PGP-UK Genomics Report for uk2293AB

1 Summary

This is the genome report was produced using collaborative research tools, including SNPedia and GetEvidence. This section shows an overview of all the small variants which were found in the genome for this individual, when compared with a reference genome. These variants are summarised in Table 1 and the pie-charts in Figures 2, 3 and 4.

This report was generated automatically and is not clinically approved. It is provided for personal and research purposes only.

This document contains hyperlinks, shown in grey, that will take you to external websites where you can find more detailed explanations. Some of the technical terms are also explained in more detail in the Ensembl Glossary. We would welcome your feedback about this report, for example, if you would like more information about anything or if any of the links have become inactive. You can contact us on: pgp-uk@ucl.ac.uk.

This summary shows an overview of all the variants which were found in the genome for this individual. The "variants remaining after filtering" refers to any differences in the DNA identified when compared to the reference genome. Of these, the majority will have already been found in some other sequenced individual and put on a database (existing variants) while others have not yet been annotated (novel variants).

"Overlapped genes" refers to the number of times where a variant was found in a region of the genome containing a gene. The diagram in Figure 1 is a simplification of the usual gene structure. "Exon" refers to the part of the gene which goes on to form a protein, and variants in this part of the gene are more likely to cause changes in the shape of the protein. Upstream, downstream, intronic and intergenic variants are more likely to alter the regulation of that gene but will not change the protein itself.

A transcript for a protein-coding gene can include the exons, introns and other gene features that are transcribed and important for gene function but might not be translated into the final protein. Not all transcripts are for protein-coding genes, with many containing non-coding RNAs that can be overlapping other genes, in introns or in intergenic regions.

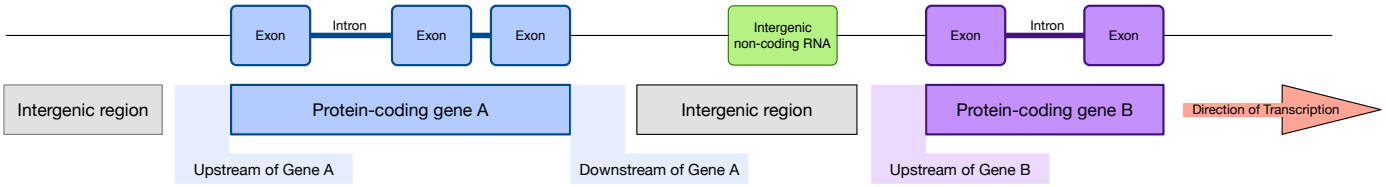

Figure 1: Diagram of gene structure indicating locations of potential variants

Feature	Count
Lines of input read	603152
Variants filtered out	468719
Novel / existing variants	0 (0.0) / 134433 (100.0)
Overlapped genes	33140
Overlapped transcripts	36466
Overlapped regulatory features	13027

Table 1: Variant calling summary

There are several different types of genomic variants. The most common change is when one single building block of the DNA (called a nucleotide) is changed, called a single nucleotide variants (SNV). Other variant types include insertions, where the DNA in the individual is longer than the reference sequence due to the insertion of one or more nucleotides; and deletions, where a few nucleotides are missing compared to the reference sequence.

Some of these changes will have no effect on the protein, while some changes may alter the protein function to varying degrees. The PolyPhen analysis software attempts to quantify the effect each mutation will have on the protein function. This ranges from "benign" where no change to the protein function is expected, to "probably damaging" where it is predicted that the mutation will affect protein function. It is nevertheless important to note that what is "damaging" for the protein is not necessarily damaging for the individual.

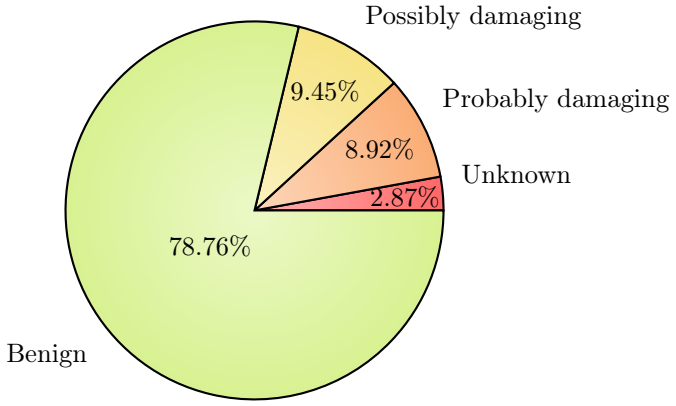

Figure 2: PolyPhen Summary

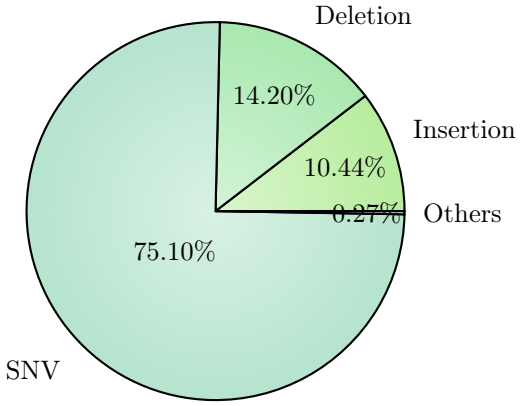

Figure 3: Variant Class

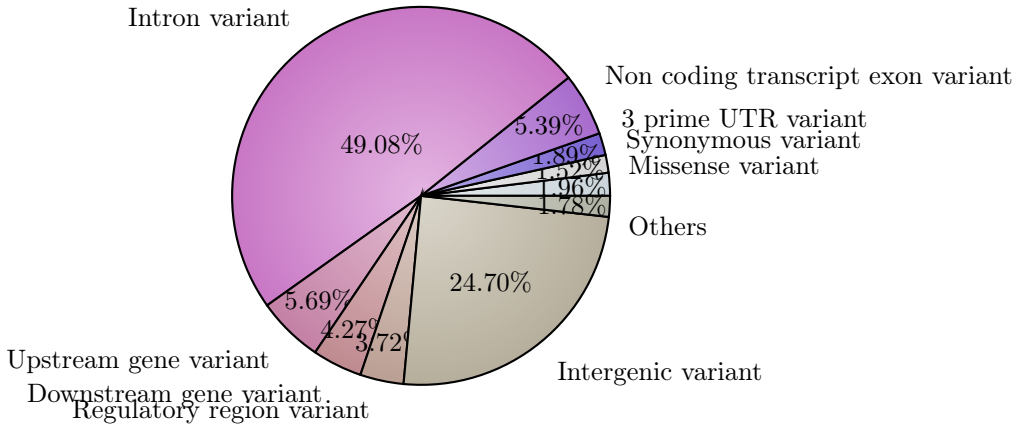

Figure 4: Consequence type

2 Ancestry

This plot shows the distribution of the genomes of different populations. Data from several studies which used whole genome sequencing was used to see the relationships between the genomes of the populations. It shows how closely related certain populations are genetically: Groups which cluster closely are more genetically similar than groups which are further apart. The black star symbol shows where this PGP-UK participant sits in relation to other populations, indicating their ancestry and their most closely related populations according to genetic sequence.

Please note that this analysis is limited by the populations available in the 1000 genomes project (1kGP) data. If there are European subpopulations reported, and the ancestry of the participant does not correspond to any of the 1kGP populations, the closest 1kGP sampled subpopulation will be shown (even though it might be different from the participant's actual ancestry).

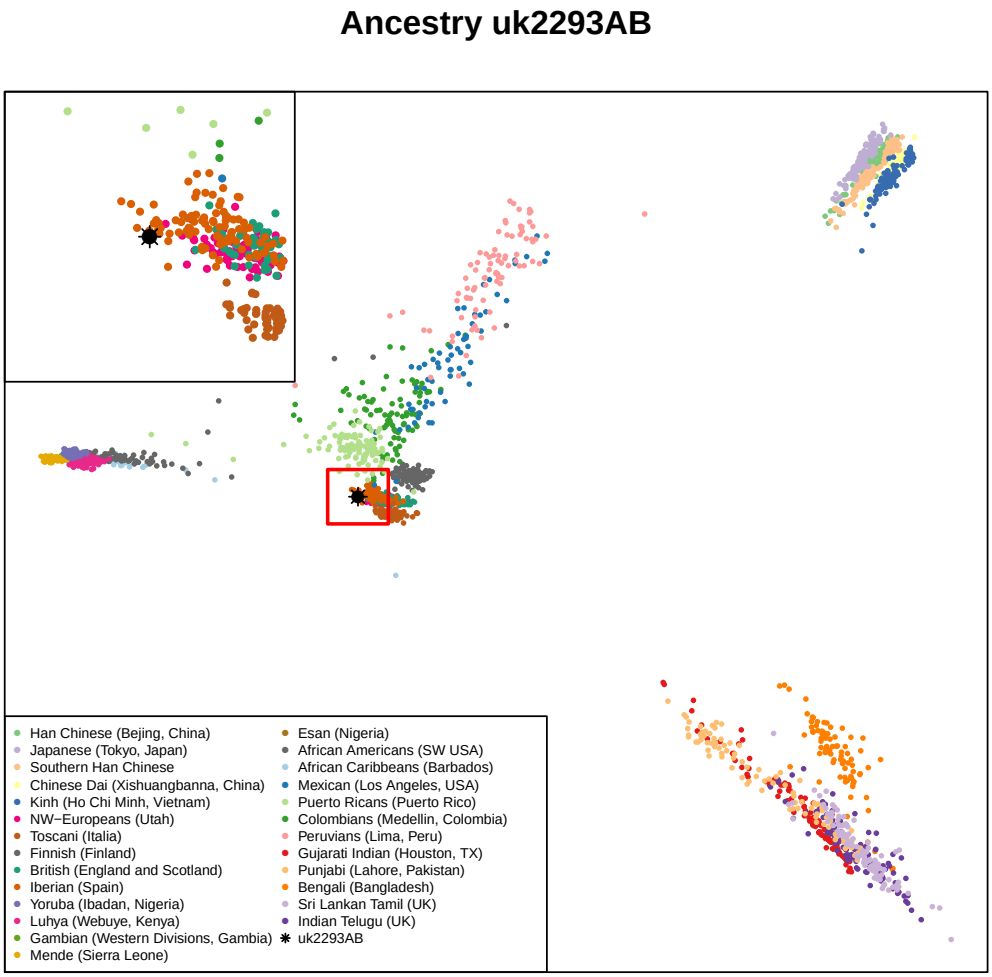

Figure 5: Ancestry Principal Component Analysis

3 Traits (based on SNPedia information)

Existing research has associated many variants with phenotypic traits, some of which can be perceived as beneficial while others appear to have a harmful effect. Some traits are complex and can be affected by several variants. It is likely that some of these would confer a higher risk while others a lower risk of trait manifestation. These can not be combined linearly to produce an actual risk of disease.

It is important to note that in most cases genomic data is probabilistic, not deterministic- i.e. having a genetic predisposition for a disease is not a diagnosis; rather, it shows an increased likelihood of developing that disease. Also, one person can have both potentially beneficial and harmful variants in the same gene, or associated with the same disease.

Some variants can also affect certain populations more, or will only affect a particular gender. For example, a variant for higher risk of endometriosis in the sequence of a male will not directly affect that person, but can be passed on to descendants.

While many traits are the result of a unique variant, many are the combination of several variants throughout the genome. In SNPedia, these are called genosets. These can integrate some of the information already present in the single variant tables, or be the combination of variants that have no phenotypic effect on their own, but contribute to a trait when together.

The variants in the following tables are sorted by magnitude. This is an subjective measure defined in SNPedia to highlight the perceived importance of the genotype described. At the moment this scale goes from 0 to 10. You can read more about it by visiting their explanatory webpage.

As our knowledge grows, the interpretation of the effect of certain variants might change. Clicking on the links in the genome report tables will take you to websites containing more information about each variant.

3.1 Possibly Beneficial Traits

Mag.	Identifier	Genotype	Summary	GnomAD	GetEvidence	ClinVar
2.5	rs3782179	(C;C)	9x lower odds of testicular cancer	Link		
2	rs10936599	(C;C)	Longer telomeres: longer life?	Link		Link
2	rs11045585	(A;A)	24% chance (lower than average) of docetaxel-in...	Link	Link	
2	rs1229984	(A;G)	0.56x decreased risk of oral/throat cancers	Link	Link	Link
2	rs12979860	(C;C)	~80% of such hepatitis C patients respond to tr...	Link	Link	Link
2	rs1544410	(G;G)	Decreased risk of low bone mineral density diso...	Link	Link	
2	rs1799884	(G;G)	Mothers have typical Birth-Weight babies. Sligh...	Link		
2	rs1864163	(A;G)	Associated with higher HDL cholesterol	Link	Link	
2	rs2241766	(G;T)	Slightly lower risk of breast cancer	Link		
2	rs261332	(A;A)	Associated with higher HDL cholesterol	Link		
2	rs3738579	(C;T)	0.5x decreased risk for cervical cancer: HNSCC:...	Link		
2	rs3819331	(T;T)	Lower risk of autism	Link		Link
2	rs4149268	(G;G)	Associated with higher HDL cholesterol	Link	Link	
2	rs6505162	(A;C)	0.58x decreased risk for esophageal cancer	Link		
2	rs7216389	(C;C)	0.69x lower risk of Childhood Asthma.	Link	Link	
1.8	rs4714156	(C;C)	<0.61x risk for restless legs	Link		
1.8	rs6897932	(C;T)	0.91x decreased risk for multiple sclerosis	Link	Link	Link
1.6	rs3775948	(C;C)	Slightly lower risk for gout	Link		
1.5	rs309375	(G;G)	Smaller mosquito bites	Link		
1.5	rs4939883	(C;C)	Associated with higher HDL cholesterol	Link	Link	
1.5	rs6427528	(A;A)	For rheumatoid arthritis patients: better respo...	Link		
1.5	rs9939609	(T;T)	Lower risk of obesity and Type-2 diabetes	Link	Link	
1.2	rs9306160	(C;T)	0.75x (reduced) risk for metastasis in LN-/ER+ ...	Link	Link	
1.1	rs2293347	(G;G)	Among NSCLC patients: better Gefitinib response...	Link		Link
1	rs2494732	(T;T)	Lower odds of psychosis	Link	Link	
1.0	rs11246226	(C;C)	Decreased risk of schizophrenia in limited stud...	Link	Link	
1.0	rs6583817	(C;T)	~0.80x (lower) risk for late onset Alzheimer's ...	Link		

3.2 Possibly Harmful Traits

Mag.	Identifier	Genotype	Summary	GnomAD	GetEvidence	ClinVar
3.5	rs1801160	(A;A)	5-fluorouracil toxicity (?)	Link	Link	Link
3	rs1143679	(A;A)	>1.78x increased risk for SLE	Link	Link	
3	rs13266634	(C;C)	Increased risk for type-2 diabetes	Link	Link	Link
3	rs16969968	(A;A)	Higher risk for nicotine dependence: lower risk...	Link	Link	Link
3	rs2237717	(T;T)	Reduced abilities related to neurocognition and...	Link		
2.6	rs8034191	(C;C)	1.80x lung cancer risk; decreased response to a...	Link	Link	
2.5	rs10490924	(G;T)	2.7x risk for age related macular degeneration	Link	Link	Link
2.5	rs1051730	(T;T)	1.8x increased risk of lung cancer; reduced res...	Link	Link	Link
2.5	rs2241880	(C;C)	2x-3x increased risk for Crohn's disease in Cau...	Link	Link	Link
2.5	rs5888	(C;T)	3x higher risk for age-related macular degenera...	Link		
2.5	rs891512	(A;G)	Higher blood pressure than G;G	Link		Link
2.2	rs964184	(G;G)	Increased risk of hypertriglyceridemia	Link	Link	
2.1	rs1050152	(T;T)	2.1x increased risk of Crohn's disease	Link	Link	Link
2.1	rs10811661	(T;T)	1.2x increased risk for type-2 diabetes	Link	Link	
2.1	rs17070145	(C;C)	Reduced memory abilities	Link		Link
2.1	rs17563	(C;C)	Risk for otosclerosis	Link	Link	Link
2.1	rs2231142	(A;C)	1.74x increased gout risk; gefinitib takers 4x ...	Link	Link	Link
2.1	rs2572886	(A;A)	1.4x increased risk of HIV infection	Link		
2.1	rs5186	(A;C)	~1.4x increased risk of hypertension	Link	Link	Link
2.1	rs5751876	(T;T)	Significantly higher anxiety levels after moder...	Link		
2	rs1050631	(C;T)	Mean Survival Time of 25 months for esophageal ...	Link		
2	rs1064395	(A;G)	Having any copies of A at this SNP heightens yo...	Link		
2	rs10883365	(G;G)	1.62x increased risk for developing Crohn's dis...	Link	Link	
2	rs10889677	(C;C)	Baseline (average) risk for certain autoimmune ...	Link	Link	
2	rs11171739	(C;C)	1.75x risk of developing Type-1 diabetes	Link	Link	
2	rs1143699	(C;C)	In men: 2.19x risk of type 2 diabetes	Link		
2	rs13254738	(C;C)	1.18x prostate cancer risk	Link	Link	
2	rs13376333	(T;T)	~2x higher risk of atrial fibrillation	Link	Link	
2	rs16942	(G;G)	Very slightly increased breast cancer risk	Link	Link	Link
2	rs17115100	(T;T)	Increased risk of developing Parkinson's Diseas...	Link	Link	
2	rs1734791	(A;A)	1.4x increased risk for lupus	Link		
2	rs1800896	(A;A)	1.8x increased prostate cancer risk	Link		
2	rs1867277	(A;A)	2x increased risk for thyroid cancer	Link		
2	rs2143340	(C;T)	Increased risk of dyslexia and poor reading per...	Link		
2	rs2305795	(A;G)	1.28x higher risk of narcolepsy compared to (G;...	Link		Link
2	rs2542151	(G;G)	2x risk for Crohn's; 1.6x for T1D	Link	Link	
2	rs25487	(G;G)	2x higher risk for skin cancer; possibly other ...	Link	Link	Link
2	rs2697962	(A;A)	Increased risk of developing Parkinson's Diseas...	Link		
2	rs2736100	(T;T)	Higher risk of Interstitial lung disease: and t...	Link	Link	Link
2	rs3025039	(C;T)	2.6x increased risk for ARMD in a Taiwanese pop...	Link		
2	rs351855	(C;T)	1.2x increased risk for prostate cancer	Link	Link	Link
2	rs3738919	(A;C)	1.94x risk of developing rheumatoid arthritis	Link		
2	rs3802842	(C;C)	>1.17x increased risk of colorectal cancer	Link	Link	
2	rs4792311	(A;G)	Increased risk of prostate cancer	Link	Link	Link
2	rs520354	(A;A)	Increased risk in men for biliary conditions	Link		
2	rs6807362	(C;C)	Increased autism risk	Link	Link	
2	rs699	(C;T)	Increased risk of hypertension	Link	Link	Link
2	rs763361	(T;T)	Increased risk for multiple autoimmune diseases...	Link	Link	
2	rs800292	(C;C)	5% higher risk of Age related macular degenerat...	Link	Link	Link
2	rs828907	(G;T)	Slightly increased risk of bladder cancer and 2...	Link		
2	rs854560	(A;T)	Higher risk for heart disease: diabetic retinop...	Link	Link	Link
2	rs9652490	(A;A)	~2x increased risk for Parkinson's disease: and...	Link	Link	
2.0	rs1434536	(A;A)	1.94x increased breast cancer risk	Link		Link

Mag.	Identifier	Genotype	Summary	GnomAD	GetEvidence	ClinVar
2.0	rs2156921	(G;G)	1.29x increased risk for depression	Link		
1.8	rs2278206	(T;T)	1.16x increased risk for asthma	Link	Link	
1.7	rs4807015	(C;T)	1.74x risk of type 2 diabetes	Link		
1.6	rs3764880	(A;A)	1.2 - 1.8x increased tuberculosis risk	Link	Link	
1.5	rs1169300	(A;G)	~1.5x increased lung cancer risk	Link		
1.5	rs12498742	(A;A)	1.25 increased risk for gout	Link		
1.5	rs13149290	(C;C)	Slightly increased risk of developing prostate ...	Link		
1.5	rs1375144	(C;C)	1.59x increased risk of developing bipolar diso...	Link		
1.5	rs140701	(A;G)	Increased risk for anxiety disorders	Link		
1.5	rs165599	(G;G)	May indicate increased susceptibility to schizo...	Link	Link	
1.5	rs1801274	(C;T)	Complex; generally greater risk for cancer prog...	Link	Link	Link
1.5	rs2076295	(G;G)	Slightly increased risk for pulmonary fibrosis ...	Link		
1.5	rs2229169	(A;A)	1.5x increased risk of heart attack and stroke ...	Link		
1.5	rs2240340	(A;A)	Slightly increased (1.5x) risk for RA	Link		
1.5	rs2272127	(C;C)	Associated with herpes and schizophrenia	Link		
1.5	rs2464196	(C;T)	~1.5x increased lung cancer risk	Link	Link	Link
1.5	rs28694718	(A;G)	2x higher risk for schizophrenia	Link		
1.5	rs2881766	(T;T)	Slightly increased risk for pregnancy-induced h...	Link		
1.5	rs356220	(T;T)	Increased risk of Parkinson's Disease	Link		
1.5	rs4585	(T;T)	Slightly poorer (0.75x) response to metformin i...	Link		Link
1.5	rs464049	(T;T)	Increased risk of schizophrenia in limited stud...	Link		
1.5	rs486907	(A;G)	1.5x increased prostate cancer risk	Link	Link	Link
1.5	rs4939827	(T;T)	1x risk for colorectal cancer	Link	Link	Link
1.5	rs5219	(C;T)	1.3x increased risk for type-2 diabetes	Link	Link	Link
1.5	rs699473	(C;C)	~1.5x increased brain tumor risk	Link		
1.5	rs995030	(G;G)	Non-protective against testicular cancer	Link	Link	
1.4	rs10865331	(A;A)	1.4x higher risk for ankylosing spondylitis	Link		
1.4	rs1126497	(C;T)	1.4x increased risk for breast cancer	Link	Link	Link
1.4	rs1801157	(A;A)	1.4x higher risk for breast cancer	Link		
1.4	rs2228314	(C;G)	1.48x risk of osteoarthritis	Link	Link	
1.4	rs3184504	(C;T)	Slightly increased risk for celiac disease	Link	Link	
1.4	rs498872	(T;T)	1.4x higher risk for glioma development	Link	Link	
1.4	rs6010620	(G;G)	1.4x higher risk for glioma development; but th...	Link	Link	
1.34	rs17465637	(C;C)	1.34x higher risk for myocardial infarction	Link	Link	
1.3	rs1042713	(A;G)	1.3x increased risk that pediatric inhaler use ...	Link	Link	Link
1.3	rs1260326	(C;T)	Slightly higher risk for gout	Link	Link	Link
1.3	rs1746048	(C;C)	1.03 increased risk for coronary heart disease	Link	Link	
1.2	rs1344706	(T;T)	1.2x increased risk for schizophrenia	Link	Link	
1.2	rs2254958	(C;T)	1.24x reported increased risk for Alzheimer's; ...	Link		
1.2	rs35677470	(A;G)	2x higher risk for scleroderma	Link	Link	
1.2	rs7514229	(G;G)	Associated with early-onset autoimmune thyroid ...	Link		
1.15	rs748404	(C;T)	Very slightly increased risk (1.15) for lung ca...	Link	Link	
1.1	rs11037909	(C;T)	1.27x type II diabetes risk	Link		
1.1	rs11650354	(C;T)	Possible risk for allergic asthma	Link		
1.1	rs2235040	(G;G)	Possibly lesser chances of remission only for i...	Link	Link	
1.1	rs2653349	(G;G)	2-6x increased risk for cluster headaches	Link	Link	
1.1	rs2828520	(G;G)	1.35x major depressive disorder risk	Link		
1.1	rs34516635	(G;G)	Less longevity for Ashkenazi Jewish women.	Link		Link
1.1	rs3740878	(A;G)	1.26x type II diabetes risk	Link		Link
1.07	rs2291834	(C;C)	Very slightly higher risk for myocardial infarc...	Link		
1	rs1010	(A;G)	1.75x risk of MI	Link	Link	
1	rs11206244	(C;T)	Slight risk of decreased thyroid hormone metabo...	Link		
1	rs1143674	(A;G)	1.3x increased autism risk	Link		
1	rs17300539	(G;G)	Increased risk of insulin resistance	Link		
1	rs3194051	(A;G)	1.12x risk of type-1 diabetes	Link	Link	Link

Mag.	Identifier	Genotype	Summary	GnomAD	GetEvidence	ClinVar
1	rs6976	(C;T)	Slight risk of osteoarthritis	Link		
0.1	rs2070744	(C;C)	Increased prostate cancer risk	Link	Link	Link
0.1	rs601338	(G;G)	Susceptible to Norovirus infections	Link	Link	Link

3.3 Genosets (Multi-variant Phenotypes)

Magnitude	Identifier	Summary
4	gs144	Male
3.0	gs291	Lower heart attack risk than average
2.9	gs192	MTHFR polymorphisms affecting homocysteine
2.5	gs100	Lactose intolerance risk
2.5	gs155	CYP3A5 non-expressor
2.5	gs281	Part of the 88% of the population claimed not t...
2.5	gs285	Claimed to lose 2.5x as much weight on a low fa...
2	gs140	NAT2 slow metabolizer
2	gs154	NAT2 Slow metabolizer
2	gs159	CYP1A2 fast metabolizer
2	gs313	Normal DPYD activity and thus 5-FU metabolism p...
1.7	gs233	Normal pain sensitivity; APS/APS: LPS/APS: and ...
1.5	gs247	Parkinson's Disease Risk

4 Report Metadata

Resource	Version	Website
Genome	GRCh37	Link
BWA	0.7.12	Link
SAMtools	1.3	Link
GATK	3.4-46	Link
PLINK	v1.90b3.35	Link
SNPedia	02-May-2019	Link
GnomAD	v2.1.1	Link
GetEvidence	10-May-2019	Link
ClinVar	10-May-2019	Link

Table 5: Analysis Pipeline Versions

Report generated on June 13, 2019.