102687	G	0.43	0.99	0.214	0.032	1.61E-11
IGP2	rs1958561	14	65106514	G	0.49	1.00	-0.241	0.031	6.10E-15
IGP2	rs12887134	14	65115296	C	0.49	0.99	-0.243	0.031	3.37E-15
IGP2	rs7155541	14	65115995	C	0.49	0.99	-0.243	0.031	3.39E-15
IGP2	rs6573615	14	65116287	G	0.40	0.99	0.180	0.032	1.25E-08
IGP2	rs7160780	14	65122466	G	0.40	0.99	0.181	0.032	9.88E-09
IGP2	rs7161123	14	65122654	G	0.51	1.00	0.240	0.031	5.95E-15
IGP2	rs2411356	14	65122914	G	0.40	0.99	0.181	0.032	9.91E-09
IGP2	rs4581615	14	65125696	C	0.51	1.00	0.240	0.031	5.94E-15
IGP2	rs17753508	14	65127205	G	0.22	1.00	0.221	0.039	9.43E-09
IGP2	rs3783709	14	65128417	T	0.51	1.00	0.240	0.031	5.95E-15
IGP2	rs12889002	14	65133335	C	0.51	1.00	0.240	0.031	5.94E-15
IGP2	rs743085	14	65137886	G	0.49	1.00	-0.240	0.031	5.94E-15
IGP2	rs8012278	14	65152326	G	0.49	1.00	-0.246	0.031	1.64E-15
IGP2	rs12890902	14	65186375	T	0.51	1.00	0.247	0.031	1.12E-15
IGP2	rs2300865	14	65189768	C	0.49	1.00	-0.247	0.031	1.09E-15
IGP2	rs11627184	14	65191196	C	0.51	1.00	0.247	0.031	1.01E-15
IGP2	rs11627185	14	65191245	G	0.49	1.00	-0.247	0.031	9.67E-16
IGP2	rs7142651	14	65202474	C	0.51	1.00	0.248	0.031	8.91E-16
IGP2	rs1998036	14	65207952	C	0.49	0.99	-0.248	0.031	8.51E-16
IGP2	rs2268959	14	65215071	C	0.78	1.00	-0.228	0.038	2.90E-09
IGP2	rs2268960	14	65215253	G	0.07	0.97	0.327	0.061	8.97E-08
IGP2	rs2268961	14	65216518	C	0.49	0.99	-0.249	0.031	6.84E-16
IGP2	rs2268962	14	65217026	G	0.49	1.00	-0.249	0.031	6.68E-16
IGP2	rs2064694	14	65217999	G	0.51	1.00	0.248	0.031	8.24E-16

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP2	rs12588838	14	65232391	G	0.51	1.00	0.248	0.031	7.88E-16
IGP2	rs11628765	14	65238202	C	0.49	1.00	-0.248	0.031	7.35E-16
IGP2	rs2411351	14	65241294	C	0.49	1.00	-0.249	0.031	7.10E-16
IGP2	rs11846546	14	65246146	G	0.14	0.99	0.251	0.045	2.22E-08
IGP2	rs8018278	14	65249841	G	0.49	1.00	-0.249	0.031	7.06E-16
IGP2	rs11627067	14	65252706	G	0.49	1.00	-0.249	0.031	7.03E-16
IGP2	rs4143898	14	65258635	T	0.44	0.99	0.221	0.031	2.13E-12
IGP2	rs11622829	14	65261535	T	0.50	1.00	0.248	0.031	9.74E-16
IGP2	rs11624104	14	65265890	G	0.50	1.00	-0.245	0.031	2.03E-15
IGP2	rs1535173	14	65268892	C	0.50	1.00	0.245	0.031	2.17E-15
IGP2	rs3742597	14	65269930	G	0.29	1.00	0.281	0.035	5.60E-16
IGP2	rs927004	14	65270664	C	0.50	1.00	-0.244	0.031	2.42E-15
IGP2	rs1950557	14	65271510	C	0.71	1.00	-0.281	0.035	5.64E-16
IGP2	rs8010876	14	65276729	G	0.50	1.00	-0.244	0.031	2.35E-15
IGP2	rs1054218	14	65278943	C	0.40	1.00	0.235	0.032	1.52E-13
IGP2	rs761830	14	65282739	G	0.40	1.00	0.235	0.032	1.53E-13
IGP2	rs10483785	14	65289270	G	0.50	1.00	0.244	0.031	2.54E-15
IGP2	rs6573624	14	65296638	G	0.50	0.98	0.245	0.031	3.12E-15
IGP2	rs2411405	14	65301839	G	0.53	0.97	-0.242	0.031	8.45E-15
IGP2	rs743084	14	65302355	C	0.52	0.97	-0.241	0.031	1.61E-14
IGP2	rs11625362	14	65302622	G	0.47	0.97	0.242	0.031	8.70E-15
IGP2	rs4080329	14	65303243	C	0.62	0.97	-0.237	0.032	2.66E-13
IGP2	rs11627605	14	65304066	G	0.47	0.97	0.242	0.031	8.98E-15
IGP2	rs11627578	14	65304201	C	0.47	0.97	0.242	0.031	9.00E-15
IGP2	rs11628840	14	65305395	G	0.53	0.97	-0.242	0.031	9.05E-15
IGP2	rs1003401	14	65307473	G	0.39	0.97	0.239	0.032	1.08E-13
IGP2	rs4902416	14	65307843	C	0.53	0.97	-0.242	0.031	9.35E-15
IGP2	rs1984855	14	65309010	C	0.61	0.97	-0.239	0.032	1.09E-13
IGP2	rs730807	14	65309043	C	0.47	0.97	0.242	0.031	9.55E-15
IGP2	rs2411404	14	65309154	C	0.47	0.97	0.242	0.031	9.64E-15
IGP2	rs1075566	14	65309210	C	0.47	0.97	0.242	0.031	9.74E-15
IGP2	rs7157449	14	65309890	G	0.53	0.97	-0.242	0.031	9.97E-15
IGP2	rs6573625	14	65310387	C	0.62	0.97	-0.236	0.032	3.18E-13
IGP2	rs6573626	14	65310448	C	0.53	0.97	-0.242	0.031	1.14E-14
IGP2	rs7158556	14	65310482	T	0.38	0.97	0.236	0.032	3.23E-13
IGP2	rs12894466	14	65310520	G	0.47	0.97	0.242	0.031	1.17E-14
IGP2	rs11625882	14	65314952	G	0.47	0.97	0.241	0.031	1.31E-14
IGP2	rs2236067	14	65317765	G	0.61	0.97	-0.238	0.032	1.43E-13
IGP2	rs968540	14	65318817	G	0.62	0.96	-0.236	0.032	4.03E-13
IGP2	rs7142165	14	65319985	G	0.53	0.96	-0.240	0.031	1.74E-14
IGP2	rs7143026	14	65320709	G	0.40	0.95	0.220	0.033	1.38E-11
IGP2	rs6573627	14	65322079	C	0.51	0.98	-0.226	0.031	5.67E-13
IGP2	rs4400971	14	65324331	C	0.42	0.99	0.188	0.032	2.27E-09
IGP2	rs7151846	14	65325534	C	0.51	0.99	-0.219	0.031	2.17E-12
IGP2	rs4073416	14	65329147	C	0.42	0.99	0.188	0.032	2.37E-09
IGP2	rs4073415	14	65329283	G	0.51	0.99	-0.219	0.031	2.20E-12
IGP2	rs11850120	14	65330132	C	0.42	0.98	0.185	0.032	6.39E-09
IGP2	rs8018379	14	65331690	C	0.56	0.95	-0.231	0.032	6.50E-13
IGP2	rs8007846	14	65332716	G	0.48	0.98	0.186	0.031	3.00E-09
IGP2	rs3924222	14	65343491	C	0.41	0.80	-0.244	0.035	2.68E-12
IGP2	rs10149325	14	65347120	G	0.41	0.80	-0.245	0.035	2.17E-12
IGP3	rs17348299	5	55358652	C	0.84	0.85	-0.266	0.045	2.39E-09
IGP3	rs16884711	5	55360559	C	0.19	0.91	0.218	0.040	6.53E-08
IGP5	rs1122979	7	150546004	G	0.88	0.91	0.295	0.049	1.89E-09

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP5	rs7812088	7	150550762	G	0.87	0.98	0.279	0.047	2.67E-09
IGP5	rs7781265	7	150581873	G	0.88	0.92	0.286	0.050	9.71E-09
IGP5	rs5757647	22	38104993	C	0.33	1.00	0.181	0.033	3.00E-08
IGP5	rs4821890	22	38107469	G	0.34	0.99	0.179	0.033	4.13E-08
IGP5	rs1010169	22	38108113	G	0.67	1.00	-0.181	0.033	2.98E-08
IGP5	rs1010170	22	38108273	C	0.67	1.00	-0.181	0.033	3.02E-08
IGP5	rs5757650	22	38108365	C	0.67	1.00	-0.181	0.033	3.02E-08
IGP5	rs9611169	22	38112973	C	0.33	1.00	0.181	0.033	3.02E-08
IGP5	rs9611170	22	38114791	C	0.66	0.99	-0.177	0.033	5.76E-08
IGP5	rs2413590	22	38120137	C	0.67	1.00	-0.179	0.033	4.28E-08
IGP5	rs5750808	22	38120933	G	0.33	1.00	0.179	0.033	4.38E-08
IGP5	rs5750811	22	38123012	G	0.67	1.00	-0.178	0.033	4.52E-08
IGP5	rs5750812	22	38123025	G	0.34	0.99	0.177	0.033	6.00E-08
IGP5	rs5757655	22	38127124	C	0.66	0.99	-0.177	0.033	5.99E-08
IGP5	rs4821893	22	38127725	G	0.33	1.00	0.179	0.033	4.05E-08
IGP5	rs5750814	22	38127933	C	0.67	1.00	-0.179	0.033	3.95E-08
IGP5	rs5757657	22	38128375	G	0.33	1.00	0.178	0.033	4.23E-08
IGP5	rs5750815	22	38128395	C	0.67	1.00	-0.178	0.033	4.23E-08
IGP5	rs4337572	22	38130650	C	0.33	1.00	0.178	0.033	4.26E-08
IGP5	rs4821894	22	38139766	C	0.67	1.00	-0.178	0.033	4.28E-08
IGP5	rs5750816	22	38140325	C	0.33	1.00	0.178	0.033	4.33E-08
IGP5	rs5757659	22	38142355	G	0.66	1.00	-0.178	0.033	4.34E-08
IGP5	rs6001587	22	38148954	C	0.66	1.00	-0.178	0.033	4.33E-08
IGP5	rs5750818	22	38150831	G	0.66	1.00	-0.178	0.033	4.31E-08
IGP5	rs5757665	22	38151587	G	0.66	1.00	-0.178	0.033	4.29E-08
IGP5	rs4821895	22	38152961	G	0.66	1.00	-0.178	0.033	4.27E-08
IGP5	rs739141	22	38154396	C	0.36	1.00	0.181	0.032	1.97E-08
IGP5	rs5750820	22	38155268	G	0.67	0.97	-0.191	0.033	7.08E-09
IGP5	rs5750822	22	38156734	G	0.34	1.00	0.179	0.033	4.01E-08
IGP5	rs7949	22	38157499	G	0.34	0.99	0.179	0.033	3.72E-08
IGP5	rs5757670	22	38159682	G	0.34	0.99	0.180	0.033	3.52E-08
IGP5	rs5750825	22	38161224	G	0.71	0.98	-0.214	0.034	4.13E-10
IGP5	rs1972280	22	38161932	T	0.29	0.98	0.215	0.034	3.43E-10
IGP5	rs4821897	22	38165533	G	0.71	0.97	-0.216	0.034	3.27E-10
IGP5	rs5750830	22	38170774	C	0.29	0.98	0.218	0.034	1.81E-10
IGP5	rs5757676	22	38171646	C	0.78	0.96	-0.199	0.037	9.08E-08
IGP5	rs8137426	22	38174296	G	0.71	0.98	-0.218	0.034	1.80E-10
IGP5	rs5757683	22	38180120	G	0.29	0.98	0.218	0.034	1.78E-10
IGP5	rs1557541	22	38181916	C	0.29	0.98	0.218	0.034	1.77E-10
IGP5	rs1557542	22	38182296	C	0.71	0.98	-0.218	0.034	1.75E-10
IGP5	rs5995735	22	38184367	C	0.29	0.98	0.218	0.034	1.73E-10
IGP5	rs738289	22	38185829	C	0.29	0.98	0.218	0.034	1.70E-10
IGP5	rs909674	22	38189115	C	0.30	0.99	0.218	0.034	1.10E-10
IGP6	rs7782210	7	50319291	G	0.38	0.98	-0.176	0.032	2.49E-08
IGP6	rs6583437	7	50320813	G	0.64	0.98	0.182	0.032	1.13E-08
IGP6	rs7789913	7	50323241	C	0.62	1.00	0.175	0.031	2.72E-08
IGP6	rs6421315	7	50325753	C	0.37	0.95	-0.181	0.032	1.95E-08
IGP6	rs7159888	14	64828395	G	0.55	0.99	-0.212	0.031	8.72E-12
IGP6	rs1256540	14	64833822	C	0.43	1.00	0.185	0.031	2.96E-09
IGP6	rs4902383	14	64834326	C	0.19	0.94	0.244	0.040	7.13E-10
IGP6	rs1269068	14	64837086	C	0.57	1.00	-0.184	0.031	3.42E-09
IGP6	rs1760978	14	64840800	G	0.43	0.98	0.214	0.031	7.37E-12
IGP6	rs10144975	14	64843735	C	0.80	0.98	-0.243	0.038	1.81E-10
IGP6	rs17102587	14	64844230	C	0.20	0.97	0.252	0.038	4.68E-11

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP6	rs8017974	14	64844940	C	0.20	0.99	0.255	0.038	2.01E-11
IGP6	rs11847263	14	64845448	G	0.39	0.98	0.248	0.032	4.69E-15
IGP6	rs10132229	14	64847313	G	0.10	1.00	0.276	0.050	4.27E-08
IGP6	rs4902386	14	64848043	C	0.80	0.99	-0.255	0.038	1.75E-11
IGP6	rs10147958	14	64848586	C	0.10	1.00	0.276	0.050	4.15E-08
IGP6	rs8019473	14	64848881	G	0.80	0.99	-0.256	0.038	1.73E-11
IGP6	rs10138662	14	64849235	G	0.20	0.99	0.256	0.038	1.65E-11
IGP6	rs10134589	14	64850987	T	0.20	0.94	0.263	0.039	2.15E-11
IGP6	rs7151212	14	64851375	C	0.80	0.99	-0.256	0.038	1.57E-11
IGP6	rs11158587	14	64852465	G	0.80	0.99	-0.256	0.038	1.55E-11
IGP6	rs8019767	14	64852538	G	0.80	1.00	-0.256	0.038	1.55E-11
IGP6	rs6573598	14	64852772	C	0.20	1.00	0.256	0.038	1.54E-11
IGP6	rs6573599	14	64852880	C	0.80	1.00	-0.256	0.038	1.46E-11
IGP6	rs10144503	14	64853862	G	0.90	1.00	-0.278	0.050	3.29E-08
IGP6	rs6573602	14	64854363	C	0.20	1.00	0.256	0.038	1.42E-11
IGP6	rs17102598	14	64854613	G	0.80	1.00	-0.256	0.038	1.42E-11
IGP6	rs12436299	14	64854947	G	0.90	1.00	-0.279	0.050	3.11E-08
IGP6	rs6573604	14	64857694	C	0.20	1.00	0.256	0.038	1.41E-11
IGP6	rs9635250	14	64869101	T	0.10	1.00	0.279	0.050	3.03E-08
IGP6	rs747541	14	64875163	C	0.45	0.98	0.208	0.032	4.29E-11
IGP6	rs1954052	14	64875462	T	0.44	0.99	0.205	0.031	6.85E-11
IGP6	rs12886005	14	64879000	C	0.45	0.87	0.220	0.033	4.93E-11
IGP6	rs12886168	14	64879039	C	0.45	0.98	0.208	0.031	4.28E-11
IGP6	rs11623920	14	64889067	C	0.56	1.00	-0.205	0.031	6.84E-11
IGP6	rs11621121	14	64892246	C	0.44	1.00	0.205	0.031	6.83E-11
IGP6	rs10148907	14	64903125	C	0.69	0.98	-0.207	0.034	1.23E-09
IGP6	rs4902393	14	64909267	C	0.56	0.99	-0.205	0.032	8.41E-11
IGP6	rs11621604	14	64910527	G	0.56	0.98	-0.200	0.032	2.52E-10
IGP6	rs12882269	14	64916897	G	0.56	0.97	-0.199	0.032	3.60E-10
IGP6	rs11158591	14	64925515	C	0.44	0.97	0.198	0.032	4.39E-10
IGP6	rs11158592	14	64929721	G	0.50	0.99	0.176	0.031	9.59E-09
IGP6	rs11158593	14	64929737	G	0.50	0.99	0.175	0.031	1.25E-08
IGP6	rs10138570	14	64929791	G	0.50	0.99	-0.174	0.031	1.26E-08
IGP6	rs2411822	14	64948148	G	0.47	1.00	-0.172	0.031	1.91E-08
IGP6	rs1953416	14	64948560	C	0.53	1.00	0.171	0.031	2.53E-08
IGP6	rs883081	14	64950374	C	0.53	1.00	0.171	0.031	2.58E-08
IGP6	rs883082	14	64950693	G	0.47	1.00	-0.172	0.031	1.96E-08
IGP6	rs12879971	14	64971357	G	0.52	0.99	0.175	0.031	1.39E-08
IGP6	rs12892058	14	64973194	C	0.47	0.99	-0.175	0.031	1.47E-08
IGP6	rs12589698	14	64990188	G	0.52	0.98	0.179	0.031	6.75E-09
IGP6	rs4899179	14	64996501	G	0.49	0.99	-0.181	0.031	4.00E-09
IGP6	rs2184603	14	65000423	C	0.49	0.99	-0.181	0.031	3.91E-09
IGP6	rs3825640	14	65030957	C	0.51	0.99	0.180	0.031	4.49E-09
IGP6	rs11627084	14	65048589	G	0.49	1.00	-0.181	0.031	3.37E-09
IGP6	rs10483780	14	65049923	C	0.50	0.99	-0.174	0.031	1.65E-08
IGP6	rs2149841	14	65080072	C	0.51	0.99	0.180	0.031	4.69E-09
IGP6	rs11621680	14	65084434	G	0.50	0.99	-0.173	0.031	1.85E-08
IGP6	rs11158601	14	65095116	G	0.49	1.00	-0.180	0.031	4.23E-09
IGP6	rs1958561	14	65106514	G	0.49	1.00	-0.180	0.031	4.25E-09
IGP6	rs12887134	14	65115296	C	0.49	0.99	-0.179	0.031	5.74E-09
IGP6	rs7155541	14	65115995	C	0.49	0.99	-0.179	0.031	5.74E-09
IGP6	rs7161123	14	65122654	G	0.51	1.00	0.180	0.031	3.88E-09
IGP6	rs4581615	14	65125696	C	0.51	1.00	0.180	0.031	3.87E-09
IGP6	rs3783709	14	65128417	T	0.51	1.00	0.180	0.031	3.87E-09

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP6	rs12889002	14	65133335	C	0.51	1.00	0.180	0.031	3.86E-09
IGP6	rs743085	14	65137886	G	0.49	1.00	-0.180	0.031	3.86E-09
IGP6	rs8012278	14	65152326	G	0.49	1.00	-0.182	0.031	2.53E-09
IGP6	rs12890902	14	65186375	T	0.51	1.00	0.183	0.031	2.40E-09
IGP6	rs2300865	14	65189768	C	0.49	1.00	-0.183	0.031	2.39E-09
IGP6	rs11627184	14	65191196	C	0.51	1.00	0.183	0.031	2.35E-09
IGP6	rs11627185	14	65191245	G	0.49	1.00	-0.183	0.031	2.31E-09
IGP6	rs7142651	14	65202474	C	0.51	1.00	0.183	0.031	2.50E-09
IGP6	rs1998036	14	65207952	C	0.49	0.99	-0.183	0.031	2.49E-09
IGP6	rs2268961	14	65216518	C	0.49	0.99	-0.183	0.031	2.35E-09
IGP6	rs2268962	14	65217026	G	0.49	1.00	-0.183	0.031	2.34E-09
IGP6	rs2064694	14	65217999	G	0.51	1.00	0.181	0.031	3.38E-09
IGP6	rs12588838	14	65232391	G	0.51	1.00	0.181	0.031	3.38E-09
IGP6	rs11628765	14	65238202	C	0.49	1.00	-0.181	0.031	3.35E-09
IGP6	rs2411351	14	65241294	C	0.49	1.00	-0.181	0.031	3.37E-09
IGP6	rs8018278	14	65249841	G	0.49	1.00	-0.181	0.031	3.45E-09
IGP6	rs11627067	14	65252706	G	0.49	1.00	-0.181	0.031	3.50E-09
IGP6	rs11622829	14	65261535	T	0.50	1.00	0.176	0.031	9.39E-09
IGP6	rs11624104	14	65265890	G	0.50	1.00	-0.176	0.031	1.06E-08
IGP6	rs1535173	14	65268892	C	0.50	1.00	0.175	0.031	1.08E-08
IGP6	rs3742597	14	65269930	G	0.29	1.00	0.206	0.034	2.13E-09
IGP6	rs927004	14	65270664	C	0.50	1.00	-0.175	0.031	1.23E-08
IGP6	rs1950557	14	65271510	C	0.71	1.00	-0.206	0.034	2.23E-09
IGP6	rs8010876	14	65276729	G	0.50	1.00	-0.175	0.031	1.25E-08
IGP6	rs10483785	14	65289270	G	0.50	1.00	0.172	0.031	2.15E-08
IGP6	rs6573624	14	65296638	G	0.50	0.98	0.171	0.031	3.19E-08
IGP6	rs2411405	14	65301839	G	0.52	0.97	-0.177	0.031	1.09E-08
IGP6	rs743084	14	65302355	C	0.52	0.97	-0.181	0.031	6.46E-09
IGP6	rs11625362	14	65302622	G	0.48	0.97	0.177	0.031	1.16E-08
IGP6	rs11627605	14	65304066	G	0.48	0.97	0.177	0.031	1.21E-08
IGP6	rs11627578	14	65304201	C	0.48	0.97	0.177	0.031	1.22E-08
IGP6	rs11628840	14	65305395	G	0.52	0.97	-0.177	0.031	1.23E-08
IGP6	rs4902416	14	65307843	C	0.52	0.97	-0.177	0.031	1.27E-08
IGP6	rs730807	14	65309043	C	0.48	0.97	0.177	0.031	1.30E-08
IGP6	rs2411404	14	65309154	C	0.48	0.97	0.176	0.031	1.32E-08
IGP6	rs1075566	14	65309210	C	0.48	0.97	0.176	0.031	1.32E-08
IGP6	rs7157449	14	65309890	G	0.52	0.97	-0.176	0.031	1.35E-08
IGP6	rs6573626	14	65310448	C	0.52	0.97	-0.176	0.031	1.48E-08
IGP6	rs12894466	14	65310520	G	0.48	0.97	0.176	0.031	1.50E-08
IGP6	rs11625882	14	65314952	G	0.48	0.97	0.176	0.031	1.60E-08
IGP6	rs7142165	14	65319985	G	0.52	0.96	-0.175	0.031	1.90E-08
IGP6	rs8006608	14	65336577	G	0.96	0.81	-0.478	0.086	2.64E-08
IGP7	rs404256	6	90714504	C	0.56	0.70	-0.209	0.036	7.49E-09
IGP9	rs17630758	22	22466542	G	0.83	0.99	0.298	0.041	4.85E-13
IGP9	rs12167679	22	22471690	C	0.80	1.00	0.219	0.039	1.52E-08
IGP9	rs17548631	22	22474125	C	0.17	0.99	-0.298	0.041	4.65E-13
IGP9	rs9620326	22	22476629	C	0.83	0.99	0.298	0.041	4.73E-13
IGP9	rs9624334	22	22496256	C	0.17	0.99	-0.301	0.041	3.59E-13
IGP9	rs2186369	22	22500996	G	0.19	0.88	-0.304	0.042	3.00E-13
IGP9	rs5757642	22	38094770	C	0.64	1.00	-0.180	0.033	3.33E-08
IGP9	rs7286714	22	38095550	C	0.36	0.97	0.178	0.033	5.71E-08
IGP9	rs5757644	22	38096386	C	0.36	0.97	0.178	0.033	5.69E-08
IGP9	rs5750806	22	38096957	G	0.64	0.97	-0.178	0.033	5.72E-08
IGP9	rs1569499	22	38099764	C	0.64	0.97	-0.182	0.033	3.57E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP9	rs4821888	22	38100543	G	0.64	0.97	-0.182	0.033	3.64E-08
IGP9	rs5750825	22	38161224	G	0.71	0.98	-0.198	0.034	8.43E-09
IGP9	rs1972280	22	38161932	T	0.29	0.98	0.199	0.034	7.54E-09
IGP9	rs4821897	22	38165533	G	0.71	0.97	-0.199	0.034	7.07E-09
IGP9	rs5750830	22	38170774	C	0.29	0.98	0.199	0.034	6.97E-09
IGP9	rs8137426	22	38174296	G	0.71	0.98	-0.199	0.034	6.85E-09
IGP9	rs5757683	22	38180120	G	0.29	0.98	0.199	0.034	6.80E-09
IGP9	rs1557541	22	38181916	C	0.29	0.98	0.198	0.034	6.84E-09
IGP9	rs1557542	22	38182296	C	0.71	0.98	-0.198	0.034	6.82E-09
IGP9	rs5995735	22	38184367	C	0.29	0.98	0.198	0.034	6.78E-09
IGP9	rs738289	22	38185829	C	0.29	0.98	0.198	0.034	6.78E-09
IGP9	rs909674	22	38189115	C	0.30	0.99	0.201	0.034	2.80E-09
IGP10	rs17630758	22	22466542	G	0.83	0.99	0.237	0.041	9.92E-09
IGP10	rs17548631	22	22474125	C	0.17	0.99	-0.236	0.041	1.01E-08
IGP10	rs9620326	22	22476629	C	0.83	0.99	0.236	0.041	1.01E-08
IGP10	rs9624334	22	22496256	C	0.17	0.99	-0.235	0.042	1.52E-08
IGP10	rs2186369	22	22500996	G	0.19	0.88	-0.256	0.042	9.32E-10
IGP11	rs7159888	14	64828395	G	0.55	0.99	-0.208	0.031	2.43E-11
IGP11	rs1256540	14	64833822	C	0.43	1.00	0.169	0.031	6.23E-08
IGP11	rs4902383	14	64834326	C	0.19	0.94	0.241	0.040	1.45E-09
IGP11	rs1269068	14	64837086	C	0.57	1.00	-0.168	0.031	7.10E-08
IGP11	rs1760978	14	64840800	G	0.43	0.98	0.198	0.031	2.62E-10
IGP11	rs10144975	14	64843735	C	0.80	0.98	-0.238	0.038	4.69E-10
IGP11	rs17102587	14	64844230	C	0.20	0.97	0.245	0.038	1.79E-10
IGP11	rs8017974	14	64844940	C	0.20	0.99	0.247	0.038	1.08E-10
IGP11	rs11847263	14	64845448	G	0.39	0.98	0.238	0.032	7.27E-14
IGP11	rs4902386	14	64848043	C	0.80	0.99	-0.246	0.038	1.03E-10
IGP11	rs8019473	14	64848881	G	0.80	0.99	-0.246	0.038	1.02E-10
IGP11	rs10138662	14	64849235	G	0.20	0.99	0.247	0.038	9.82E-11
IGP11	rs10134589	14	64850987	T	0.19	0.94	0.259	0.039	5.28E-11
IGP11	rs7151212	14	64851375	C	0.80	0.99	-0.247	0.038	9.45E-11
IGP11	rs11158587	14	64852465	G	0.80	0.99	-0.247	0.038	9.43E-11
IGP11	rs8019767	14	64852538	G	0.80	1.00	-0.247	0.038	9.47E-11
IGP11	rs6573598	14	64852772	C	0.20	1.00	0.247	0.038	9.45E-11
IGP11	rs6573599	14	64852880	C	0.80	1.00	-0.247	0.038	9.01E-11
IGP11	rs6573602	14	64854363	C	0.20	1.00	0.247	0.038	8.81E-11
IGP11	rs17102598	14	64854613	G	0.80	1.00	-0.247	0.038	8.87E-11
IGP11	rs6573604	14	64857694	C	0.20	1.00	0.247	0.038	8.87E-11
IGP11	rs747541	14	64875163	C	0.45	0.98	0.206	0.032	6.84E-11
IGP11	rs1954052	14	64875462	T	0.44	0.99	0.203	0.032	1.15E-10
IGP11	rs12886005	14	64879000	C	0.45	0.87	0.215	0.034	1.45E-10
IGP11	rs12886168	14	64879039	C	0.45	0.98	0.206	0.032	6.66E-11
IGP11	rs11623920	14	64889067	C	0.56	1.00	-0.203	0.032	1.12E-10
IGP11	rs11621121	14	64892246	C	0.44	1.00	0.203	0.031	1.12E-10
IGP11	rs10148907	14	64903125	C	0.69	0.98	-0.208	0.034	1.28E-09
IGP11	rs4902393	14	64909267	C	0.56	0.99	-0.203	0.032	1.47E-10
IGP11	rs11621604	14	64910527	G	0.56	0.98	-0.198	0.032	4.63E-10
IGP11	rs12882269	14	64916897	G	0.56	0.97	-0.196	0.032	6.87E-10
IGP11	rs11158591	14	64925515	C	0.44	0.97	0.195	0.032	8.58E-10
IGP11	rs12879971	14	64971357	G	0.52	0.99	0.165	0.031	8.45E-08
IGP11	rs12589698	14	64990188	G	0.52	0.98	0.174	0.031	2.06E-08
IGP11	rs4899179	14	64996501	G	0.49	0.99	-0.176	0.031	1.12E-08
IGP11	rs2184603	14	65000423	C	0.49	0.99	-0.177	0.031	1.04E-08
IGP11	rs3825640	14	65030957	C	0.51	0.99	0.175	0.031	1.24E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP11	rs11627084	14	65048589	G	0.49	1.00	-0.177	0.031	8.26E-09
IGP11	rs10483780	14	65049923	C	0.50	0.99	-0.171	0.031	2.99E-08
IGP11	rs2149841	14	65080072	C	0.51	0.99	0.175	0.031	1.28E-08
IGP11	rs11621680	14	65084434	G	0.50	0.99	-0.170	0.031	3.21E-08
IGP11	rs11158601	14	65095116	G	0.49	1.00	-0.176	0.031	9.40E-09
IGP11	rs1958561	14	65106514	G	0.49	1.00	-0.176	0.031	9.25E-09
IGP11	rs12887134	14	65115296	C	0.49	0.99	-0.175	0.031	1.40E-08
IGP11	rs7155541	14	65115995	C	0.49	0.99	-0.175	0.031	1.40E-08
IGP11	rs7161123	14	65122654	G	0.51	1.00	0.177	0.031	8.22E-09
IGP11	rs4581615	14	65125696	C	0.51	1.00	0.177	0.031	8.23E-09
IGP11	rs3783709	14	65128417	T	0.51	1.00	0.177	0.031	8.25E-09
IGP11	rs12889002	14	65133335	C	0.51	1.00	0.177	0.031	8.27E-09
IGP11	rs743085	14	65137886	G	0.49	1.00	-0.177	0.031	8.29E-09
IGP11	rs8012278	14	65152326	G	0.49	1.00	-0.178	0.031	6.43E-09
IGP11	rs12890902	14	65186375	T	0.51	1.00	0.178	0.031	6.86E-09
IGP11	rs2300865	14	65189768	C	0.49	1.00	-0.178	0.031	6.89E-09
IGP11	rs11627184	14	65191196	C	0.51	1.00	0.178	0.031	6.83E-09
IGP11	rs11627185	14	65191245	G	0.49	1.00	-0.178	0.031	6.75E-09
IGP11	rs7142651	14	65202474	C	0.51	1.00	0.177	0.031	7.63E-09
IGP11	rs1998036	14	65207952	C	0.49	0.99	-0.177	0.031	7.65E-09
IGP11	rs2268961	14	65216518	C	0.49	0.99	-0.178	0.031	7.37E-09
IGP11	rs2268962	14	65217026	G	0.49	1.00	-0.178	0.031	7.35E-09
IGP11	rs2064694	14	65217999	G	0.51	1.00	0.175	0.031	1.14E-08
IGP11	rs12588838	14	65232391	G	0.51	1.00	0.175	0.031	1.14E-08
IGP11	rs11628765	14	65238202	C	0.49	1.00	-0.175	0.031	1.14E-08
IGP11	rs2411351	14	65241294	C	0.49	1.00	-0.175	0.031	1.16E-08
IGP11	rs8018278	14	65249841	G	0.49	1.00	-0.175	0.031	1.20E-08
IGP11	rs11627067	14	65252706	G	0.49	1.00	-0.175	0.031	1.24E-08
IGP11	rs11622829	14	65261535	T	0.50	1.00	0.168	0.031	4.83E-08
IGP11	rs11624104	14	65265890	G	0.50	1.00	-0.170	0.031	3.53E-08
IGP11	rs1535173	14	65268892	C	0.50	1.00	0.168	0.031	4.38E-08
IGP11	rs3742597	14	65269930	G	0.29	1.00	0.201	0.035	5.91E-09
IGP11	rs927004	14	65270664	C	0.50	1.00	-0.167	0.031	4.94E-08
IGP11	rs1950557	14	65271510	C	0.71	1.00	-0.201	0.035	6.09E-09
IGP11	rs8010876	14	65276729	G	0.50	1.00	-0.167	0.031	4.96E-08
IGP11	rs10483785	14	65289270	G	0.50	1.00	0.165	0.031	7.00E-08
IGP11	rs6573624	14	65296638	G	0.50	0.98	0.166	0.031	7.62E-08
IGP11	rs2411405	14	65301839	G	0.53	0.97	-0.177	0.031	1.16E-08
IGP11	rs743084	14	65302355	C	0.52	0.97	-0.177	0.031	1.32E-08
IGP11	rs11625362	14	65302622	G	0.47	0.97	0.177	0.031	1.20E-08
IGP11	rs11627605	14	65304066	G	0.47	0.97	0.177	0.031	1.23E-08
IGP11	rs11627578	14	65304201	C	0.47	0.97	0.177	0.031	1.24E-08
IGP11	rs11628840	14	65305395	G	0.53	0.97	-0.177	0.031	1.24E-08
IGP11	rs4902416	14	65307843	C	0.53	0.97	-0.177	0.031	1.26E-08
IGP11	rs730807	14	65309043	C	0.47	0.97	0.177	0.031	1.27E-08
IGP11	rs2411404	14	65309154	C	0.47	0.97	0.177	0.031	1.28E-08
IGP11	rs1075566	14	65309210	C	0.47	0.97	0.177	0.031	1.28E-08
IGP11	rs7157449	14	65309890	G	0.52	0.97	-0.177	0.031	1.29E-08
IGP11	rs6573626	14	65310448	C	0.52	0.97	-0.177	0.031	1.33E-08
IGP11	rs12894466	14	65310520	G	0.48	0.97	0.177	0.031	1.34E-08
IGP11	rs11625882	14	65314952	G	0.48	0.97	0.177	0.031	1.37E-08
IGP11	rs7142165	14	65319985	G	0.52	0.96	-0.177	0.031	1.44E-08
IGP11	rs6573627	14	65322079	C	0.51	0.98	-0.171	0.031	3.99E-08
IGP11	rs7151846	14	65325534	C	0.51	0.99	-0.170	0.031	4.04E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP11	rs4073415	14	65329283	G	0.51	0.99	-0.170	0.031	3.98E-08
IGP13	rs17348299	5	55358652	C	0.84	0.85	0.287	0.045	1.27E-10
IGP13	rs16884711	5	55360559	C	0.19	0.91	-0.242	0.041	2.63E-09
IGP13	rs10454831	5	55374548	T	0.80	0.90	0.224	0.040	2.35E-08
IGP13	rs955768	5	55374759	T	0.20	0.90	-0.225	0.040	2.32E-08
IGP13	rs12342831	9	33114872	C	0.26	0.97	-0.193	0.036	5.19E-08
IGP13	rs10813951	9	33118021	G	0.26	0.97	-0.193	0.036	5.19E-08
IGP13	rs2067749	9	33120640	G	0.11	0.98	0.270	0.050	6.91E-08
IGP13	rs10511909	9	33122518	C	0.11	0.98	0.270	0.050	7.10E-08
IGP13	rs3780486	9	33129453	C	0.74	0.97	0.194	0.036	5.13E-08
IGP13	rs10813957	9	33143527	G	0.74	0.96	0.196	0.036	4.73E-08
IGP14	rs17776120	3	188215373	C	0.64	0.80	-0.216	0.035	5.98E-10
IGP14	rs3821819	3	188215419	G	0.63	0.81	-0.213	0.035	7.02E-10
IGP14	rs967367	3	188217160	G	0.63	0.81	-0.213	0.035	6.75E-10
IGP14	rs278541	8	94292121	C	0.98	0.50	-0.802	0.146	4.24E-08
IGP14	rs9624334	22	22496256	C	0.17	0.99	-0.225	0.041	4.93E-08
IGP14	rs2186369	22	22500996	G	0.19	0.88	-0.229	0.042	3.40E-08
IGP15	rs11923417	3	188188484	C	0.60	0.45	-0.314	0.046	1.04E-11
IGP15	rs759602	3	188191498	G	0.78	0.98	-0.200	0.037	6.59E-08
IGP15	rs4012171	3	188194147	C	0.75	0.75	-0.297	0.040	2.04E-13
IGP15	rs16848727	3	188195657	G	0.25	0.71	-0.520	0.042	8.08E-36
IGP15	rs13322676	3	188201439	C	0.28	0.87	-0.492	0.036	7.06E-42
IGP15	rs6808800	3	188202068	G	0.51	0.85	-0.323	0.033	5.02E-23
IGP15	rs17775791	3	188205056	C	0.28	0.89	-0.492	0.036	2.62E-42
IGP15	rs7617523	3	188205144	G	0.34	0.89	-0.399	0.034	6.56E-32
IGP15	rs7652995	3	188205638	G	0.18	0.83	0.391	0.044	5.43E-19
IGP15	rs6764279	3	188206669	C	0.71	0.95	0.489	0.035	1.59E-45
IGP15	rs6788832	3	188206913	G	0.34	0.89	-0.397	0.034	6.15E-32
IGP15	rs3872721	3	188208185	G	0.24	0.89	0.384	0.038	3.62E-24
IGP15	rs11710456	3	188208581	G	0.70	0.88	0.498	0.035	2.05E-45
IGP15	rs3872722	3	188208971	C	0.41	0.89	0.328	0.033	2.09E-23
IGP15	rs7621161	3	188209864	C	0.72	0.94	0.491	0.035	1.68E-45
IGP15	rs10937278	3	188210509	T	0.23	0.94	0.372	0.037	2.99E-23
IGP15	rs10937279	3	188210530	G	0.77	0.94	-0.371	0.037	3.14E-23
IGP15	rs7619468	3	188210872	C	0.77	0.94	-0.371	0.037	3.21E-23
IGP15	rs4686830	3	188211259	G	0.77	0.96	-0.368	0.037	4.81E-23
IGP15	rs10804908	3	188211536	T	0.23	0.96	0.367	0.037	5.05E-23
IGP15	rs4686834	3	188211848	G	0.77	0.97	-0.364	0.037	6.92E-23
IGP15	rs4686835	3	188211912	C	0.23	0.97	0.364	0.037	7.40E-23
IGP15	rs4686836	3	188212059	C	0.23	0.97	0.363	0.037	7.81E-23
IGP15	rs4012256	3	188213035	C	0.77	0.97	-0.363	0.037	8.30E-23
IGP15	rs4012257	3	188213090	C	0.77	0.98	-0.362	0.037	8.69E-23
IGP15	rs7619989	3	188214443	C	0.59	0.89	-0.322	0.033	8.24E-23
IGP15	rs17776120	3	188215373	C	0.64	0.80	0.430	0.035	2.53E-34
IGP15	rs3821819	3	188215419	G	0.63	0.81	0.432	0.035	2.28E-35
IGP15	rs6444193	3	188216882	G	0.23	0.99	0.359	0.037	1.31E-22
IGP15	rs967367	3	188217160	G	0.63	0.81	0.432	0.035	2.92E-35
IGP15	rs4686837	3	188222371	G	0.70	0.86	0.287	0.036	1.62E-15
IGP15	rs9941987	3	188225221	G	0.18	0.79	0.364	0.045	1.18E-15
IGP15	rs4686838	3	188225747	G	0.45	0.71	-0.233	0.036	1.12E-10
IGP15	rs16861533	3	188237416	G	0.84	0.67	0.399	0.050	2.42E-15
IGP15	rs2268536	3	188239602	G	0.16	0.68	-0.391	0.050	7.40E-15
IGP15	rs9876699	3	188248791	C	0.56	0.92	-0.174	0.033	8.91E-08
IGP15	rs257101	3	188261522	C	0.23	0.49	-0.367	0.050	3.12E-13

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP17	rs17775791	3	188205056	C	0.28	0.89	-0.192	0.036	9.32E-08
IGP17	rs6764279	3	188206669	C	0.71	0.95	0.191	0.034	2.70E-08
IGP17	rs11710456	3	188208581	G	0.70	0.88	0.200	0.035	1.18E-08
IGP17	rs7621161	3	188209864	C	0.71	0.94	0.192	0.035	2.79E-08
IGP17	rs3818593	9	33110706	G	0.20	1.00	-0.232	0.039	2.68E-09
IGP17	rs10971418	9	33112024	C	0.80	0.98	0.231	0.039	3.23E-09
IGP17	rs10113903	9	33112645	C	0.31	0.99	-0.193	0.034	1.31E-08
IGP17	rs10738905	9	33113627	G	0.31	0.99	-0.192	0.034	1.39E-08
IGP17	rs10971419	9	33114161	C	0.31	0.99	-0.191	0.034	1.54E-08
IGP17	rs12342831	9	33114872	C	0.26	0.97	-0.237	0.036	2.70E-11
IGP17	rs10758189	9	33115804	C	0.31	0.92	-0.193	0.035	3.35E-08
IGP17	rs10813950	9	33117640	G	0.69	1.00	0.190	0.034	1.64E-08
IGP17	rs10813951	9	33118021	G	0.26	0.97	-0.236	0.036	2.74E-11
IGP17	rs3780490	9	33119839	G	0.31	1.00	-0.190	0.034	1.65E-08
IGP17	rs2067749	9	33120640	G	0.11	0.98	0.283	0.050	1.53E-08
IGP17	rs10758192	9	33121651	G	0.69	1.00	0.190	0.034	1.66E-08
IGP17	rs10511909	9	33122518	C	0.11	0.98	0.283	0.050	1.57E-08
IGP17	rs913214	9	33125085	G	0.69	1.00	0.190	0.034	1.68E-08
IGP17	rs10738906	9	33125634	C	0.31	1.00	-0.190	0.034	1.69E-08
IGP17	rs10124479	9	33126233	G	0.31	1.00	-0.190	0.034	1.70E-08
IGP17	rs10813954	9	33127596	C	0.31	1.00	-0.190	0.034	1.71E-08
IGP17	rs3780486	9	33129453	C	0.74	0.97	0.237	0.036	2.77E-11
IGP17	rs7864705	9	33130352	C	0.31	1.00	-0.190	0.034	1.72E-08
IGP17	rs7865745	9	33130976	G	0.69	1.00	0.190	0.034	1.72E-08
IGP17	rs7873903	9	33132728	G	0.69	0.99	0.191	0.034	1.73E-08
IGP17	rs3824458	9	33134809	C	0.69	0.99	0.191	0.034	1.66E-08
IGP17	rs10813957	9	33143527	G	0.74	0.96	0.239	0.036	2.78E-11
IGP17	rs10971438	9	33170308	G	0.30	0.75	-0.251	0.039	9.27E-11
IGP17	rs10813960	9	33170362	C	0.70	0.74	0.252	0.039	9.01E-11
IGP17	rs10971439	9	33170813	C	0.23	0.71	-0.260	0.043	2.06E-09
IGP17	rs4878639	9	36089399	C	0.26	0.95	-0.196	0.036	3.51E-08
IGP22	rs5750825	22	38161224	G	0.71	0.98	0.197	0.034	1.01E-08
IGP22	rs1972280	22	38161932	T	0.29	0.98	-0.198	0.034	9.01E-09
IGP22	rs4821897	22	38165533	G	0.71	0.97	0.198	0.034	8.68E-09
IGP22	rs5750830	22	38170774	C	0.29	0.98	-0.203	0.034	3.45E-09
IGP22	rs8137426	22	38174296	G	0.71	0.98	0.203	0.034	3.34E-09
IGP22	rs5757683	22	38180120	G	0.29	0.98	-0.202	0.034	3.34E-09
IGP22	rs1557541	22	38181916	C	0.29	0.98	-0.202	0.034	3.34E-09
IGP22	rs1557542	22	38182296	C	0.71	0.98	0.202	0.034	3.32E-09
IGP22	rs5995735	22	38184367	C	0.29	0.98	-0.202	0.034	3.30E-09
IGP22	rs738289	22	38185829	C	0.29	0.98	-0.202	0.034	3.27E-09
IGP22	rs909674	22	38189115	C	0.30	0.99	-0.210	0.034	5.33E-10
IGP23	rs16848727	3	188195657	G	0.25	0.71	-0.227	0.041	4.39E-08
IGP23	rs13322676	3	188201439	C	0.28	0.87	-0.218	0.036	1.58E-09
IGP23	rs17775791	3	188205056	C	0.28	0.89	-0.220	0.036	9.07E-10
IGP23	rs7617523	3	188205144	G	0.34	0.89	-0.202	0.034	2.11E-09
IGP23	rs6764279	3	188206669	C	0.71	0.95	0.227	0.034	4.11E-11
IGP23	rs6788832	3	188206913	G	0.34	0.89	-0.202	0.034	1.82E-09
IGP23	rs11710456	3	188208581	G	0.70	0.88	0.230	0.035	5.92E-11
IGP23	rs7621161	3	188209864	C	0.72	0.94	0.228	0.035	3.92E-11
IGP23	rs17776120	3	188215373	C	0.64	0.80	0.203	0.035	7.64E-09
IGP23	rs3821819	3	188215419	G	0.63	0.81	0.200	0.035	8.28E-09
IGP23	rs967367	3	188217160	G	0.63	0.81	0.200	0.035	8.78E-09
IGP23	rs9296009	6	32222493	T	0.20	0.76	-0.211	0.038	3.79E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP24	rs11923417	3	188188484	C	0.60	0.45	-0.258	0.046	1.72E-08
IGP24	rs759602	3	188191498	G	0.78	0.98	-0.198	0.037	6.71E-08
IGP24	rs4012171	3	188194147	C	0.75	0.75	-0.264	0.040	4.59E-11
IGP24	rs16848727	3	188195657	G	0.25	0.71	-0.429	0.041	2.65E-25
IGP24	rs13322676	3	188201439	C	0.28	0.87	-0.406	0.036	1.70E-29
IGP24	rs6808800	3	188202068	G	0.51	0.85	-0.273	0.032	3.66E-17
IGP24	rs17775791	3	188205056	C	0.28	0.89	-0.406	0.036	9.08E-30
IGP24	rs7617523	3	188205144	G	0.34	0.89	-0.351	0.034	1.47E-25
IGP24	rs7652995	3	188205638	G	0.18	0.83	0.353	0.043	4.46E-16
IGP24	rs6764279	3	188206669	C	0.71	0.95	0.396	0.034	5.33E-31
IGP24	rs6788832	3	188206913	G	0.34	0.89	-0.350	0.033	1.41E-25
IGP24	rs3872721	3	188208185	G	0.24	0.89	0.300	0.038	1.15E-15
IGP24	rs11710456	3	188208581	G	0.70	0.88	0.405	0.035	4.30E-31
IGP24	rs3872722	3	188208971	C	0.41	0.89	0.275	0.033	3.29E-17
IGP24	rs7621161	3	188209864	C	0.71	0.94	0.398	0.034	5.13E-31
IGP24	rs10937278	3	188210509	T	0.23	0.94	0.293	0.037	2.70E-15
IGP24	rs10937279	3	188210530	G	0.77	0.94	-0.292	0.037	2.77E-15
IGP24	rs7619468	3	188210872	C	0.77	0.94	-0.292	0.037	2.80E-15
IGP24	rs4686830	3	188211259	G	0.77	0.96	-0.290	0.037	3.01E-15
IGP24	rs10804908	3	188211536	T	0.23	0.96	0.290	0.037	3.08E-15
IGP24	rs4686834	3	188211848	G	0.77	0.97	-0.288	0.037	3.71E-15
IGP24	rs4686835	3	188211912	C	0.23	0.97	0.287	0.037	3.84E-15
IGP24	rs4686836	3	188212059	C	0.23	0.97	0.287	0.037	3.93E-15
IGP24	rs4012256	3	188213035	C	0.77	0.97	-0.287	0.037	4.08E-15
IGP24	rs4012257	3	188213090	C	0.77	0.98	-0.286	0.036	4.19E-15
IGP24	rs7619989	3	188214443	C	0.59	0.89	-0.270	0.032	6.64E-17
IGP24	rs17776120	3	188215373	C	0.64	0.80	0.355	0.035	2.52E-24
IGP24	rs3821819	3	188215419	G	0.63	0.81	0.356	0.034	5.32E-25
IGP24	rs6444193	3	188216882	G	0.23	0.99	0.284	0.036	5.33E-15
IGP24	rs967367	3	188217160	G	0.63	0.81	0.355	0.035	7.07E-25
IGP24	rs4686837	3	188222371	G	0.70	0.86	0.245	0.036	6.09E-12
IGP24	rs9941987	3	188225221	G	0.18	0.79	0.338	0.045	4.54E-14
IGP24	rs4686838	3	188225747	G	0.45	0.71	-0.204	0.036	1.01E-08
IGP24	rs16861533	3	188237416	G	0.84	0.67	0.343	0.050	6.69E-12
IGP24	rs2268536	3	188239602	G	0.16	0.68	-0.336	0.050	1.56E-11
IGP24	rs257101	3	188261522	C	0.23	0.49	-0.346	0.050	3.94E-12
IGP24	rs10113903	9	33112645	C	0.31	0.99	-0.202	0.034	2.23E-09
IGP24	rs10738905	9	33113627	G	0.31	0.99	-0.202	0.034	2.35E-09
IGP24	rs10971419	9	33114161	C	0.31	0.99	-0.201	0.034	2.57E-09
IGP24	rs12342831	9	33114872	C	0.26	0.97	-0.223	0.035	2.70E-10
IGP24	rs10758189	9	33115804	C	0.31	0.92	-0.200	0.035	9.83E-09
IGP24	rs10813950	9	33117640	G	0.69	1.00	0.200	0.034	2.76E-09
IGP24	rs10813951	9	33118021	G	0.26	0.97	-0.223	0.035	2.79E-10
IGP24	rs3780490	9	33119839	G	0.31	1.00	-0.200	0.034	2.84E-09
IGP24	rs10758192	9	33121651	G	0.69	1.00	0.200	0.034	2.91E-09
IGP24	rs913214	9	33125085	G	0.69	1.00	0.199	0.034	3.14E-09
IGP24	rs10738906	9	33125634	C	0.31	1.00	-0.199	0.034	3.21E-09
IGP24	rs10124479	9	33126233	G	0.31	1.00	-0.199	0.034	3.26E-09
IGP24	rs10813954	9	33127596	C	0.31	1.00	-0.199	0.034	3.38E-09
IGP24	rs10971424	9	33128775	C	0.34	0.90	-0.184	0.034	9.46E-08
IGP24	rs3780486	9	33129453	C	0.74	0.97	0.223	0.035	3.27E-10
IGP24	rs7864705	9	33130352	C	0.31	1.00	-0.199	0.034	3.40E-09
IGP24	rs7865745	9	33130976	G	0.69	1.00	0.199	0.034	3.40E-09
IGP24	rs7873903	9	33132728	G	0.69	0.99	0.199	0.034	3.43E-09

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP24	rs3824458	9	33134809	C	0.69	0.99	0.200	0.034	3.35E-09
IGP24	rs10813957	9	33143527	G	0.74	0.96	0.224	0.036	3.56E-10
IGP24	rs10971438	9	33170308	G	0.30	0.75	-0.238	0.039	7.30E-10
IGP24	rs10813960	9	33170362	C	0.70	0.74	0.238	0.039	7.17E-10
IGP26	rs16848727	3	188195657	G	0.25	0.71	-0.268	0.041	1.02E-10
IGP26	rs13322676	3	188201439	C	0.28	0.87	-0.251	0.036	3.63E-12
IGP26	rs17775791	3	188205056	C	0.28	0.89	-0.252	0.036	2.32E-12
IGP26	rs7617523	3	188205144	G	0.34	0.89	-0.221	0.034	5.55E-11
IGP26	rs6764279	3	188206669	C	0.71	0.95	0.249	0.034	3.89E-13
IGP26	rs6788832	3	188206913	G	0.34	0.89	-0.220	0.034	5.16E-11
IGP26	rs11710456	3	188208581	G	0.70	0.88	0.256	0.035	2.47E-13
IGP26	rs7621161	3	188209864	C	0.71	0.94	0.250	0.034	4.10E-13
IGP26	rs17776120	3	188215373	C	0.64	0.80	0.202	0.035	7.72E-09
IGP26	rs3821819	3	188215419	G	0.63	0.81	0.204	0.035	3.95E-09
IGP26	rs967367	3	188217160	G	0.63	0.81	0.203	0.035	4.51E-09
IGP26	rs3818593	9	33110706	G	0.20	1.00	-0.231	0.039	2.81E-09
IGP26	rs10971418	9	33112024	C	0.80	0.98	0.230	0.039	3.31E-09
IGP26	rs10113903	9	33112645	C	0.31	0.99	-0.194	0.034	9.24E-09
IGP26	rs10738905	9	33113627	G	0.31	0.99	-0.194	0.034	9.69E-09
IGP26	rs10971419	9	33114161	C	0.31	0.99	-0.193	0.034	1.05E-08
IGP26	rs12342831	9	33114872	C	0.26	0.97	-0.236	0.035	2.96E-11
IGP26	rs10758189	9	33115804	C	0.31	0.92	-0.194	0.035	2.52E-08
IGP26	rs10813950	9	33117640	G	0.69	1.00	0.192	0.034	1.12E-08
IGP26	rs10813951	9	33118021	G	0.26	0.97	-0.236	0.035	3.04E-11
IGP26	rs3780490	9	33119839	G	0.31	1.00	-0.192	0.034	1.14E-08
IGP26	rs10758192	9	33121651	G	0.69	1.00	0.192	0.034	1.16E-08
IGP26	rs913214	9	33125085	G	0.69	1.00	0.192	0.034	1.22E-08
IGP26	rs10738906	9	33125634	C	0.31	1.00	-0.192	0.034	1.24E-08
IGP26	rs10124479	9	33126233	G	0.31	1.00	-0.192	0.034	1.25E-08
IGP26	rs10813954	9	33127596	C	0.31	1.00	-0.192	0.034	1.28E-08
IGP26	rs3780486	9	33129453	C	0.74	0.97	0.235	0.036	3.36E-11
IGP26	rs7864705	9	33130352	C	0.31	1.00	-0.192	0.034	1.29E-08
IGP26	rs7865745	9	33130976	G	0.69	1.00	0.192	0.034	1.29E-08
IGP26	rs7873903	9	33132728	G	0.69	0.99	0.192	0.034	1.30E-08
IGP26	rs3824458	9	33134809	C	0.69	0.99	0.193	0.034	1.26E-08
IGP26	rs10813957	9	33143527	G	0.74	0.96	0.237	0.036	3.50E-11
IGP26	rs10971438	9	33170308	G	0.30	0.75	-0.248	0.039	1.52E-10
IGP26	rs10813960	9	33170362	C	0.70	0.74	0.248	0.039	1.49E-10
IGP26	rs10971439	9	33170813	C	0.23	0.71	-0.260	0.043	1.93E-09
IGP28	rs11923417	3	188188484	C	0.60	0.45	-0.302	0.046	4.37E-11
IGP28	rs759602	3	188191498	G	0.78	0.98	-0.212	0.037	7.85E-09
IGP28	rs4012171	3	188194147	C	0.75	0.75	-0.302	0.040	6.22E-14
IGP28	rs16848727	3	188195657	G	0.25	0.71	-0.451	0.041	9.13E-28
IGP28	rs13322676	3	188201439	C	0.28	0.87	-0.438	0.036	8.16E-34
IGP28	rs6808800	3	188202068	G	0.51	0.85	-0.311	0.032	8.62E-22
IGP28	rs17775791	3	188205056	C	0.28	0.89	-0.437	0.036	3.64E-34
IGP28	rs7617523	3	188205144	G	0.34	0.89	-0.371	0.034	3.75E-28
IGP28	rs7652995	3	188205638	G	0.18	0.83	0.404	0.044	2.04E-20
IGP28	rs6764279	3	188206669	C	0.71	0.95	0.435	0.034	8.43E-37
IGP28	rs6788832	3	188206913	G	0.34	0.89	-0.370	0.034	3.33E-28
IGP28	rs3872721	3	188208185	G	0.24	0.89	0.363	0.038	5.22E-22
IGP28	rs11710456	3	188208581	G	0.70	0.88	0.444	0.035	8.53E-37
IGP28	rs3872722	3	188208971	C	0.41	0.89	0.298	0.033	8.50E-20
IGP28	rs7621161	3	188209864	C	0.71	0.94	0.437	0.034	8.45E-37

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP28	rs10937278	3	188210509	T	0.23	0.94	0.351	0.037	3.43E-21
IGP28	rs10937279	3	188210530	G	0.77	0.94	-0.351	0.037	3.60E-21
IGP28	rs7619468	3	188210872	C	0.77	0.94	-0.351	0.037	3.65E-21
IGP28	rs4686830	3	188211259	G	0.77	0.96	-0.347	0.037	5.24E-21
IGP28	rs10804908	3	188211536	T	0.23	0.96	0.347	0.037	5.44E-21
IGP28	rs4686834	3	188211848	G	0.77	0.97	-0.344	0.037	7.68E-21
IGP28	rs4686835	3	188211912	C	0.23	0.97	0.344	0.037	8.13E-21
IGP28	rs4686836	3	188212059	C	0.23	0.97	0.343	0.037	8.51E-21
IGP28	rs4012256	3	188213035	C	0.77	0.97	-0.343	0.037	9.05E-21
IGP28	rs4012257	3	188213090	C	0.77	0.98	-0.342	0.037	9.43E-21
IGP28	rs7619989	3	188214443	C	0.59	0.89	-0.293	0.033	2.33E-19
IGP28	rs17776120	3	188215373	C	0.64	0.80	0.379	0.035	2.55E-27
IGP28	rs3821819	3	188215419	G	0.63	0.81	0.382	0.035	1.93E-28
IGP28	rs6444193	3	188216882	G	0.23	0.99	0.339	0.036	1.39E-20
IGP28	rs967367	3	188217160	G	0.63	0.81	0.382	0.035	2.50E-28
IGP28	rs4686837	3	188222371	G	0.70	0.86	0.276	0.036	1.19E-14
IGP28	rs9941987	3	188225221	G	0.18	0.79	0.386	0.045	1.07E-17
IGP28	rs4686838	3	188225747	G	0.45	0.71	-0.221	0.036	7.24E-10
IGP28	rs16861533	3	188237416	G	0.84	0.67	0.333	0.050	2.99E-11
IGP28	rs2268536	3	188239602	G	0.16	0.68	-0.326	0.050	7.02E-11
IGP28	rs257101	3	188261522	C	0.23	0.49	-0.315	0.050	2.56E-10
IGP29	rs11923417	3	188188484	C	0.60	0.45	-0.452	0.046	5.88E-23
IGP29	rs759602	3	188191498	G	0.78	0.98	-0.336	0.037	4.89E-20
IGP29	rs4012171	3	188194147	C	0.75	0.75	-0.451	0.040	3.23E-29
IGP29	rs16848727	3	188195657	G	0.25	0.71	-0.677	0.041	3.57E-60
IGP29	rs13322676	3	188201439	C	0.28	0.87	-0.644	0.036	6.10E-71
IGP29	rs6808800	3	188202068	G	0.51	0.85	-0.435	0.033	1.15E-40
IGP29	rs17775791	3	188205056	C	0.28	0.89	-0.643	0.036	1.69E-71
IGP29	rs7617523	3	188205144	G	0.34	0.89	-0.559	0.034	2.28E-61
IGP29	rs7652995	3	188205638	G	0.18	0.83	0.580	0.044	2.75E-40
IGP29	rs6764279	3	188206669	C	0.72	0.95	0.627	0.034	2.53E-74
IGP29	rs6788832	3	188206913	G	0.34	0.89	-0.557	0.034	2.24E-61
IGP29	rs3872721	3	188208185	G	0.24	0.89	0.494	0.038	2.50E-39
IGP29	rs11710456	3	188208581	G	0.70	0.88	0.643	0.035	6.12E-75
IGP29	rs3872722	3	188208971	C	0.41	0.89	0.442	0.033	1.36E-41
IGP29	rs7621161	3	188209864	C	0.72	0.94	0.631	0.035	1.95E-74
IGP29	rs10937278	3	188210509	T	0.23	0.94	0.476	0.037	1.36E-37
IGP29	rs10937279	3	188210530	G	0.77	0.94	-0.476	0.037	1.43E-37
IGP29	rs7619468	3	188210872	C	0.77	0.94	-0.476	0.037	1.47E-37
IGP29	rs4686830	3	188211259	G	0.77	0.96	-0.472	0.037	2.41E-37
IGP29	rs10804908	3	188211536	T	0.23	0.96	0.471	0.037	2.54E-37
IGP29	rs4686834	3	188211848	G	0.77	0.97	-0.467	0.037	4.85E-37
IGP29	rs4686835	3	188211912	C	0.23	0.97	0.466	0.037	5.42E-37
IGP29	rs4686836	3	188212059	C	0.23	0.97	0.466	0.037	5.86E-37
IGP29	rs4012256	3	188213035	C	0.77	0.97	-0.465	0.037	6.48E-37
IGP29	rs4012257	3	188213090	C	0.77	0.98	-0.465	0.037	6.85E-37
IGP29	rs7619989	3	188214443	C	0.59	0.89	-0.434	0.033	1.17E-40
IGP29	rs17776120	3	188215373	C	0.64	0.80	0.569	0.035	2.73E-59
IGP29	rs3821819	3	188215419	G	0.63	0.81	0.569	0.035	1.50E-60
IGP29	rs6444193	3	188216882	G	0.23	0.99	0.461	0.036	1.34E-36
IGP29	rs967367	3	188217160	G	0.63	0.81	0.568	0.035	2.71E-60
IGP29	rs4686837	3	188222371	G	0.70	0.86	0.391	0.036	1.28E-27
IGP29	rs9941987	3	188225221	G	0.18	0.79	0.538	0.045	9.37E-33
IGP29	rs4686838	3	188225747	G	0.45	0.71	-0.348	0.036	3.22E-22

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP29	rs16861533	3	188237416	G	0.84	0.67	0.527	0.050	1.10E-25
IGP29	rs2268536	3	188239602	G	0.16	0.68	-0.516	0.050	8.07E-25
IGP29	rs4686844	3	188247829	G	0.41	0.75	0.191	0.036	8.28E-08
IGP29	rs9876699	3	188248791	C	0.56	0.92	-0.214	0.032	3.81E-11
IGP29	rs6800338	3	188248816	C	0.56	0.94	-0.207	0.032	9.90E-11
IGP29	rs4012245	3	188250134	G	0.44	0.98	0.191	0.031	1.30E-09
IGP29	rs257105	3	188258413	C	0.38	0.87	0.195	0.034	1.01E-08
IGP29	rs4012246	3	188261076	C	0.44	0.99	0.189	0.031	1.77E-09
IGP29	rs257101	3	188261522	C	0.23	0.49	-0.509	0.050	2.74E-24
IGP29	rs10433485	3	188263560	G	0.38	0.86	0.198	0.034	5.41E-09
IGP30	rs17776120	3	188215373	C	0.64	0.80	0.195	0.035	2.77E-08
IGP30	rs3821819	3	188215419	G	0.63	0.81	0.192	0.035	2.95E-08
IGP30	rs967367	3	188217160	G	0.63	0.81	0.192	0.035	2.98E-08
IGP31	rs16848727	3	188195657	G	0.25	0.71	0.283	0.041	8.74E-12
IGP31	rs13322676	3	188201439	C	0.28	0.87	0.274	0.036	3.46E-14
IGP31	rs6808800	3	188202068	G	0.51	0.85	0.186	0.033	1.07E-08
IGP31	rs17775791	3	188205056	C	0.28	0.89	0.275	0.036	1.93E-14
IGP31	rs7617523	3	188205144	G	0.34	0.89	0.237	0.034	2.11E-12
IGP31	rs6764279	3	188206669	C	0.71	0.95	-0.283	0.034	1.89E-16
IGP31	rs6788832	3	188206913	G	0.34	0.89	0.237	0.034	1.85E-12
IGP31	rs3872721	3	188208185	G	0.24	0.89	-0.208	0.038	3.79E-08
IGP31	rs11710456	3	188208581	G	0.70	0.88	-0.293	0.035	5.66E-17
IGP31	rs3872722	3	188208971	C	0.41	0.89	-0.189	0.033	8.52E-09
IGP31	rs7621161	3	188209864	C	0.72	0.94	-0.284	0.035	2.10E-16
IGP31	rs10937278	3	188210509	T	0.23	0.94	-0.202	0.037	6.07E-08
IGP31	rs10937279	3	188210530	G	0.77	0.94	0.202	0.037	6.17E-08
IGP31	rs7619468	3	188210872	C	0.77	0.94	0.202	0.037	6.27E-08
IGP31	rs4686830	3	188211259	G	0.77	0.96	0.198	0.037	9.76E-08
IGP31	rs10804908	3	188211536	T	0.23	0.96	-0.198	0.037	9.87E-08
IGP31	rs7619989	3	188214443	C	0.59	0.89	0.181	0.033	3.09E-08
IGP31	rs17776120	3	188215373	C	0.64	0.80	-0.228	0.035	7.01E-11
IGP31	rs3821819	3	188215419	G	0.63	0.81	-0.228	0.035	4.38E-11
IGP31	rs967367	3	188217160	G	0.63	0.81	-0.227	0.035	5.51E-11
IGP31	rs2659005	17	76833309	C	0.52	0.88	0.176	0.033	5.83E-08
IGP31	rs7224668	17	76850383	C	0.52	0.94	0.173	0.031	3.33E-08
IGP31	rs7223939	17	76856116	G	0.36	0.98	0.172	0.032	8.35E-08
IGP31	rs8077394	17	76873382	G	0.49	0.93	0.171	0.031	5.33E-08
IGP31	rs9914093	17	76875248	C	0.49	0.95	-0.171	0.031	4.80E-08
IGP32	rs4012171	3	188194147	C	0.75	0.75	-0.273	0.040	1.23E-11
IGP32	rs16848727	3	188195657	G	0.25	0.71	-0.462	0.041	8.24E-29
IGP32	rs13322676	3	188201439	C	0.28	0.87	-0.443	0.036	2.12E-34
IGP32	rs6808800	3	188202068	G	0.51	0.85	-0.252	0.033	1.32E-14
IGP32	rs17775791	3	188205056	C	0.28	0.89	-0.443	0.036	7.36E-35
IGP32	rs7617523	3	188205144	G	0.34	0.89	-0.371	0.034	5.17E-28
IGP32	rs7652995	3	188205638	G	0.18	0.83	0.339	0.044	9.02E-15
IGP32	rs6764279	3	188206669	C	0.72	0.95	0.441	0.034	1.24E-37
IGP32	rs6788832	3	188206913	G	0.34	0.89	-0.370	0.034	4.42E-28
IGP32	rs3872721	3	188208185	G	0.24	0.89	0.322	0.038	1.41E-17
IGP32	rs11710456	3	188208581	G	0.70	0.88	0.448	0.035	3.13E-37
IGP32	rs3872722	3	188208971	C	0.41	0.89	0.330	0.033	9.54E-24
IGP32	rs7621161	3	188209864	C	0.72	0.94	0.444	0.035	1.07E-37
IGP32	rs10937278	3	188210509	T	0.23	0.94	0.312	0.037	6.03E-17
IGP32	rs10937279	3	188210530	G	0.77	0.94	-0.312	0.037	6.08E-17
IGP32	rs7619468	3	188210872	C	0.77	0.94	-0.312	0.037	6.18E-17

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP32	rs4686830	3	188211259	G	0.77	0.96	-0.309	0.037	7.06E-17
IGP32	rs10804908	3	188211536	T	0.23	0.96	0.309	0.037	7.21E-17
IGP32	rs4686834	3	188211848	G	0.77	0.97	-0.306	0.037	9.19E-17
IGP32	rs4686835	3	188211912	C	0.23	0.97	0.306	0.037	9.61E-17
IGP32	rs4686836	3	188212059	C	0.23	0.97	0.306	0.037	9.86E-17
IGP32	rs4012256	3	188213035	C	0.77	0.97	-0.305	0.037	1.03E-16
IGP32	rs4012257	3	188213090	C	0.77	0.98	-0.305	0.037	1.04E-16
IGP32	rs7619989	3	188214443	C	0.59	0.89	-0.325	0.033	2.45E-23
IGP32	rs17776120	3	188215373	C	0.64	0.80	0.431	0.035	1.12E-34
IGP32	rs3821819	3	188215419	G	0.63	0.81	0.427	0.035	1.05E-34
IGP32	rs6444193	3	188216882	G	0.23	0.99	0.303	0.037	1.35E-16
IGP32	rs967367	3	188217160	G	0.63	0.81	0.426	0.035	1.40E-34
IGP32	rs4686837	3	188222371	G	0.70	0.86	0.287	0.036	1.49E-15
IGP32	rs9941987	3	188225221	G	0.18	0.79	0.319	0.045	1.83E-12
IGP32	rs4686838	3	188225747	G	0.45	0.71	-0.240	0.036	2.74E-11
IGP32	rs16861533	3	188237416	G	0.84	0.67	0.389	0.050	1.05E-14
IGP32	rs2268536	3	188239602	G	0.16	0.68	-0.383	0.050	2.41E-14
IGP32	rs9876699	3	188248791	C	0.56	0.92	-0.174	0.033	8.41E-08
IGP32	rs257101	3	188261522	C	0.23	0.49	-0.365	0.050	3.89E-13
IGP34	rs5750825	22	38161224	G	0.71	0.98	-0.208	0.034	1.26E-09
IGP34	rs1972280	22	38161932	T	0.29	0.98	0.208	0.034	1.24E-09
IGP34	rs4821897	22	38165533	G	0.71	0.97	-0.209	0.034	1.20E-09
IGP34	rs5750830	22	38170774	C	0.29	0.98	0.208	0.034	1.17E-09
IGP34	rs8137426	22	38174296	G	0.71	0.98	-0.208	0.034	1.16E-09
IGP34	rs5757683	22	38180120	G	0.29	0.98	0.208	0.034	1.17E-09
IGP34	rs1557541	22	38181916	C	0.29	0.98	0.208	0.034	1.17E-09
IGP34	rs1557542	22	38182296	C	0.71	0.98	-0.208	0.034	1.18E-09
IGP34	rs5995735	22	38184367	C	0.29	0.98	0.207	0.034	1.22E-09
IGP34	rs738289	22	38185829	C	0.29	0.98	0.207	0.034	1.23E-09
IGP34	rs909674	22	38189115	C	0.30	0.99	0.214	0.034	2.48E-10
IGP35	rs4012171	3	188194147	C	0.75	0.75	0.280	0.040	3.50E-12
IGP35	rs16848727	3	188195657	G	0.25	0.71	0.490	0.041	2.72E-32
IGP35	rs13322676	3	188201439	C	0.28	0.87	0.475	0.036	3.32E-39
IGP35	rs6808800	3	188202068	G	0.51	0.85	0.285	0.033	2.52E-18
IGP35	rs17775791	3	188205056	C	0.28	0.89	0.475	0.036	7.89E-40
IGP35	rs7617523	3	188205144	G	0.34	0.89	0.398	0.034	6.87E-32
IGP35	rs7652995	3	188205638	G	0.18	0.83	-0.366	0.044	6.84E-17
IGP35	rs6764279	3	188206669	C	0.72	0.95	-0.478	0.034	1.11E-43
IGP35	rs6788832	3	188206913	G	0.34	0.89	0.397	0.034	5.22E-32
IGP35	rs3872721	3	188208185	G	0.24	0.89	-0.350	0.038	2.11E-20
IGP35	rs11710456	3	188208581	G	0.70	0.88	-0.489	0.035	5.11E-44
IGP35	rs3872722	3	188208971	C	0.41	0.89	-0.343	0.033	1.91E-25
IGP35	rs7621161	3	188209864	C	0.72	0.94	-0.480	0.035	1.12E-43
IGP35	rs10937278	3	188210509	T	0.23	0.94	-0.340	0.037	8.94E-20
IGP35	rs10937279	3	188210530	G	0.77	0.94	0.340	0.037	9.13E-20
IGP35	rs7619468	3	188210872	C	0.77	0.94	0.339	0.037	9.39E-20
IGP35	rs4686830	3	188211259	G	0.77	0.96	0.335	0.037	1.67E-19
IGP35	rs10804908	3	188211536	T	0.23	0.96	-0.335	0.037	1.71E-19
IGP35	rs4686834	3	188211848	G	0.77	0.97	0.331	0.037	2.66E-19
IGP35	rs4686835	3	188211912	C	0.23	0.97	-0.331	0.037	2.81E-19
IGP35	rs4686836	3	188212059	C	0.23	0.97	-0.331	0.037	2.97E-19
IGP35	rs4012256	3	188213035	C	0.77	0.97	0.330	0.037	3.17E-19
IGP35	rs4012257	3	188213090	C	0.77	0.98	0.330	0.037	3.24E-19
IGP35	rs7619989	3	188214443	C	0.59	0.89	0.335	0.033	1.44E-24

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP35	rs17776120	3	188215373	C	0.64	0.80	-0.442	0.035	2.64E-36
IGP35	rs3821819	3	188215419	G	0.63	0.81	-0.438	0.035	1.48E-36
IGP35	rs6444193	3	188216882	G	0.23	0.99	-0.327	0.037	4.84E-19
IGP35	rs967367	3	188217160	G	0.63	0.81	-0.438	0.035	2.38E-36
IGP35	rs4686837	3	188222371	G	0.70	0.86	-0.277	0.036	1.59E-14
IGP35	rs9941987	3	188225221	G	0.18	0.79	-0.336	0.045	1.23E-13
IGP35	rs4686838	3	188225747	G	0.45	0.71	0.208	0.036	8.46E-09
IGP35	rs16861533	3	188237416	G	0.84	0.67	-0.361	0.050	7.83E-13
IGP35	rs2268536	3	188239602	G	0.16	0.68	0.353	0.050	2.03E-12
IGP35	rs257101	3	188261522	C	0.23	0.49	0.322	0.050	1.54E-10
IGP36	rs3818593	9	33110706	G	0.20	1.00	0.222	0.039	1.25E-08
IGP36	rs10971418	9	33112024	C	0.80	0.98	-0.222	0.039	1.24E-08
IGP36	rs10113903	9	33112645	C	0.31	0.99	0.193	0.034	1.39E-08
IGP36	rs10738905	9	33113627	G	0.31	0.99	0.192	0.034	1.46E-08
IGP36	rs10971419	9	33114161	C	0.31	0.99	0.191	0.034	1.59E-08
IGP36	rs12342831	9	33114872	C	0.26	0.97	0.230	0.036	1.05E-10
IGP36	rs10813950	9	33117640	G	0.69	1.00	-0.191	0.034	1.70E-08
IGP36	rs10813951	9	33118021	G	0.26	0.97	0.230	0.036	1.07E-10
IGP36	rs3780490	9	33119839	G	0.31	1.00	0.190	0.034	1.72E-08
IGP36	rs10758192	9	33121651	G	0.69	1.00	-0.190	0.034	1.73E-08
IGP36	rs913214	9	33125085	G	0.69	1.00	-0.190	0.034	1.73E-08
IGP36	rs10738906	9	33125634	C	0.31	1.00	0.190	0.034	1.74E-08
IGP36	rs10124479	9	33126233	G	0.31	1.00	0.190	0.034	1.74E-08
IGP36	rs10813954	9	33127596	C	0.31	1.00	0.190	0.034	1.76E-08
IGP36	rs3780486	9	33129453	C	0.74	0.97	-0.230	0.036	1.07E-10
IGP36	rs7864705	9	33130352	C	0.31	1.00	0.191	0.034	1.76E-08
IGP36	rs7865745	9	33130976	G	0.69	1.00	-0.191	0.034	1.76E-08
IGP36	rs7873903	9	33132728	G	0.69	0.99	-0.191	0.034	1.77E-08
IGP36	rs3824458	9	33134809	C	0.69	0.99	-0.191	0.034	1.76E-08
IGP36	rs10813957	9	33143527	G	0.74	0.96	-0.231	0.036	1.27E-10
IGP36	rs10971438	9	33170308	G	0.30	0.75	0.236	0.039	1.31E-09
IGP36	rs10813960	9	33170362	C	0.70	0.74	-0.236	0.039	1.29E-09
IGP36	rs10971439	9	33170813	C	0.23	0.71	0.245	0.043	1.73E-08
IGP37	rs16848727	3	188195657	G	0.25	0.71	0.305	0.042	2.26E-13
IGP37	rs13322676	3	188201439	C	0.28	0.87	0.284	0.036	5.14E-15
IGP37	rs6808800	3	188202068	G	0.51	0.85	0.186	0.033	1.28E-08
IGP37	rs17775791	3	188205056	C	0.28	0.89	0.283	0.036	3.83E-15
IGP37	rs7617523	3	188205144	G	0.34	0.89	0.232	0.034	7.81E-12
IGP37	rs7652995	3	188205638	G	0.18	0.83	-0.239	0.044	5.11E-08
IGP37	rs6764279	3	188206669	C	0.71	0.95	-0.280	0.034	4.35E-16
IGP37	rs6788832	3	188206913	G	0.34	0.89	0.231	0.034	7.89E-12
IGP37	rs3872721	3	188208185	G	0.24	0.89	-0.226	0.038	2.63E-09
IGP37	rs11710456	3	188208581	G	0.70	0.88	-0.293	0.035	8.21E-17
IGP37	rs3872722	3	188208971	C	0.41	0.89	-0.198	0.033	1.71E-09
IGP37	rs7621161	3	188209864	C	0.71	0.94	-0.281	0.035	4.76E-16
IGP37	rs10937278	3	188210509	T	0.23	0.94	-0.221	0.037	3.76E-09
IGP37	rs10937279	3	188210530	G	0.77	0.94	0.220	0.037	3.83E-09
IGP37	rs7619468	3	188210872	C	0.77	0.94	0.220	0.037	3.88E-09
IGP37	rs4686830	3	188211259	G	0.77	0.96	0.217	0.037	5.61E-09
IGP37	rs10804908	3	188211536	T	0.23	0.96	-0.217	0.037	5.70E-09
IGP37	rs4686834	3	188211848	G	0.77	0.97	0.215	0.037	6.49E-09
IGP37	rs4686835	3	188211912	C	0.23	0.97	-0.214	0.037	6.71E-09
IGP37	rs4686836	3	188212059	C	0.23	0.97	-0.214	0.037	6.96E-09
IGP37	rs4012256	3	188213035	C	0.77	0.97	0.214	0.037	7.10E-09

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP37	rs4012257	3	188213090	C	0.77	0.98	0.213	0.037	7.20E-09
IGP37	rs7619989	3	188214443	C	0.59	0.89	0.192	0.033	4.24E-09
IGP37	rs17776120	3	188215373	C	0.64	0.80	-0.244	0.035	4.18E-12
IGP37	rs3821819	3	188215419	G	0.63	0.81	-0.245	0.035	2.05E-12
IGP37	rs6444193	3	188216882	G	0.23	0.99	-0.211	0.037	8.43E-09
IGP37	rs967367	3	188217160	G	0.63	0.81	-0.244	0.035	2.43E-12
IGP37	rs3818593	9	33110706	G	0.20	1.00	0.226	0.039	6.55E-09
IGP37	rs10971418	9	33112024	C	0.80	0.98	-0.226	0.039	6.92E-09
IGP37	rs10113903	9	33112645	C	0.31	0.99	0.195	0.034	9.01E-09
IGP37	rs10738905	9	33113627	G	0.31	0.99	0.194	0.034	9.55E-09
IGP37	rs10971419	9	33114161	C	0.31	0.99	0.193	0.034	1.05E-08
IGP37	rs12342831	9	33114872	C	0.26	0.97	0.230	0.036	9.37E-11
IGP37	rs10813950	9	33117640	G	0.69	1.00	-0.193	0.034	1.14E-08
IGP37	rs10813951	9	33118021	G	0.26	0.97	0.230	0.036	9.58E-11
IGP37	rs3780490	9	33119839	G	0.31	1.00	0.193	0.034	1.15E-08
IGP37	rs10758192	9	33121651	G	0.69	1.00	-0.193	0.034	1.16E-08
IGP37	rs913214	9	33125085	G	0.69	1.00	-0.193	0.034	1.12E-08
IGP37	rs10738906	9	33125634	C	0.31	1.00	0.193	0.034	1.12E-08
IGP37	rs10124479	9	33126233	G	0.31	1.00	0.193	0.034	1.11E-08
IGP37	rs10813954	9	33127596	C	0.31	1.00	0.193	0.034	1.10E-08
IGP37	rs3780486	9	33129453	C	0.74	0.97	-0.231	0.036	8.98E-11
IGP37	rs7864705	9	33130352	C	0.31	1.00	0.193	0.034	1.10E-08
IGP37	rs7865745	9	33130976	G	0.69	1.00	-0.193	0.034	1.10E-08
IGP37	rs7873903	9	33132728	G	0.69	0.99	-0.193	0.034	1.12E-08
IGP37	rs3824458	9	33134809	C	0.69	0.99	-0.194	0.034	1.11E-08
IGP37	rs10813957	9	33143527	G	0.74	0.96	-0.232	0.036	1.11E-10
IGP37	rs10971438	9	33170308	G	0.30	0.75	0.237	0.039	1.08E-09
IGP37	rs10813960	9	33170362	C	0.70	0.74	-0.237	0.039	1.07E-09
IGP37	rs10971439	9	33170813	C	0.23	0.71	0.247	0.043	1.19E-08
IGP38	rs16848727	3	188195657	G	0.25	0.71	0.309	0.042	1.12E-13
IGP38	rs13322676	3	188201439	C	0.28	0.87	0.286	0.036	2.87E-15
IGP38	rs6808800	3	188202068	G	0.51	0.85	0.183	0.033	2.29E-08
IGP38	rs17775791	3	188205056	C	0.28	0.89	0.286	0.036	2.24E-15
IGP38	rs7617523	3	188205144	G	0.34	0.89	0.230	0.034	1.22E-11
IGP38	rs7652995	3	188205638	G	0.18	0.83	-0.240	0.044	4.82E-08
IGP38	rs6764279	3	188206669	C	0.71	0.95	-0.282	0.034	3.03E-16
IGP38	rs6788832	3	188206913	G	0.34	0.89	0.229	0.034	1.24E-11
IGP38	rs3872721	3	188208185	G	0.24	0.89	-0.231	0.038	1.18E-09
IGP38	rs11710456	3	188208581	G	0.70	0.88	-0.295	0.035	5.43E-17
IGP38	rs3872722	3	188208971	C	0.41	0.89	-0.203	0.033	6.82E-10
IGP38	rs7621161	3	188209864	C	0.71	0.94	-0.283	0.035	3.24E-16
IGP38	rs10937278	3	188210509	T	0.23	0.94	-0.225	0.037	1.71E-09
IGP38	rs10937279	3	188210530	G	0.77	0.94	0.225	0.037	1.74E-09
IGP38	rs7619468	3	188210872	C	0.77	0.94	0.225	0.037	1.77E-09
IGP38	rs4686830	3	188211259	G	0.77	0.96	0.222	0.037	2.53E-09
IGP38	rs10804908	3	188211536	T	0.23	0.96	-0.221	0.037	2.57E-09
IGP38	rs4686834	3	188211848	G	0.77	0.97	0.219	0.037	2.95E-09
IGP38	rs4686835	3	188211912	C	0.23	0.97	-0.219	0.037	3.07E-09
IGP38	rs4686836	3	188212059	C	0.23	0.97	-0.219	0.037	3.18E-09
IGP38	rs4012256	3	188213035	C	0.77	0.97	0.218	0.037	3.25E-09
IGP38	rs4012257	3	188213090	C	0.77	0.98	0.218	0.037	3.29E-09
IGP38	rs7619989	3	188214443	C	0.59	0.89	0.197	0.033	1.69E-09
IGP38	rs17776120	3	188215373	C	0.64	0.80	-0.245	0.035	3.16E-12
IGP38	rs3821819	3	188215419	G	0.63	0.81	-0.246	0.035	1.59E-12

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP38	rs6444193	3	188216882	G	0.23	0.99	-0.216	0.037	3.88E-09
IGP38	rs967367	3	188217160	G	0.63	0.81	-0.245	0.035	1.86E-12
IGP38	rs3818593	9	33110706	G	0.20	1.00	0.229	0.039	4.01E-09
IGP38	rs10971418	9	33112024	C	0.80	0.98	-0.230	0.039	4.08E-09
IGP38	rs10113903	9	33112645	C	0.31	0.99	0.197	0.034	6.60E-09
IGP38	rs10738905	9	33113627	G	0.31	0.99	0.196	0.034	7.01E-09
IGP38	rs10971419	9	33114161	C	0.31	0.99	0.195	0.034	7.75E-09
IGP38	rs12342831	9	33114872	C	0.26	0.97	0.234	0.036	4.96E-11
IGP38	rs10813950	9	33117640	G	0.69	1.00	-0.195	0.034	8.39E-09
IGP38	rs10813951	9	33118021	G	0.26	0.97	0.234	0.036	5.06E-11
IGP38	rs3780490	9	33119839	G	0.31	1.00	0.194	0.034	8.47E-09
IGP38	rs10758192	9	33121651	G	0.69	1.00	-0.194	0.034	8.55E-09
IGP38	rs913214	9	33125085	G	0.69	1.00	-0.195	0.034	8.42E-09
IGP38	rs10738906	9	33125634	C	0.31	1.00	0.195	0.034	8.43E-09
IGP38	rs10124479	9	33126233	G	0.31	1.00	0.195	0.034	8.43E-09
IGP38	rs10813954	9	33127596	C	0.31	1.00	0.195	0.034	8.44E-09
IGP38	rs3780486	9	33129453	C	0.74	0.97	-0.234	0.036	4.95E-11
IGP38	rs7864705	9	33130352	C	0.31	1.00	0.195	0.034	8.44E-09
IGP38	rs7865745	9	33130976	G	0.69	1.00	-0.195	0.034	8.45E-09
IGP38	rs7873903	9	33132728	G	0.69	0.99	-0.195	0.034	8.56E-09
IGP38	rs3824458	9	33134809	C	0.69	0.99	-0.195	0.034	8.56E-09
IGP38	rs10813957	9	33143527	G	0.74	0.96	-0.235	0.036	6.39E-11
IGP38	rs10971438	9	33170308	G	0.30	0.75	0.239	0.039	7.65E-10
IGP38	rs10813960	9	33170362	C	0.70	0.74	-0.239	0.039	7.58E-10
IGP38	rs10971439	9	33170813	C	0.23	0.71	0.251	0.043	7.19E-09
IGP39	rs3818593	9	33110706	G	0.20	1.00	0.213	0.039	4.18E-08
IGP39	rs10971418	9	33112024	C	0.80	0.98	-0.214	0.039	3.59E-08
IGP39	rs10113903	9	33112645	C	0.31	0.99	0.207	0.034	9.65E-10
IGP39	rs10738905	9	33113627	G	0.31	0.99	0.206	0.034	9.90E-10
IGP39	rs10971419	9	33114161	C	0.31	0.99	0.206	0.034	1.02E-09
IGP39	rs12342831	9	33114872	C	0.26	0.97	0.217	0.035	9.57E-10
IGP39	rs10758189	9	33115804	C	0.31	0.92	0.204	0.035	4.84E-09
IGP39	rs10813950	9	33117640	G	0.69	1.00	-0.205	0.034	1.04E-09
IGP39	rs10813951	9	33118021	G	0.26	0.97	0.217	0.035	9.40E-10
IGP39	rs3780490	9	33119839	G	0.31	1.00	0.205	0.034	1.04E-09
IGP39	rs10758192	9	33121651	G	0.69	1.00	-0.205	0.034	1.04E-09
IGP39	rs913214	9	33125085	G	0.69	1.00	-0.205	0.034	1.18E-09
IGP39	rs10738906	9	33125634	C	0.31	1.00	0.205	0.034	1.23E-09
IGP39	rs10124479	9	33126233	G	0.31	1.00	0.204	0.034	1.27E-09
IGP39	rs10813954	9	33127596	C	0.31	1.00	0.204	0.034	1.35E-09
IGP39	rs10971424	9	33128775	C	0.34	0.90	0.194	0.035	2.01E-08
IGP39	rs3780486	9	33129453	C	0.74	0.97	-0.216	0.035	1.17E-09
IGP39	rs7864705	9	33130352	C	0.31	1.00	0.204	0.034	1.34E-09
IGP39	rs7865745	9	33130976	G	0.69	1.00	-0.204	0.034	1.34E-09
IGP39	rs7873903	9	33132728	G	0.69	0.99	-0.204	0.034	1.35E-09
IGP39	rs7036812	9	33133822	C	0.33	0.89	0.193	0.035	3.61E-08
IGP39	rs3824458	9	33134809	C	0.69	0.99	-0.205	0.034	1.35E-09
IGP39	rs10813957	9	33143527	G	0.74	0.96	-0.217	0.036	1.30E-09
IGP39	rs10971438	9	33170308	G	0.30	0.75	0.228	0.039	3.92E-09
IGP39	rs10813960	9	33170362	C	0.70	0.74	-0.228	0.039	3.89E-09
IGP39	rs10971439	9	33170813	C	0.23	0.71	0.234	0.043	6.11E-08
IGP39	rs17630758	22	22466542	G	0.83	0.99	0.260	0.041	2.61E-10
IGP39	rs17548631	22	22474125	C	0.17	0.99	-0.260	0.041	2.26E-10
IGP39	rs9620326	22	22476629	C	0.83	0.99	0.260	0.041	2.24E-10

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP39	rs9624334	22	22496256	C	0.17	0.99	-0.259	0.041	3.51E-10
IGP39	rs2186369	22	22500996	G	0.19	0.88	-0.267	0.042	1.34E-10
IGP39	rs137682	22	38068371	C	0.78	1.00	-0.207	0.037	1.57E-08
IGP39	rs137683	22	38068447	C	0.78	0.96	-0.219	0.037	2.73E-09
IGP39	rs137686	22	38069584	C	0.24	0.89	0.252	0.037	1.13E-11
IGP39	rs137699	22	38078800	G	0.69	0.89	-0.211	0.035	1.49E-09
IGP39	rs2049986	22	38086800	C	0.69	0.88	-0.212	0.035	1.16E-09
IGP39	rs5757636	22	38088455	G	0.87	0.77	-0.292	0.051	1.04E-08
IGP39	rs5757637	22	38088487	G	0.87	0.77	-0.295	0.051	6.94E-09
IGP39	rs5757642	22	38094770	C	0.64	1.00	-0.276	0.032	1.80E-17
IGP39	rs7286714	22	38095550	C	0.36	0.97	0.280	0.033	1.07E-17
IGP39	rs5757644	22	38096386	C	0.36	0.97	0.280	0.033	1.04E-17
IGP39	rs5750806	22	38096957	G	0.64	0.97	-0.280	0.033	1.04E-17
IGP39	rs1569499	22	38099764	C	0.64	0.97	-0.281	0.033	1.16E-17
IGP39	rs4821888	22	38100543	G	0.64	0.97	-0.281	0.033	1.18E-17
IGP39	rs5757647	22	38104993	C	0.33	1.00	0.284	0.033	4.25E-18
IGP39	rs4821890	22	38107469	G	0.34	0.99	0.285	0.033	2.98E-18
IGP39	rs1010169	22	38108113	G	0.67	1.00	-0.284	0.033	4.31E-18
IGP39	rs1010170	22	38108273	C	0.67	1.00	-0.283	0.033	4.47E-18
IGP39	rs5757650	22	38108365	C	0.67	1.00	-0.283	0.033	4.54E-18
IGP39	rs9611169	22	38112973	C	0.33	1.00	0.283	0.033	4.67E-18
IGP39	rs9611170	22	38114791	C	0.67	0.99	-0.282	0.033	6.34E-18
IGP39	rs2413590	22	38120137	C	0.67	1.00	-0.280	0.033	8.90E-18
IGP39	rs5750808	22	38120933	G	0.33	1.00	0.280	0.033	8.80E-18
IGP39	rs5750811	22	38123012	G	0.67	1.00	-0.280	0.033	8.67E-18
IGP39	rs5750812	22	38123025	G	0.34	0.99	0.284	0.033	3.54E-18
IGP39	rs5757655	22	38127124	C	0.66	0.99	-0.284	0.033	3.35E-18
IGP39	rs4821893	22	38127725	G	0.33	1.00	0.284	0.033	3.27E-18
IGP39	rs5750814	22	38127933	C	0.67	1.00	-0.284	0.033	2.86E-18
IGP39	rs5757657	22	38128375	G	0.33	1.00	0.284	0.033	2.75E-18
IGP39	rs5750815	22	38128395	C	0.67	1.00	-0.284	0.033	2.59E-18
IGP39	rs4337572	22	38130650	C	0.33	1.00	0.284	0.033	2.50E-18
IGP39	rs4821894	22	38139766	C	0.67	1.00	-0.284	0.033	2.38E-18
IGP39	rs5750816	22	38140325	C	0.33	1.00	0.285	0.033	2.27E-18
IGP39	rs5757659	22	38142355	G	0.67	1.00	-0.285	0.033	2.14E-18
IGP39	rs6001585	22	38142932	C	0.22	1.00	0.297	0.037	5.28E-16
IGP39	rs6001587	22	38148954	C	0.67	1.00	-0.285	0.033	2.17E-18
IGP39	rs5750818	22	38150831	G	0.67	1.00	-0.285	0.033	2.18E-18
IGP39	rs5757665	22	38151587	G	0.67	1.00	-0.285	0.033	2.18E-18
IGP39	rs4821895	22	38152961	G	0.67	1.00	-0.285	0.033	2.19E-18
IGP39	rs739141	22	38154396	C	0.36	1.00	0.263	0.032	3.37E-16
IGP39	rs5750820	22	38155268	G	0.68	0.97	-0.303	0.033	5.96E-20
IGP39	rs5750822	22	38156734	G	0.33	1.00	0.285	0.033	1.95E-18
IGP39	rs7949	22	38157499	G	0.33	0.99	0.286	0.033	1.71E-18
IGP39	rs5757670	22	38159682	G	0.33	0.99	0.287	0.033	1.51E-18
IGP39	rs5750825	22	38161224	G	0.71	0.98	-0.333	0.034	2.26E-22
IGP39	rs1972280	22	38161932	T	0.29	0.98	0.334	0.034	1.82E-22
IGP39	rs4821897	22	38165533	G	0.71	0.97	-0.335	0.034	1.46E-22
IGP39	rs5750830	22	38170774	C	0.29	0.98	0.341	0.034	1.67E-23
IGP39	rs5757676	22	38171646	C	0.78	0.96	-0.318	0.037	1.16E-17
IGP39	rs8137426	22	38174296	G	0.71	0.98	-0.341	0.034	1.58E-23
IGP39	rs5757683	22	38180120	G	0.29	0.98	0.341	0.034	1.51E-23
IGP39	rs1557541	22	38181916	C	0.29	0.98	0.341	0.034	1.52E-23
IGP39	rs1557542	22	38182296	C	0.71	0.98	-0.341	0.034	1.52E-23

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP39	rs5995735	22	38184367	C	0.29	0.98	0.341	0.034	1.54E-23
IGP39	rs738289	22	38185829	C	0.29	0.98	0.341	0.034	1.54E-23
IGP39	rs909674	22	38189115	C	0.30	0.99	0.339	0.034	8.87E-24
IGP39	rs4820378	22	38199155	C	0.47	0.99	-0.177	0.031	1.40E-08
IGP39	rs1003538	22	38202653	G	0.49	0.95	-0.191	0.032	1.62E-09
IGP39	rs9306336	22	38203416	T	0.54	0.99	0.170	0.031	4.91E-08
IGP39	rs5757731	22	38297731	C	0.43	0.90	-0.173	0.032	8.67E-08
IGP39	rs3788556	22	38302108	C	0.56	0.85	0.180	0.033	4.90E-08
IGP40	rs3818593	9	33110706	G	0.20	1.00	0.211	0.039	5.10E-08
IGP40	rs10971418	9	33112024	C	0.80	0.98	-0.212	0.039	4.54E-08
IGP40	rs10113903	9	33112645	C	0.31	0.99	0.209	0.034	6.07E-10
IGP40	rs10738905	9	33113627	G	0.31	0.99	0.208	0.034	6.23E-10
IGP40	rs10971419	9	33114161	C	0.31	0.99	0.208	0.034	6.44E-10
IGP40	rs12342831	9	33114872	C	0.26	0.97	0.219	0.035	5.59E-10
IGP40	rs10758189	9	33115804	C	0.31	0.92	0.204	0.035	4.02E-09
IGP40	rs10813950	9	33117640	G	0.69	1.00	-0.207	0.034	6.59E-10
IGP40	rs10813951	9	33118021	G	0.26	0.97	0.219	0.035	5.49E-10
IGP40	rs3780490	9	33119839	G	0.31	1.00	0.207	0.034	6.58E-10
IGP40	rs10758192	9	33121651	G	0.69	1.00	-0.207	0.034	6.58E-10
IGP40	rs913214	9	33125085	G	0.69	1.00	-0.207	0.034	7.40E-10
IGP40	rs10738906	9	33125634	C	0.31	1.00	0.206	0.034	7.71E-10
IGP40	rs10124479	9	33126233	G	0.31	1.00	0.206	0.034	7.91E-10
IGP40	rs10813954	9	33127596	C	0.31	1.00	0.206	0.034	8.38E-10
IGP40	rs10971424	9	33128775	C	0.34	0.90	0.196	0.034	1.35E-08
IGP40	rs3780486	9	33129453	C	0.74	0.97	-0.218	0.035	6.77E-10
IGP40	rs7864705	9	33130352	C	0.31	1.00	0.206	0.034	8.35E-10
IGP40	rs7865745	9	33130976	G	0.69	1.00	-0.206	0.034	8.35E-10
IGP40	rs7873903	9	33132728	G	0.69	0.99	-0.206	0.034	8.42E-10
IGP40	rs7036812	9	33133822	C	0.33	0.89	0.195	0.035	2.37E-08
IGP40	rs3824458	9	33134809	C	0.69	0.99	-0.207	0.034	8.39E-10
IGP40	rs10813957	9	33143527	G	0.74	0.96	-0.220	0.036	7.63E-10
IGP40	rs10971438	9	33170308	G	0.30	0.75	0.230	0.039	2.64E-09
IGP40	rs10813960	9	33170362	C	0.70	0.74	-0.230	0.039	2.64E-09
IGP40	rs10971439	9	33170813	C	0.23	0.71	0.231	0.043	8.64E-08
IGP40	rs17630758	22	22466542	G	0.83	0.99	0.260	0.041	1.86E-10
IGP40	rs17548631	22	22474125	C	0.17	0.99	-0.261	0.041	1.62E-10
IGP40	rs9620326	22	22476629	C	0.83	0.99	0.261	0.041	1.60E-10
IGP40	rs9624334	22	22496256	C	0.17	0.99	-0.258	0.041	3.41E-10
IGP40	rs2186369	22	22500996	G	0.19	0.88	-0.265	0.041	1.43E-10
IGP40	rs137682	22	38068371	C	0.78	1.00	-0.217	0.036	2.11E-09
IGP40	rs137683	22	38068447	C	0.78	0.96	-0.230	0.037	3.44E-10
IGP40	rs137686	22	38069584	C	0.24	0.89	0.261	0.037	1.60E-12
IGP40	rs137699	22	38078800	G	0.69	0.89	-0.224	0.035	9.98E-11
IGP40	rs2049986	22	38086800	C	0.69	0.88	-0.225	0.035	7.74E-11
IGP40	rs5757636	22	38088455	G	0.87	0.77	-0.307	0.051	1.44E-09
IGP40	rs5757637	22	38088487	G	0.87	0.77	-0.310	0.051	9.42E-10
IGP40	rs5757642	22	38094770	C	0.64	1.00	-0.282	0.032	2.51E-18
IGP40	rs7286714	22	38095550	C	0.36	0.97	0.286	0.033	1.41E-18
IGP40	rs5757644	22	38096386	C	0.36	0.97	0.286	0.033	1.37E-18
IGP40	rs5750806	22	38096957	G	0.64	0.97	-0.286	0.033	1.36E-18
IGP40	rs1569499	22	38099764	C	0.64	0.97	-0.287	0.033	1.53E-18
IGP40	rs4821888	22	38100543	G	0.64	0.97	-0.287	0.033	1.55E-18
IGP40	rs5757647	22	38104993	C	0.33	1.00	0.292	0.033	2.79E-19
IGP40	rs4821890	22	38107469	G	0.34	0.99	0.294	0.033	1.92E-19

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP40	rs1010169	22	38108113	G	0.67	1.00	-0.292	0.033	2.84E-19
IGP40	rs1010170	22	38108273	C	0.67	1.00	-0.292	0.033	2.95E-19
IGP40	rs5757650	22	38108365	C	0.67	1.00	-0.292	0.033	3.00E-19
IGP40	rs9611169	22	38112973	C	0.33	1.00	0.291	0.033	3.08E-19
IGP40	rs9611170	22	38114791	C	0.66	0.99	-0.290	0.032	3.73E-19
IGP40	rs2413590	22	38120137	C	0.67	1.00	-0.289	0.032	5.35E-19
IGP40	rs5750808	22	38120933	G	0.33	1.00	0.289	0.032	5.28E-19
IGP40	rs5750811	22	38123012	G	0.67	1.00	-0.289	0.032	5.18E-19
IGP40	rs5750812	22	38123025	G	0.34	0.99	0.293	0.032	2.01E-19
IGP40	rs5757655	22	38127124	C	0.66	0.99	-0.293	0.032	1.90E-19
IGP40	rs4821893	22	38127725	G	0.33	1.00	0.292	0.032	1.86E-19
IGP40	rs5750814	22	38127933	C	0.67	1.00	-0.293	0.032	1.63E-19
IGP40	rs5757657	22	38128375	G	0.33	1.00	0.293	0.032	1.57E-19
IGP40	rs5750815	22	38128395	C	0.67	1.00	-0.293	0.032	1.47E-19
IGP40	rs4337572	22	38130650	C	0.33	1.00	0.293	0.032	1.42E-19
IGP40	rs4821894	22	38139766	C	0.66	1.00	-0.293	0.032	1.36E-19
IGP40	rs5750816	22	38140325	C	0.34	1.00	0.293	0.032	1.29E-19
IGP40	rs5757659	22	38142355	G	0.66	1.00	-0.293	0.032	1.22E-19
IGP40	rs6001585	22	38142932	C	0.22	1.00	0.308	0.036	3.28E-17
IGP40	rs6001587	22	38148954	C	0.66	1.00	-0.293	0.032	1.24E-19
IGP40	rs5750818	22	38150831	G	0.66	1.00	-0.293	0.032	1.24E-19
IGP40	rs5757665	22	38151587	G	0.66	1.00	-0.293	0.032	1.25E-19
IGP40	rs4821895	22	38152961	G	0.66	1.00	-0.293	0.032	1.25E-19
IGP40	rs739141	22	38154396	C	0.36	1.00	0.271	0.032	2.77E-17
IGP40	rs5750820	22	38155268	G	0.67	0.97	-0.311	0.033	2.98E-21
IGP40	rs5750822	22	38156734	G	0.34	1.00	0.294	0.032	1.10E-19
IGP40	rs7949	22	38157499	G	0.34	0.99	0.295	0.032	9.53E-20
IGP40	rs5757670	22	38159682	G	0.34	0.99	0.296	0.032	8.31E-20
IGP40	rs5750825	22	38161224	G	0.71	0.98	-0.338	0.034	3.24E-23
IGP40	rs1972280	22	38161932	T	0.29	0.98	0.340	0.034	2.56E-23
IGP40	rs4821897	22	38165533	G	0.71	0.97	-0.341	0.034	2.04E-23
IGP40	rs5750830	22	38170774	C	0.29	0.98	0.347	0.034	2.01E-24
IGP40	rs5757676	22	38171646	C	0.78	0.96	-0.329	0.037	6.14E-19
IGP40	rs8137426	22	38174296	G	0.71	0.98	-0.347	0.034	1.88E-24
IGP40	rs5757683	22	38180120	G	0.29	0.98	0.347	0.034	1.81E-24
IGP40	rs1557541	22	38181916	C	0.29	0.98	0.347	0.034	1.81E-24
IGP40	rs1557542	22	38182296	C	0.71	0.98	-0.347	0.034	1.81E-24
IGP40	rs5995735	22	38184367	C	0.29	0.98	0.347	0.034	1.83E-24
IGP40	rs738289	22	38185829	C	0.29	0.98	0.346	0.034	1.82E-24
IGP40	rs909674	22	38189115	C	0.30	0.99	0.345	0.034	9.66E-25
IGP40	rs4820378	22	38199155	C	0.47	0.99	-0.177	0.031	1.06E-08
IGP40	rs1003538	22	38202653	G	0.49	0.95	-0.190	0.032	1.57E-09
IGP40	rs9306336	22	38203416	T	0.54	0.99	0.171	0.031	3.40E-08
IGP40	rs2899319	22	38204260	C	0.66	0.99	0.174	0.033	8.91E-08
IGP40	rs9607658	22	38287686	C	0.57	1.00	0.165	0.031	6.09E-08
IGP40	rs5757731	22	38297731	C	0.43	0.90	-0.177	0.032	3.92E-08
IGP40	rs3788556	22	38302108	C	0.56	0.85	0.186	0.033	1.46E-08
IGP41	rs1894204	11	67686247	C	0.59	0.88	0.191	0.033	5.66E-09
IGP41	rs10896298	11	67688035	C	0.51	1.00	0.185	0.030	8.90E-10
IGP41	rs4930561	11	67688337	G	0.51	1.00	0.185	0.030	8.88E-10
IGP41	rs7931502	11	67716183	C	0.59	0.89	0.189	0.033	6.24E-09
IGP41	rs4930564	11	67739857	G	0.41	0.86	-0.192	0.033	6.37E-09
IGP41	rs7973719	12	7226080	C	0.49	0.92	0.177	0.032	4.48E-08
IGP41	rs12828421	12	7226484	C	0.51	0.92	-0.177	0.032	4.48E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP42	rs2859113	6	32805763	C	0.38	0.91	0.181	0.033	5.72E-08
IGP42	rs7751856	6	32806966	C	0.38	0.90	0.181	0.033	6.27E-08
IGP42	rs9276197	6	32807565	C	0.62	0.90	-0.180	0.033	6.47E-08
IGP42	rs9276234	6	32808826	T	0.62	0.90	-0.180	0.033	6.45E-08
IGP42	rs2859071	6	32811344	C	0.62	0.92	-0.180	0.033	6.51E-08
IGP42	rs9276311	6	32812637	C	0.62	0.94	-0.179	0.033	6.75E-08
IGP42	rs7773149	6	32814020	G	0.62	0.94	-0.179	0.033	7.23E-08
IGP42	rs1049110	6	32834781	C	0.35	0.98	0.191	0.034	1.64E-08
IGP42	rs7782210	7	50319291	G	0.38	0.98	-0.190	0.032	2.04E-09
IGP42	rs6583437	7	50320813	G	0.64	0.98	0.197	0.032	6.66E-10
IGP42	rs7789913	7	50323241	C	0.62	1.00	0.189	0.032	2.13E-09
IGP42	rs6421315	7	50325753	C	0.37	0.95	-0.194	0.032	2.22E-09
IGP42	rs1122979	7	150546004	G	0.87	0.91	0.298	0.049	1.41E-09
IGP42	rs7812088	7	150550762	G	0.87	0.98	0.283	0.047	1.82E-09
IGP42	rs7781265	7	150581873	G	0.88	0.92	0.281	0.050	2.01E-08
IGP42	rs8021641	14	64782173	C	0.15	0.95	0.234	0.044	9.64E-08
IGP42	rs1256519	14	64806077	G	0.44	0.89	-0.198	0.033	1.03E-09
IGP42	rs1256526	14	64809658	G	0.39	1.00	0.170	0.032	9.20E-08
IGP42	rs7159888	14	64828395	G	0.55	0.99	-0.262	0.031	5.01E-17
IGP42	rs12431963	14	64829447	C	0.92	0.92	-0.431	0.059	2.48E-13
IGP42	rs1256540	14	64833822	C	0.43	1.00	0.257	0.031	2.38E-16
IGP42	rs4902383	14	64834326	C	0.19	0.94	0.274	0.040	7.17E-12
IGP42	rs1269068	14	64837086	C	0.57	1.00	-0.257	0.031	2.51E-16
IGP42	rs10135194	14	64840731	C	0.94	0.84	-0.434	0.071	8.50E-10
IGP42	rs1760978	14	64840800	G	0.43	0.98	0.288	0.031	4.65E-20
IGP42	rs10144975	14	64843735	C	0.80	0.98	-0.288	0.038	5.87E-14
IGP42	rs17102587	14	64844230	C	0.20	0.97	0.295	0.038	1.88E-14
IGP42	rs8017974	14	64844940	C	0.20	0.99	0.296	0.038	1.17E-14
IGP42	rs11847263	14	64845448	G	0.39	0.98	0.303	0.032	2.76E-21
IGP42	rs10132229	14	64847313	G	0.10	1.00	0.393	0.051	1.38E-14
IGP42	rs4902386	14	64848043	C	0.81	0.99	-0.296	0.038	1.07E-14
IGP42	rs10147958	14	64848586	C	0.10	1.00	0.393	0.051	1.37E-14
IGP42	rs8019473	14	64848881	G	0.81	0.99	-0.296	0.038	1.05E-14
IGP42	rs10138662	14	64849235	G	0.19	0.99	0.296	0.038	1.01E-14
IGP42	rs10134589	14	64850987	T	0.19	0.94	0.318	0.040	1.04E-15
IGP42	rs7151212	14	64851375	C	0.81	0.99	-0.296	0.038	9.63E-15
IGP42	rs11158587	14	64852465	G	0.81	0.99	-0.296	0.038	9.51E-15
IGP42	rs8019767	14	64852538	G	0.81	1.00	-0.296	0.038	9.41E-15
IGP42	rs6573598	14	64852772	C	0.19	1.00	0.296	0.038	9.27E-15
IGP42	rs6573599	14	64852880	C	0.81	1.00	-0.296	0.038	8.99E-15
IGP42	rs10144503	14	64853862	G	0.90	1.00	-0.393	0.051	1.25E-14
IGP42	rs6573602	14	64854363	C	0.19	1.00	0.296	0.038	8.73E-15
IGP42	rs17102598	14	64854613	G	0.81	1.00	-0.296	0.038	8.65E-15
IGP42	rs12436299	14	64854947	G	0.90	1.00	-0.393	0.051	1.23E-14
IGP42	rs6573604	14	64857694	C	0.19	1.00	0.297	0.038	8.48E-15
IGP42	rs9635250	14	64869101	T	0.10	1.00	0.394	0.051	1.20E-14
IGP42	rs12881755	14	64871564	G	0.65	0.96	-0.245	0.033	2.24E-13
IGP42	rs747541	14	64875163	C	0.45	0.98	0.280	0.032	1.28E-18
IGP42	rs1954052	14	64875462	T	0.44	0.99	0.280	0.032	1.11E-18
IGP42	rs12436465	14	64876630	C	0.72	0.98	-0.205	0.035	6.53E-09
IGP42	rs12886005	14	64879000	C	0.45	0.87	0.283	0.034	4.17E-17
IGP42	rs12886168	14	64879039	C	0.45	0.98	0.279	0.032	1.27E-18
IGP42	rs11623920	14	64889067	C	0.56	1.00	-0.279	0.032	1.11E-18
IGP42	rs11621121	14	64892246	C	0.44	1.00	0.279	0.032	1.13E-18

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP42	rs10148907	14	64903125	C	0.69	0.98	-0.286	0.034	8.94E-17
IGP42	rs4902393	14	64909267	C	0.56	0.99	-0.278	0.032	1.99E-18
IGP42	rs11621604	14	64910527	G	0.56	0.98	-0.274	0.032	9.11E-18
IGP42	rs12882269	14	64916897	G	0.56	0.97	-0.272	0.032	1.63E-17
IGP42	rs11158591	14	64925515	C	0.44	0.97	0.270	0.032	2.39E-17
IGP42	rs11158592	14	64929721	G	0.50	0.99	0.251	0.031	3.93E-16
IGP42	rs11158593	14	64929737	G	0.50	0.99	0.253	0.031	1.96E-16
IGP42	rs10138570	14	64929791	G	0.50	0.99	-0.253	0.031	1.99E-16
IGP42	rs10138671	14	64929845	G	0.58	0.99	-0.172	0.031	3.96E-08
IGP42	rs4587890	14	64933537	T	0.42	0.99	0.171	0.031	4.02E-08
IGP42	rs2411823	14	64934819	C	0.42	0.99	0.171	0.031	4.10E-08
IGP42	rs17246007	14	64935424	C	0.08	0.99	0.323	0.059	5.77E-08
IGP42	rs11844747	14	64939881	C	0.08	0.99	0.323	0.059	5.69E-08
IGP42	rs17246035	14	64943883	G	0.08	1.00	0.323	0.059	5.23E-08
IGP42	rs2411822	14	64948148	G	0.48	1.00	-0.235	0.031	2.48E-14
IGP42	rs1953416	14	64948560	C	0.53	1.00	0.237	0.031	1.36E-14
IGP42	rs1953417	14	64948662	C	0.92	1.00	-0.323	0.059	5.11E-08
IGP42	rs883081	14	64950374	C	0.53	1.00	0.237	0.031	1.41E-14
IGP42	rs883082	14	64950693	G	0.48	1.00	-0.235	0.031	2.59E-14
IGP42	rs7145574	14	64954155	C	0.92	1.00	-0.324	0.059	5.06E-08
IGP42	rs867972	14	64965514	C	0.48	0.97	-0.237	0.031	2.86E-14
IGP42	rs11851576	14	64970036	C	0.54	0.99	-0.206	0.031	4.51E-11
IGP42	rs12879971	14	64971357	G	0.52	0.99	0.237	0.031	1.66E-14
IGP42	rs12892058	14	64973194	C	0.47	0.99	-0.241	0.031	7.51E-15
IGP42	rs10483776	14	64984620	G	0.22	1.00	0.220	0.038	1.04E-08
IGP42	rs17826580	14	64985015	C	0.08	1.00	0.325	0.059	4.40E-08
IGP42	rs2184602	14	64985425	G	0.08	1.00	0.325	0.059	4.40E-08
IGP42	rs2152375	14	64985531	C	0.08	1.00	0.325	0.059	4.40E-08
IGP42	rs12589698	14	64990188	G	0.52	0.98	0.246	0.031	2.63E-15
IGP42	rs4899179	14	64996501	G	0.49	0.99	-0.243	0.031	4.25E-15
IGP42	rs2184603	14	65000423	C	0.49	0.99	-0.243	0.031	4.18E-15
IGP42	rs11850847	14	65003551	C	0.92	1.00	-0.325	0.059	4.33E-08
IGP42	rs12434585	14	65008121	G	0.08	1.00	0.325	0.059	4.33E-08
IGP42	rs3825640	14	65030957	C	0.51	0.99	0.245	0.031	2.19E-15
IGP42	rs11627084	14	65048589	G	0.49	1.00	-0.243	0.031	3.98E-15
IGP42	rs10483780	14	65049923	C	0.50	0.99	-0.239	0.031	1.14E-14
IGP42	rs2149841	14	65080072	C	0.51	0.99	0.245	0.031	2.12E-15
IGP42	rs7153679	14	65082707	G	0.08	0.99	0.326	0.059	4.09E-08
IGP42	rs11621680	14	65084434	G	0.50	0.99	-0.239	0.031	1.07E-14
IGP42	rs11851013	14	65085965	G	0.08	0.99	0.326	0.059	4.09E-08
IGP42	rs11623662	14	65090945	G	0.60	0.99	-0.178	0.032	1.65E-08
IGP42	rs11851772	14	65091800	C	0.92	0.99	-0.326	0.059	4.09E-08
IGP42	rs9972106	14	65092884	T	0.60	0.99	-0.178	0.032	1.63E-08
IGP42	rs11158601	14	65095116	G	0.49	1.00	-0.242	0.031	3.80E-15
IGP42	rs7146742	14	65102687	G	0.43	0.99	0.217	0.032	8.53E-12
IGP42	rs1958561	14	65106514	G	0.49	1.00	-0.242	0.031	4.03E-15
IGP42	rs12887134	14	65115296	C	0.49	0.99	-0.245	0.031	2.24E-15
IGP42	rs7155541	14	65115995	C	0.49	0.99	-0.245	0.031	2.25E-15
IGP42	rs6573615	14	65116287	G	0.40	0.99	0.178	0.032	1.67E-08
IGP42	rs7160780	14	65122466	G	0.40	0.99	0.179	0.031	1.32E-08
IGP42	rs7161123	14	65122654	G	0.51	1.00	0.242	0.031	3.84E-15
IGP42	rs2411356	14	65122914	G	0.40	0.99	0.179	0.031	1.32E-08
IGP42	rs12433827	14	65125363	G	0.92	1.00	-0.327	0.059	3.96E-08
IGP42	rs4581615	14	65125696	C	0.51	1.00	0.242	0.031	3.84E-15

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP42	rs8005309	14	65126261	T	0.92	1.00	-0.327	0.059	3.96E-08
IGP42	rs17753508	14	65127205	G	0.22	1.00	0.223	0.038	6.94E-09
IGP42	rs3783709	14	65128417	T	0.51	1.00	0.242	0.031	3.84E-15
IGP42	rs12889002	14	65133335	C	0.51	1.00	0.242	0.031	3.84E-15
IGP42	rs743085	14	65137886	G	0.49	1.00	-0.242	0.031	3.84E-15
IGP42	rs17826724	14	65138073	C	0.08	1.00	0.327	0.060	3.93E-08
IGP42	rs11849252	14	65139522	G	0.92	1.00	-0.327	0.060	3.93E-08
IGP42	rs17826736	14	65151955	C	0.08	1.00	0.327	0.060	3.91E-08
IGP42	rs2073294	14	65152246	C	0.92	1.00	-0.327	0.060	3.91E-08
IGP42	rs8012278	14	65152326	G	0.49	1.00	-0.247	0.031	1.09E-15
IGP42	rs11849862	14	65167778	G	0.07	1.00	0.327	0.060	3.91E-08
IGP42	rs2268957	14	65182986	C	0.93	1.00	-0.327	0.060	3.92E-08
IGP42	rs12890902	14	65186375	T	0.51	1.00	0.248	0.031	7.47E-16
IGP42	rs2300865	14	65189768	C	0.49	1.00	-0.248	0.031	7.28E-16
IGP42	rs11627184	14	65191196	C	0.51	1.00	0.249	0.031	6.80E-16
IGP42	rs12435908	14	65191221	C	0.93	1.00	-0.327	0.060	3.91E-08
IGP42	rs11627185	14	65191245	G	0.49	1.00	-0.249	0.031	6.49E-16
IGP42	rs1998035	14	65195983	G	0.07	1.00	0.327	0.060	3.89E-08
IGP42	rs2268958	14	65197991	T	0.07	1.00	0.327	0.060	3.88E-08
IGP42	rs7142651	14	65202474	C	0.51	1.00	0.249	0.031	6.11E-16
IGP42	rs1998036	14	65207952	C	0.49	0.99	-0.249	0.031	5.85E-16
IGP42	rs2268959	14	65215071	C	0.78	1.00	-0.229	0.038	2.33E-09
IGP42	rs2268960	14	65215253	G	0.07	0.97	0.344	0.061	1.84E-08
IGP42	rs2268961	14	65216518	C	0.49	0.99	-0.250	0.031	4.70E-16
IGP42	rs2268962	14	65217026	G	0.49	1.00	-0.250	0.031	4.59E-16
IGP42	rs2300871	14	65217447	C	0.07	1.00	0.327	0.060	3.81E-08
IGP42	rs2300872	14	65217514	G	0.07	1.00	0.328	0.060	4.03E-08
IGP42	rs2064694	14	65217999	G	0.51	1.00	0.249	0.031	5.90E-16
IGP42	rs12588838	14	65232391	G	0.51	1.00	0.249	0.031	5.65E-16
IGP42	rs8019491	14	65237863	G	0.07	1.00	0.328	0.060	4.01E-08
IGP42	rs11628765	14	65238202	C	0.49	1.00	-0.250	0.031	5.27E-16
IGP42	rs2411351	14	65241294	C	0.49	1.00	-0.250	0.031	5.09E-16
IGP42	rs11846546	14	65246146	G	0.14	0.99	0.259	0.045	7.31E-09
IGP42	rs8018278	14	65249841	G	0.49	1.00	-0.250	0.031	5.06E-16
IGP42	rs11627067	14	65252706	G	0.49	1.00	-0.250	0.031	5.04E-16
IGP42	rs4143898	14	65258635	T	0.44	0.99	0.223	0.031	1.40E-12
IGP42	rs11622829	14	65261535	T	0.50	1.00	0.249	0.031	7.25E-16
IGP42	rs11624104	14	65265890	G	0.50	1.00	-0.247	0.031	1.35E-15
IGP42	rs1535173	14	65268892	C	0.50	1.00	0.246	0.031	1.45E-15
IGP42	rs3742597	14	65269930	G	0.29	1.00	0.288	0.035	9.84E-17
IGP42	rs927004	14	65270664	C	0.50	1.00	-0.246	0.031	1.61E-15
IGP42	rs1950557	14	65271510	C	0.71	1.00	-0.288	0.035	9.89E-17
IGP42	rs8010876	14	65276729	G	0.50	1.00	-0.246	0.031	1.56E-15
IGP42	rs1054218	14	65278943	C	0.40	1.00	0.238	0.032	6.66E-14
IGP42	rs761830	14	65282739	G	0.40	1.00	0.238	0.032	6.68E-14
IGP42	rs10483785	14	65289270	G	0.50	1.00	0.245	0.031	1.68E-15
IGP42	rs6573624	14	65296638	G	0.50	0.98	0.248	0.031	1.65E-15
IGP42	rs2411405	14	65301839	G	0.53	0.97	-0.246	0.031	3.18E-15
IGP42	rs743084	14	65302355	C	0.52	0.97	-0.245	0.031	5.83E-15
IGP42	rs11625362	14	65302622	G	0.47	0.97	0.246	0.031	3.22E-15
IGP42	rs4080329	14	65303243	C	0.62	0.97	-0.243	0.032	6.35E-14
IGP42	rs11627605	14	65304066	G	0.47	0.97	0.246	0.031	3.29E-15
IGP42	rs11627578	14	65304201	C	0.47	0.97	0.246	0.031	3.29E-15
IGP42	rs11628840	14	65305395	G	0.53	0.97	-0.246	0.031	3.30E-15

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP42	rs1003401	14	65307473	G	0.39	0.97	0.244	0.032	2.87E-14
IGP42	rs4902416	14	65307843	C	0.53	0.97	-0.246	0.031	3.37E-15
IGP42	rs1984855	14	65309010	C	0.61	0.97	-0.244	0.032	2.89E-14
IGP42	rs730807	14	65309043	C	0.47	0.97	0.246	0.031	3.43E-15
IGP42	rs2411404	14	65309154	C	0.47	0.97	0.246	0.031	3.46E-15
IGP42	rs1075566	14	65309210	C	0.47	0.97	0.246	0.031	3.49E-15
IGP42	rs7157449	14	65309890	G	0.53	0.97	-0.246	0.031	3.56E-15
IGP42	rs6573625	14	65310387	C	0.62	0.97	-0.243	0.032	7.33E-14
IGP42	rs6573626	14	65310448	C	0.53	0.97	-0.246	0.031	4.11E-15
IGP42	rs7158556	14	65310482	T	0.38	0.97	0.242	0.032	7.42E-14
IGP42	rs12894466	14	65310520	G	0.47	0.97	0.246	0.031	4.18E-15
IGP42	rs11625882	14	65314952	G	0.47	0.97	0.245	0.031	4.74E-15
IGP42	rs2236067	14	65317765	G	0.61	0.97	-0.244	0.032	3.78E-14
IGP42	rs968540	14	65318817	G	0.62	0.96	-0.242	0.032	8.88E-14
IGP42	rs7142165	14	65319985	G	0.53	0.96	-0.245	0.031	6.00E-15
IGP42	rs7143026	14	65320709	G	0.40	0.95	0.226	0.033	3.92E-12
IGP42	rs6573627	14	65322079	C	0.51	0.98	-0.230	0.031	2.13E-13
IGP42	rs4400971	14	65324331	C	0.43	0.99	0.193	0.031	8.89E-10
IGP42	rs7151846	14	65325534	C	0.51	0.99	-0.222	0.031	8.85E-13
IGP42	rs4073416	14	65329147	C	0.43	0.99	0.193	0.031	9.27E-10
IGP42	rs4073415	14	65329283	G	0.51	0.99	-0.223	0.031	8.96E-13
IGP42	rs11850120	14	65330132	C	0.42	0.98	0.190	0.032	2.31E-09
IGP42	rs8018379	14	65331690	C	0.56	0.95	-0.232	0.032	5.80E-13
IGP42	rs8007846	14	65332716	G	0.48	0.98	0.186	0.031	3.21E-09
IGP42	rs4078408	14	65342587	G	0.29	0.86	-0.198	0.037	8.41E-08
IGP42	rs3924222	14	65343491	C	0.41	0.80	-0.246	0.035	1.58E-12
IGP42	rs10149325	14	65347120	G	0.41	0.80	-0.247	0.035	1.30E-12
IGP43	rs17348299	5	55358652	C	0.84	0.85	-0.280	0.045	3.09E-10
IGP43	rs16884711	5	55360559	C	0.19	0.91	0.227	0.040	1.89E-08
IGP43	rs10454831	5	55374548	T	0.80	0.90	-0.217	0.040	5.59E-08
IGP43	rs955768	5	55374759	T	0.20	0.90	0.217	0.040	5.59E-08
IGP45	rs1122979	7	150546004	G	0.88	0.91	0.305	0.049	6.06E-10
IGP45	rs7812088	7	150550762	G	0.87	0.98	0.288	0.047	9.67E-10
IGP45	rs7781265	7	150581873	G	0.88	0.92	0.287	0.050	9.22E-09
IGP45	rs5757647	22	38104993	C	0.33	1.00	0.206	0.033	3.28E-10
IGP45	rs4821890	22	38107469	G	0.34	0.99	0.206	0.033	3.31E-10
IGP45	rs1010169	22	38108113	G	0.67	1.00	-0.206	0.033	3.26E-10
IGP45	rs1010170	22	38108273	C	0.67	1.00	-0.206	0.033	3.30E-10
IGP45	rs5757650	22	38108365	C	0.67	1.00	-0.206	0.033	3.29E-10
IGP45	rs9611169	22	38112973	C	0.33	1.00	0.206	0.033	3.29E-10
IGP45	rs9611170	22	38114791	C	0.66	0.99	-0.204	0.033	4.12E-10
IGP45	rs2413590	22	38120137	C	0.67	1.00	-0.204	0.033	4.14E-10
IGP45	rs5750808	22	38120933	G	0.33	1.00	0.204	0.033	4.21E-10
IGP45	rs5750811	22	38123012	G	0.67	1.00	-0.204	0.033	4.32E-10
IGP45	rs5750812	22	38123025	G	0.34	0.99	0.205	0.033	3.91E-10
IGP45	rs5757655	22	38127124	C	0.66	0.99	-0.205	0.033	3.88E-10
IGP45	rs4821893	22	38127725	G	0.33	1.00	0.205	0.033	3.35E-10
IGP45	rs5750814	22	38127933	C	0.67	1.00	-0.205	0.033	3.24E-10
IGP45	rs5757657	22	38128375	G	0.33	1.00	0.205	0.033	3.46E-10
IGP45	rs5750815	22	38128395	C	0.67	1.00	-0.205	0.033	3.43E-10
IGP45	rs4337572	22	38130650	C	0.33	1.00	0.205	0.033	3.45E-10
IGP45	rs4821894	22	38139766	C	0.66	1.00	-0.205	0.033	3.46E-10
IGP45	rs5750816	22	38140325	C	0.34	1.00	0.204	0.033	3.49E-10
IGP45	rs5757659	22	38142355	G	0.66	1.00	-0.204	0.033	3.49E-10

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP45	rs6001585	22	38142932	C	0.22	1.00	0.212	0.037	7.63E-09
IGP45	rs6001587	22	38148954	C	0.66	1.00	-0.204	0.033	3.48E-10
IGP45	rs5750818	22	38150831	G	0.66	1.00	-0.204	0.033	3.46E-10
IGP45	rs5757665	22	38151587	G	0.66	1.00	-0.204	0.033	3.45E-10
IGP45	rs4821895	22	38152961	G	0.66	1.00	-0.204	0.033	3.43E-10
IGP45	rs739141	22	38154396	C	0.36	1.00	0.208	0.032	1.10E-10
IGP45	rs5750820	22	38155268	G	0.67	0.97	-0.219	0.033	3.93E-11
IGP45	rs5750822	22	38156734	G	0.34	1.00	0.205	0.033	3.17E-10
IGP45	rs7949	22	38157499	G	0.34	0.99	0.206	0.033	2.89E-10
IGP45	rs5757670	22	38159682	G	0.34	0.99	0.206	0.033	2.70E-10
IGP45	rs5750825	22	38161224	G	0.71	0.98	-0.243	0.034	1.34E-12
IGP45	rs1972280	22	38161932	T	0.29	0.98	0.245	0.034	1.08E-12
IGP45	rs4821897	22	38165533	G	0.71	0.97	-0.245	0.034	1.02E-12
IGP45	rs5750830	22	38170774	C	0.29	0.98	0.250	0.034	3.24E-13
IGP45	rs5757676	22	38171646	C	0.78	0.96	-0.227	0.037	1.14E-09
IGP45	rs8137426	22	38174296	G	0.71	0.98	-0.249	0.034	3.21E-13
IGP45	rs5757683	22	38180120	G	0.29	0.98	0.249	0.034	3.17E-13
IGP45	rs1557541	22	38181916	C	0.29	0.98	0.249	0.034	3.14E-13
IGP45	rs1557542	22	38182296	C	0.71	0.98	-0.249	0.034	3.11E-13
IGP45	rs5995735	22	38184367	C	0.29	0.98	0.249	0.034	3.07E-13
IGP45	rs738289	22	38185829	C	0.29	0.98	0.249	0.034	3.02E-13
IGP45	rs909674	22	38189115	C	0.30	0.99	0.247	0.034	2.84E-13
IGP46	rs6583437	7	50320813	G	0.64	0.98	0.174	0.032	3.95E-08
IGP46	rs6421315	7	50325753	C	0.37	0.95	-0.173	0.032	7.38E-08
IGP46	rs7159888	14	64828395	G	0.55	0.99	-0.200	0.031	1.06E-10
IGP46	rs1256540	14	64833822	C	0.43	1.00	0.168	0.031	6.83E-08
IGP46	rs4902383	14	64834326	C	0.19	0.94	0.221	0.040	2.57E-08
IGP46	rs1269068	14	64837086	C	0.57	1.00	-0.167	0.031	7.65E-08
IGP46	rs1760978	14	64840800	G	0.43	0.98	0.198	0.031	2.04E-10
IGP46	rs10144975	14	64843735	C	0.80	0.98	-0.220	0.038	7.06E-09
IGP46	rs17102587	14	64844230	C	0.20	0.97	0.228	0.038	2.70E-09
IGP46	rs8017974	14	64844940	C	0.20	0.99	0.230	0.038	1.55E-09
IGP46	rs11847263	14	64845448	G	0.39	0.98	0.233	0.032	1.81E-13
IGP46	rs4902386	14	64848043	C	0.80	0.99	-0.230	0.038	1.42E-09
IGP46	rs8019473	14	64848881	G	0.80	0.99	-0.230	0.038	1.41E-09
IGP46	rs10138662	14	64849235	G	0.20	0.99	0.230	0.038	1.36E-09
IGP46	rs10134589	14	64850987	T	0.19	0.94	0.239	0.039	1.20E-09
IGP46	rs7151212	14	64851375	C	0.80	0.99	-0.231	0.038	1.30E-09
IGP46	rs11158587	14	64852465	G	0.80	0.99	-0.231	0.038	1.29E-09
IGP46	rs8019767	14	64852538	G	0.80	1.00	-0.231	0.038	1.28E-09
IGP46	rs6573598	14	64852772	C	0.20	1.00	0.231	0.038	1.27E-09
IGP46	rs6573599	14	64852880	C	0.80	1.00	-0.231	0.038	1.22E-09
IGP46	rs6573602	14	64854363	C	0.20	1.00	0.231	0.038	1.19E-09
IGP46	rs17102598	14	64854613	G	0.80	1.00	-0.231	0.038	1.19E-09
IGP46	rs6573604	14	64857694	C	0.20	1.00	0.231	0.038	1.18E-09
IGP46	rs747541	14	64875163	C	0.45	0.98	0.194	0.031	7.23E-10
IGP46	rs1954052	14	64875462	T	0.44	0.99	0.191	0.031	1.13E-09
IGP46	rs12886005	14	64879000	C	0.45	0.87	0.202	0.033	1.28E-09
IGP46	rs12886168	14	64879039	C	0.45	0.98	0.193	0.031	7.15E-10
IGP46	rs11623920	14	64889067	C	0.56	1.00	-0.191	0.031	1.12E-09
IGP46	rs11621121	14	64892246	C	0.44	1.00	0.190	0.031	1.11E-09
IGP46	rs10148907	14	64903125	C	0.69	0.98	-0.195	0.034	9.86E-09
IGP46	rs4902393	14	64909267	C	0.56	0.99	-0.190	0.031	1.42E-09
IGP46	rs11621604	14	64910527	G	0.56	0.98	-0.186	0.032	4.09E-09

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP46	rs12882269	14	64916897	G	0.56	0.97	-0.184	0.032	5.76E-09
IGP46	rs11158591	14	64925515	C	0.44	0.97	0.183	0.032	7.00E-09
IGP46	rs11158592	14	64929721	G	0.50	0.99	0.167	0.031	5.00E-08
IGP46	rs11158593	14	64929737	G	0.50	0.99	0.165	0.031	6.40E-08
IGP46	rs10138570	14	64929791	G	0.50	0.99	-0.165	0.031	6.47E-08
IGP46	rs2411822	14	64948148	G	0.47	1.00	-0.166	0.031	6.13E-08
IGP46	rs1953416	14	64948560	C	0.53	1.00	0.164	0.031	8.01E-08
IGP46	rs883081	14	64950374	C	0.53	1.00	0.164	0.031	8.13E-08
IGP46	rs883082	14	64950693	G	0.47	1.00	-0.165	0.031	6.26E-08
IGP46	rs12879971	14	64971357	G	0.52	0.99	0.168	0.031	4.64E-08
IGP46	rs12892058	14	64973194	C	0.47	0.99	-0.168	0.031	4.90E-08
IGP46	rs12589698	14	64990188	G	0.52	0.98	0.171	0.031	2.79E-08
IGP46	rs4899179	14	64996501	G	0.49	0.99	-0.173	0.031	1.74E-08
IGP46	rs2184603	14	65000423	C	0.49	0.99	-0.173	0.031	1.72E-08
IGP46	rs3825640	14	65030957	C	0.51	0.99	0.172	0.031	2.01E-08
IGP46	rs11627084	14	65048589	G	0.49	1.00	-0.173	0.031	1.55E-08
IGP46	rs10483780	14	65049923	C	0.50	0.99	-0.165	0.031	7.59E-08
IGP46	rs2149841	14	65080072	C	0.51	0.99	0.172	0.031	2.14E-08
IGP46	rs11621680	14	65084434	G	0.50	0.99	-0.164	0.031	8.82E-08
IGP46	rs11158601	14	65095116	G	0.49	1.00	-0.171	0.031	2.06E-08
IGP46	rs1958561	14	65106514	G	0.49	1.00	-0.171	0.031	2.06E-08
IGP46	rs12887134	14	65115296	C	0.49	0.99	-0.170	0.031	2.71E-08
IGP46	rs7155541	14	65115995	C	0.49	0.99	-0.170	0.031	2.71E-08
IGP46	rs7161123	14	65122654	G	0.51	1.00	0.172	0.031	1.84E-08
IGP46	rs4581615	14	65125696	C	0.51	1.00	0.172	0.031	1.84E-08
IGP46	rs3783709	14	65128417	T	0.51	1.00	0.172	0.031	1.83E-08
IGP46	rs12889002	14	65133335	C	0.51	1.00	0.172	0.031	1.83E-08
IGP46	rs743085	14	65137886	G	0.49	1.00	-0.172	0.031	1.83E-08
IGP46	rs8012278	14	65152326	G	0.49	1.00	-0.174	0.031	1.27E-08
IGP46	rs12890902	14	65186375	T	0.51	1.00	0.174	0.031	1.20E-08
IGP46	rs2300865	14	65189768	C	0.49	1.00	-0.174	0.031	1.20E-08
IGP46	rs11627184	14	65191196	C	0.51	1.00	0.174	0.031	1.18E-08
IGP46	rs11627185	14	65191245	G	0.49	1.00	-0.174	0.031	1.17E-08
IGP46	rs7142651	14	65202474	C	0.51	1.00	0.174	0.031	1.30E-08
IGP46	rs1998036	14	65207952	C	0.49	0.99	-0.174	0.031	1.30E-08
IGP46	rs2268961	14	65216518	C	0.49	0.99	-0.174	0.031	1.24E-08
IGP46	rs2268962	14	65217026	G	0.49	1.00	-0.174	0.031	1.24E-08
IGP46	rs2064694	14	65217999	G	0.51	1.00	0.172	0.031	1.85E-08
IGP46	rs12588838	14	65232391	G	0.51	1.00	0.172	0.031	1.86E-08
IGP46	rs11628765	14	65238202	C	0.49	1.00	-0.172	0.031	1.85E-08
IGP46	rs2411351	14	65241294	C	0.49	1.00	-0.172	0.031	1.87E-08
IGP46	rs8018278	14	65249841	G	0.49	1.00	-0.172	0.031	1.92E-08
IGP46	rs11627067	14	65252706	G	0.49	1.00	-0.172	0.031	1.96E-08
IGP46	rs11622829	14	65261535	T	0.50	1.00	0.166	0.031	5.64E-08
IGP46	rs11624104	14	65265890	G	0.50	1.00	-0.166	0.031	5.95E-08
IGP46	rs1535173	14	65268892	C	0.50	1.00	0.166	0.031	6.25E-08
IGP46	rs3742597	14	65269930	G	0.29	1.00	0.191	0.034	2.87E-08
IGP46	rs927004	14	65270664	C	0.50	1.00	-0.165	0.031	7.11E-08
IGP46	rs1950557	14	65271510	C	0.71	1.00	-0.190	0.034	2.99E-08
IGP46	rs8010876	14	65276729	G	0.50	1.00	-0.165	0.031	7.23E-08
IGP46	rs2411405	14	65301839	G	0.52	0.97	-0.167	0.031	7.29E-08
IGP46	rs743084	14	65302355	C	0.52	0.97	-0.171	0.031	3.69E-08
IGP46	rs11625362	14	65302622	G	0.48	0.97	0.166	0.031	7.65E-08
IGP46	rs11627605	14	65304066	G	0.48	0.97	0.166	0.031	7.95E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP46	rs11627578	14	65304201	C	0.48	0.97	0.166	0.031	7.99E-08
IGP46	rs11628840	14	65305395	G	0.52	0.97	-0.166	0.031	8.06E-08
IGP46	rs4902416	14	65307843	C	0.52	0.97	-0.166	0.031	8.28E-08
IGP46	rs730807	14	65309043	C	0.48	0.97	0.166	0.031	8.45E-08
IGP46	rs2411404	14	65309154	C	0.48	0.97	0.166	0.031	8.53E-08
IGP46	rs1075566	14	65309210	C	0.48	0.97	0.166	0.031	8.58E-08
IGP46	rs7157449	14	65309890	G	0.52	0.97	-0.166	0.031	8.75E-08
IGP46	rs6573626	14	65310448	C	0.52	0.97	-0.165	0.031	9.56E-08
IGP46	rs12894466	14	65310520	G	0.48	0.97	0.165	0.031	9.70E-08
IGP49	rs5760020	22	22463092	G	0.30	1.00	-0.185	0.034	4.77E-08
IGP49	rs2073389	22	22463493	C	0.30	1.00	-0.185	0.034	4.52E-08
IGP49	rs17630758	22	22466542	G	0.83	0.99	0.327	0.041	2.33E-15
IGP49	rs5760023	22	22468301	C	0.30	1.00	-0.186	0.034	3.73E-08
IGP49	rs12167679	22	22471690	C	0.80	1.00	0.256	0.039	3.95E-11
IGP49	rs17548631	22	22474125	C	0.17	0.99	-0.326	0.041	2.27E-15
IGP49	rs9620326	22	22476629	C	0.83	0.99	0.326	0.041	2.32E-15
IGP49	rs9624334	22	22496256	C	0.17	0.99	-0.332	0.041	1.12E-15
IGP49	rs2186369	22	22500996	G	0.19	0.88	-0.336	0.042	7.34E-16
IGP49	rs6519476	22	22512500	G	0.76	0.99	0.215	0.036	3.56E-09
IGP49	rs5757642	22	38094770	C	0.64	1.00	-0.182	0.033	2.54E-08
IGP49	rs7286714	22	38095550	C	0.36	0.97	0.182	0.033	2.97E-08
IGP49	rs5757644	22	38096386	C	0.36	0.97	0.182	0.033	2.96E-08
IGP49	rs5750806	22	38096957	G	0.64	0.97	-0.182	0.033	2.97E-08
IGP49	rs1569499	22	38099764	C	0.64	0.97	-0.184	0.033	2.70E-08
IGP49	rs4821888	22	38100543	G	0.64	0.97	-0.183	0.033	2.75E-08
IGP49	rs5750820	22	38155268	G	0.67	0.97	-0.180	0.033	5.71E-08
IGP49	rs5750825	22	38161224	G	0.71	0.98	-0.199	0.034	6.65E-09
IGP49	rs1972280	22	38161932	T	0.29	0.98	0.200	0.034	6.12E-09
IGP49	rs4821897	22	38165533	G	0.71	0.97	-0.200	0.034	5.74E-09
IGP49	rs5750830	22	38170774	C	0.29	0.98	0.201	0.034	4.37E-09
IGP49	rs8137426	22	38174296	G	0.71	0.98	-0.201	0.034	4.32E-09
IGP49	rs5757683	22	38180120	G	0.29	0.98	0.201	0.034	4.30E-09
IGP49	rs1557541	22	38181916	C	0.29	0.98	0.201	0.034	4.31E-09
IGP49	rs1557542	22	38182296	C	0.71	0.98	-0.201	0.034	4.31E-09
IGP49	rs5995735	22	38184367	C	0.29	0.98	0.201	0.034	4.33E-09
IGP49	rs738289	22	38185829	C	0.29	0.98	0.201	0.034	4.35E-09
IGP49	rs909674	22	38189115	C	0.30	0.99	0.200	0.034	3.26E-09
IGP50	rs17630758	22	22466542	G	0.83	0.99	0.239	0.041	6.21E-09
IGP50	rs12167679	22	22471690	C	0.80	1.00	0.227	0.039	5.16E-09
IGP50	rs17548631	22	22474125	C	0.17	0.99	-0.239	0.041	6.61E-09
IGP50	rs9620326	22	22476629	C	0.83	0.99	0.238	0.041	6.63E-09
IGP50	rs9624334	22	22496256	C	0.17	0.99	-0.239	0.041	7.86E-09
IGP50	rs2186369	22	22500996	G	0.19	0.88	-0.259	0.042	5.34E-10
IGP51	rs7159888	14	64828395	G	0.55	0.99	-0.199	0.031	1.63E-10
IGP51	rs4902383	14	64834326	C	0.19	0.94	0.230	0.040	7.18E-09
IGP51	rs1760978	14	64840800	G	0.43	0.98	0.190	0.031	1.25E-09
IGP51	rs10144975	14	64843735	C	0.80	0.98	-0.230	0.038	1.73E-09
IGP51	rs17102587	14	64844230	C	0.20	0.97	0.236	0.038	7.98E-10
IGP51	rs8017974	14	64844940	C	0.20	0.99	0.237	0.038	5.56E-10
IGP51	rs11847263	14	64845448	G	0.39	0.98	0.232	0.032	2.35E-13
IGP51	rs4902386	14	64848043	C	0.80	0.99	-0.236	0.038	5.46E-10
IGP51	rs8019473	14	64848881	G	0.80	0.99	-0.236	0.038	5.43E-10
IGP51	rs10138662	14	64849235	G	0.20	0.99	0.236	0.038	5.24E-10
IGP51	rs10134589	14	64850987	T	0.19	0.94	0.245	0.039	4.94E-10

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP51	rs7151212	14	64851375	C	0.80	0.99	-0.237	0.038	5.05E-10
IGP51	rs11158587	14	64852465	G	0.80	0.99	-0.237	0.038	5.04E-10
IGP51	rs8019767	14	64852538	G	0.80	1.00	-0.237	0.038	5.05E-10
IGP51	rs6573598	14	64852772	C	0.20	1.00	0.237	0.038	5.04E-10
IGP51	rs6573599	14	64852880	C	0.80	1.00	-0.237	0.038	4.83E-10
IGP51	rs6573602	14	64854363	C	0.20	1.00	0.237	0.038	4.73E-10
IGP51	rs17102598	14	64854613	G	0.80	1.00	-0.237	0.038	4.76E-10
IGP51	rs6573604	14	64857694	C	0.20	1.00	0.237	0.038	4.75E-10
IGP51	rs747541	14	64875163	C	0.45	0.98	0.192	0.032	1.05E-09
IGP51	rs1954052	14	64875462	T	0.44	0.99	0.190	0.031	1.65E-09
IGP51	rs12886005	14	64879000	C	0.45	0.87	0.201	0.033	1.94E-09
IGP51	rs12886168	14	64879039	C	0.45	0.98	0.192	0.031	1.05E-09
IGP51	rs11623920	14	64889067	C	0.56	1.00	-0.189	0.031	1.65E-09
IGP51	rs11621121	14	64892246	C	0.44	1.00	0.189	0.031	1.65E-09
IGP51	rs10148907	14	64903125	C	0.69	0.98	-0.204	0.034	2.41E-09
IGP51	rs4902393	14	64909267	C	0.56	0.99	-0.188	0.032	2.28E-09
IGP51	rs11621604	14	64910527	G	0.56	0.98	-0.183	0.032	7.06E-09
IGP51	rs12882269	14	64916897	G	0.56	0.97	-0.181	0.032	1.07E-08
IGP51	rs11158591	14	64925515	C	0.44	0.97	0.180	0.032	1.33E-08
IGP51	rs3742597	14	65269930	G	0.29	1.00	0.194	0.034	1.69E-08
IGP51	rs1950557	14	65271510	C	0.71	1.00	-0.194	0.034	1.71E-08
IGP53	rs17348299	5	55358652	C	0.84	0.85	0.292	0.045	6.88E-11
IGP53	rs16884711	5	55360559	C	0.19	0.91	-0.247	0.041	1.23E-09
IGP53	rs10454831	5	55374548	T	0.80	0.90	0.228	0.040	1.31E-08
IGP53	rs955768	5	55374759	T	0.20	0.90	-0.229	0.040	1.31E-08
IGP53	rs3818593	9	33110706	G	0.20	1.00	-0.215	0.039	3.48E-08
IGP53	rs10971418	9	33112024	C	0.80	0.98	0.214	0.039	3.79E-08
IGP53	rs12342831	9	33114872	C	0.26	0.97	-0.214	0.035	1.68E-09
IGP53	rs10813951	9	33118021	G	0.26	0.97	-0.214	0.035	1.70E-09
IGP53	rs2067749	9	33120640	G	0.11	0.98	0.294	0.050	3.97E-09
IGP53	rs10511909	9	33122518	C	0.11	0.98	0.294	0.050	4.08E-09
IGP53	rs3780486	9	33129453	C	0.74	0.97	0.214	0.036	1.74E-09
IGP53	rs10813957	9	33143527	G	0.74	0.96	0.216	0.036	1.60E-09
IGP53	rs10971438	9	33170308	G	0.30	0.75	-0.224	0.039	6.74E-09
IGP53	rs10813960	9	33170362	C	0.70	0.74	0.225	0.039	6.58E-09
IGP53	rs10971439	9	33170813	C	0.23	0.71	-0.242	0.043	2.26E-08
IGP54	rs278541	8	94292121	C	0.98	0.50	-0.805	0.147	3.87E-08
IGP55	rs17348299	5	55358652	C	0.84	0.85	-0.286	0.045	1.35E-10
IGP55	rs16884711	5	55360559	C	0.19	0.91	0.239	0.040	3.59E-09
IGP55	rs10454831	5	55374548	T	0.80	0.90	-0.225	0.040	2.03E-08
IGP55	rs955768	5	55374759	T	0.20	0.90	0.225	0.040	2.02E-08
IGP57	rs17348299	5	55358652	C	0.84	0.85	0.287	0.045	1.32E-10
IGP57	rs16884711	5	55360559	C	0.19	0.91	-0.237	0.041	5.05E-09
IGP57	rs10454831	5	55374548	T	0.80	0.90	0.223	0.040	2.73E-08
IGP57	rs955768	5	55374759	T	0.20	0.90	-0.223	0.040	2.73E-08
IGP57	rs3818593	9	33110706	G	0.20	1.00	-0.209	0.039	7.16E-08
IGP57	rs10971418	9	33112024	C	0.80	0.98	0.209	0.039	7.96E-08
IGP57	rs12342831	9	33114872	C	0.26	0.97	-0.210	0.035	3.03E-09
IGP57	rs10813951	9	33118021	G	0.26	0.97	-0.210	0.035	3.07E-09
IGP57	rs2067749	9	33120640	G	0.11	0.98	0.276	0.050	3.56E-08
IGP57	rs10511909	9	33122518	C	0.11	0.98	0.275	0.050	3.64E-08
IGP57	rs3780486	9	33129453	C	0.74	0.97	0.210	0.036	3.26E-09
IGP57	rs10813957	9	33143527	G	0.74	0.96	0.213	0.036	2.99E-09
IGP57	rs10971438	9	33170308	G	0.30	0.75	-0.218	0.039	1.85E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP57	rs10813960	9	33170362	C	0.70	0.74	0.218	0.039	1.81E-08
IGP57	rs10971439	9	33170813	C	0.23	0.71	-0.234	0.043	6.36E-08
IGP58	rs7782210	7	50319291	G	0.38	0.98	0.171	0.032	6.91E-08
IGP58	rs6583437	7	50320813	G	0.64	0.98	-0.177	0.032	2.50E-08
IGP58	rs7789913	7	50323241	C	0.62	1.00	-0.169	0.031	7.96E-08
IGP58	rs6421315	7	50325753	C	0.37	0.95	0.178	0.032	3.16E-08
IGP58	rs7159888	14	64828395	G	0.55	0.99	0.246	0.031	2.31E-15
IGP58	rs12431963	14	64829447	C	0.92	0.92	0.357	0.058	7.41E-10
IGP58	rs1256540	14	64833822	C	0.43	1.00	-0.213	0.031	8.16E-12
IGP58	rs4902383	14	64834326	C	0.19	0.94	-0.290	0.040	2.37E-13
IGP58	rs1269068	14	64837086	C	0.57	1.00	0.212	0.031	9.53E-12
IGP58	rs10135194	14	64840731	C	0.94	0.84	0.390	0.070	2.15E-08
IGP58	rs1760978	14	64840800	G	0.43	0.98	-0.250	0.031	1.16E-15
IGP58	rs10144975	14	64843735	C	0.80	0.98	0.293	0.038	1.27E-14
IGP58	rs17102587	14	64844230	C	0.20	0.97	-0.301	0.038	3.74E-15
IGP58	rs8017974	14	64844940	C	0.20	0.99	-0.302	0.038	2.15E-15
IGP58	rs11847263	14	64845448	G	0.39	0.98	-0.285	0.032	2.36E-19
IGP58	rs10132229	14	64847313	G	0.10	1.00	-0.342	0.050	1.16E-11
IGP58	rs4902386	14	64848043	C	0.80	0.99	0.302	0.038	2.03E-15
IGP58	rs10147958	14	64848586	C	0.10	1.00	-0.342	0.050	1.13E-11
IGP58	rs8019473	14	64848881	G	0.80	0.99	0.302	0.038	2.01E-15
IGP58	rs10138662	14	64849235	G	0.20	0.99	-0.302	0.038	1.93E-15
IGP58	rs10134589	14	64850987	T	0.20	0.94	-0.316	0.039	1.00E-15
IGP58	rs7151212	14	64851375	C	0.80	0.99	0.302	0.038	1.84E-15
IGP58	rs11158587	14	64852465	G	0.80	0.99	0.302	0.038	1.83E-15
IGP58	rs8019767	14	64852538	G	0.80	1.00	0.302	0.038	1.83E-15
IGP58	rs6573598	14	64852772	C	0.20	1.00	-0.302	0.038	1.81E-15
IGP58	rs6573599	14	64852880	C	0.80	1.00	0.302	0.038	1.74E-15
IGP58	rs10144503	14	64853862	G	0.90	1.00	0.344	0.050	8.93E-12
IGP58	rs6573602	14	64854363	C	0.20	1.00	-0.302	0.038	1.69E-15
IGP58	rs17102598	14	64854613	G	0.80	1.00	0.302	0.038	1.70E-15
IGP58	rs12436299	14	64854947	G	0.90	1.00	0.344	0.050	8.47E-12
IGP58	rs6573604	14	64857694	C	0.20	1.00	-0.302	0.038	1.68E-15
IGP58	rs9635250	14	64869101	T	0.10	1.00	-0.345	0.050	8.19E-12
IGP58	rs12881755	14	64871564	G	0.65	0.96	0.186	0.033	2.23E-08
IGP58	rs747541	14	64875163	C	0.45	0.98	-0.239	0.032	3.91E-14
IGP58	rs1954052	14	64875462	T	0.44	0.99	-0.237	0.031	4.74E-14
IGP58	rs12886005	14	64879000	C	0.45	0.87	-0.248	0.033	1.37E-13
IGP58	rs12886168	14	64879039	C	0.45	0.98	-0.238	0.032	3.84E-14
IGP58	rs11623920	14	64889067	C	0.56	1.00	0.237	0.031	4.66E-14
IGP58	rs11621121	14	64892246	C	0.44	1.00	-0.237	0.031	4.72E-14
IGP58	rs10148907	14	64903125	C	0.69	0.98	0.244	0.034	8.51E-13
IGP58	rs4902393	14	64909267	C	0.56	0.99	0.237	0.032	6.49E-14
IGP58	rs11621604	14	64910527	G	0.56	0.98	0.232	0.032	2.62E-13
IGP58	rs12882269	14	64916897	G	0.56	0.97	0.230	0.032	4.20E-13
IGP58	rs11158591	14	64925515	C	0.44	0.97	-0.229	0.032	5.47E-13
IGP58	rs11158592	14	64929721	G	0.50	0.99	-0.206	0.031	1.85E-11
IGP58	rs11158593	14	64929737	G	0.50	0.99	-0.206	0.031	2.01E-11
IGP58	rs10138570	14	64929791	G	0.50	0.99	0.205	0.031	2.04E-11
IGP58	rs2411822	14	64948148	G	0.47	1.00	0.202	0.031	4.28E-11
IGP58	rs1953416	14	64948560	C	0.53	1.00	-0.202	0.031	4.91E-11
IGP58	rs883081	14	64950374	C	0.53	1.00	-0.202	0.031	4.91E-11
IGP58	rs883082	14	64950693	G	0.47	1.00	0.202	0.031	4.29E-11
IGP58	rs867972	14	64965514	C	0.48	0.97	0.194	0.031	4.50E-10

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP58	rs11851576	14	64970036	C	0.54	0.99	0.166	0.031	9.69E-08
IGP58	rs12879971	14	64971357	G	0.52	0.99	-0.205	0.031	2.55E-11
IGP58	rs12892058	14	64973194	C	0.47	0.99	0.206	0.031	2.26E-11
IGP58	rs12589698	14	64990188	G	0.52	0.98	-0.212	0.031	7.27E-12
IGP58	rs4899179	14	64996501	G	0.49	0.99	0.213	0.031	4.83E-12
IGP58	rs2184603	14	65000423	C	0.49	0.99	0.213	0.031	4.68E-12
IGP58	rs3825640	14	65030957	C	0.51	0.99	-0.213	0.031	4.46E-12
IGP58	rs11627084	14	65048589	G	0.49	1.00	0.213	0.031	4.00E-12
IGP58	rs10483780	14	65049923	C	0.50	0.99	0.205	0.031	2.39E-11
IGP58	rs2149841	14	65080072	C	0.51	0.99	-0.212	0.031	5.16E-12
IGP58	rs11621680	14	65084434	G	0.50	0.99	0.204	0.031	3.44E-11
IGP58	rs11158601	14	65095116	G	0.49	1.00	0.210	0.031	7.46E-12
IGP58	rs7146742	14	65102687	G	0.43	0.99	-0.172	0.032	5.03E-08
IGP58	rs1958561	14	65106514	G	0.49	1.00	0.210	0.031	7.17E-12
IGP58	rs12887134	14	65115296	C	0.49	0.99	0.210	0.031	8.02E-12
IGP58	rs7155541	14	65115995	C	0.49	0.99	0.210	0.031	8.00E-12
IGP58	rs7161123	14	65122654	G	0.51	1.00	-0.212	0.031	4.55E-12
IGP58	rs4581615	14	65125696	C	0.51	1.00	-0.212	0.031	4.55E-12
IGP58	rs3783709	14	65128417	T	0.51	1.00	-0.212	0.031	4.55E-12
IGP58	rs12889002	14	65133335	C	0.51	1.00	-0.212	0.031	4.55E-12
IGP58	rs743085	14	65137886	G	0.49	1.00	0.212	0.031	4.55E-12
IGP58	rs8012278	14	65152326	G	0.49	1.00	0.215	0.031	2.39E-12
IGP58	rs12890902	14	65186375	T	0.51	1.00	-0.215	0.031	2.27E-12
IGP58	rs2300865	14	65189768	C	0.49	1.00	0.215	0.031	2.28E-12
IGP58	rs11627184	14	65191196	C	0.51	1.00	-0.215	0.031	2.26E-12
IGP58	rs11627185	14	65191245	G	0.49	1.00	0.215	0.031	2.24E-12
IGP58	rs7142651	14	65202474	C	0.51	1.00	-0.214	0.031	3.00E-12
IGP58	rs1998036	14	65207952	C	0.49	0.99	0.214	0.031	3.06E-12
IGP58	rs2268961	14	65216518	C	0.49	0.99	0.214	0.031	3.01E-12
IGP58	rs2268962	14	65217026	G	0.49	1.00	0.214	0.031	3.00E-12
IGP58	rs2064694	14	65217999	G	0.51	1.00	-0.210	0.031	6.66E-12
IGP58	rs12588838	14	65232391	G	0.51	1.00	-0.210	0.031	6.79E-12
IGP58	rs11628765	14	65238202	C	0.49	1.00	0.210	0.031	6.85E-12
IGP58	rs2411351	14	65241294	C	0.49	1.00	0.210	0.031	7.10E-12
IGP58	rs8018278	14	65249841	G	0.49	1.00	0.210	0.031	7.25E-12
IGP58	rs11627067	14	65252706	G	0.49	1.00	0.210	0.031	7.38E-12
IGP58	rs4143898	14	65258635	T	0.44	0.99	-0.179	0.031	1.00E-08
IGP58	rs11622829	14	65261535	T	0.50	1.00	-0.205	0.031	2.17E-11
IGP58	rs11624104	14	65265890	G	0.50	1.00	0.206	0.031	2.10E-11
IGP58	rs1535173	14	65268892	C	0.50	1.00	-0.205	0.031	2.52E-11
IGP58	rs3742597	14	65269930	G	0.29	1.00	-0.244	0.034	1.34E-12
IGP58	rs927004	14	65270664	C	0.50	1.00	0.204	0.031	2.88E-11
IGP58	rs1950557	14	65271510	C	0.71	1.00	0.244	0.034	1.39E-12
IGP58	rs8010876	14	65276729	G	0.50	1.00	0.204	0.031	2.91E-11
IGP58	rs1054218	14	65278943	C	0.40	1.00	-0.184	0.032	5.55E-09
IGP58	rs761830	14	65282739	G	0.40	1.00	-0.184	0.032	5.58E-09
IGP58	rs10483785	14	65289270	G	0.50	1.00	-0.201	0.031	4.83E-11
IGP58	rs6573624	14	65296638	G	0.50	0.98	-0.203	0.031	5.48E-11
IGP58	rs2411405	14	65301839	G	0.52	0.97	0.208	0.031	1.93E-11
IGP58	rs743084	14	65302355	C	0.52	0.97	0.210	0.031	1.70E-11
IGP58	rs11625362	14	65302622	G	0.48	0.97	-0.208	0.031	2.01E-11
IGP58	rs4080329	14	65303243	C	0.62	0.97	0.192	0.032	2.66E-09
IGP58	rs11627605	14	65304066	G	0.48	0.97	-0.208	0.031	2.08E-11
IGP58	rs11627578	14	65304201	C	0.48	0.97	-0.208	0.031	2.09E-11

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP58	rs11628840	14	65305395	G	0.52	0.97	0.208	0.031	2.10E-11
IGP58	rs1003401	14	65307473	G	0.39	0.97	-0.197	0.032	6.42E-10
IGP58	rs4902416	14	65307843	C	0.52	0.97	0.208	0.031	2.16E-11
IGP58	rs1984855	14	65309010	C	0.61	0.97	0.197	0.032	6.49E-10
IGP58	rs730807	14	65309043	C	0.48	0.97	-0.208	0.031	2.20E-11
IGP58	rs2411404	14	65309154	C	0.48	0.97	-0.208	0.031	2.22E-11
IGP58	rs1075566	14	65309210	C	0.48	0.97	-0.208	0.031	2.23E-11
IGP58	rs7157449	14	65309890	G	0.52	0.97	0.208	0.031	2.29E-11
IGP58	rs6573625	14	65310387	C	0.62	0.97	0.191	0.032	3.24E-09
IGP58	rs6573626	14	65310448	C	0.52	0.97	0.207	0.031	2.59E-11
IGP58	rs7158556	14	65310482	T	0.38	0.97	-0.191	0.032	3.28E-09
IGP58	rs12894466	14	65310520	G	0.48	0.97	-0.207	0.031	2.63E-11
IGP58	rs11625882	14	65314952	G	0.48	0.97	-0.207	0.031	2.90E-11
IGP58	rs2236067	14	65317765	G	0.61	0.97	0.197	0.032	8.30E-10
IGP58	rs968540	14	65318817	G	0.62	0.96	0.190	0.032	3.74E-09
IGP58	rs7142165	14	65319985	G	0.52	0.96	0.207	0.031	3.22E-11
IGP58	rs7143026	14	65320709	G	0.40	0.95	-0.180	0.032	2.39E-08
IGP58	rs6573627	14	65322079	C	0.51	0.98	0.196	0.031	3.39E-10
IGP58	rs7151846	14	65325534	C	0.51	0.99	0.192	0.031	5.51E-10
IGP58	rs4073415	14	65329283	G	0.51	0.99	0.192	0.031	5.45E-10
IGP58	rs8018379	14	65331690	C	0.56	0.95	0.196	0.032	7.68E-10
IGP58	rs8006608	14	65336577	G	0.96	0.81	0.481	0.086	2.27E-08
IGP58	rs3924222	14	65343491	C	0.41	0.80	0.193	0.035	2.41E-08
IGP58	rs10149325	14	65347120	G	0.41	0.80	0.194	0.035	2.02E-08
IGP59	rs2859113	6	32805763	C	0.38	0.91	-0.182	0.033	5.64E-08
IGP59	rs7751856	6	32806966	C	0.38	0.90	-0.181	0.033	6.24E-08
IGP59	rs9276197	6	32807565	C	0.62	0.89	0.181	0.033	6.50E-08
IGP59	rs9276234	6	32808826	T	0.62	0.90	0.181	0.033	6.53E-08
IGP59	rs2859071	6	32811344	C	0.62	0.92	0.180	0.033	6.68E-08
IGP59	rs9276311	6	32812637	C	0.62	0.94	0.180	0.033	6.89E-08
IGP59	rs7773149	6	32814020	G	0.62	0.94	0.179	0.033	7.40E-08
IGP59	rs1049110	6	32834781	C	0.35	0.98	-0.182	0.034	7.97E-08
IGP59	rs7782210	7	50319291	G	0.38	0.98	0.192	0.032	1.57E-09
IGP59	rs6583437	7	50320813	G	0.64	0.98	-0.195	0.032	1.05E-09
IGP59	rs7789913	7	50323241	C	0.62	1.00	-0.190	0.032	1.80E-09
IGP59	rs6421315	7	50325753	C	0.37	0.95	0.197	0.032	1.15E-09
IGP59	rs1256519	14	64806077	G	0.44	0.89	0.190	0.032	4.86E-09
IGP59	rs7159888	14	64828395	G	0.55	0.99	0.270	0.031	5.34E-18
IGP59	rs12431963	14	64829447	C	0.92	0.92	0.425	0.059	4.16E-13
IGP59	rs1256540	14	64833822	C	0.43	1.00	-0.258	0.031	1.50E-16
IGP59	rs4902383	14	64834326	C	0.19	0.94	-0.301	0.040	3.81E-14
IGP59	rs1269068	14	64837086	C	0.57	1.00	0.258	0.031	1.60E-16
IGP59	rs10135194	14	64840731	C	0.94	0.84	0.423	0.071	2.21E-09
IGP59	rs1760978	14	64840800	G	0.43	0.98	-0.291	0.031	1.58E-20
IGP59	rs10144975	14	64843735	C	0.80	0.98	0.309	0.038	5.13E-16
IGP59	rs17102587	14	64844230	C	0.20	0.97	-0.315	0.038	2.39E-16
IGP59	rs8017974	14	64844940	C	0.20	0.99	-0.314	0.038	2.23E-16
IGP59	rs11847263	14	64845448	G	0.39	0.98	-0.312	0.032	1.08E-22
IGP59	rs10132229	14	64847313	G	0.10	1.00	-0.387	0.051	2.91E-14
IGP59	rs4902386	14	64848043	C	0.80	0.99	0.313	0.038	2.35E-16
IGP59	rs10147958	14	64848586	C	0.10	1.00	-0.387	0.051	2.91E-14
IGP59	rs8019473	14	64848881	G	0.80	0.99	0.313	0.038	2.35E-16
IGP59	rs10138662	14	64849235	G	0.20	0.99	-0.312	0.038	2.35E-16
IGP59	rs10134589	14	64850987	T	0.19	0.94	-0.336	0.039	1.71E-17

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP59	rs7151212	14	64851375	C	0.80	0.99	0.312	0.038	2.36E-16
IGP59	rs11158587	14	64852465	G	0.80	0.99	0.312	0.038	2.36E-16
IGP59	rs8019767	14	64852538	G	0.80	1.00	0.312	0.038	2.36E-16
IGP59	rs6573598	14	64852772	C	0.20	1.00	-0.312	0.038	2.36E-16
IGP59	rs6573599	14	64852880	C	0.80	1.00	0.312	0.038	2.38E-16
IGP59	rs10144503	14	64853862	G	0.90	1.00	0.387	0.051	2.94E-14
IGP59	rs6573602	14	64854363	C	0.20	1.00	-0.312	0.038	2.40E-16
IGP59	rs17102598	14	64854613	G	0.80	1.00	0.312	0.038	2.41E-16
IGP59	rs12436299	14	64854947	G	0.90	1.00	0.387	0.051	2.97E-14
IGP59	rs6573604	14	64857694	C	0.20	1.00	-0.312	0.038	2.41E-16
IGP59	rs9635250	14	64869101	T	0.10	1.00	-0.387	0.051	2.91E-14
IGP59	rs12881755	14	64871564	G	0.65	0.96	0.236	0.033	1.55E-12
IGP59	rs747541	14	64875163	C	0.45	0.98	-0.286	0.032	1.90E-19
IGP59	rs1954052	14	64875462	T	0.44	0.99	-0.285	0.032	2.16E-19
IGP59	rs12436465	14	64876630	C	0.72	0.98	0.194	0.035	3.70E-08
IGP59	rs12886005	14	64879000	C	0.45	0.87	-0.291	0.034	5.32E-18
IGP59	rs12886168	14	64879039	C	0.45	0.98	-0.286	0.032	1.87E-19
IGP59	rs11623920	14	64889067	C	0.56	1.00	0.285	0.032	2.12E-19
IGP59	rs11621121	14	64892246	C	0.44	1.00	-0.284	0.032	2.19E-19
IGP59	rs10148907	14	64903125	C	0.69	0.98	0.286	0.034	8.00E-17
IGP59	rs4902393	14	64909267	C	0.56	0.99	0.285	0.032	2.32E-19
IGP59	rs11621604	14	64910527	G	0.56	0.98	0.283	0.032	7.13E-19
IGP59	rs12882269	14	64916897	G	0.56	0.97	0.281	0.032	1.27E-18
IGP59	rs11158591	14	64925515	C	0.44	0.97	-0.280	0.032	1.59E-18
IGP59	rs11158592	14	64929721	G	0.50	0.99	-0.244	0.031	2.23E-15
IGP59	rs11158593	14	64929737	G	0.50	0.99	-0.247	0.031	1.08E-15
IGP59	rs10138570	14	64929791	G	0.50	0.99	0.247	0.031	1.08E-15
IGP59	rs17246007	14	64935424	C	0.08	0.99	-0.318	0.059	8.18E-08
IGP59	rs11844747	14	64939881	C	0.08	0.99	-0.318	0.059	8.05E-08
IGP59	rs17246035	14	64943883	G	0.08	1.00	-0.319	0.059	7.15E-08
IGP59	rs2411822	14	64948148	G	0.47	1.00	0.232	0.031	4.82E-14
IGP59	rs1953416	14	64948560	C	0.53	1.00	-0.235	0.031	2.49E-14
IGP59	rs1953417	14	64948662	C	0.92	1.00	0.319	0.059	6.98E-08
IGP59	rs883081	14	64950374	C	0.53	1.00	-0.235	0.031	2.57E-14
IGP59	rs883082	14	64950693	G	0.47	1.00	0.232	0.031	5.02E-14
IGP59	rs7145574	14	64954155	C	0.92	1.00	0.319	0.059	6.91E-08
IGP59	rs867972	14	64965514	C	0.48	0.97	0.232	0.031	1.07E-13
IGP59	rs11851576	14	64970036	C	0.54	0.99	0.194	0.031	5.35E-10
IGP59	rs12879971	14	64971357	G	0.52	0.99	-0.235	0.031	2.93E-14
IGP59	rs12892058	14	64973194	C	0.47	0.99	0.239	0.031	1.29E-14
IGP59	rs10483776	14	64984620	G	0.22	1.00	-0.224	0.038	4.98E-09
IGP59	rs17826580	14	64985015	C	0.08	1.00	-0.320	0.059	6.35E-08
IGP59	rs2184602	14	64985425	G	0.08	1.00	-0.320	0.059	6.35E-08
IGP59	rs2152375	14	64985531	C	0.08	1.00	-0.320	0.059	6.35E-08
IGP59	rs12589698	14	64990188	G	0.52	0.98	-0.246	0.031	2.33E-15
IGP59	rs4899179	14	64996501	G	0.49	0.99	0.244	0.031	3.68E-15
IGP59	rs2184603	14	65000423	C	0.49	0.99	0.244	0.031	3.54E-15
IGP59	rs11850847	14	65003551	C	0.92	1.00	0.321	0.059	6.25E-08
IGP59	rs12434585	14	65008121	G	0.08	1.00	-0.321	0.059	6.25E-08
IGP59	rs3825640	14	65030957	C	0.51	0.99	-0.246	0.031	1.51E-15
IGP59	rs11627084	14	65048589	G	0.49	1.00	0.244	0.031	2.85E-15
IGP59	rs10483780	14	65049923	C	0.50	0.99	0.240	0.031	8.49E-15
IGP59	rs2149841	14	65080072	C	0.51	0.99	-0.247	0.031	1.40E-15
IGP59	rs7153679	14	65082707	G	0.08	0.99	-0.321	0.059	5.92E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP59	rs11621680	14	65084434	G	0.50	0.99	0.240	0.031	7.18E-15
IGP59	rs11851013	14	65085965	G	0.08	0.99	-0.321	0.059	5.92E-08
IGP59	rs11623662	14	65090945	G	0.59	0.99	0.175	0.031	2.53E-08
IGP59	rs11851772	14	65091800	C	0.92	0.99	0.321	0.059	5.91E-08
IGP59	rs9972106	14	65092884	T	0.59	0.99	0.176	0.031	2.50E-08
IGP59	rs11158601	14	65095116	G	0.49	1.00	0.244	0.031	2.30E-15
IGP59	rs7146742	14	65102687	G	0.43	0.99	-0.209	0.032	4.29E-11
IGP59	rs1958561	14	65106514	G	0.49	1.00	0.244	0.031	2.43E-15
IGP59	rs12887134	14	65115296	C	0.49	0.99	0.247	0.031	1.31E-15
IGP59	rs7155541	14	65115995	C	0.49	0.99	0.247	0.031	1.32E-15
IGP59	rs6573615	14	65116287	G	0.41	0.99	-0.176	0.031	2.47E-08
IGP59	rs7160780	14	65122466	G	0.41	0.99	-0.177	0.031	1.99E-08
IGP59	rs7161123	14	65122654	G	0.51	1.00	-0.244	0.031	2.45E-15
IGP59	rs2411356	14	65122914	G	0.41	0.99	-0.177	0.031	2.00E-08
IGP59	rs12433827	14	65125363	G	0.92	1.00	0.322	0.059	5.66E-08
IGP59	rs4581615	14	65125696	C	0.51	1.00	-0.244	0.031	2.45E-15
IGP59	rs8005309	14	65126261	T	0.92	1.00	0.322	0.059	5.66E-08
IGP59	rs17753508	14	65127205	G	0.22	1.00	-0.228	0.038	3.05E-09
IGP59	rs3783709	14	65128417	T	0.51	1.00	-0.244	0.031	2.46E-15
IGP59	rs12889002	14	65133335	C	0.51	1.00	-0.244	0.031	2.46E-15
IGP59	rs743085	14	65137886	G	0.49	1.00	0.244	0.031	2.46E-15
IGP59	rs17826724	14	65138073	C	0.08	1.00	-0.322	0.059	5.69E-08
IGP59	rs11849252	14	65139522	G	0.92	1.00	0.322	0.059	5.70E-08
IGP59	rs17826736	14	65151955	C	0.08	1.00	-0.322	0.059	5.69E-08
IGP59	rs2073294	14	65152246	C	0.92	1.00	0.322	0.059	5.69E-08
IGP59	rs8012278	14	65152326	G	0.49	1.00	0.248	0.031	8.28E-16
IGP59	rs11849862	14	65167778	G	0.08	1.00	-0.322	0.059	5.71E-08
IGP59	rs2268957	14	65182986	C	0.92	1.00	0.322	0.059	5.76E-08
IGP59	rs12890902	14	65186375	T	0.51	1.00	-0.249	0.031	6.17E-16
IGP59	rs2300865	14	65189768	C	0.49	1.00	0.249	0.031	6.06E-16
IGP59	rs11627184	14	65191196	C	0.51	1.00	-0.249	0.031	5.66E-16
IGP59	rs12435908	14	65191221	C	0.92	1.00	0.322	0.059	5.74E-08
IGP59	rs11627185	14	65191245	G	0.49	1.00	0.249	0.031	5.40E-16
IGP59	rs1998035	14	65195983	G	0.08	1.00	-0.322	0.059	5.72E-08
IGP59	rs2268958	14	65197991	T	0.08	1.00	-0.322	0.059	5.71E-08
IGP59	rs7142651	14	65202474	C	0.51	1.00	-0.250	0.031	4.77E-16
IGP59	rs1998036	14	65207952	C	0.49	0.99	0.250	0.031	4.54E-16
IGP59	rs2268959	14	65215071	C	0.78	1.00	0.233	0.038	1.16E-09
IGP59	rs2268960	14	65215253	G	0.07	0.97	-0.341	0.061	2.10E-08
IGP59	rs2268961	14	65216518	C	0.49	0.99	0.251	0.031	3.65E-16
IGP59	rs2268962	14	65217026	G	0.49	1.00	0.251	0.031	3.56E-16
IGP59	rs2300871	14	65217447	C	0.08	1.00	-0.322	0.059	5.62E-08
IGP59	rs2300872	14	65217514	G	0.08	1.00	-0.321	0.059	6.53E-08
IGP59	rs2064694	14	65217999	G	0.51	1.00	-0.250	0.031	4.18E-16
IGP59	rs12588838	14	65232391	G	0.51	1.00	-0.250	0.031	4.00E-16
IGP59	rs8019491	14	65237863	G	0.08	1.00	-0.321	0.060	6.58E-08
IGP59	rs11628765	14	65238202	C	0.49	1.00	0.251	0.031	3.74E-16
IGP59	rs2411351	14	65241294	C	0.49	1.00	0.251	0.031	3.61E-16
IGP59	rs11846546	14	65246146	G	0.14	0.99	-0.274	0.044	7.59E-10
IGP59	rs8018278	14	65249841	G	0.49	1.00	0.251	0.031	3.60E-16
IGP59	rs11627067	14	65252706	G	0.49	1.00	0.251	0.031	3.59E-16
IGP59	rs4143898	14	65258635	T	0.44	0.99	-0.214	0.031	1.02E-11
IGP59	rs11622829	14	65261535	T	0.50	1.00	-0.249	0.031	6.13E-16
IGP59	rs11624104	14	65265890	G	0.50	1.00	0.248	0.031	9.61E-16

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP59	rs1535173	14	65268892	C	0.50	1.00	-0.247	0.031	1.01E-15
IGP59	rs3742597	14	65269930	G	0.29	1.00	-0.290	0.035	6.05E-17
IGP59	rs927004	14	65270664	C	0.50	1.00	0.247	0.031	1.16E-15
IGP59	rs1950557	14	65271510	C	0.71	1.00	0.290	0.035	6.37E-17
IGP59	rs8010876	14	65276729	G	0.50	1.00	0.247	0.031	1.17E-15
IGP59	rs1054218	14	65278943	C	0.40	1.00	-0.224	0.032	1.75E-12
IGP59	rs761830	14	65282739	G	0.40	1.00	-0.224	0.032	1.76E-12
IGP59	rs10483785	14	65289270	G	0.50	1.00	-0.244	0.031	2.16E-15
IGP59	rs6573624	14	65296638	G	0.50	0.98	-0.246	0.031	2.57E-15
IGP59	rs2411405	14	65301839	G	0.52	0.97	0.249	0.031	1.25E-15
IGP59	rs743084	14	65302355	C	0.52	0.97	0.250	0.031	1.46E-15
IGP59	rs11625362	14	65302622	G	0.48	0.97	-0.249	0.031	1.30E-15
IGP59	rs4080329	14	65303243	C	0.62	0.97	0.231	0.032	1.04E-12
IGP59	rs11627605	14	65304066	G	0.48	0.97	-0.249	0.031	1.34E-15
IGP59	rs11627578	14	65304201	C	0.48	0.97	-0.249	0.031	1.34E-15
IGP59	rs11628840	14	65305395	G	0.52	0.97	0.249	0.031	1.35E-15
IGP59	rs1003401	14	65307473	G	0.39	0.97	-0.232	0.032	4.76E-13
IGP59	rs4902416	14	65307843	C	0.52	0.97	0.249	0.031	1.39E-15
IGP59	rs1984855	14	65309010	C	0.61	0.97	0.232	0.032	4.81E-13
IGP59	rs730807	14	65309043	C	0.48	0.97	-0.249	0.031	1.42E-15
IGP59	rs2411404	14	65309154	C	0.48	0.97	-0.249	0.031	1.43E-15
IGP59	rs1075566	14	65309210	C	0.48	0.97	-0.249	0.031	1.44E-15
IGP59	rs7157449	14	65309890	G	0.52	0.97	0.249	0.031	1.48E-15
IGP59	rs6573625	14	65310387	C	0.62	0.97	0.230	0.032	1.26E-12
IGP59	rs6573626	14	65310448	C	0.52	0.97	0.249	0.031	1.72E-15
IGP59	rs7158556	14	65310482	T	0.38	0.97	-0.230	0.032	1.28E-12
IGP59	rs12894466	14	65310520	G	0.48	0.97	-0.249	0.031	1.75E-15
IGP59	rs11625882	14	65314952	G	0.48	0.97	-0.248	0.031	1.98E-15
IGP59	rs2236067	14	65317765	G	0.61	0.97	0.232	0.032	6.34E-13
IGP59	rs968540	14	65318817	G	0.62	0.96	0.229	0.032	1.59E-12
IGP59	rs7142165	14	65319985	G	0.52	0.96	0.248	0.031	2.50E-15
IGP59	rs7143026	14	65320709	G	0.40	0.95	-0.215	0.033	4.11E-11
IGP59	rs6573627	14	65322079	C	0.51	0.98	0.235	0.031	6.44E-14
IGP59	rs4400971	14	65324331	C	0.43	0.99	-0.188	0.031	2.18E-09
IGP59	rs7151846	14	65325534	C	0.51	0.99	0.228	0.031	2.13E-13
IGP59	rs4073416	14	65329147	C	0.43	0.99	-0.188	0.031	2.28E-09
IGP59	rs4073415	14	65329283	G	0.51	0.99	0.228	0.031	2.15E-13
IGP59	rs11850120	14	65330132	C	0.42	0.98	-0.185	0.032	5.60E-09
IGP59	rs8018379	14	65331690	C	0.56	0.95	0.241	0.032	5.74E-14
IGP59	rs8007846	14	65332716	G	0.48	0.98	-0.195	0.031	4.76E-10
IGP59	rs8006608	14	65336577	G	0.96	0.81	0.514	0.086	2.58E-09
IGP59	rs3924222	14	65343491	C	0.41	0.80	0.240	0.035	5.30E-12
IGP59	rs10149325	14	65347120	G	0.41	0.80	0.241	0.035	4.40E-12
IGP60	rs17732497	7	50306619	C	0.70	0.97	-0.178	0.033	9.85E-08
IGP60	rs7805434	7	50311296	C	0.30	0.99	0.177	0.033	9.66E-08
IGP60	rs7781977	7	50316680	C	0.70	1.00	-0.177	0.033	8.93E-08
IGP60	rs7782210	7	50319291	G	0.38	0.98	0.180	0.032	1.31E-08
IGP60	rs6583437	7	50320813	G	0.64	0.98	-0.186	0.032	4.60E-09
IGP60	rs7789913	7	50323241	C	0.62	1.00	-0.178	0.031	1.48E-08
IGP60	rs6421315	7	50325753	C	0.37	0.95	0.185	0.032	8.55E-09
IGP60	rs7159888	14	64828395	G	0.55	0.99	0.208	0.031	1.82E-11
IGP60	rs1256540	14	64833822	C	0.43	1.00	-0.173	0.031	2.69E-08
IGP60	rs4902383	14	64834326	C	0.19	0.94	-0.229	0.040	7.35E-09
IGP60	rs1269068	14	64837086	C	0.57	1.00	0.172	0.031	3.04E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP60	rs1760978	14	64840800	G	0.43	0.98	-0.205	0.031	4.59E-11
IGP60	rs10144975	14	64843735	C	0.80	0.98	0.233	0.038	9.22E-10
IGP60	rs17102587	14	64844230	C	0.20	0.97	-0.242	0.038	2.52E-10
IGP60	rs8017974	14	64844940	C	0.20	0.99	-0.246	0.038	1.11E-10
IGP60	rs11847263	14	64845448	G	0.39	0.98	-0.240	0.032	3.08E-14
IGP60	rs4902386	14	64848043	C	0.80	0.99	0.246	0.038	9.57E-11
IGP60	rs8019473	14	64848881	G	0.80	0.99	0.246	0.038	9.39E-11
IGP60	rs10138662	14	64849235	G	0.20	0.99	-0.246	0.038	8.93E-11
IGP60	rs10134589	14	64850987	T	0.19	0.94	-0.255	0.039	8.13E-11
IGP60	rs7151212	14	64851375	C	0.80	0.99	0.247	0.038	8.36E-11
IGP60	rs11158587	14	64852465	G	0.80	0.99	0.247	0.038	8.26E-11
IGP60	rs8019767	14	64852538	G	0.80	1.00	0.247	0.038	8.23E-11
IGP60	rs6573598	14	64852772	C	0.20	1.00	-0.247	0.038	8.13E-11
IGP60	rs6573599	14	64852880	C	0.80	1.00	0.247	0.038	7.68E-11
IGP60	rs6573602	14	64854363	C	0.20	1.00	-0.247	0.038	7.38E-11
IGP60	rs17102598	14	64854613	G	0.80	1.00	0.247	0.038	7.36E-11
IGP60	rs6573604	14	64857694	C	0.20	1.00	-0.247	0.038	7.25E-11
IGP60	rs747541	14	64875163	C	0.45	0.98	-0.198	0.031	2.74E-10
IGP60	rs1954052	14	64875462	T	0.44	0.99	-0.197	0.031	3.58E-10
IGP60	rs12886005	14	64879000	C	0.45	0.87	-0.209	0.033	3.38E-10
IGP60	rs12886168	14	64879039	C	0.45	0.98	-0.198	0.031	2.72E-10
IGP60	rs11623920	14	64889067	C	0.56	1.00	0.196	0.031	3.55E-10
IGP60	rs11621121	14	64892246	C	0.44	1.00	-0.196	0.031	3.53E-10
IGP60	rs10148907	14	64903125	C	0.69	0.98	0.199	0.034	5.51E-09
IGP60	rs4902393	14	64909267	C	0.56	0.99	0.196	0.031	4.51E-10
IGP60	rs11621604	14	64910527	G	0.56	0.98	0.191	0.032	1.39E-09
IGP60	rs12882269	14	64916897	G	0.56	0.97	0.189	0.032	2.05E-09
IGP60	rs11158591	14	64925515	C	0.44	0.97	-0.188	0.032	2.52E-09
IGP60	rs11158592	14	64929721	G	0.50	0.99	-0.177	0.031	7.21E-09
IGP60	rs11158593	14	64929737	G	0.50	0.99	-0.175	0.031	9.87E-09
IGP60	rs10138570	14	64929791	G	0.50	0.99	0.175	0.031	9.98E-09
IGP60	rs2411822	14	64948148	G	0.47	1.00	0.172	0.031	1.78E-08
IGP60	rs1953416	14	64948560	C	0.53	1.00	-0.170	0.031	2.47E-08
IGP60	rs883081	14	64950374	C	0.53	1.00	-0.170	0.031	2.49E-08
IGP60	rs883082	14	64950693	G	0.47	1.00	0.172	0.031	1.80E-08
IGP60	rs12879971	14	64971357	G	0.52	0.99	-0.175	0.031	1.27E-08
IGP60	rs12892058	14	64973194	C	0.47	0.99	0.174	0.031	1.39E-08
IGP60	rs12589698	14	64990188	G	0.52	0.98	-0.178	0.031	7.65E-09
IGP60	rs4899179	14	64996501	G	0.49	0.99	0.180	0.031	4.37E-09
IGP60	rs2184603	14	65000423	C	0.49	0.99	0.180	0.031	4.31E-09
IGP60	rs3825640	14	65030957	C	0.51	0.99	-0.179	0.031	5.29E-09
IGP60	rs11627084	14	65048589	G	0.49	1.00	0.180	0.031	3.77E-09
IGP60	rs10483780	14	65049923	C	0.50	0.99	0.172	0.031	2.11E-08
IGP60	rs2149841	14	65080072	C	0.51	0.99	-0.179	0.031	5.52E-09
IGP60	rs11621680	14	65084434	G	0.50	0.99	0.171	0.031	2.37E-08
IGP60	rs11158601	14	65095116	G	0.49	1.00	0.179	0.031	4.68E-09
IGP60	rs1958561	14	65106514	G	0.49	1.00	0.179	0.031	4.65E-09
IGP60	rs12887134	14	65115296	C	0.49	0.99	0.178	0.031	6.56E-09
IGP60	rs7155541	14	65115995	C	0.49	0.99	0.178	0.031	6.56E-09
IGP60	rs7161123	14	65122654	G	0.51	1.00	-0.180	0.030	3.91E-09
IGP60	rs4581615	14	65125696	C	0.51	1.00	-0.180	0.030	3.90E-09
IGP60	rs3783709	14	65128417	T	0.51	1.00	-0.180	0.030	3.90E-09
IGP60	rs12889002	14	65133335	C	0.51	1.00	-0.180	0.030	3.89E-09
IGP60	rs743085	14	65137886	G	0.49	1.00	0.180	0.030	3.89E-09

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP60	rs8012278	14	65152326	G	0.49	1.00	0.182	0.031	2.48E-09
IGP60	rs12890902	14	65186375	T	0.51	1.00	-0.182	0.030	2.34E-09
IGP60	rs2300865	14	65189768	C	0.49	1.00	0.182	0.030	2.33E-09
IGP60	rs11627184	14	65191196	C	0.51	1.00	-0.182	0.030	2.30E-09
IGP60	rs11627185	14	65191245	G	0.49	1.00	0.182	0.031	2.28E-09
IGP60	rs7142651	14	65202474	C	0.51	1.00	-0.182	0.031	2.58E-09
IGP60	rs1998036	14	65207952	C	0.49	0.99	0.182	0.031	2.59E-09
IGP60	rs2268961	14	65216518	C	0.49	0.99	0.182	0.031	2.50E-09
IGP60	rs2268962	14	65217026	G	0.49	1.00	0.182	0.031	2.49E-09
IGP60	rs2064694	14	65217999	G	0.51	1.00	-0.180	0.031	3.85E-09
IGP60	rs12588838	14	65232391	G	0.51	1.00	-0.180	0.031	3.88E-09
IGP60	rs11628765	14	65238202	C	0.49	1.00	0.180	0.031	3.88E-09
IGP60	rs2411351	14	65241294	C	0.49	1.00	0.180	0.031	3.95E-09
IGP60	rs8018278	14	65249841	G	0.49	1.00	0.180	0.031	4.03E-09
IGP60	rs11627067	14	65252706	G	0.49	1.00	0.180	0.031	4.10E-09
IGP60	rs11622829	14	65261535	T	0.50	1.00	-0.175	0.031	1.04E-08
IGP60	rs11624104	14	65265890	G	0.50	1.00	0.175	0.031	1.17E-08
IGP60	rs1535173	14	65268892	C	0.50	1.00	-0.174	0.031	1.26E-08
IGP60	rs3742597	14	65269930	G	0.29	1.00	-0.198	0.034	8.83E-09
IGP60	rs927004	14	65270664	C	0.50	1.00	0.173	0.031	1.41E-08
IGP60	rs1950557	14	65271510	C	0.71	1.00	0.197	0.034	9.05E-09
IGP60	rs8010876	14	65276729	G	0.50	1.00	0.173	0.031	1.41E-08
IGP60	rs10483785	14	65289270	G	0.50	1.00	-0.171	0.031	1.97E-08
IGP60	rs6573624	14	65296638	G	0.50	0.98	-0.171	0.031	2.62E-08
IGP60	rs2411405	14	65301839	G	0.52	0.97	0.176	0.031	1.18E-08
IGP60	rs743084	14	65302355	C	0.52	0.97	0.180	0.031	6.29E-09
IGP60	rs11625362	14	65302622	G	0.48	0.97	-0.176	0.031	1.23E-08
IGP60	rs11627605	14	65304066	G	0.48	0.97	-0.176	0.031	1.28E-08
IGP60	rs11627578	14	65304201	C	0.48	0.97	-0.176	0.031	1.29E-08
IGP60	rs11628840	14	65305395	G	0.52	0.97	0.176	0.031	1.30E-08
IGP60	rs4902416	14	65307843	C	0.52	0.97	0.176	0.031	1.33E-08
IGP60	rs730807	14	65309043	C	0.48	0.97	-0.176	0.031	1.36E-08
IGP60	rs2411404	14	65309154	C	0.48	0.97	-0.176	0.031	1.37E-08
IGP60	rs1075566	14	65309210	C	0.48	0.97	-0.176	0.031	1.38E-08
IGP60	rs7157449	14	65309890	G	0.52	0.97	0.176	0.031	1.41E-08
IGP60	rs6573626	14	65310448	C	0.52	0.97	0.175	0.031	1.55E-08
IGP60	rs12894466	14	65310520	G	0.48	0.97	-0.175	0.031	1.57E-08
IGP60	rs11625882	14	65314952	G	0.48	0.97	-0.175	0.031	1.69E-08
IGP60	rs7142165	14	65319985	G	0.52	0.96	0.174	0.031	1.97E-08
IGP60	rs8006608	14	65336577	G	0.96	0.81	0.488	0.086	1.30E-08
IGP61	rs7159888	14	64828395	G	0.55	0.99	0.238	0.031	1.34E-14
IGP61	rs1256540	14	64833822	C	0.43	1.00	-0.196	0.031	2.48E-10
IGP61	rs4902383	14	64834326	C	0.19	0.94	-0.257	0.039	6.84E-11
IGP61	rs1269068	14	64837086	C	0.57	1.00	0.195	0.031	2.92E-10
IGP61	rs1760978	14	64840800	G	0.43	0.98	-0.227	0.031	2.99E-13
IGP61	rs10144975	14	64843735	C	0.80	0.98	0.264	0.038	3.13E-12
IGP61	rs17102587	14	64844230	C	0.20	0.97	-0.274	0.038	6.30E-13
IGP61	rs8017974	14	64844940	C	0.20	0.99	-0.278	0.038	2.36E-13
IGP61	rs11847263	14	64845448	G	0.39	0.98	-0.268	0.032	2.60E-17
IGP61	rs10132229	14	64847313	G	0.10	1.00	-0.299	0.050	3.01E-09
IGP61	rs4902386	14	64848043	C	0.80	0.99	0.279	0.038	1.97E-13
IGP61	rs10147958	14	64848586	C	0.10	1.00	-0.299	0.050	2.90E-09
IGP61	rs8019473	14	64848881	G	0.80	0.99	0.279	0.038	1.93E-13
IGP61	rs10138662	14	64849235	G	0.20	0.99	-0.279	0.038	1.82E-13

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP61	rs10134589	14	64850987	T	0.20	0.94	-0.289	0.039	1.86E-13
IGP61	rs7151212	14	64851375	C	0.80	0.99	0.279	0.038	1.68E-13
IGP61	rs11158587	14	64852465	G	0.80	0.99	0.279	0.038	1.66E-13
IGP61	rs8019767	14	64852538	G	0.80	1.00	0.279	0.038	1.65E-13
IGP61	rs6573598	14	64852772	C	0.20	1.00	-0.279	0.038	1.63E-13
IGP61	rs6573599	14	64852880	C	0.80	1.00	0.280	0.038	1.52E-13
IGP61	rs10144503	14	64853862	G	0.90	1.00	0.301	0.050	2.17E-09
IGP61	rs6573602	14	64854363	C	0.20	1.00	-0.280	0.038	1.45E-13
IGP61	rs17102598	14	64854613	G	0.80	1.00	0.280	0.038	1.45E-13
IGP61	rs12436299	14	64854947	G	0.90	1.00	0.302	0.050	2.04E-09
IGP61	rs6573604	14	64857694	C	0.20	1.00	-0.280	0.038	1.42E-13
IGP61	rs9635250	14	64869101	T	0.10	1.00	-0.302	0.050	1.96E-09
IGP61	rs747541	14	64875163	C	0.45	0.98	-0.221	0.031	2.00E-12
IGP61	rs1954052	14	64875462	T	0.44	0.99	-0.222	0.031	1.71E-12
IGP61	rs12886005	14	64879000	C	0.45	0.87	-0.229	0.033	6.13E-12
IGP61	rs12886168	14	64879039	C	0.45	0.98	-0.221	0.031	1.98E-12
IGP61	rs11623920	14	64889067	C	0.56	1.00	0.221	0.031	1.69E-12
IGP61	rs11621121	14	64892246	C	0.44	1.00	-0.221	0.031	1.68E-12
IGP61	rs10148907	14	64903125	C	0.69	0.98	0.226	0.034	3.28E-11
IGP61	rs4902393	14	64909267	C	0.56	0.99	0.222	0.031	1.59E-12
IGP61	rs11621604	14	64910527	G	0.56	0.98	0.220	0.032	3.17E-12
IGP61	rs12882269	14	64916897	G	0.56	0.97	0.220	0.032	3.94E-12
IGP61	rs11158591	14	64925515	C	0.44	0.97	-0.219	0.032	4.38E-12
IGP61	rs11158592	14	64929721	G	0.50	0.99	-0.210	0.031	6.95E-12
IGP61	rs11158593	14	64929737	G	0.50	0.99	-0.208	0.031	1.13E-11
IGP61	rs10138570	14	64929791	G	0.50	0.99	0.208	0.031	1.15E-11
IGP61	rs2411822	14	64948148	G	0.47	1.00	0.207	0.031	1.24E-11
IGP61	rs1953416	14	64948560	C	0.53	1.00	-0.205	0.031	2.04E-11
IGP61	rs883081	14	64950374	C	0.53	1.00	-0.205	0.031	2.12E-11
IGP61	rs883082	14	64950693	G	0.47	1.00	0.207	0.031	1.30E-11
IGP61	rs867972	14	64965514	C	0.48	0.97	0.200	0.031	1.13E-10
IGP61	rs11851576	14	64970036	C	0.54	0.99	0.167	0.031	6.87E-08
IGP61	rs12879971	14	64971357	G	0.52	0.99	-0.209	0.031	9.38E-12
IGP61	rs12892058	14	64973194	C	0.47	0.99	0.208	0.031	1.29E-11
IGP61	rs12589698	14	64990188	G	0.52	0.98	-0.212	0.031	5.36E-12
IGP61	rs4899179	14	64996501	G	0.49	0.99	0.215	0.031	2.82E-12
IGP61	rs2184603	14	65000423	C	0.49	0.99	0.215	0.031	2.75E-12
IGP61	rs3825640	14	65030957	C	0.51	0.99	-0.212	0.031	4.34E-12
IGP61	rs11627084	14	65048589	G	0.49	1.00	0.214	0.031	2.70E-12
IGP61	rs10483780	14	65049923	C	0.50	0.99	0.204	0.031	2.75E-11
IGP61	rs2149841	14	65080072	C	0.51	0.99	-0.212	0.031	4.47E-12
IGP61	rs11621680	14	65084434	G	0.50	0.99	0.204	0.031	2.93E-11
IGP61	rs11158601	14	65095116	G	0.49	1.00	0.213	0.031	3.23E-12
IGP61	rs7146742	14	65102687	G	0.43	0.99	-0.172	0.031	4.28E-08
IGP61	rs1958561	14	65106514	G	0.49	1.00	0.213	0.031	3.38E-12
IGP61	rs12887134	14	65115296	C	0.49	0.99	0.211	0.031	5.49E-12
IGP61	rs7155541	14	65115995	C	0.49	0.99	0.211	0.031	5.51E-12
IGP61	rs7161123	14	65122654	G	0.51	1.00	-0.212	0.031	3.77E-12
IGP61	rs4581615	14	65125696	C	0.51	1.00	-0.212	0.031	3.77E-12
IGP61	rs3783709	14	65128417	T	0.51	1.00	-0.212	0.031	3.77E-12
IGP61	rs12889002	14	65133335	C	0.51	1.00	-0.212	0.031	3.77E-12
IGP61	rs743085	14	65137886	G	0.49	1.00	0.212	0.031	3.77E-12
IGP61	rs8012278	14	65152326	G	0.49	1.00	0.215	0.031	1.86E-12
IGP61	rs12890902	14	65186375	T	0.51	1.00	-0.215	0.031	1.68E-12

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP61	rs2300865	14	65189768	C	0.49	1.00	0.215	0.031	1.68E-12
IGP61	rs11627184	14	65191196	C	0.51	1.00	-0.216	0.031	1.63E-12
IGP61	rs11627185	14	65191245	G	0.49	1.00	0.216	0.031	1.59E-12
IGP61	rs7142651	14	65202474	C	0.51	1.00	-0.215	0.031	1.78E-12
IGP61	rs1998036	14	65207952	C	0.49	0.99	0.216	0.031	1.76E-12
IGP61	rs2268961	14	65216518	C	0.49	0.99	0.216	0.031	1.59E-12
IGP61	rs2268962	14	65217026	G	0.49	1.00	0.216	0.031	1.57E-12
IGP61	rs2064694	14	65217999	G	0.51	1.00	-0.214	0.031	2.57E-12
IGP61	rs12588838	14	65232391	G	0.51	1.00	-0.214	0.031	2.54E-12
IGP61	rs11628765	14	65238202	C	0.49	1.00	0.214	0.031	2.48E-12
IGP61	rs2411351	14	65241294	C	0.49	1.00	0.214	0.031	2.49E-12
IGP61	rs8018278	14	65249841	G	0.49	1.00	0.214	0.031	2.53E-12
IGP61	rs11627067	14	65252706	G	0.49	1.00	0.214	0.031	2.57E-12
IGP61	rs4143898	14	65258635	T	0.44	0.99	-0.182	0.031	4.84E-09
IGP61	rs11622829	14	65261535	T	0.50	1.00	-0.209	0.031	7.79E-12
IGP61	rs11624104	14	65265890	G	0.50	1.00	0.210	0.031	6.44E-12
IGP61	rs1535173	14	65268892	C	0.50	1.00	-0.209	0.031	7.68E-12
IGP61	rs3742597	14	65269930	G	0.29	1.00	-0.234	0.034	9.82E-12
IGP61	rs927004	14	65270664	C	0.50	1.00	0.209	0.031	8.44E-12
IGP61	rs1950557	14	65271510	C	0.71	1.00	0.234	0.034	9.66E-12
IGP61	rs8010876	14	65276729	G	0.50	1.00	0.209	0.031	8.18E-12
IGP61	rs1054218	14	65278943	C	0.40	1.00	-0.186	0.031	3.75E-09
IGP61	rs761830	14	65282739	G	0.40	1.00	-0.186	0.031	3.74E-09
IGP61	rs10483785	14	65289270	G	0.50	1.00	-0.209	0.031	6.88E-12
IGP61	rs6573624	14	65296638	G	0.50	0.98	-0.213	0.031	4.94E-12
IGP61	rs2411405	14	65301839	G	0.53	0.97	0.213	0.031	6.04E-12
IGP61	rs743084	14	65302355	C	0.52	0.97	0.212	0.031	8.41E-12
IGP61	rs11625362	14	65302622	G	0.47	0.97	-0.213	0.031	6.06E-12
IGP61	rs4080329	14	65303243	C	0.62	0.97	0.192	0.032	2.10E-09
IGP61	rs11627605	14	65304066	G	0.48	0.97	-0.213	0.031	6.11E-12
IGP61	rs11627578	14	65304201	C	0.48	0.97	-0.213	0.031	6.11E-12
IGP61	rs11628840	14	65305395	G	0.52	0.97	0.213	0.031	6.11E-12
IGP61	rs1003401	14	65307473	G	0.39	0.97	-0.201	0.032	2.92E-10
IGP61	rs4902416	14	65307843	C	0.52	0.97	0.213	0.031	6.14E-12
IGP61	rs1984855	14	65309010	C	0.61	0.97	0.201	0.032	2.93E-10
IGP61	rs730807	14	65309043	C	0.48	0.97	-0.213	0.031	6.19E-12
IGP61	rs2411404	14	65309154	C	0.48	0.97	-0.213	0.031	6.22E-12
IGP61	rs1075566	14	65309210	C	0.48	0.97	-0.213	0.031	6.25E-12
IGP61	rs7157449	14	65309890	G	0.52	0.97	0.213	0.031	6.35E-12
IGP61	rs6573625	14	65310387	C	0.62	0.97	0.192	0.032	2.37E-09
IGP61	rs6573626	14	65310448	C	0.52	0.97	0.213	0.031	7.08E-12
IGP61	rs7158556	14	65310482	T	0.38	0.97	-0.192	0.032	2.39E-09
IGP61	rs12894466	14	65310520	G	0.48	0.97	-0.212	0.031	7.17E-12
IGP61	rs11625882	14	65314952	G	0.48	0.97	-0.212	0.031	7.86E-12
IGP61	rs2236067	14	65317765	G	0.61	0.97	0.200	0.032	3.64E-10
IGP61	rs968540	14	65318817	G	0.62	0.96	0.192	0.032	2.55E-09
IGP61	rs7142165	14	65319985	G	0.52	0.96	0.212	0.031	7.97E-12
IGP61	rs7143026	14	65320709	G	0.40	0.95	-0.177	0.032	3.96E-08
IGP61	rs6573627	14	65322079	C	0.51	0.98	0.200	0.031	1.12E-10
IGP61	rs7151846	14	65325534	C	0.51	0.99	0.196	0.031	2.37E-10
IGP61	rs4073415	14	65329283	G	0.51	0.99	0.196	0.031	2.35E-10
IGP61	rs8018379	14	65331690	C	0.56	0.95	0.193	0.032	1.39E-09
IGP61	rs8006608	14	65336577	G	0.96	0.81	0.483	0.086	1.70E-08
IGP61	rs3924222	14	65343491	C	0.41	0.80	0.206	0.035	2.61E-09

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP61	rs10149325	14	65347120	G	0.41	0.80	0.206	0.035	2.25E-09
IGP62	rs4917017	7	50305778	G	0.71	0.92	-0.218	0.035	3.38E-10
IGP62	rs17732497	7	50306619	C	0.70	0.97	-0.212	0.033	2.31E-10
IGP62	rs9886239	7	50307097	C	0.32	0.98	0.207	0.033	3.45E-10
IGP62	rs7805434	7	50311296	C	0.30	0.99	0.210	0.033	2.04E-10
IGP62	rs7781977	7	50316680	C	0.70	1.00	-0.210	0.033	1.92E-10
IGP62	rs7782210	7	50319291	G	0.38	0.98	0.209	0.032	3.24E-11
IGP62	rs6583437	7	50320813	G	0.64	0.98	-0.212	0.032	2.30E-11
IGP62	rs7789913	7	50323241	C	0.62	1.00	-0.206	0.031	4.50E-11
IGP62	rs6421315	7	50325753	C	0.37	0.95	0.220	0.032	8.11E-12
IGP62	rs7802443	7	50328511	C	0.39	0.99	0.170	0.032	7.14E-08
IGP62	rs6583440	7	50332228	G	0.63	0.99	-0.173	0.032	5.75E-08
IGP62	rs17630758	22	22466542	G	0.83	0.99	-0.260	0.041	2.34E-10
IGP62	rs17548631	22	22474125	C	0.17	0.99	0.260	0.041	2.18E-10
IGP62	rs9620326	22	22476629	C	0.83	0.99	-0.260	0.041	2.17E-10
IGP62	rs9624334	22	22496256	C	0.17	0.99	0.282	0.041	8.76E-12
IGP62	rs2186369	22	22500996	G	0.19	0.88	0.295	0.042	1.23E-12
IGP62	rs5757647	22	38104993	C	0.33	1.00	-0.186	0.033	1.31E-08
IGP62	rs4821890	22	38107469	G	0.34	0.99	-0.188	0.033	9.60E-09
IGP62	rs1010169	22	38108113	G	0.67	1.00	0.186	0.033	1.32E-08
IGP62	rs1010170	22	38108273	C	0.67	1.00	0.186	0.033	1.35E-08
IGP62	rs5757650	22	38108365	C	0.67	1.00	0.186	0.033	1.35E-08
IGP62	rs9611169	22	38112973	C	0.33	1.00	-0.185	0.033	1.36E-08
IGP62	rs9611170	22	38114791	C	0.66	0.99	0.185	0.033	1.45E-08
IGP62	rs2413590	22	38120137	C	0.67	1.00	0.183	0.033	2.03E-08
IGP62	rs5750808	22	38120933	G	0.33	1.00	-0.183	0.033	2.06E-08
IGP62	rs5750811	22	38123012	G	0.67	1.00	0.183	0.033	2.11E-08
IGP62	rs5750812	22	38123025	G	0.34	0.99	-0.185	0.033	1.36E-08
IGP62	rs5757655	22	38127124	C	0.66	0.99	0.185	0.033	1.37E-08
IGP62	rs4821893	22	38127725	G	0.33	1.00	-0.184	0.033	1.71E-08
IGP62	rs5750814	22	38127933	C	0.67	1.00	0.183	0.033	1.75E-08
IGP62	rs5757657	22	38128375	G	0.33	1.00	-0.183	0.033	1.82E-08
IGP62	rs5750815	22	38128395	C	0.67	1.00	0.183	0.033	1.84E-08
IGP62	rs4337572	22	38130650	C	0.33	1.00	-0.183	0.033	1.87E-08
IGP62	rs4821894	22	38139766	C	0.67	1.00	0.183	0.033	1.90E-08
IGP62	rs5750816	22	38140325	C	0.33	1.00	-0.183	0.032	1.95E-08
IGP62	rs5757659	22	38142355	G	0.66	1.00	0.182	0.032	1.99E-08
IGP62	rs6001587	22	38148954	C	0.66	1.00	0.182	0.032	1.99E-08
IGP62	rs5750818	22	38150831	G	0.66	1.00	0.182	0.032	1.99E-08
IGP62	rs5757665	22	38151587	G	0.66	1.00	0.182	0.032	1.99E-08
IGP62	rs4821895	22	38152961	G	0.66	1.00	0.182	0.032	1.98E-08
IGP62	rs739141	22	38154396	C	0.36	1.00	-0.189	0.032	4.41E-09
IGP62	rs5750820	22	38155268	G	0.67	0.97	0.199	0.033	1.80E-09
IGP62	rs5750822	22	38156734	G	0.34	1.00	-0.183	0.033	1.89E-08
IGP62	rs7949	22	38157499	G	0.34	0.99	-0.183	0.033	1.81E-08
IGP62	rs5757670	22	38159682	G	0.34	0.99	-0.184	0.033	1.73E-08
IGP62	rs5750825	22	38161224	G	0.71	0.98	0.214	0.034	3.87E-10
IGP62	rs1972280	22	38161932	T	0.29	0.98	-0.215	0.034	3.67E-10
IGP62	rs4821897	22	38165533	G	0.71	0.97	0.215	0.034	3.48E-10
IGP62	rs5750830	22	38170774	C	0.29	0.98	-0.217	0.034	2.28E-10
IGP62	rs8137426	22	38174296	G	0.71	0.98	0.217	0.034	2.33E-10
IGP62	rs5757683	22	38180120	G	0.29	0.98	-0.217	0.034	2.33E-10
IGP62	rs1557541	22	38181916	C	0.29	0.98	-0.217	0.034	2.32E-10
IGP62	rs1557542	22	38182296	C	0.71	0.98	0.216	0.034	2.34E-10

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP62	rs5995735	22	38184367	C	0.29	0.98	-0.216	0.034	2.41E-10
IGP62	rs738289	22	38185829	C	0.29	0.98	-0.216	0.034	2.44E-10
IGP62	rs909674	22	38189115	C	0.30	0.99	-0.215	0.034	1.93E-10
IGP63	rs716719	7	50296263	C	0.71	0.80	-0.198	0.037	7.01E-08
IGP63	rs4917017	7	50305778	G	0.71	0.92	-0.217	0.035	3.52E-10
IGP63	rs17732497	7	50306619	C	0.70	0.97	-0.207	0.033	4.99E-10
IGP63	rs9886239	7	50307097	C	0.32	0.98	0.210	0.033	1.60E-10
IGP63	rs7805434	7	50311296	C	0.30	0.99	0.205	0.033	4.69E-10
IGP63	rs7781977	7	50316680	C	0.70	1.00	-0.205	0.033	4.56E-10
IGP63	rs7782210	7	50319291	G	0.38	0.98	0.230	0.031	3.02E-13
IGP63	rs6583437	7	50320813	G	0.64	0.98	-0.225	0.032	1.12E-12
IGP63	rs7789913	7	50323241	C	0.62	1.00	-0.225	0.031	6.82E-13
IGP63	rs6421315	7	50325753	C	0.37	0.95	0.236	0.032	1.87E-13
IGP63	rs7802443	7	50328511	C	0.39	0.99	0.198	0.032	3.45E-10
IGP63	rs6583440	7	50332228	G	0.63	0.99	-0.193	0.032	1.15E-09
IGP63	rs11847263	14	64845448	G	0.39	0.98	-0.175	0.032	3.34E-08
IGP63	rs300032	16	85238497	G	0.15	0.89	-0.243	0.046	9.11E-08
IGP63	rs9624334	22	22496256	C	0.17	0.99	0.233	0.041	1.61E-08
IGP63	rs2186369	22	22500996	G	0.19	0.88	0.244	0.041	3.68E-09
IGP63	rs5757642	22	38094770	C	0.64	1.00	0.174	0.032	8.65E-08
IGP63	rs7286714	22	38095550	C	0.36	0.97	-0.175	0.033	8.35E-08
IGP63	rs5757644	22	38096386	C	0.36	0.97	-0.175	0.033	8.32E-08
IGP63	rs5750806	22	38096957	G	0.64	0.97	0.175	0.033	8.31E-08
IGP63	rs1569499	22	38099764	C	0.64	0.97	0.176	0.033	7.90E-08
IGP63	rs4821888	22	38100543	G	0.64	0.97	0.176	0.033	7.97E-08
IGP63	rs5757647	22	38104993	C	0.33	1.00	-0.199	0.033	1.02E-09
IGP63	rs4821890	22	38107469	G	0.34	0.99	-0.200	0.033	1.02E-09
IGP63	rs1010169	22	38108113	G	0.67	1.00	0.199	0.033	1.03E-09
IGP63	rs1010170	22	38108273	C	0.67	1.00	0.199	0.033	1.06E-09
IGP63	rs5757650	22	38108365	C	0.67	1.00	0.199	0.033	1.07E-09
IGP63	rs9611169	22	38112973	C	0.33	1.00	-0.199	0.033	1.08E-09
IGP63	rs9611170	22	38114791	C	0.66	0.99	0.198	0.033	1.19E-09
IGP63	rs2413590	22	38120137	C	0.67	1.00	0.198	0.033	1.21E-09
IGP63	rs5750808	22	38120933	G	0.33	1.00	-0.198	0.033	1.21E-09
IGP63	rs5750811	22	38123012	G	0.67	1.00	0.198	0.033	1.20E-09
IGP63	rs5750812	22	38123025	G	0.34	0.99	-0.199	0.033	9.60E-10
IGP63	rs5757655	22	38127124	C	0.66	0.99	0.199	0.033	9.51E-10
IGP63	rs4821893	22	38127725	G	0.33	1.00	-0.199	0.033	8.54E-10
IGP63	rs5750814	22	38127933	C	0.67	1.00	0.199	0.033	8.48E-10
IGP63	rs5757657	22	38128375	G	0.33	1.00	-0.199	0.032	8.49E-10
IGP63	rs5750815	22	38128395	C	0.67	1.00	0.199	0.032	8.45E-10
IGP63	rs4337572	22	38130650	C	0.33	1.00	-0.199	0.032	8.46E-10
IGP63	rs4821894	22	38139766	C	0.67	1.00	0.199	0.032	8.48E-10
IGP63	rs5750816	22	38140325	C	0.33	1.00	-0.199	0.032	8.51E-10
IGP63	rs5757659	22	38142355	G	0.67	1.00	0.199	0.032	8.54E-10
IGP63	rs6001587	22	38148954	C	0.67	1.00	0.199	0.032	8.58E-10
IGP63	rs5750818	22	38150831	G	0.67	1.00	0.199	0.032	8.59E-10
IGP63	rs5757665	22	38151587	G	0.67	1.00	0.199	0.032	8.61E-10
IGP63	rs4821895	22	38152961	G	0.67	1.00	0.199	0.032	8.62E-10
IGP63	rs739141	22	38154396	C	0.36	1.00	-0.207	0.032	1.30E-10
IGP63	rs5750820	22	38155268	G	0.67	0.97	0.218	0.033	3.84E-11
IGP63	rs5750822	22	38156734	G	0.33	1.00	-0.199	0.032	8.39E-10
IGP63	rs7949	22	38157499	G	0.33	0.99	-0.200	0.033	8.15E-10
IGP63	rs5757670	22	38159682	G	0.33	0.99	-0.200	0.033	7.84E-10

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP63	rs5750825	22	38161224	G	0.71	0.98	0.238	0.034	3.35E-12
IGP63	rs1972280	22	38161932	T	0.29	0.98	-0.238	0.034	3.42E-12
IGP63	rs4821897	22	38165533	G	0.71	0.97	0.239	0.034	3.17E-12
IGP63	rs5750830	22	38170774	C	0.29	0.98	-0.236	0.034	4.72E-12
IGP63	rs8137426	22	38174296	G	0.71	0.98	0.236	0.034	4.93E-12
IGP63	rs5757683	22	38180120	G	0.29	0.98	-0.236	0.034	4.95E-12
IGP63	rs1557541	22	38181916	C	0.29	0.98	-0.236	0.034	4.91E-12
IGP63	rs1557542	22	38182296	C	0.71	0.98	0.236	0.034	5.00E-12
IGP63	rs5995735	22	38184367	C	0.29	0.98	-0.235	0.034	5.32E-12
IGP63	rs738289	22	38185829	C	0.29	0.98	-0.235	0.034	5.47E-12
IGP63	rs909674	22	38189115	C	0.30	0.99	-0.231	0.034	6.44E-12
IGP64	rs17630758	22	22466542	G	0.83	0.99	-0.291	0.041	1.48E-12
IGP64	rs12167679	22	22471690	C	0.80	1.00	-0.230	0.039	3.16E-09
IGP64	rs17548631	22	22474125	C	0.17	0.99	0.291	0.041	1.39E-12
IGP64	rs9620326	22	22476629	C	0.83	0.99	-0.291	0.041	1.39E-12
IGP64	rs9624334	22	22496256	C	0.17	0.99	0.309	0.041	7.87E-14
IGP64	rs2186369	22	22500996	G	0.19	0.88	0.318	0.042	2.08E-14
IGP64	rs6519476	22	22512500	G	0.76	0.99	-0.198	0.036	5.06E-08
IGP64	rs1972280	22	38161932	T	0.29	0.98	-0.183	0.034	9.45E-08
IGP64	rs4821897	22	38165533	G	0.71	0.97	0.183	0.034	9.24E-08
IGP64	rs5750830	22	38170774	C	0.29	0.98	-0.188	0.034	4.11E-08
IGP64	rs8137426	22	38174296	G	0.71	0.98	0.188	0.034	4.09E-08
IGP64	rs5757683	22	38180120	G	0.29	0.98	-0.188	0.034	4.09E-08
IGP64	rs1557541	22	38181916	C	0.29	0.98	-0.188	0.034	4.09E-08
IGP64	rs1557542	22	38182296	C	0.71	0.98	0.188	0.034	4.07E-08
IGP64	rs5995735	22	38184367	C	0.29	0.98	-0.188	0.034	4.07E-08
IGP64	rs738289	22	38185829	C	0.29	0.98	-0.188	0.034	4.05E-08
IGP64	rs909674	22	38189115	C	0.30	0.99	-0.187	0.034	3.02E-08
IGP65	rs7159888	14	64828395	G	0.55	0.99	0.186	0.031	1.91E-09
IGP65	rs1760978	14	64840800	G	0.43	0.98	-0.172	0.031	3.26E-08
IGP65	rs17102587	14	64844230	C	0.20	0.97	-0.206	0.038	6.43E-08
IGP65	rs8017974	14	64844940	C	0.20	0.99	-0.212	0.038	2.34E-08
IGP65	rs11847263	14	64845448	G	0.39	0.98	-0.202	0.032	1.47E-10
IGP65	rs4902386	14	64848043	C	0.80	0.99	0.213	0.038	1.87E-08
IGP65	rs8019473	14	64848881	G	0.80	0.99	0.213	0.038	1.83E-08
IGP65	rs10138662	14	64849235	G	0.20	0.99	-0.213	0.038	1.72E-08
IGP65	rs10134589	14	64850987	T	0.20	0.94	-0.219	0.039	2.17E-08
IGP65	rs7151212	14	64851375	C	0.80	0.99	0.214	0.038	1.58E-08
IGP65	rs11158587	14	64852465	G	0.80	0.99	0.214	0.038	1.56E-08
IGP65	rs8019767	14	64852538	G	0.80	1.00	0.214	0.038	1.54E-08
IGP65	rs6573598	14	64852772	C	0.20	1.00	-0.214	0.038	1.52E-08
IGP65	rs6573599	14	64852880	C	0.80	1.00	0.214	0.038	1.42E-08
IGP65	rs6573602	14	64854363	C	0.20	1.00	-0.215	0.038	1.34E-08
IGP65	rs17102598	14	64854613	G	0.80	1.00	0.215	0.038	1.33E-08
IGP65	rs6573604	14	64857694	C	0.20	1.00	-0.215	0.038	1.30E-08
IGP65	rs11158592	14	64929721	G	0.50	0.99	-0.171	0.031	2.36E-08
IGP65	rs11158593	14	64929737	G	0.50	0.99	-0.166	0.031	5.51E-08
IGP65	rs10138570	14	64929791	G	0.50	0.99	0.166	0.031	5.54E-08
IGP65	rs2411822	14	64948148	G	0.47	1.00	0.170	0.031	2.66E-08
IGP65	rs1953416	14	64948560	C	0.53	1.00	-0.165	0.031	6.16E-08
IGP65	rs883081	14	64950374	C	0.53	1.00	-0.165	0.031	6.29E-08
IGP65	rs883082	14	64950693	G	0.47	1.00	0.170	0.031	2.74E-08
IGP65	rs12879971	14	64971357	G	0.52	0.99	-0.171	0.031	2.32E-08
IGP65	rs12892058	14	64973194	C	0.47	0.99	0.168	0.031	4.37E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP65	rs12589698	14	64990188	G	0.52	0.98	-0.168	0.031	4.38E-08
IGP65	rs4899179	14	64996501	G	0.49	0.99	0.173	0.031	1.75E-08
IGP65	rs2184603	14	65000423	C	0.49	0.99	0.173	0.031	1.77E-08
IGP65	rs3825640	14	65030957	C	0.51	0.99	-0.168	0.031	4.06E-08
IGP65	rs11627084	14	65048589	G	0.49	1.00	0.172	0.031	1.82E-08
IGP65	rs2149841	14	65080072	C	0.51	0.99	-0.168	0.031	4.07E-08
IGP65	rs11158601	14	65095116	G	0.49	1.00	0.172	0.031	1.90E-08
IGP65	rs1958561	14	65106514	G	0.49	1.00	0.172	0.031	1.96E-08
IGP65	rs12887134	14	65115296	C	0.49	0.99	0.167	0.031	4.38E-08
IGP65	rs7155541	14	65115995	C	0.49	0.99	0.167	0.031	4.40E-08
IGP65	rs7161123	14	65122654	G	0.51	1.00	-0.170	0.030	2.25E-08
IGP65	rs4581615	14	65125696	C	0.51	1.00	-0.170	0.030	2.25E-08
IGP65	rs3783709	14	65128417	T	0.51	1.00	-0.170	0.030	2.25E-08
IGP65	rs12889002	14	65133335	C	0.51	1.00	-0.170	0.030	2.25E-08
IGP65	rs743085	14	65137886	G	0.49	1.00	0.170	0.030	2.25E-08
IGP65	rs8012278	14	65152326	G	0.49	1.00	0.173	0.031	1.30E-08
IGP65	rs12890902	14	65186375	T	0.51	1.00	-0.174	0.030	1.15E-08
IGP65	rs2300865	14	65189768	C	0.49	1.00	0.174	0.030	1.14E-08
IGP65	rs11627184	14	65191196	C	0.51	1.00	-0.174	0.030	1.11E-08
IGP65	rs11627185	14	65191245	G	0.49	1.00	0.174	0.030	1.08E-08
IGP65	rs7142651	14	65202474	C	0.51	1.00	-0.174	0.031	1.11E-08
IGP65	rs1998036	14	65207952	C	0.49	0.99	0.175	0.031	1.09E-08
IGP65	rs2268961	14	65216518	C	0.49	0.99	0.175	0.031	9.66E-09
IGP65	rs2268962	14	65217026	G	0.49	1.00	0.175	0.031	9.53E-09
IGP65	rs2064694	14	65217999	G	0.51	1.00	-0.174	0.031	1.23E-08
IGP65	rs12588838	14	65232391	G	0.51	1.00	-0.174	0.030	1.21E-08
IGP65	rs11628765	14	65238202	C	0.49	1.00	0.174	0.030	1.16E-08
IGP65	rs2411351	14	65241294	C	0.49	1.00	0.174	0.030	1.14E-08
IGP65	rs8018278	14	65249841	G	0.49	1.00	0.174	0.030	1.13E-08
IGP65	rs11627067	14	65252706	G	0.49	1.00	0.174	0.031	1.12E-08
IGP65	rs11622829	14	65261535	T	0.50	1.00	-0.174	0.031	1.31E-08
IGP65	rs11624104	14	65265890	G	0.50	1.00	0.175	0.031	1.10E-08
IGP65	rs1535173	14	65268892	C	0.50	1.00	-0.174	0.031	1.21E-08
IGP65	rs927004	14	65270664	C	0.50	1.00	0.174	0.031	1.22E-08
IGP65	rs8010876	14	65276729	G	0.50	1.00	0.174	0.031	1.19E-08
IGP65	rs10483785	14	65289270	G	0.50	1.00	-0.175	0.030	8.77E-09
IGP65	rs6573624	14	65296638	G	0.50	0.98	-0.180	0.031	4.98E-09
IGP65	rs2411405	14	65301839	G	0.52	0.97	0.176	0.031	1.30E-08
IGP65	rs743084	14	65302355	C	0.52	0.97	0.178	0.031	9.82E-09
IGP65	rs11625362	14	65302622	G	0.48	0.97	-0.176	0.031	1.26E-08
IGP65	rs11627605	14	65304066	G	0.48	0.97	-0.176	0.031	1.24E-08
IGP65	rs11627578	14	65304201	C	0.48	0.97	-0.176	0.031	1.24E-08
IGP65	rs11628840	14	65305395	G	0.52	0.97	0.176	0.031	1.23E-08
IGP65	rs4902416	14	65307843	C	0.52	0.97	0.176	0.031	1.21E-08
IGP65	rs730807	14	65309043	C	0.48	0.97	-0.176	0.031	1.21E-08
IGP65	rs2411404	14	65309154	C	0.48	0.97	-0.176	0.031	1.20E-08
IGP65	rs1075566	14	65309210	C	0.48	0.97	-0.176	0.031	1.20E-08
IGP65	rs7157449	14	65309890	G	0.52	0.97	0.176	0.031	1.20E-08
IGP65	rs6573626	14	65310448	C	0.52	0.97	0.176	0.031	1.24E-08
IGP65	rs12894466	14	65310520	G	0.48	0.97	-0.176	0.031	1.24E-08
IGP65	rs11625882	14	65314952	G	0.48	0.97	-0.176	0.031	1.28E-08
IGP65	rs7142165	14	65319985	G	0.52	0.96	0.177	0.031	1.19E-08
IGP65	rs6573627	14	65322079	C	0.51	0.98	0.170	0.031	3.95E-08
IGP65	rs7151846	14	65325534	C	0.51	0.99	0.167	0.031	5.70E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP65	rs4073415	14	65329283	G	0.51	0.99	0.168	0.031	5.65E-08
IGP66	rs17630758	22	22466542	G	0.83	0.99	0.319	0.041	1.09E-14
IGP66	rs12167679	22	22471690	C	0.80	1.00	0.246	0.039	2.49E-10
IGP66	rs17548631	22	22474125	C	0.17	0.99	-0.319	0.041	9.55E-15
IGP66	rs9620326	22	22476629	C	0.83	0.99	0.319	0.041	9.55E-15
IGP66	rs9624334	22	22496256	C	0.17	0.99	-0.334	0.041	8.52E-16
IGP66	rs2186369	22	22500996	G	0.19	0.88	-0.347	0.042	8.84E-17
IGP66	rs6519476	22	22512500	G	0.76	0.99	0.208	0.036	1.05E-08
IGP66	rs5757642	22	38094770	C	0.64	1.00	-0.219	0.033	2.14E-11
IGP66	rs7286714	22	38095550	C	0.36	0.97	0.221	0.033	2.09E-11
IGP66	rs5757644	22	38096386	C	0.36	0.97	0.221	0.033	2.06E-11
IGP66	rs5750806	22	38096957	G	0.64	0.97	-0.221	0.033	2.06E-11
IGP66	rs1569499	22	38099764	C	0.64	0.97	-0.222	0.033	1.75E-11
IGP66	rs4821888	22	38100543	G	0.64	0.97	-0.222	0.033	1.78E-11
IGP66	rs5757647	22	38104993	C	0.33	1.00	0.235	0.033	7.80E-13
IGP66	rs4821890	22	38107469	G	0.34	0.99	0.235	0.033	8.10E-13
IGP66	rs1010169	22	38108113	G	0.67	1.00	-0.235	0.033	7.86E-13
IGP66	rs1010170	22	38108273	C	0.67	1.00	-0.235	0.033	8.12E-13
IGP66	rs5757650	22	38108365	C	0.67	1.00	-0.235	0.033	8.17E-13
IGP66	rs9611169	22	38112973	C	0.33	1.00	0.235	0.033	8.29E-13
IGP66	rs9611170	22	38114791	C	0.66	0.99	-0.230	0.033	2.33E-12
IGP66	rs2413590	22	38120137	C	0.67	1.00	-0.230	0.033	2.29E-12
IGP66	rs5750808	22	38120933	G	0.33	1.00	0.230	0.033	2.32E-12
IGP66	rs5750811	22	38123012	G	0.67	1.00	-0.229	0.033	2.36E-12
IGP66	rs5750812	22	38123025	G	0.34	0.99	0.231	0.033	1.67E-12
IGP66	rs5757655	22	38127124	C	0.66	0.99	-0.231	0.033	1.64E-12
IGP66	rs4821893	22	38127725	G	0.33	1.00	0.233	0.033	1.11E-12
IGP66	rs5750814	22	38127933	C	0.67	1.00	-0.233	0.033	1.07E-12
IGP66	rs5757657	22	38128375	G	0.33	1.00	0.233	0.033	1.10E-12
IGP66	rs5750815	22	38128395	C	0.67	1.00	-0.233	0.033	1.07E-12
IGP66	rs4337572	22	38130650	C	0.33	1.00	0.233	0.033	1.07E-12
IGP66	rs4821894	22	38139766	C	0.66	1.00	-0.233	0.033	1.06E-12
IGP66	rs5750816	22	38140325	C	0.34	1.00	0.233	0.033	1.06E-12
IGP66	rs5757659	22	38142355	G	0.66	1.00	-0.232	0.033	1.06E-12
IGP66	rs6001585	22	38142932	C	0.22	1.00	0.213	0.037	8.13E-09
IGP66	rs6001587	22	38148954	C	0.66	1.00	-0.232	0.033	1.07E-12
IGP66	rs5750818	22	38150831	G	0.66	1.00	-0.232	0.033	1.07E-12
IGP66	rs5757665	22	38151587	G	0.66	1.00	-0.232	0.033	1.07E-12
IGP66	rs4821895	22	38152961	G	0.66	1.00	-0.232	0.033	1.07E-12
IGP66	rs739141	22	38154396	C	0.36	1.00	0.236	0.032	2.96E-13
IGP66	rs5750820	22	38155268	G	0.67	0.97	-0.254	0.033	2.17E-14
IGP66	rs5750822	22	38156734	G	0.34	1.00	0.233	0.033	9.75E-13
IGP66	rs7949	22	38157499	G	0.34	0.99	0.234	0.033	8.79E-13
IGP66	rs5757670	22	38159682	G	0.34	0.99	0.234	0.033	8.06E-13
IGP66	rs5750825	22	38161224	G	0.71	0.98	-0.281	0.034	2.85E-16
IGP66	rs1972280	22	38161932	T	0.29	0.98	0.282	0.034	2.35E-16
IGP66	rs4821897	22	38165533	G	0.71	0.97	-0.283	0.034	2.22E-16
IGP66	rs5750830	22	38170774	C	0.29	0.98	0.285	0.034	1.15E-16
IGP66	rs5757676	22	38171646	C	0.78	0.96	-0.227	0.037	1.40E-09
IGP66	rs8137426	22	38174296	G	0.71	0.98	-0.284	0.034	1.15E-16
IGP66	rs5757683	22	38180120	G	0.29	0.98	0.284	0.034	1.16E-16
IGP66	rs1557541	22	38181916	C	0.29	0.98	0.284	0.034	1.16E-16
IGP66	rs1557542	22	38182296	C	0.71	0.98	-0.284	0.034	1.16E-16
IGP66	rs5995735	22	38184367	C	0.29	0.98	0.284	0.034	1.17E-16

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP66	rs738289	22	38185829	C	0.29	0.98	0.284	0.034	1.17E-16
IGP66	rs909674	22	38189115	C	0.30	0.99	0.281	0.034	1.08E-16
IGP67	rs4917017	7	50305778	G	0.71	0.92	0.194	0.035	2.15E-08
IGP67	rs17732497	7	50306619	C	0.70	0.97	0.186	0.033	2.18E-08
IGP67	rs9886239	7	50307097	C	0.32	0.98	-0.189	0.033	8.75E-09
IGP67	rs7805434	7	50311296	C	0.30	0.99	-0.185	0.033	2.10E-08
IGP67	rs7781977	7	50316680	C	0.70	1.00	0.185	0.033	2.03E-08
IGP67	rs7782210	7	50319291	G	0.38	0.98	-0.204	0.032	1.04E-10
IGP67	rs6583437	7	50320813	G	0.64	0.98	0.200	0.032	3.00E-10
IGP67	rs7789913	7	50323241	C	0.62	1.00	0.198	0.031	2.38E-10
IGP67	rs6421315	7	50325753	C	0.37	0.95	-0.210	0.032	7.11E-11
IGP67	rs7802443	7	50328511	C	0.39	0.99	-0.172	0.032	5.21E-08
IGP67	rs17630758	22	22466542	G	0.83	0.99	0.267	0.041	7.14E-11
IGP67	rs17548631	22	22474125	C	0.17	0.99	-0.267	0.041	6.73E-11
IGP67	rs9620326	22	22476629	C	0.83	0.99	0.267	0.041	6.79E-11
IGP67	rs9624334	22	22496256	C	0.17	0.99	-0.283	0.041	7.19E-12
IGP67	rs2186369	22	22500996	G	0.19	0.88	-0.294	0.042	1.45E-12
IGP67	rs5757642	22	38094770	C	0.64	1.00	-0.217	0.032	2.23E-11
IGP67	rs7286714	22	38095550	C	0.36	0.97	0.219	0.033	2.46E-11
IGP67	rs5757644	22	38096386	C	0.36	0.97	0.219	0.033	2.43E-11
IGP67	rs5750806	22	38096957	G	0.64	0.97	-0.219	0.033	2.43E-11
IGP67	rs1569499	22	38099764	C	0.64	0.97	-0.221	0.033	1.71E-11
IGP67	rs4821888	22	38100543	G	0.64	0.97	-0.221	0.033	1.74E-11
IGP67	rs5757647	22	38104993	C	0.33	1.00	0.251	0.033	1.67E-14
IGP67	rs4821890	22	38107469	G	0.34	0.99	0.250	0.033	2.14E-14
IGP67	rs1010169	22	38108113	G	0.67	1.00	-0.251	0.033	1.69E-14
IGP67	rs1010170	22	38108273	C	0.67	1.00	-0.251	0.033	1.76E-14
IGP67	rs5757650	22	38108365	C	0.67	1.00	-0.250	0.033	1.77E-14
IGP67	rs9611169	22	38112973	C	0.33	1.00	0.250	0.033	1.81E-14
IGP67	rs9611170	22	38114791	C	0.66	0.99	-0.246	0.033	4.38E-14
IGP67	rs2413590	22	38120137	C	0.67	1.00	-0.247	0.033	3.45E-14
IGP67	rs5750808	22	38120933	G	0.33	1.00	0.247	0.033	3.43E-14
IGP67	rs5750811	22	38123012	G	0.67	1.00	-0.247	0.033	3.40E-14
IGP67	rs5750812	22	38123025	G	0.34	0.99	0.248	0.033	2.81E-14
IGP67	rs5757655	22	38127124	C	0.66	0.99	-0.248	0.033	2.77E-14
IGP67	rs4821893	22	38127725	G	0.33	1.00	0.250	0.033	1.58E-14
IGP67	rs5750814	22	38127933	C	0.67	1.00	-0.250	0.033	1.55E-14
IGP67	rs5757657	22	38128375	G	0.33	1.00	0.250	0.033	1.56E-14
IGP67	rs5750815	22	38128395	C	0.67	1.00	-0.250	0.033	1.52E-14
IGP67	rs4337572	22	38130650	C	0.33	1.00	0.250	0.033	1.53E-14
IGP67	rs4821894	22	38139766	C	0.66	1.00	-0.250	0.033	1.53E-14
IGP67	rs5750816	22	38140325	C	0.34	1.00	0.250	0.032	1.54E-14
IGP67	rs5757659	22	38142355	G	0.66	1.00	-0.250	0.032	1.54E-14
IGP67	rs6001585	22	38142932	C	0.22	1.00	0.221	0.037	1.60E-09
IGP67	rs6001587	22	38148954	C	0.66	1.00	-0.250	0.032	1.57E-14
IGP67	rs5750818	22	38150831	G	0.66	1.00	-0.250	0.032	1.58E-14
IGP67	rs5757665	22	38151587	G	0.66	1.00	-0.250	0.032	1.58E-14
IGP67	rs4821895	22	38152961	G	0.66	1.00	-0.250	0.032	1.59E-14
IGP67	rs739141	22	38154396	C	0.36	1.00	0.253	0.032	4.19E-15
IGP67	rs5750820	22	38155268	G	0.67	0.97	-0.271	0.033	2.46E-16
IGP67	rs5750822	22	38156734	G	0.34	1.00	0.250	0.033	1.52E-14
IGP67	rs7949	22	38157499	G	0.34	0.99	0.251	0.033	1.42E-14
IGP67	rs5757670	22	38159682	G	0.34	0.99	0.251	0.033	1.33E-14
IGP67	rs5750825	22	38161224	G	0.71	0.98	-0.296	0.034	4.50E-18

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP67	rs1972280	22	38161932	T	0.29	0.98	0.297	0.034	4.28E-18
IGP67	rs4821897	22	38165533	G	0.71	0.97	-0.298	0.034	3.98E-18
IGP67	rs5750830	22	38170774	C	0.29	0.98	0.294	0.034	7.09E-18
IGP67	rs5757676	22	38171646	C	0.78	0.96	-0.229	0.037	8.11E-10
IGP67	rs8137426	22	38174296	G	0.71	0.98	-0.294	0.034	7.49E-18
IGP67	rs5757683	22	38180120	G	0.29	0.98	0.294	0.034	7.60E-18
IGP67	rs1557541	22	38181916	C	0.29	0.98	0.294	0.034	7.54E-18
IGP67	rs1557542	22	38182296	C	0.71	0.98	-0.294	0.034	7.69E-18
IGP67	rs5995735	22	38184367	C	0.29	0.98	0.293	0.034	8.21E-18
IGP67	rs738289	22	38185829	C	0.29	0.98	0.293	0.034	8.47E-18
IGP67	rs909674	22	38189115	C	0.30	0.99	0.289	0.034	1.12E-17
IGP68	rs17630758	22	22466542	G	0.83	0.99	0.300	0.041	3.54E-13
IGP68	rs12167679	22	22471690	C	0.80	1.00	0.236	0.039	1.13E-09
IGP68	rs17548631	22	22474125	C	0.17	0.99	-0.300	0.041	3.22E-13
IGP68	rs9620326	22	22476629	C	0.83	0.99	0.300	0.041	3.23E-13
IGP68	rs9624334	22	22496256	C	0.17	0.99	-0.311	0.041	5.92E-14
IGP68	rs2186369	22	22500996	G	0.19	0.88	-0.324	0.042	8.05E-15
IGP68	rs5750820	22	38155268	G	0.67	0.97	-0.182	0.033	4.34E-08
IGP68	rs5750825	22	38161224	G	0.71	0.98	-0.206	0.034	2.03E-09
IGP68	rs1972280	22	38161932	T	0.29	0.98	0.207	0.034	1.78E-09
IGP68	rs4821897	22	38165533	G	0.71	0.97	-0.207	0.034	1.72E-09
IGP68	rs5750830	22	38170774	C	0.29	0.98	0.210	0.034	8.99E-10
IGP68	rs8137426	22	38174296	G	0.71	0.98	-0.210	0.034	8.83E-10
IGP68	rs5757683	22	38180120	G	0.29	0.98	0.210	0.034	8.82E-10
IGP68	rs1557541	22	38181916	C	0.29	0.98	0.210	0.034	8.82E-10
IGP68	rs1557542	22	38182296	C	0.71	0.98	-0.210	0.034	8.78E-10
IGP68	rs5995735	22	38184367	C	0.29	0.98	0.210	0.034	8.74E-10
IGP68	rs738289	22	38185829	C	0.29	0.98	0.210	0.034	8.67E-10
IGP68	rs909674	22	38189115	C	0.30	0.99	0.209	0.034	6.24E-10
IGP69	rs2072209	7	107379434	G	0.06	0.97	-0.374	0.066	1.16E-08
IGP69	rs12342831	9	33114872	C	0.26	0.97	0.193	0.036	6.90E-08
IGP69	rs10813951	9	33118021	G	0.26	0.97	0.193	0.036	6.83E-08
IGP69	rs3780486	9	33129453	C	0.74	0.97	-0.192	0.036	7.69E-08
IGP69	rs10813957	9	33143527	G	0.74	0.96	-0.193	0.036	8.48E-08
IGP69	rs2186369	22	22500996	G	0.19	0.88	-0.234	0.042	2.37E-08
IGP70	rs4917017	7	50305778	G	0.71	0.92	0.197	0.035	1.40E-08
IGP70	rs17732497	7	50306619	C	0.70	0.97	0.185	0.033	3.47E-08
IGP70	rs9886239	7	50307097	C	0.32	0.98	-0.180	0.033	5.10E-08
IGP70	rs7805434	7	50311296	C	0.30	0.99	-0.183	0.033	3.24E-08
IGP70	rs7781977	7	50316680	C	0.70	1.00	0.183	0.033	3.10E-08
IGP70	rs7782210	7	50319291	G	0.38	0.98	-0.174	0.032	3.59E-08
IGP70	rs6583437	7	50320813	G	0.64	0.98	0.177	0.032	2.72E-08
IGP70	rs7789913	7	50323241	C	0.62	1.00	0.171	0.031	4.83E-08
IGP70	rs6421315	7	50325753	C	0.37	0.95	-0.182	0.032	1.57E-08
IGP70	rs17630758	22	22466542	G	0.83	0.99	0.314	0.041	2.52E-14
IGP70	rs12167679	22	22471690	C	0.80	1.00	0.242	0.039	4.00E-10
IGP70	rs17548631	22	22474125	C	0.17	0.99	-0.314	0.041	2.23E-14
IGP70	rs9620326	22	22476629	C	0.83	0.99	0.314	0.041	2.22E-14
IGP70	rs9624334	22	22496256	C	0.17	0.99	-0.330	0.041	1.50E-15
IGP70	rs2186369	22	22500996	G	0.19	0.88	-0.345	0.042	1.18E-16
IGP70	rs6519476	22	22512500	G	0.76	0.99	0.212	0.036	5.93E-09
IGP70	rs5757642	22	38094770	C	0.64	1.00	-0.212	0.033	7.43E-11
IGP70	rs7286714	22	38095550	C	0.36	0.97	0.214	0.033	6.84E-11
IGP70	rs5757644	22	38096386	C	0.36	0.97	0.215	0.033	6.74E-11

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP70	rs5750806	22	38096957	G	0.64	0.97	-0.215	0.033	6.71E-11
IGP70	rs1569499	22	38099764	C	0.64	0.97	-0.216	0.033	5.75E-11
IGP70	rs4821888	22	38100543	G	0.64	0.97	-0.216	0.033	5.85E-11
IGP70	rs5757647	22	38104993	C	0.33	1.00	0.233	0.033	1.31E-12
IGP70	rs4821890	22	38107469	G	0.34	0.99	0.233	0.033	1.32E-12
IGP70	rs1010169	22	38108113	G	0.67	1.00	-0.232	0.033	1.32E-12
IGP70	rs1010170	22	38108273	C	0.67	1.00	-0.232	0.033	1.36E-12
IGP70	rs5757650	22	38108365	C	0.67	1.00	-0.232	0.033	1.36E-12
IGP70	rs9611169	22	38112973	C	0.33	1.00	0.232	0.033	1.38E-12
IGP70	rs9611170	22	38114791	C	0.66	0.99	-0.228	0.033	3.26E-12
IGP70	rs2413590	22	38120137	C	0.67	1.00	-0.228	0.033	3.27E-12
IGP70	rs5750808	22	38120933	G	0.33	1.00	0.228	0.033	3.30E-12
IGP70	rs5750811	22	38123012	G	0.67	1.00	-0.227	0.033	3.33E-12
IGP70	rs5750812	22	38123025	G	0.34	0.99	0.229	0.033	2.45E-12
IGP70	rs5757655	22	38127124	C	0.66	0.99	-0.229	0.033	2.42E-12
IGP70	rs4821893	22	38127725	G	0.33	1.00	0.230	0.033	1.84E-12
IGP70	rs5750814	22	38127933	C	0.67	1.00	-0.230	0.033	1.81E-12
IGP70	rs5757657	22	38128375	G	0.33	1.00	0.230	0.033	1.86E-12
IGP70	rs5750815	22	38128395	C	0.67	1.00	-0.230	0.033	1.82E-12
IGP70	rs4337572	22	38130650	C	0.33	1.00	0.230	0.033	1.83E-12
IGP70	rs4821894	22	38139766	C	0.66	1.00	-0.230	0.033	1.84E-12
IGP70	rs5750816	22	38140325	C	0.34	1.00	0.230	0.033	1.85E-12
IGP70	rs5757659	22	38142355	G	0.66	1.00	-0.230	0.033	1.86E-12
IGP70	rs6001585	22	38142932	C	0.22	1.00	0.208	0.037	1.52E-08
IGP70	rs6001587	22	38148954	C	0.66	1.00	-0.230	0.033	1.87E-12
IGP70	rs5750818	22	38150831	G	0.66	1.00	-0.230	0.033	1.87E-12
IGP70	rs5757665	22	38151587	G	0.66	1.00	-0.230	0.033	1.87E-12
IGP70	rs4821895	22	38152961	G	0.66	1.00	-0.230	0.033	1.87E-12
IGP70	rs739141	22	38154396	C	0.36	1.00	0.231	0.032	7.70E-13
IGP70	rs5750820	22	38155268	G	0.67	0.97	-0.250	0.033	4.20E-14
IGP70	rs5750822	22	38156734	G	0.34	1.00	0.230	0.033	1.71E-12
IGP70	rs7949	22	38157499	G	0.34	0.99	0.231	0.033	1.57E-12
IGP70	rs5757670	22	38159682	G	0.34	0.99	0.231	0.033	1.45E-12
IGP70	rs5750825	22	38161224	G	0.71	0.98	-0.276	0.034	8.04E-16
IGP70	rs1972280	22	38161932	T	0.29	0.98	0.277	0.034	6.94E-16
IGP70	rs4821897	22	38165533	G	0.71	0.97	-0.278	0.034	6.55E-16
IGP70	rs5750830	22	38170774	C	0.29	0.98	0.279	0.034	4.15E-16
IGP70	rs5757676	22	38171646	C	0.78	0.96	-0.221	0.037	3.24E-09
IGP70	rs8137426	22	38174296	G	0.71	0.98	-0.279	0.034	4.19E-16
IGP70	rs5757683	22	38180120	G	0.29	0.98	0.279	0.034	4.22E-16
IGP70	rs1557541	22	38181916	C	0.29	0.98	0.278	0.034	4.22E-16
IGP70	rs1557542	22	38182296	C	0.71	0.98	-0.278	0.034	4.24E-16
IGP70	rs5995735	22	38184367	C	0.29	0.98	0.278	0.034	4.34E-16
IGP70	rs738289	22	38185829	C	0.29	0.98	0.278	0.034	4.37E-16
IGP70	rs909674	22	38189115	C	0.30	0.99	0.275	0.034	3.91E-16
IGP71	rs4917017	7	50305778	G	0.71	0.92	0.196	0.035	1.90E-08
IGP71	rs17732497	7	50306619	C	0.70	0.97	0.184	0.033	4.24E-08
IGP71	rs9886239	7	50307097	C	0.32	0.98	-0.180	0.033	5.36E-08
IGP71	rs7805434	7	50311296	C	0.30	0.99	-0.182	0.033	3.90E-08
IGP71	rs7781977	7	50316680	C	0.70	1.00	0.182	0.033	3.75E-08
IGP71	rs7782210	7	50319291	G	0.38	0.98	-0.175	0.032	3.47E-08
IGP71	rs6583437	7	50320813	G	0.64	0.98	0.176	0.032	3.00E-08
IGP71	rs7789913	7	50323241	C	0.62	1.00	0.172	0.031	4.69E-08
IGP71	rs6421315	7	50325753	C	0.37	0.95	-0.183	0.032	1.49E-08

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP71	rs17630758	22	22466542	G	0.83	0.99	0.316	0.041	1.73E-14
IGP71	rs12167679	22	22471690	C	0.80	1.00	0.244	0.039	3.38E-10
IGP71	rs17548631	22	22474125	C	0.17	0.99	-0.317	0.041	1.51E-14
IGP71	rs9620326	22	22476629	C	0.83	0.99	0.317	0.041	1.50E-14
IGP71	rs9624334	22	22496256	C	0.17	0.99	-0.334	0.041	8.09E-16
IGP71	rs2186369	22	22500996	G	0.19	0.88	-0.347	0.042	8.75E-17
IGP71	rs6519476	22	22512500	G	0.76	0.99	0.211	0.036	6.82E-09
IGP71	rs5757642	22	38094770	C	0.64	1.00	-0.212	0.033	7.77E-11
IGP71	rs7286714	22	38095550	C	0.36	0.97	0.215	0.033	6.75E-11
IGP71	rs5757644	22	38096386	C	0.36	0.97	0.215	0.033	6.66E-11
IGP71	rs5750806	22	38096957	G	0.64	0.97	-0.215	0.033	6.63E-11
IGP71	rs1569499	22	38099764	C	0.64	0.97	-0.216	0.033	6.04E-11
IGP71	rs4821888	22	38100543	G	0.64	0.97	-0.216	0.033	6.14E-11
IGP71	rs5757647	22	38104993	C	0.33	1.00	0.231	0.033	1.80E-12
IGP71	rs4821890	22	38107469	G	0.34	0.99	0.232	0.033	1.70E-12
IGP71	rs1010169	22	38108113	G	0.67	1.00	-0.231	0.033	1.81E-12
IGP71	rs1010170	22	38108273	C	0.67	1.00	-0.231	0.033	1.87E-12
IGP71	rs5757650	22	38108365	C	0.67	1.00	-0.231	0.033	1.88E-12
IGP71	rs9611169	22	38112973	C	0.33	1.00	0.231	0.033	1.91E-12
IGP71	rs9611170	22	38114791	C	0.66	0.99	-0.227	0.033	4.19E-12
IGP71	rs2413590	22	38120137	C	0.67	1.00	-0.226	0.033	4.51E-12
IGP71	rs5750808	22	38120933	G	0.33	1.00	0.226	0.033	4.57E-12
IGP71	rs5750811	22	38123012	G	0.67	1.00	-0.226	0.033	4.64E-12
IGP71	rs5750812	22	38123025	G	0.34	0.99	0.228	0.033	3.15E-12
IGP71	rs5757655	22	38127124	C	0.66	0.99	-0.228	0.033	3.11E-12
IGP71	rs4821893	22	38127725	G	0.33	1.00	0.229	0.033	2.46E-12
IGP71	rs5750814	22	38127933	C	0.67	1.00	-0.229	0.033	2.41E-12
IGP71	rs5757657	22	38128375	G	0.33	1.00	0.229	0.033	2.47E-12
IGP71	rs5750815	22	38128395	C	0.67	1.00	-0.229	0.033	2.42E-12
IGP71	rs4337572	22	38130650	C	0.33	1.00	0.229	0.033	2.43E-12
IGP71	rs4821894	22	38139766	C	0.66	1.00	-0.229	0.033	2.43E-12
IGP71	rs5750816	22	38140325	C	0.34	1.00	0.229	0.033	2.45E-12
IGP71	rs5757659	22	38142355	G	0.66	1.00	-0.229	0.033	2.45E-12
IGP71	rs6001585	22	38142932	C	0.22	1.00	0.208	0.037	1.57E-08
IGP71	rs6001587	22	38148954	C	0.66	1.00	-0.228	0.033	2.47E-12
IGP71	rs5750818	22	38150831	G	0.66	1.00	-0.229	0.033	2.46E-12
IGP71	rs5757665	22	38151587	G	0.66	1.00	-0.229	0.033	2.46E-12
IGP71	rs4821895	22	38152961	G	0.66	1.00	-0.229	0.033	2.46E-12
IGP71	rs739141	22	38154396	C	0.36	1.00	0.233	0.032	5.80E-13
IGP71	rs5750820	22	38155268	G	0.67	0.97	-0.249	0.033	5.66E-14
IGP71	rs5750822	22	38156734	G	0.34	1.00	0.229	0.033	2.26E-12
IGP71	rs7949	22	38157499	G	0.34	0.99	0.230	0.033	2.06E-12
IGP71	rs5757670	22	38159682	G	0.34	0.99	0.230	0.033	1.90E-12
IGP71	rs5750825	22	38161224	G	0.71	0.98	-0.274	0.034	1.49E-15
IGP71	rs1972280	22	38161932	T	0.29	0.98	0.275	0.034	1.27E-15
IGP71	rs4821897	22	38165533	G	0.71	0.97	-0.275	0.034	1.20E-15
IGP71	rs5750830	22	38170774	C	0.29	0.98	0.277	0.034	6.63E-16
IGP71	rs5757676	22	38171646	C	0.78	0.96	-0.222	0.037	2.97E-09
IGP71	rs8137426	22	38174296	G	0.71	0.98	-0.277	0.034	6.69E-16
IGP71	rs5757683	22	38180120	G	0.29	0.98	0.277	0.034	6.72E-16
IGP71	rs1557541	22	38181916	C	0.29	0.98	0.277	0.034	6.72E-16
IGP71	rs1557542	22	38182296	C	0.71	0.98	-0.277	0.034	6.74E-16
IGP71	rs5995735	22	38184367	C	0.29	0.98	0.276	0.034	6.87E-16
IGP71	rs738289	22	38185829	C	0.29	0.98	0.276	0.034	6.90E-16

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP71	rs909674	22	38189115	C	0.30	0.99	0.274	0.034	6.19E-16
IGP72	rs4917017	7	50305778	G	0.71	0.92	-0.197	0.035	1.54E-08
IGP72	rs17732497	7	50306619	C	0.70	0.97	-0.185	0.033	3.01E-08
IGP72	rs9886239	7	50307097	C	0.32	0.98	0.182	0.033	3.81E-08
IGP72	rs7805434	7	50311296	C	0.30	0.99	0.184	0.033	2.77E-08
IGP72	rs7781977	7	50316680	C	0.70	1.00	-0.184	0.033	2.64E-08
IGP72	rs7782210	7	50319291	G	0.38	0.98	0.178	0.032	2.00E-08
IGP72	rs6583437	7	50320813	G	0.64	0.98	-0.179	0.032	1.73E-08
IGP72	rs7789913	7	50323241	C	0.62	1.00	-0.175	0.031	2.72E-08
IGP72	rs6421315	7	50325753	C	0.37	0.95	0.186	0.032	7.97E-09
IGP72	rs17630758	22	22466542	G	0.83	0.99	-0.317	0.041	1.57E-14
IGP72	rs12167679	22	22471690	C	0.80	1.00	-0.245	0.039	2.59E-10
IGP72	rs17548631	22	22474125	C	0.17	0.99	0.317	0.041	1.38E-14
IGP72	rs9620326	22	22476629	C	0.83	0.99	-0.317	0.041	1.37E-14
IGP72	rs9624334	22	22496256	C	0.17	0.99	0.334	0.041	7.62E-16
IGP72	rs2186369	22	22500996	G	0.19	0.88	0.347	0.042	8.63E-17
IGP72	rs6519476	22	22512500	G	0.76	0.99	-0.209	0.036	1.04E-08
IGP72	rs5757642	22	38094770	C	0.64	1.00	0.211	0.033	9.58E-11
IGP72	rs7286714	22	38095550	C	0.36	0.97	-0.214	0.033	7.72E-11
IGP72	rs5757644	22	38096386	C	0.36	0.97	-0.214	0.033	7.60E-11
IGP72	rs5750806	22	38096957	G	0.64	0.97	0.214	0.033	7.57E-11
IGP72	rs1569499	22	38099764	C	0.64	0.97	0.215	0.033	7.11E-11
IGP72	rs4821888	22	38100543	G	0.64	0.97	0.215	0.033	7.20E-11
IGP72	rs5757647	22	38104993	C	0.34	1.00	-0.229	0.033	2.80E-12
IGP72	rs4821890	22	38107469	G	0.34	0.99	-0.230	0.033	2.52E-12
IGP72	rs1010169	22	38108113	G	0.66	1.00	0.229	0.033	2.82E-12
IGP72	rs1010170	22	38108273	C	0.66	1.00	0.229	0.033	2.90E-12
IGP72	rs5757650	22	38108365	C	0.66	1.00	0.229	0.033	2.92E-12
IGP72	rs9611169	22	38112973	C	0.34	1.00	-0.229	0.033	2.95E-12
IGP72	rs9611170	22	38114791	C	0.66	0.99	0.225	0.033	6.10E-12
IGP72	rs2413590	22	38120137	C	0.67	1.00	0.224	0.033	6.89E-12
IGP72	rs5750808	22	38120933	G	0.33	1.00	-0.224	0.033	6.97E-12
IGP72	rs5750811	22	38123012	G	0.67	1.00	0.224	0.033	7.07E-12
IGP72	rs5750812	22	38123025	G	0.34	0.99	-0.226	0.033	4.58E-12
IGP72	rs5757655	22	38127124	C	0.66	0.99	0.226	0.033	4.53E-12
IGP72	rs4821893	22	38127725	G	0.33	1.00	-0.227	0.033	3.79E-12
IGP72	rs5750814	22	38127933	C	0.67	1.00	0.227	0.033	3.72E-12
IGP72	rs5757657	22	38128375	G	0.33	1.00	-0.227	0.033	3.82E-12
IGP72	rs5750815	22	38128395	C	0.66	1.00	0.227	0.033	3.74E-12
IGP72	rs4337572	22	38130650	C	0.34	1.00	-0.227	0.033	3.76E-12
IGP72	rs4821894	22	38139766	C	0.66	1.00	0.227	0.033	3.77E-12
IGP72	rs5750816	22	38140325	C	0.34	1.00	-0.227	0.033	3.80E-12
IGP72	rs5757659	22	38142355	G	0.66	1.00	0.226	0.033	3.81E-12
IGP72	rs6001585	22	38142932	C	0.22	1.00	-0.203	0.037	3.44E-08
IGP72	rs6001587	22	38148954	C	0.66	1.00	0.226	0.033	3.84E-12
IGP72	rs5750818	22	38150831	G	0.66	1.00	0.226	0.033	3.83E-12
IGP72	rs5757665	22	38151587	G	0.66	1.00	0.226	0.033	3.83E-12
IGP72	rs4821895	22	38152961	G	0.66	1.00	0.226	0.033	3.83E-12
IGP72	rs739141	22	38154396	C	0.36	1.00	-0.231	0.032	8.98E-13
IGP72	rs5750820	22	38155268	G	0.67	0.97	0.247	0.033	1.04E-13
IGP72	rs5750822	22	38156734	G	0.34	1.00	-0.227	0.033	3.53E-12
IGP72	rs7949	22	38157499	G	0.34	0.99	-0.228	0.033	3.23E-12
IGP72	rs5757670	22	38159682	G	0.34	0.99	-0.228	0.033	3.00E-12
IGP72	rs5750825	22	38161224	G	0.71	0.98	0.270	0.034	3.69E-15

Trait	SNP	Chr	Position	EA	EAF	RSq	Beta*	SE	P
IGP72	rs1972280	22	38161932	T	0.29	0.98	-0.271	0.034	3.20E-15
IGP72	rs4821897	22	38165533	G	0.71	0.97	0.271	0.034	3.04E-15
IGP72	rs5750830	22	38170774	C	0.29	0.98	-0.273	0.034	1.77E-15
IGP72	rs5757676	22	38171646	C	0.78	0.96	0.217	0.037	6.80E-09
IGP72	rs8137426	22	38174296	G	0.71	0.98	0.273	0.034	1.79E-15
IGP72	rs5757683	22	38180120	G	0.29	0.98	-0.273	0.034	1.81E-15
IGP72	rs1557541	22	38181916	C	0.29	0.98	-0.273	0.034	1.81E-15
IGP72	rs1557542	22	38182296	C	0.71	0.98	0.272	0.034	1.82E-15
IGP72	rs5995735	22	38184367	C	0.29	0.98	-0.272	0.034	1.86E-15
IGP72	rs738289	22	38185829	C	0.29	0.98	-0.272	0.034	1.87E-15
IGP72	rs909674	22	38189115	C	0.30	0.99	-0.270	0.034	1.69E-15
IGP74	rs9624334	22	22496256	C	0.17	0.99	-0.226	0.042	5.33E-08
IGP74	rs2186369	22	22500996	G	0.19	0.88	-0.236	0.042	1.66E-08
IGP75	rs17630758	22	22466542	G	0.83	0.99	0.223	0.041	5.82E-08
IGP75	rs17548631	22	22474125	C	0.17	0.99	-0.224	0.041	5.13E-08
IGP75	rs9620326	22	22476629	C	0.83	0.99	0.224	0.041	5.06E-08
IGP75	rs9624334	22	22496256	C	0.17	0.99	-0.234	0.041	1.73E-08
IGP75	rs2186369	22	22500996	G	0.19	0.88	-0.245	0.042	3.96E-09
IGP76	rs9624334	22	22496256	C	0.17	0.99	0.222	0.041	7.77E-08
IGP76	rs2186369	22	22500996	G	0.19	0.88	0.233	0.042	2.09E-08

Chr= chromosome; Position= position (build 36); EA= effect allele; EAF= effect allele frequency; RSq= average imputation quality (RSq) across meta-analysis populations; SE= standard error of beta

*effect expressed in standard deviation units after adjustment for sex, age and the first 3 principal components

Table 26: Pearson correlation coefficients and p-values for FA2 glycan as measured by UPLC, MALDI-TOF-MS, LC-ESI-MS and xCGE-LIF.

METHOD	IgG Class	UPLC Total	MALDI-TOF-MS IgG1	MALDI-TOF-MS IgG2&3	LC-ESI-MS IgG1	LC-ESI-MS IgG2&3	xCGE-LIF Total
UPLC	Total		0	0	0	0	0
MALDI-TOF-MS	IgG1	0.895		0	0	0	0
	IgG2&3	0.853	0.804		0	0	0
LC-ESI-MS	IgG1	0.912	0.943	0.774		0	0
	IgG2&3	0.881	0.790	0.953	0.809		0
xCGE-LIF	Total	0.928	0.882	0.833	0.914	0.865	

The bottom triangle contains the correlation coefficient; the top triangle contains the p-value and a p-value of 0 indicates that it was beyond the number of significant digits in R (~1x10^{-320})

Table 27: Pearson correlation coefficients and p-values for FA2B glycan as measured by UPLC, MALDI-TOF-MS, LC-ESI-MS and xCGE-LIF.

METHOD	IgG Class	UPLC Total	MALDI-TOF-MS IgG1	MALDI-TOF-MS IgG2&3	LC-ESI-MS IgG1	LC-ESI-MS IgG2&3	xCGE-LIF Total
UPLC	Total		0	0	0	0	0
MALDI-TOF-MS	IgG1	0.738		0	0	0	0
	IgG2&3	0.747	0.716		0	0	0
LC-ESI-MS	IgG1	0.807	0.899	0.654		0	0
	IgG2&3	0.828	0.686	0.921	0.731		0
xCGE-LIF	Total	0.862	0.792	0.724	0.901	0.813	

The bottom triangle contains the correlation coefficient; the top triangle contains the p-value and a p-value of 0 indicates that it was beyond the number of significant digits in R (~1x10^{-320})

Table 28: Pearson correlation coefficients and p-values for FA2G1* glycan as measured by UPLC, MALDI-TOF-MS, LC-ESI-MS and xCGE-LIF.

METHOD	IgG Class	UPLC Total		MALDI-TOF-MS IgG1	MALDI-TOF-MS IgG2&3	LC-ESI-MS IgG1	LC-ESI-MS IgG2&3	xCGE-LIF Total	
UPLC	Total		4.31E-04	0	0	0	0	0	4.10E-03
		0.106		0	0	0	0	0.160	0
MALDI-TOF-MS	IgG1	0.691	0.374		0	0	0	0	0
	IgG2&3	0.417	0.368	0.676		0	0	0	0
LC-ESI-MS	IgG1	0.711	0.538	0.677	0.319		0	0	0
	IgG2&3	0.506	0.508	0.587	0.817	0.550		0	0
xCGE-LIF	Total	0.872	0.042	0.620	0.336	0.675	0.448		0.536
		0.087	0.912	0.333	0.326	0.527	0.456	0.019	

The bottom triangle contains the correlation coefficient; the top triangle contains the p-value and a p-value of 0 indicates that it was beyond the number of significant digits in R (~1x10^{-320})

*This structure is measured as two isomers with UPLCand xCGE-LIF but as only one mass by MS-based methods

Table 29: Pearson correlation coefficients and p-values for FA2BG1* glycan as measured by UPLC, MALDI-TOF-MS, LC-ESI-MS and xCGE-LIF.

METHOD		UPLC		MALDI-TOF-MS		LC-ESI-MS		xCGE-LIF	
	IgG Class	Total		IgG1	IgG2&3	IgG1	IgG2&3	Total	
UPLC	Total		0	0	0	0	0	0	0
		0.256		8.42E-14	7.31E-05	0	4.44E-16	0	0
MALDI-TOF-MS	IgG1	0.777	0.223		0	0	0	0	0
	IgG2&3	0.665	0.119	0.740		0	0	0	4.44E-16
LC-ESI-MS	IgG1	0.866	0.288	0.881	0.612		0	0	0
	IgG2&3	0.835	0.241	0.743	0.841	0.775		0	0
xCGE-LIF	Total	0.858	0.286	0.718	0.563	0.771	0.768		0
		0.400	0.494	0.388	0.243	0.477	0.375	0.547	

The bottom triangle contains the correlation coefficient; the top triangle contains the p-value and a p-value of 0 indicates that it was beyond the number of significant digits in R ($\sim 1 \times 10^{-320}$)

*This structure is measured as two isomers with UPLCand xCGE-LIF but as only one mass by MS-based methods

Table 30: Pearson correlation coefficients and p-values for FA2G2 glycan as measured by UPLC, MALDI-TOF-MS, LC-ESI-MS and xCGE-LIF.

METHOD		UPLC	MALDI-TOF-MS		LC-ESI-MS		xCGE-LIF
	IgG Class	Total	IgG1	IgG2&3	IgG1	IgG2&3	Total
UPLC	Total		0	0	0	0	0
MALDI-TOF-MS	IgG1	0.913		0	0	0	0
	IgG2&3	0.851	0.853		0	0	0
LC-ESI-MS	IgG1	0.940	0.931	0.808		0	0
	IgG2&3	0.890	0.839	0.924	0.877		0
xCGE-LIF	Total	0.947	0.909	0.842	0.937	0.886	

The bottom triangle contains the correlation coefficient; the top triangle contains the p-value and a p-value of 0 indicates that it was beyond the number of significant digits in R ($\sim 1 \times 10^{-320}$)

Table 31: Pearson correlation coefficients and p-values for FA2BG2 glycan as measured by UPLC, MALDI-TOF-MS, LC-ESI-MS and xCGE-LIF.

METHOD		UPLC	MALDI-TOF-MS		LC-ESI-MS		xCGE-LIF
	IgG Class	Total	IgG1	IgG2&3	IgG1	IgG2&3	Total
UPLC	Total		0	0	0	0	0
MALDI-TOF-MS	IgG1	0.644		0	0	0	0
	IgG2&3	0.672	0.687		0	0	0
LC-ESI-MS	IgG1	0.830	0.791	0.717		0	0
	IgG2&3	0.777	0.648	0.844	0.831		0
xCGE-LIF	Total	0.768	0.650	0.670	0.819	0.773	

The bottom triangle contains the correlation coefficient; the top triangle contains the p-value and a p-value of 0 indicates that it was beyond the number of significant digits in R ($\sim 1 \times 10^{-320}$)

Table 32: Pearson correlation coefficients and p-values for FA2G1S1 glycan as measured by UPLC, MALDI-TOF-MS, LC-ESI-MS and xCGE-LIF.

METHOD		UPLC	MALDI-TOF-MS		LC-ESI-MS		xCGE-LIF
	IgG Class	Total	IgG1	IgG2&3	IgG1	IgG2&3	Total
UPLC	Total		0.084	0	0	0	0
MALDI-TOF-MS	IgG1	0.052		1.12E-05	0.071	2.42E-03	0
	IgG2&3	0.302	0.132		0	0	0
LC-ESI-MS	IgG1	0.362	0.055	0.276		0	0
	IgG2&3	0.411	0.091	0.697	0.554		0
xCGE-LIF	Total	0.604	0.284	0.356	0.422	0.467	

The bottom triangle contains the correlation coefficient; the top triangle contains the p-value and a p-value of 0 indicates that it was beyond the number of significant digits in R ($\sim 1\times10^{-320}$)

Table 33: Pearson correlation coefficients and p-values for FGS/(FG+FGS) as measured by UPLC, MALDI-TOF-MS, LC-ESI-MS and xCGE-LIF.

METHOD		UPLC	MALDI-TOF-MS		LC-ESI-MS		xCGE-LIF
	IgG Class	Total	IgG1	IgG2&3	IgG1	IgG2&3	Total
UPLC	Total		0	0	0	0	0
MALDI-TOF-MS	IgG1	0.292		0	0	0	0
	IgG2&3	0.413	0.419		0	0	0
LC-ESI-MS	IgG1	0.581	0.332	0.555		0	0
	IgG2&3	0.443	0.341	0.703	0.727		0
xCGE-LIF	Total	0.775	0.379	0.516	0.703	0.551	

The bottom triangle contains the correlation coefficient; the top triangle contains the p-value and a p-value of 0 indicates that it was beyond the number of significant digits in R ($\sim 1\times10^{-320}$)

Table 34: Pearson correlation coefficients and p-values for FGS/(F+FG+FGS) as measured by UPLC, MALDI-TOF-MS, LC-ESI-MS and xCGE-LIF.

METHOD		UPLC	MALDI-TOF-MS		LC-ESI-MS		xCGE-LIF
	IgG Class	Total	IgG1	IgG2&3	IgG1	IgG2&3	Total
UPLC	Total		0	0	0	0	0
MALDI-TOF-MS	IgG1	0.495		0	0	0	0
	IgG2&3	0.666	0.561		0	0	0
LC-ESI-MS	IgG1	0.794	0.528	0.668		0	0
	IgG2&3	0.713	0.491	0.839	0.775		0
xCGE-LIF	Total	0.884	0.542	0.690	0.826	0.752	

The bottom triangle contains the correlation coefficient; the top triangle contains the p-value and a p-value of 0 indicates that it was beyond the number of significant digits in R ($\sim 1\times10^{-320}$)

Table 35: Pearson correlation coefficients and p-values for FG1S1/ (FG1 + FG1S1) as measured by UPLC, MALDI-TOF-MS, LC-ESI-MS and xCGE-LIF.

METHOD		UPLC	MALDI-TOF-MS		LC-ESI-MS		xCGE-LIF
	IgG Class	Total	IgG1	IgG2&3	IgG1	IgG2&3	Total
UPLC	Total		5.55E-04	3.15E-12	0	0	0
MALDI-TOF-MS	IgG1	0.104		1.83E-03	8.85E-03	1.92E-04	0
	IgG2&3	0.208	0.094		0	0	0
LC-ESI-MS	IgG1	0.254	0.079	0.512		0	0
	IgG2&3	0.278	0.112	0.659	0.732		0
xCGE-LIF	Total	0.581	0.303	0.263	0.309	0.347	

The bottom triangle contains the correlation coefficient; the top triangle contains the p-value and a p-value of 0 indicates that it was beyond the number of significant digits in R (~1×10^{-320})

Table 36: Pearson correlation coefficients and p-values for FG2S1/ (FG2 + FG2S1) as measured by UPLC, MALDI-TOF-MS, LC-ESI-MS and xCGE-LIF.

METHOD		UPLC	MALDI-TOF-MS		LC-ESI-MS		xCGE-LIF
	IgG Class	Total	IgG1	IgG2&3	IgG1	IgG2&3	Total
UPLC	Total		0	0	0	0	0
MALDI-TOF-MS	IgG1	0.361		0	0	0	0
	IgG2&3	0.339	0.485		0	0	0
LC-ESI-MS	IgG1	0.399	0.366	0.471		0	0
	IgG2&3	0.399	0.377	0.611	0.777		0
xCGE-LIF	Total	0.750	0.414	0.390	0.457	0.443	

The bottom triangle contains the correlation coefficient; the top triangle contains the p-value and a p-value of 0 indicates that it was beyond the number of significant digits in R (~1×10^{-320})

Table 37: Pearson correlation coefficients and p-values for G0n as measured by UPLC, MALDI-TOF-MS, LC-ESI-MS and xCGE-LIF.

METHOD		UPLC	MALDI-TOF-MS		LC-ESI-MS		xCGE-LIF
	IgG Class	Total	IgG1	IgG2&3	IgG1	IgG2&3	Total
UPLC	Total		0	0	0	0	0
MALDI-TOF-MS	IgG1	0.914		0	0	0	0
	IgG2&3	0.862	0.796		0	0	0
LC-ESI-MS	IgG1	0.929	0.967	0.782		0	0
	IgG2&3	0.877	0.782	0.972	0.795		0
xCGE-LIF	Total	0.942	0.914	0.849	0.934	0.866	

The bottom triangle contains the correlation coefficient; the top triangle contains the p-value and a p-value of 0 indicates that it was beyond the number of significant digits in R (~1×10^{-320})

Table 38: Pearson correlation coefficients and p-values for G1n as measured by UPLC, MALDI-TOF-MS, LC-ESI-MS and xCGE-LIF.

METHOD		UPLC	MALDI-TOF-MS		LC-ESI-MS		xCGE-LIF
	IgG Class	Total	IgG1	IgG2&3	IgG1	IgG2&3	Total
UPLC	Total		0	0	0	0	0
MALDI-TOF-MS	IgG1	0.876		0	0	0	0
	IgG2&3	0.747	0.716		0	0	0
LC-ESI-MS	IgG1	0.908	0.915	0.612		0	0
	IgG2&3	0.784	0.702	0.959	0.640		0
xCGE-LIF	Total	0.917	0.860	0.710	0.916	0.748	

The bottom triangle contains the correlation coefficient; the top triangle contains the p-value and a p-value of 0 indicates that it was beyond the number of significant digits in R ($\sim 1 \times 10^{-320}$)

Table 39: Pearson correlation coefficients and p-values for G2n as measured by UPLC, MALDI-TOF-MS, LC-ESI-MS and xCGE-LIF.

METHOD		UPLC	MALDI-TOF-MS		LC-ESI-MS		xCGE-LIF
	IgG Class	Total	IgG1	IgG2&3	IgG1	IgG2&3	Total
UPLC	Total		0	0	0	0	0
MALDI-TOF-MS	IgG1	0.922		0	0	0	0
	IgG2&3	0.863	0.856		0	0	0
LC-ESI-MS	IgG1	0.950	0.949	0.827		0	0
	IgG2&3	0.902	0.846	0.948	0.875		0
xCGE-LIF	Total	0.951	0.922	0.858	0.952	0.898	

The bottom triangle contains the correlation coefficient; the top triangle contains the p-value and a p-value of 0 indicates that it was beyond the number of significant digits in R ($\sim 1 \times 10^{-320}$)

9.3 Papers Published From This Work

1. Lauc G*, Essafi A*, **Huffman JE***, Hayward C*, Knežević A, et al. (2010) Genomics meets glycomics-the first GWAS study of human N-Glycome identifies HNF1α as a master regulator of plasma protein fucosylation. PLoS Genet 6: e1001256. URL: http://www.plosgenetics.org/article/info%3Adoi%2F10.1371%2Fjournal.pgen.1001256

2. **Huffman JE**, Knezevic A, Vitart V, Kattla J, Adamczyk B, et al. (2011) Polymorphisms in B3GAT1, SLC9A9 and MGAT5 are associated with variation within the human plasma N-glycome of 3533 European adults. Hum Mol Genet 20: 5000-5011. URL: http://hmg.oxfordjournals.org/content/20/24/5000.long

3. Thanabalasingham G*, **Huffman JE***, Kattla JJ*, Novokmet M*, Rudan I*, et al. (2013) Mutations in HNF1A Result in Marked Alterations of Plasma Glycan Profile. Diabetes 62: 1329-1337. URL: http://diabetes.diabetesjournals.org/content/62/4/1329.long

4. Lauc G*, **Huffman JE***, Pučić M*, Zgaga L*, Adamczyk B*, et al. (2013) Loci associated with N-glycosylation of human immunoglobulin G show pleiotropy with autoimmune diseases and haematological cancers. PLoS Genet 9: e1003225. URL: http://www.plosgenetics.org/article/info%3Adoi%2F10.1371%2Fjournal.pgen.1003225

5. **Huffman JE***, Pučić-Baković M*, Klarić L*, Hennig R*, Selman MH*, et al. (2014) Comparative performance of four methods for high-throughput glycosylation analysis of immunoglobulin G in genetic and epidemiological research. Mol Cell Proteomics. 13(6):1598:610. URL: http://www.mcponline.org/content/13/6/1598.long

* co-first authors