

gwascat: structuring and querying the NHGRI GWAS catalog

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May 4, 2020

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*Generous support of Robert Gentleman and the Computational Biology Group of Genentech, Inc. is gratefully acknowledged

1 Introduction

NHGRI maintains and routinely updates a database of selected genome-wide association studies. This document describes R/Bioconductor facilities for working with contents of this database.

1.1 Installation

The package can be installed using Bioconductor's *BiocManager* package, with the sequence

```
library(BiocManager)
BiocManager::install("gwascats")
```

1.2 Attachment and access to documentation

Once the package has been installed, use `library(gwascats)` to obtain interactive access to all the facilities. After executing this command, use `help(package="gwascats")` to obtain an overview. The current version of this vignette can always be accessed at www.bioconductor.org, or by suitably navigating the web pages generated with `help.start()`.

1.3 Illustrations: computing

Available functions are:

```
> library(gwascats)
> objects("package:gwascats")
```

```
[1] "bindcadd_snv"      "chklocs"          "ebicat37"
[4] "ebicat37UCSC"      "ebicat38"          "ebicat_b37"
[7] "ebicat_b38"        "efo.obo.g"         "g17SM"
[10] "getRsids"          "getTraits"         "gg17N"
[13] "gw6.rs_17"         "gwastagger"        "gwcecx2gviz"
[16] "gwdf_2014_09_08"   "gwrngs19"          "gwrngs38"
[19] "ldtagr"            "locon6"            "locs4trait"
[22] "low17"             "makeCurrentGwascats" "obo2graphNEL"
[25] "riskyAlleleCount"  "rules_6.0_1kg_17"  "si.hs.37"
[28] "si.hs.38"          "subsetByChromosome" "subsetByTraits"
[31] "topTraits"         "traitsManh"
```

The extended `GRanges` instance with all SNP-disease associations is obtained as follows, using the hg19 genome build (GRCh38/hg38-based ranges are also available as `ebicat38`).

```
> data(ebicat37)
```

To determine the most frequently occurring traits:

```
> topTraits(ebicat37)
```

Obesity-related traits	Height	IgG glycosylation
957	822	699
Type 2 diabetes	Rheumatoid arthritis	Crohn's disease
340	294	249
Schizophrenia	Blood metabolite levels	HDL cholesterol
248	245	220
Breast cancer		
199		

For a given trait, obtain a GRanges with all recorded associations; here only three associations are shown:

```
> subsetByTraits(ebicat37, tr="LDL cholesterol")[1:3]
```

gwasloc instance with 3 records and 36 attributes per record.

Extracted: 2016-01-18

Genome: GRCh37

Excerpt:

GRanges object with 3 ranges and 3 metadata columns:

	seqnames	ranges	strand	DISEASE/TRAIT	SNPS	P-VALUE
	<Rle>	<IRanges>	<Rle>	<character>	<character>	<numeric>
[1]	chr2	44072576	*	LDL cholesterol	rs4299376	4e-72
[2]	chr1	150958836	*	LDL cholesterol	rs267733	5e-09
[3]	chr2	21263900	*	LDL cholesterol	rs1367117	1e-182

seqinfo: 23 sequences from GRCh37 genome

2 Some visualizations

2.1 Basic Manhattan plot

A basic Manhattan plot is easily constructed with the ggbio package facilities. Here we confine attention to chromosomes 4:6. First, we create a version of the catalog with $-\log_{10}p$ truncated at a maximum value of 25.

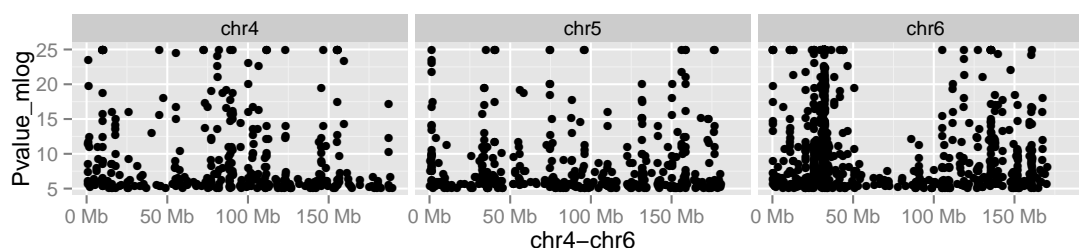
```
> gwtrunc = ebicat37
> requireNamespace("S4Vectors")
> mcols = S4Vectors::mcols
```

```

> mlpv = mcols(ebicat37)$PVALUE_MLOG
> mlpv = ifelse(mlpv > 25, 25, mlpv)
> S4Vectors::mcols(gwtrunc)$PVALUE_MLOG = mlpv
> library(GenomeInfoDb)
> seqlevelsStyle(gwtrunc) = "UCSC"
> gwlit = gwtrunc[ which(as.character(seqnames(gwtrunc)) %in% c("chr4", "chr5", "chr6")) ]
> library(ggbio)
> mlpv = mcols(gwlit)$PVALUE_MLOG
> mlpv = ifelse(mlpv > 25, 25, mlpv)
> S4Vectors::mcols(gwlit)$PVALUE_MLOG = mlpv

> methods:::bind_activation(FALSE)
> autoplot(gwlit, geom="point", aes(y=PVALUE_MLOG), xlab="chr4-chr6")

```



2.2 Annotated Manhattan plot

A simple call permits visualization of GWAS results for a small number of traits. Note the defaults in this call.

July 2018: The following is unevaluated owing to ggbio.

```

> args(traitsManh)

function (gwr, selr = GRanges(seqnames = "chr17", IRanges(3e+07,
  5e+07)), traits = c("Asthma", "Parkinson's disease", "Height",
  "Crohn's disease"), truncmlp = 25, ...)
NULL

> traitsManh(gwtrunc)

```

2.3 Integrative view of potential genetic determinants

The following chunk uses GFF3 data on eQTL and related phenomena distributed at the GBrowse instance at eqtl.uchicago.edu. A request for all information at 43-45 Mb was made on 2 June 2012, yielding the GFF3 referenced below. Of interest are locations and scores of genetic associations with DNaseI hypersensitivity (scores identifying dsQTL, see Degner et al 2012).

```
> gffpath = system.file("gff3/chr17_43000000_45000000.gff3", package="gwascat")
> library(rtracklayer)
> c17tg = import(gffpath)
```

We make a Gviz DataTrack of the dsQTL scores.

```
> c17td = c17tg[ which(S4Vectors::mcols(c17tg)$type == "Degner_dsQTL") ]
> library(Gviz)
> dsqs = DataTrack( c17td, chrom="chr17", genome="hg19", data="score",
+   name="dsQTL")
```

We start the construction of the graph here.

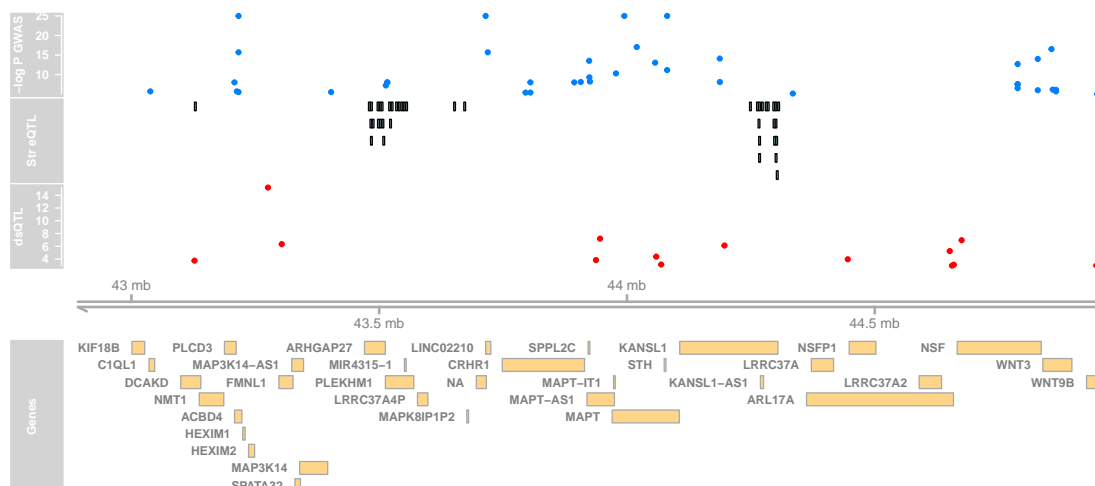
```
> g2 = GRanges(seqnames="chr17", IRanges(start=4.3e7, width=2e6))
> seqlevelsStyle(ebicat37) = "UCSC"
> basic = gwcex2gviz(basegr = ebicat37, contextGR=g2, plot.it=FALSE)
```

We also collect locations of eQTL in the Stranger 2007 multipopulation eQTL study.

```
> c17ts = c17tg[ which(S4Vectors::mcols(c17tg)$type == "Stranger_eqtl") ]
> eqloc = AnnotationTrack(c17ts, chrom="chr17", genome="hg19", name="Str eQTL")
> displayPars(eqloc)$col = "black"
> displayPars(dsqs)$col = "red"
> integ = list(basic[[1]], eqloc, dsqs, basic[[2]], basic[[3]])
```

Now use Gviz.

```
> plotTracks(integ)
```



3 SNP sets and trait sets

3.1 SNPs by name

We can regard the content of a SNP chip as a set of SNP, referenced by name. The `pd.genomewidesnp.6` package describes the Affymetrix SNP 6.0 chip. We can determine which traits are associated with loci interrogated by the chip as follows. We work with a subset of the 1 million loci for illustration.

The `locon6` data frame has information on 10000 probes, acquired through the following code (not executed here to reduce dependence on the `pd.genomewidesnp.6` package, which is very large).

```
> library(pd.genomewidesnp.6)
> con = pd.genomewidesnp.6@getdb()
> locon6 = dbGetQuery(con,
+   "select dbsnp_rs_id, chrom, physical_pos from featureSet limit 10000")
```

Instead use the serialized information:

```
> data(locon6)
> rson6 = as.character(locon6[[1]])
> rson6[1:5]
```

```
[1] "rs2887286" "rs1496555" "rs41477744" "rs3890745" "rs10492936"
```

We subset the GWAS ranges structure with rsids that are common to both the chip and the GWAS catalog. We then tabulate the diseases associated with the common loci.

```
> intr = ebicat37[ intersect(getRsids(ebicat37), rson6) ]
> sort(table(getTraits(intr)), decreasing=TRUE)[1:10]
```

Height	6
Select biomarker traits	3
Bipolar disorder	2
Dental caries	2
Homocysteine levels	2
IgG glycosylation	2
Immune reponse to smallpox (secreted IFN-alpha)	2

```

Metabolic traits
2
Mitochondrial DNA levels
2
Response to cytidine analogues (cytosine arabinoside)
2

```

3.2 Traits by genomic location

We will assemble genomic coordinates for SNP on the Affymetrix 6.0 chip and show the effects of identifying the trait-associated loci with regions of width 1000bp instead of 1bp.

The following code retrieves coordinates for SNP interrogated on 10000 probes (to save time) on the 6.0 chip, and stores the results in a GRanges instance.

```

> gr6.0 = GRanges(seqnames=ifelse(is.na(locon6$chrom),0,locon6$chrom),
+               IRanges(ifelse(is.na(locon6$phys),1,locon6$phys), width=1))
> S4Vectors::mcols(gr6.0)$rsid = as.character(locon6$dbSNP_rs_id)
> seqlevels(gr6.0) = paste("chr", seqlevels(gr6.0), sep="")

```

Here we compute overlaps with both the raw disease-associated locus addresses, and with the locus address \pm 500bp.

```

> ag = function(x) as(x, "GRanges")
> ovraw = suppressWarnings(subsetByOverlaps(ag(ebicat37), gr6.0))
> length(ovraw)

[1] 128

> ovaug = suppressWarnings(subsetByOverlaps(ag(ebicat37+500), gr6.0))
> length(ovaug)

[1] 207

```

To acquire the subset of the catalog to which 6.0 probes are within 500bp, use:

```

> rawrs = mcols(ovraw)$SNPS
> augrs = mcols(ovaug)$SNPS
> ebicat37[augrs]

```

gwasloc instance with 207 records and 36 attributes per record.

Extracted: 2016-01-18

Genome: GRCh37

Excerpt:

GRanges object with 5 ranges and 3 metadata columns:

	seqnames	ranges	strand	
	<Rle>	<IRanges>	<Rle>	
[1]	chr11	4605195	*	
[2]	chr11	46761055	*	
[3]	chr1	169519049	*	
[4]	chr11	61640379	*	
[5]	chr1	8495945	*	

	DISEASE/TRAIT
	<character>
[1]	Response to serotonin reuptake inhibitors in major depressive disorder
[2]	Venous thromboembolism
[3]	Venous thromboembolism
[4]	Trans fatty acid levels
[5]	Optic cup area

	SNPS	P-VALUE
	<character>	<numeric>
[1]	rs2566255	2e-06
[2]	rs1799963	2e-09
[3]	rs6025	1e-96
[4]	rs174449	8e-07
[5]	rs301801	3e-08

seqinfo: 23 sequences from GRCh37 genome

Relaxing the intersection criterion in this limited case leads to a larger set of traits.

```
> setdiff( getTraits(ebicat37[augrs]), getTraits(ebicat37[rawrs]) )
```

```
[1] "Response to serotonin reuptake inhibitors in major depressive disorder"
[2] "Venous thromboembolism"
[3] "Hippocampal volume"
[4] "Red blood cell fatty acid levels"
[5] "Febrile seizures (MMR vaccine-related)"
[6] "Eosinophilic esophagitis"
[7] "QT interval"
[8] "Smoking cessation"
[9] "Systolic blood pressure (alcohol consumption interaction)"
[10] "QRS duration in Tripanosoma cruzi seropositivity"
[11] "Functional impairment in major depressive disorder, bipolar disorder and schizop
[12] "Periodontitis (CDC/AAP)"
[13] "Odorant perception (&beta;-damascenone)"
[14] "Bronchopulmonary dysplasia"
[15] "Self-reported allergy"
```



```

[16] "Migraine"
[17] "Reading and spelling"
[18] "Adverse response to chemotherapy (neutropenia/leucopenia) (carboplatin)"
[19] "Obesity"
[20] "Autism spectrum disorder, attention deficit-hyperactivity disorder, bipolar disorder"
[21] "Response to taxane treatment (docetaxel)"
[22] "Response to amphetamines"
[23] "Neuroblastoma"
[24] "Lentiform nucleus volume"
[25] "Capecitabine sensitivity"
[26] "Fasting glucose-related traits (interaction with BMI)"
[27] "Response to angiotensin II receptor blocker therapy"
[28] "Response to hepatitis C treatment"
[29] "Response to anti-depressant treatment in major depressive disorder"
[30] "Phospholipid levels (plasma)"
[31] "Endometrial cancer"
[32] "MRI atrophy measures"
[33] "Self-rated health"
[34] "Neonatal lupus"
[35] "Crohn's disease"
[36] "Response to statin therapy"
[37] "Tanning"
[38] "Osteonecrosis of the jaw"
[39] "Hip geometry"
[40] "Parkinson's disease"

```

4 Counting alleles associated with traits

We can use `riskyAlleleCount` to count risky alleles enumerated in the GWAS catalog. This particular function assumes that we have genotyped at the catalogued loci. Below we will discuss how to impute from non-catalogued loci to those enumerated in the catalog.

```

> data(gg17N) # translated from GGdata chr 17 calls using ABmat2nuc
> gg17N[1:5,1:5]

```

	rs6565733	rs1106175	rs17054921	rs8064924	rs8070440
NA06985	"G/G"	"A/G"	"C/C"	"G/G"	"G/G"
NA06991	"G/G"	"A/A"	"C/C"	"G/G"	"G/G"
NA06993	"G/G"	"A/A"	"C/C"	"G/G"	"G/G"
NA06994	"A/G"	"A/G"	"C/C"	"A/G"	"G/G"
NA07000	"G/G"	"A/A"	"C/C"	"G/G"	"G/G"

This function can use genotype information in the A/B format, assuming that B denotes the alphabetically later nucleotide. Because we have direct nucleotide coding in our matrix, we set the `matIsAB` parameter to false in this call.

```
> h17 = riskyAlleleCount(gg17N, matIsAB=FALSE, chr="ch17",
+ gwwl = ebicat37)
> h17[1:5,1:5]
```

	rs7217319	rs684232	rs623323	rs747685	rs747687
NA06985	0	0	2	1	1
NA06991	0	0	2	2	2
NA06993	0	0	2	1	1
NA06994	0	0	2	2	2
NA07000	0	0	2	2	2

```
> table(as.numeric(h17))
```

0	1	2
23876	9954	7570

It is of interest to bind the counts back to the catalog data.

```
> gwr = ebicat37
> gwr = gwr[colnames(h17),]
> S4Vectors::mcols(gwr) = cbind(mcols(gwr), DataFrame(t(h17)))
> sn = rownames(h17)
> gwr[,c("DISEASE/TRAIT", sn[1:4])]
```

gwasloc instance with 460 records and 5 attributes per record.

Extracted: 2016-01-18

Genome: GRCh37

Excerpt:

GRanges object with 5 ranges and 5 metadata columns:

	seqnames	ranges	strand	DISEASE/TRAIT	NA06985	NA06991
	<Rle>	<IRanges>	<Rle>	<character>	<integer>	<integer>
[1]	chr17	38924	*	AIDS progression	0	0
[2]	chr17	618965	*	Prostate cancer	0	0
[3]	chr17	700020	*	Type 2 diabetes	2	2
[4]	chr17	775051	*	Blood pressure	1	2
[5]	chr17	775334	*	Blood pressure	1	2
	NA06993	NA06994				
	<integer>	<integer>				
[1]	0	0				
[2]	0	0				

[3]	2	2
[4]	1	2
[5]	1	2

seqinfo: 23 sequences from GRCh37 genome

Now by programming on the metadata columns, we can identify individuals with particular risk profiles.

5 Imputation to unobserved loci

If we lack information on a specific locus s , but have reasonably dense genotyping on a subject, population genetics may allow a reasonable guess at the genotype at s for this subject. Many algorithms for genotype imputation have been proposed. Here we use a very simple approach due to David Clayton in the *snpStats* package.

We use the “low coverage” 1000 genomes genotypes for the CEU (central European) HapMap cohort as a base for constructing imputation rules. We focus on chromosome 17 for illustration.

The base data are

```
> data(low17)
> low17
```

An object of class "SnpMatrix"

```
chr17:1869 chr17:2220 chr17:6689 rs34663111 rs62054999 chr17:13074
chr17:14008 chr17:19979 chr17:27268 chr17:31906 chr17:32249 chr17:32309
chr17:32311 chr17:32579 chr17:32869 chr17:33766 chr17:33817 chr17:33865
chr17:34206 chr17:34276 chr17:34401 chr17:36164 chr17:36169 chr17:36642
rs62054056 chr17:38761 chr17:44399 rs62057000 chr17:46107 rs34794059
rs35498575 rs11656530 rs12941744 chr17:48400 rs12945606 rs59865068
chr17:48474 rs7501441 chr17:48878 rs4890179 rs4890180 rs4890181
rs62057022 rs62057023 rs4890182 rs55715614 chr17:49783 rs56209223
chr17:49868 rs8070685 rs62057026 chr17:50776 rs11658619 rs11656429
rs9900783 chr17:51088 rs11657419 rs9911285 rs4890184 chr17:51196
rs4890185 rs1882990 rs1109902 rs4424950 rs56200345 rs7503116 rs4890188
rs1136388 chr17:53181 rs1609550 chr17:53324 rs34979521 rs9913041
chr17:54373 rs1109995 chr17:55518 chr17:55533 rs9903623 rs4305131
rs7213008 chr17:57029 chr17:57897 rs55639116 rs62057047 rs11654695
chr17:59056 chr17:59096 chr17:59137 chr17:59340 rs4353523 chr17:59389
rs11649979 chr17:60469 rs12938802 chr17:60733 chr17:61665 chr17:61849
rs1138504 rs11150884 rs9907477 chr17:63097 rs11150885 rs11150886
chr17:63683 chr17:63824 chr17:63927 rs62057048 rs8077096 chr17:64175
```

rs62057049 rs7226358 chr17:65360 rs62057050 rs7207457 rs11868664
rs4417592 rs4417593 chr17:66507 rs62057051 rs8066107 chr17:68293
chr17:68317 chr17:68329 rs62057055 rs56377713 rs12941133 rs55767019
rs55737141 chr17:69067 rs62057059 rs62059560 rs62059561 rs62059562
rs62059563 rs12450789 chr17:71465 chr17:71471 rs12943724 rs56871222
rs62059580 rs9915268 rs35292180 chr17:72213 chr17:72267 chr17:72335
chr17:72338 rs12450662 rs28698090 rs4442878 rs9890183 rs8078223
rs9896436 rs35147412 rs11867332 rs34778113 rs36016398 rs35147390
rs11867900 rs35698541 chr17:74922 chr17:75264 rs61618085 chr17:75839
chr17:76431 rs12939784 chr17:76628 rs9915328 rs34372025 rs12452457
chr17:77285 rs11150887 rs8081881 rs8078929 rs8069524 rs9675043
rs28521142 rs8075539 chr17:80061 chr17:80433 rs11150888 rs11150889
rs4890193 rs4550502 rs11150890 rs11150891 rs12945036 rs11150892
rs55708782 chr17:81113 rs4890194 rs4890195 chr17:81254 chr17:81349
chr17:81369 rs9674467 chr17:81659 rs9674571 chr17:81768 chr17:81921
chr17:81922 chr17:81923 rs8075084 rs8075208 chr17:82229 chr17:82312
rs34314694 rs4890196 rs4890171 chr17:82992 rs4890197 rs4890198
rs12941826 rs28529202 rs28690679 chr17:84521 rs8073847 rs35286566
chr17:84936 rs8076034 chr17:85592 chr17:85776 rs4531790 rs3923019
chr17:85842 rs11655874 rs11651610 rs3923018 rs11651800 rs3923017
rs11654890 chr17:86853 rs9905036 chr17:86925 rs55708732 rs11652984
rs35315427 rs11150893 rs11150894 rs11653255 rs12603796 chr17:87964
rs34347588 rs8074031 rs7213583 rs7213702 rs12449638 rs7217872
chr17:89055 rs12937656 chr17:90050 rs62056563 rs9912863 rs9908467
rs9908519 rs9894303 rs9913392 rs9909439 rs9892331 rs35026216 rs55904681
rs34170095 rs35445227 rs12942097 rs12949408 chr17:92005 chr17:93709
chr17:94243 rs12150065 chr17:94595 chr17:94869 rs12150077 chr17:94873
rs9896350 rs58055127 chr17:95303 chr17:95332 rs9892040 rs7207284
rs62622824 rs58153628 rs57953101 rs7405600 rs4985571 rs4352099
chr17:97378 rs4353524 rs4426400 chr17:97720 rs12948758 rs12449506
rs12451407 rs4357997 chr17:98250 rs11651297 rs4395128 chr17:98469
chr17:98717 rs59337913 chr17:98915 rs4129926 rs56252542 chr17:100246
rs7406880 chr17:100371 rs62056571 rs56384259 chr17:100691 rs7405713
rs12451219 rs12451236 rs12600698 rs12602957 chr17:101766 rs9901911
chr17:102171 rs7208985 rs58485634 rs7223759 rs7209151 rs58315634
rs9892618 rs7209688 rs7221298 rs7217222 rs7214608 rs28747076 rs7214637
rs12451029 rs4458053 rs28515912 rs28706104 rs28556780 rs62056574
rs9900685 rs60727688 rs12601375 rs4890202 rs4890203 chr17:108015
rs12452527 rs11150870 rs9906110 chr17:109220 chr17:109235 rs9907635
rs7406768 chr17:109423 rs4985595 rs7224163 rs7215219 chr17:110522
rs7219680 rs7212156 rs9903116 rs8073479 rs8073513 rs10454094
chr17:111460 chr17:111519 chr17:111665 rs56702013 rs28468376 rs28404325

chr17:112970 rs7208188 rs55695413 rs6565702 rs4985594 chr17:113584
chr17:113604 rs34427628 rs4985593 rs4985592 chr17:113738 rs12947571
rs12449625 chr17:114530 rs4617924 rs8075999 chr17:115031 chr17:115115
rs60794269 rs4985591 rs4985590 rs4247500 rs4985589 rs4371209 rs4471739
chr17:115802 rs4471740 rs7224768 rs7224674 rs12940704 chr17:116375
chr17:116431 chr17:116499 chr17:117204 chr17:117452 rs28593623
rs56960944 chr17:118657 rs12451051 chr17:118962 rs7504058 rs7501898
chr17:119999 rs4985588 rs12937990 chr17:122582 rs8079261 rs9789021
chr17:123540 rs9891976 chr17:123961 rs9915796 rs59849037 chr17:125579
rs7207517 chr17:126030 rs7211665 rs9902230 rs10871511 rs9915647
rs9915649 chr17:126885 chr17:127753 rs56101945 rs12936802 rs7223270
rs9789059 rs9789037 rs9789038 rs9788983 chr17:129697 rs35128325
rs56210084 rs56005157 rs7208824 chr17:130149 chr17:130369 chr17:130451
chr17:130529 rs4985587 chr17:130892 rs12949507 rs9894715 rs12449754
rs12942829 rs11150871 rs12451279 rs12452629 rs9906685 chr17:132008
rs9901478 rs12453152 rs9891894 rs9891903 chr17:132276 rs10871512
rs11657652 chr17:132364 rs35035943 rs4985586 rs9913843 rs35478781
rs9909445 rs12936617 chr17:133111 rs12949092 chr17:133392 chr17:133497
rs12451101 rs9889392 rs9901577 rs11650789 rs11650933 rs10871513
rs55995547 rs55856972 rs62052705 chr17:135075 rs55868427 rs12951184
rs12951413 chr17:135237 rs9915773 chr17:135524 chr17:135981 rs11652478
rs11653478 rs12946667 chr17:136397 chr17:136464 rs34700119 rs36047229
chr17:138726 rs28705960 chr17:139250 rs9891792 rs9912566 chr17:139747
chr17:139853 chr17:139901 chr17:139984 rs9912795 rs9905901 chr17:140586
rs12950277 rs9913719 rs11650366 rs9675256 chr17:141286 rs57803378
chr17:143043 rs7502760 rs7212943 rs6565707 rs7501694 rs12450463
rs7213496 rs12940213 rs12452413 chr17:144037 rs34724309 rs34223743
chr17:146378 rs11867532 rs34927789 rs11869552 rs28583833 chr17:147237
rs11658390 chr17:147332 chr17:147595 rs11655614 rs62053674 rs9902691
rs9893423 rs9903406 rs17879541 chr17:148623 rs57766060 chr17:149102
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rs9897769 rs9909725 chr17:78654024 rs12937511 chr17:78654554
[ reached getOption("max.print") -- omitted 60 rows ]

```

A somewhat sparser set of genotypes (HapMap phase II, genomewide 4 million loci) on chromosome 17 is archived as `g17SM`. This has a compact `Snpmatrix` encoding of genotypes.

```

> data(g17SM)
> g17SM

```

An object of class "Snpmatrix"

```

      rs6565733 rs1106175 rs17054921 rs8064924 rs8070440 rs3794811 rs8066551
NA06985      03      02      03      03      03      02      02
      rs7215271 rs7224313 rs7217319 rs17055015 rs4890199 rs10459967 rs4890183
NA06985      02      01      02      01      03      01      02
      rs11654491 rs1882990 rs4424950 rs7503116 rs1136388 rs1609550 rs12937885

```

NA06985	00	03	03	01	03	02	03
	rs7213008	rs7212865	rs10153238	rs11654695	rs8072649	rs8072804	
NA06985	01	03	03	03	03	03	
	rs11649979	rs12938802	rs11650641	rs1138504	rs11150884	rs9907477	
NA06985	01	01	03	01	03	02	
	rs7226358	rs8066107	rs9915268	rs8078223	rs9896436	rs4890192	rs8078929
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	rs4890194	rs9674467	rs8075084	rs4890171	rs4890197	rs4890198	rs12941826
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	rs8073847	rs3923018	rs11651800	rs3923017	rs11654890	rs11652984	
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	rs7213702	rs12449638	rs7217872	rs12937656	rs9908467	rs9896350	rs7207284
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	rs7222853	rs12602957	rs7223759	rs7221298	rs12452527	rs11150870	
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	rs4074549	rs11656610	rs7502120	rs12941632	rs4073769	rs7212603	
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	rs7208299	rs11869174	rs6565714	rs3934764	rs6565715	rs7215343	rs12942009
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	rs2465803	rs8078047	rs6502870	rs11657525	rs3926687	rs4790781	rs2716945
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	rs12952184	rs16944437	rs9900828	rs9903630	rs9904109	rs11871700	
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	rs3744579	rs3744580	rs3826450	rs16945280	rs4792166	rs972947	rs9896157
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	rs2011094	rs7212419	rs4791475	rs4792176	rs4791476	rs9890025	rs7218761
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	rs16940757	rs11650055	rs2322052	rs2322053	rs2874669	rs7217598	rs9913751
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	rs726800	rs1005637	rs1005639	rs6502283	rs8074072	rs17663499	rs4513137
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	rs11867181	rs2079627	rs8080210	rs11078169	rs11078170	rs11078171	
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	rs4508458	rs12453186	rs11652847	rs11654550	rs10521233	rs17587876	
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	rs11651688	rs11651718	rs765475	rs765476	rs917388	rs7222364	rs7222105
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	rs12449826	rs2322939	rs9890735	rs12450186	rs11658332	rs9914411	
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	rs11078176	rs9900362	rs7216617	rs2218343	rs2120187	rs11868265	
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	rs9910557	rs16948423	rs9890442	rs12937820	rs1867232	rs16948430	
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	rs16948435	rs12601543	rs12941937	rs16948439	rs7216216	rs12948848	
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	rs17590660	rs16948456	rs4519361	rs4542695	rs2322968	rs997205	rs16948476
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	rs4792396	rs7207162	rs9915220	rs17667266	rs2322969	rs1530361	rs1530358
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	rs1530357	rs9902668	rs9909073	rs9909353	rs4792397	rs4792398	rs8064349
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	rs9303099	rs1029688	rs1029687	rs7210165	rs11078224	rs11652668	
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	rs11078225	rs8079640	rs12943936	rs12945821	rs16949067	rs722554	
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	rs8071165	rs11078226	rs11871117	rs12450626	rs4792438	rs17616525	
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	rs16949074	rs9891372	rs17616591	rs12452978	rs17678774	rs11652402	
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	rs8073382	rs9905776	rs11657441	rs16949080	rs6502337	rs8065848	rs3785681
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	rs3785680	rs11868899	rs9910671	rs7210500	rs12603348	rs2323093	rs2323094
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	rs8073984	rs12449610	rs12937279	rs12939377	rs2323095	rs2323096	

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	rs2323097	rs2874958	rs1990234	rs9303100	rs16949103	rs7212977	rs8070339
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	rs8075612	rs8079642	rs8081414	rs12936411	rs2530377	rs12453546	rs2856183
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	rs2530376	rs2530375	rs9913639	rs2530373	rs2530370	rs2530368	rs2259118
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	rs2856185	rs16949118	rs2856147	rs3020869	rs12941439	rs2158978	
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	rs16949234	rs12449595	rs2529629	rs12453877	rs2529627	rs2856177	
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	rs2023485	rs9901316	rs2529626	rs917309	rs2856178	rs10521264	rs8077231
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	rs2529625	rs3826366	rs917308	rs9901549	rs12452172	rs3785662	rs3785659
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	rs12601148	rs4792446	rs1050214	rs2230355	rs11078233	rs11078234	
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	rs7214082	rs1802618	rs2071245	rs1050216	rs1050223	rs11869719	rs11869759
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	rs11869709	rs4792447	rs7211577	rs7212116	rs12951559	rs12944270	
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	rs12945766	rs12150130	rs12150136	rs4792448	rs11871019	rs8080585	
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	rs16949277	rs11656595	rs8065030	rs4792449	rs11655445	rs12946884	
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	rs17617684	rs7218697	rs7223903	rs17679866	rs4792453	rs4792454	rs2323221
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	rs9903896	rs8067063	rs1859905	rs1859904	rs17680043	rs2874993	rs7503943
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	rs12453856	rs12453899	rs11078236	rs11078237	rs12450424	rs16949314	
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	rs11868525	rs16949319	rs7214616	rs4792461	rs9911711	rs960296	rs3815271
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	rs4284690	rs4303583	rs4303584	rs4303585	rs4303586	rs1465243	rs1465242

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	rs7220012	rs755732	rs755730	rs733769	rs12942020	rs7223714	rs2190626
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	rs886864	rs886863	rs719470	rs16949359	rs9896731	rs2190625	rs11870163
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	rs4792467	rs4791571	rs886862	rs9890556	rs4791573	rs16949371	rs4791574
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	rs2323174	rs9907589	rs9908363	rs3785658	rs9303102	rs1005322	rs1005321
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	rs740379	rs11078240	rs4792468	rs4792469	rs3826365	rs9890648	rs758049
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	rs7221273	rs11870395	rs12373159	rs12103925	rs7222205	rs4792471	
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	rs8080590	rs726942	rs7211702	rs2108461	rs9900779	rs1015663	rs2058044
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	rs9890916	rs9891555	rs740376	rs6502345	rs11870724	rs9909862	rs720873
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	rs7222164	rs1859906	rs917310	rs1871784	rs7217818	rs11552190	rs1053326
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	rs2291208	rs2086515	rs6502346	rs2199998	rs7225272	rs7226075	rs2127998
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	rs16949420	rs1994029	rs8069341	rs17619418	rs17619424	rs11078245	
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	rs16949426	rs8077326	rs17692591	rs11657444	rs17692633	rs17619645	
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	rs9914530	rs3912261	rs3912262	rs3912263	rs3912264	rs11651598	rs11651699
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	rs9303104	rs3848445	rs9972938	rs16949435	rs9909883	rs9916577	rs9898158
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	rs2109168	rs2109169	rs2109173	rs8081226	rs8081719	rs9892049	rs9892569
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	rs12953125	rs10521277	rs9895361	rs12947004	rs12945756	rs1019153	
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	rs1019155	rs17704478	rs16950020	rs7221028	rs9890809	rs16950022	
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	rs16950027	rs4424942	rs16950031	rs9900688	rs1465268	rs16950032	

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	rs16940920	rs8074303	rs8074490	rs8074531	rs9901465	rs8074969	rs16950033
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	rs12941773	rs12936630	rs9890349	rs12602267	rs12602281	rs9899112	
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	rs4791613	rs8075196	rs17647512	rs11869796	rs8079915	rs8080696	
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	rs8080479	rs6502424	rs6502425	rs6502426	rs1005751	rs16950909	rs8067507
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	rs11078366	rs6502556	rs8068587	rs4985714	rs8066877	rs8070944	rs16961288
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	rs12944514	rs11658544	rs16960167	rs7214134	rs2428589	rs2428588	
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	rs12451469	rs2428580	rs2453614	rs16960177	rs9906930	rs7225055	rs7225894
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	rs2240097	rs2240096	rs7213572	rs8068853	rs7214851	rs8078268	rs4924996
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	rs8076975	rs2453603	rs8072992	rs7211758	rs7222869	rs8067420	rs1470318

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	rs11871259	rs2440153	rs2453580	rs751259	rs894680	rs12943918	rs8080953
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	rs2018675	rs2453583	rs735579	rs2453584	rs9905246	rs2440154	rs12451696
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	rs2440155	rs2453585	rs2453576	rs1808941	rs2014082	rs2453574	rs2453573
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	rs7219149	rs11650156	rs2247518	rs2289668	rs8076893	rs9909350	rs16960201
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	rs2453569	rs2453568	rs720252	rs16960202	rs16960203	rs2244280	rs2440150
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	rs1443460	rs2289669	rs16960206	rs2289670	rs8081204	rs9900821	rs8076891
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	rs8065082	rs11657807	rs2289667	rs2289666	rs11871177	rs716126	rs1961669
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	rs2253611	rs2250486	rs2453599	rs10735	rs3803838	rs2453594	rs2120273
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	rs2453589	rs2165894	rs7222948	rs2245724	rs2245639	rs2453586	rs2165895
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	rs7216938	rs9674673	rs2440161	rs11656199	rs12949521	rs2440162	rs2440163
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	rs2453602	rs17684040	rs4598966	rs2012843	rs2453604	rs1806922	rs11654072
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	rs7342960	rs11650399	rs12604069	rs12946324	rs8080984	rs2120274	
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	rs16960251	rs4273101	rs2453608	rs7405862	rs7502992	rs12941194	rs7215257
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	rs9914765	rs8079648	rs7225451	rs7210433	rs1470317	rs11871420	rs9889632
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	rs8064748	rs8074500	rs4925026	rs8065688	rs11871642	rs4621031	rs3888642
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	rs11204407	rs9901895	rs4925036	rs1004490	rs1004491	rs4646794	rs4646795
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	rs962801	rs962800	rs2072332	rs4646798	rs1034897	rs2386145	rs16960280
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	rs1800869	rs4646801	rs4646802	rs2108971	rs8073767	rs4646804	rs4244600
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	rs7216	rs7215	rs3760489	rs11868363	rs4646807	rs8074204	rs12937179

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	rs12453474	rs11658227	rs8081130	rs16960349	rs8064572	rs8079625	
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	rs4925044	rs16960360	rs12325921	rs7222445	rs9900497	rs4925045	rs758427
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	rs2891935	rs7213388	rs11656096	rs7206967	rs11657205	rs9910370	rs2010744
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	rs7214841	rs4924793	rs1006553	rs12948881	rs11650088	rs2108967	rs1006556
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	rs4319825	rs1042183	rs917520	rs2228100	rs3744695	rs3744694	rs3744693
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	rs3744692	rs3786036	rs2072330	rs2072329	rs9895030	rs4646790	rs2072328
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	rs887241	rs887240	rs887239	rs4646789	rs4646788	rs4646787	rs12951039
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	rs2072327	rs4646786	rs4646785	rs4646784	rs4646783	rs3760487	rs7221211
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	rs9905570	rs205094	rs1662214	rs1638522	rs205093	rs205090	rs176098
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	rs9897295	rs184006	rs205088	rs169512	rs9915902	rs11656704	rs9894723
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	rs157397	rs157398	rs169513	rs205103	rs205104	rs9905538	rs8064549
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	rs6587207	rs8080190	rs7224567	rs7224875	rs9915039	rs4925067	rs8079093
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	rs9901862	rs10459970	rs8082671	rs6587208	rs6587209	rs4577147	rs7210751
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	rs9914328	rs7221669	rs3909257	rs1182231	rs12946508	rs7219688	rs16960644
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	rs8072517	rs3930821	rs11656284	rs9908154	rs9907149	rs9916049	rs2958478
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	rs7223285	rs11657497	rs1564296	rs17052362	rs11656087	rs1985718	
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	rs7214074	rs2342184	rs7216763	rs9912295	rs17052370	rs2342183	rs12948022
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	rs4889746	rs8081093	rs8069215	rs11867688	rs899418	rs2880273	rs2880272
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	rs8076832	rs7359574	rs1121327	rs2169915	rs7502023	rs8079247	rs1842110
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	rs899414	rs11871520	rs755583	rs755584	rs2199698	rs4993505	rs12949684
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	rs4993506	rs4993507	rs4993511	rs981637	rs12051613	rs12601480	rs8069077
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	rs8066323	rs7215861	rs7215892	rs1871323	rs6565377	rs12943366	rs1159589
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	rs1842109	rs12450492	rs4393617	rs4889721	rs9989453	rs2169914	rs2169913
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	rs6565378	rs1985878	rs1985877	rs7218015	rs11651208	rs17052396	rs2061853
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	rs7225244	rs6565381	rs8068034	rs11150718	rs7350915	rs12940235	
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	rs12948134	rs2880292	rs12103516	rs11658486	rs8075964	rs7218889	
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	rs2169916	rs1877500	rs1817415	rs1382623	rs12950467	rs2219805	rs9897562
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	rs12937394	rs6565386	rs8072844	rs402052	rs3751916	rs2019216	rs8073228
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	rs907708	rs907707	rs9896042	rs2342216	rs12450390	rs1850565	rs8065425
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	rs8066357	rs1512846	rs12452224	rs12450074	rs907704	rs17052434	rs1518049
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	rs7215275	rs12940712	rs4889733	rs17808614	rs11150722	rs9891438	
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	rs8079620	rs12937428	rs7220319	rs12449520	rs4889742	rs1040269	rs932219
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	rs7212653	rs1915048	rs11150728	rs2002203	rs8076748	rs2077219	rs1829489
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	rs7213631	rs1818692	rs4889744	rs11868088	rs9908622	rs11869580	rs1829491
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	rs11868335	rs2203931	rs7222514	rs8070275	rs8066332	rs11658968	
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	rs8080725	rs7225129	rs12942556	rs11868559	rs12150105	rs12944067	
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	rs1850005	rs1515750	rs1973661	rs2292697	rs2292698	rs9807046	rs12453646
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	rs11080119	rs8079454	rs7503713	rs3930206	rs9748137	rs9748024	rs9893017
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	rs4302084	rs7213094	rs1976838	rs5015403	rs4795878	rs11868485	rs11653494
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	rs9910343	rs16966494	rs11867343	rs7218531	rs11656707	rs11871417	
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	rs2313050	rs4795077	rs7215009	rs4796099	rs1851271	rs7226210	rs7221571
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	rs12600900	rs12600912	rs2139942	rs11080048	rs11658274	rs9912637	
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	rs1969373	rs1521563	rs12103473	rs11657456	rs7225143	rs12453728	
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	rs7212623	rs11871008	rs2948534	rs2948533	rs2945384	rs2948532	rs10775412
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	rs4795816	rs4267373	rs9303666	rs9898153	rs9912493	rs2241906	rs1075952
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	rs9905566	rs3094272	rs4795835	rs4794975	rs12949932	rs3094274	rs732222
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	rs4239242	rs361499	rs4794976	rs16966434	rs3107064	rs8368	rs9899312

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	rs8075943	rs11080261	rs9899871	rs11080266	rs9896280	rs4523974	
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	rs9907600	rs9891469	rs12952498	rs4538061	rs4239246	rs9890882	rs4794996
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	rs11868072	rs6505406	rs4795911	rs7209966	rs10454091	rs10454092	
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	rs11080289	rs12948602	rs7218693	rs9901359	rs9908208	rs9897012	rs9897029
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	rs9901551	rs7208810	rs12952168	rs917631	rs16965715	rs11080124	
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	rs17803815	rs2058284	rs3764417	rs717663	rs7220213	rs9913111	rs4795549

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	rs216451	rs216452	rs186262	rs2874671	rs216455	rs216457	rs170053
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	rs315439	rs4795630	rs315440	rs1126172	rs1126173	rs12452086	rs1421131
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	rs385535	rs373531	rs17246595	rs9896472	rs9915783	rs952581	rs7223114
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	rs1948606	rs11657231	rs9303662	rs8081544	rs1908958	rs10432046	
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	rs10432047	rs10432048	rs12103815	rs8078963	rs6505334	rs4499288	
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	rs1391077	rs11651260	rs11651326	rs9914417	rs8081703	rs8080646	rs9916185
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	rs10459963	rs320643	rs9911125	rs9905033	rs12449358	rs320645	rs8081861
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	rs7207679	rs35024811	rs320628	rs320629	rs1504575	rs63953	rs63954
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	rs320631	rs7223147	rs963048	rs320633	rs320637	rs320638	rs320641

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	rs400843	rs445907	rs1875873	rs424892	rs447040	rs17836780	rs1874604
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	rs12449721	rs17249146	rs320642	rs2036537	rs9674859	rs3104299	rs7217704
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	rs2174341	rs12449923	rs17184727	rs12943787	rs12937449	rs12937459	
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	rs377066	rs412602	rs374430	rs431564	rs2645983	rs2656087	rs16963766
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	rs4795768	rs17836785	rs733136	rs452439	rs439783	rs9915690	rs4795769
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	rs12946336	rs2014285	rs2014268	rs17249181	rs11653379	rs7224450	rs950537
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	rs6505336	rs7501738	rs1504573	rs1394388	rs12449795	rs9901182	rs7503350
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	rs959338	rs12450971	rs11868983	rs11868989	rs10512443	rs7213724	
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	rs1394387	rs1394386	rs1394385	rs7223760	rs11080213	rs7219978	rs7224859
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	rs1504582	rs16968252	rs924846	rs924847	rs1007034	rs1007035	rs16968253
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	rs1007033	rs17184825	rs1039578	rs1979909	rs4795770	rs1394393	rs1394394
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	rs1394395	rs6505337	rs7220131	rs11652103	rs11656759	rs7215745	rs8074678
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	rs6505338	rs9896958	rs2347154	rs905754	rs871764	rs17782182	rs1394392
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	rs1394391	rs931796	rs1995526	rs1995525	rs1504581	rs17184873	rs8072171
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	rs1875875	rs931795	rs1504580	rs11080214	rs7224966	rs7226138	rs7207448
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	rs12150421	rs7207801	rs11867162	rs1021892	rs12946750	rs1021891	
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	rs2089164	rs12941575	rs7225320	rs7220791	rs8074495	rs11652948	rs1504577
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	rs1394389	rs12946200	rs11652495	rs1394390	rs11658120	rs12951547	
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	rs4353517	rs9895229	rs7207476	rs11080216	rs4794947	rs11657729	
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	rs17184908	rs10853155	rs9898140	rs11080217	rs4795778	rs9914451	
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	rs11080218	rs12950864	rs11655499	rs12601602	rs8073613	rs7207391	

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	rs1504579	rs8078262	rs17185000	rs8076691	rs8082353	rs8076841	rs16968314
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	rs4794949	rs4795781	rs16968318	rs17782332	rs1827650	rs17782343	
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	rs17185036	rs16963769	rs9901960	rs9902936	rs17185057	rs16968321	
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	rs17185084	rs9904433	rs7213646	rs8075266	rs4572456	rs17836803	rs2036535
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	rs9915725	rs4795783	rs4795784	rs4795785	rs1472742	rs12953219	rs1504576
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	rs9709314	rs9709422	rs9894658	rs4795791	rs7502868	rs11656800	rs11656544
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	rs9913678	rs12940736	rs1354489	rs972860	rs12162163	rs2347151	rs4286149
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	rs13341020	rs7221119	rs12602581	rs2347155	rs905752	rs9903070	rs11656936
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	rs11657983	rs12450871	rs1123025	rs1123024	rs12451584	rs7210023	
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	rs17836818	rs12450545	rs9898160	rs4510072	rs4794950	rs9892208	
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	rs9914228	rs9908799	rs7219482	rs12603550	rs7221002	rs12601996	rs1995523
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	rs12952607	rs952541	rs1394384	rs952540	rs12601163	rs869097	rs2881565
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	rs9635766	rs12944010	rs17836824	rs1472740	rs1472741	rs12937545	
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	rs4513141	rs7208436	rs7209964	rs1504570	rs1875872	rs1857737	rs17249479
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	rs9915618	rs7222281	rs7207388	rs1504571	rs1553495	rs9894197	rs1553496
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	rs4795795	rs4795797	rs17249521	rs12602517	rs12600630	rs12600538	
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	rs10512445	rs17249577	rs1347351	rs17249591	rs12103532	rs1865392	
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	rs12185231	rs12185267	rs9909130	rs4794966	rs977296	rs977295	rs7502177
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	rs16968774	rs11869137	rs12938529	rs2046898	rs2046899	rs4474738	
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	rs2347558	rs2347559	rs16968785	rs4795826	rs6505373	rs7207102	rs989956
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	rs989957	rs9897152	rs6505374	rs2029531	rs12938719	rs989353	rs7223612
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	rs16969415	rs17809012	rs3744508	rs1860184	rs3815341	rs4795898	rs1019109
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	rs12601294	rs12601396	rs714910	rs1860182	rs1860181	rs12453516	rs9913706
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	rs4795904	rs8081356	rs1860180	rs8073784	rs17809115	rs3919504	rs7504095

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	rs11656007	rs11656109	rs11652256	rs8075846	rs9905791	rs2215185	
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	rs12451323	rs2041190	rs2215184	rs16969449	rs4795908	rs16969454	
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	rs12453746	rs16969457	rs12449657	rs12452741	rs4100073	rs1233653	
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	rs12602707	rs12602722	rs885691	rs12453143	rs1233650	rs3890641	rs3138034
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	rs8082480	rs8081376	rs4374216	rs4795910	rs12449308	rs3138035	rs3138036
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	rs3138037	rs1133763	rs16969479	rs4310920	rs11575056	rs11575057	
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	rs1431991	rs3136674	rs3136675	rs3136676	rs3136677	rs159313	rs2072069
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	rs2072070	rs159314	rs159315	rs159316	rs11575025	rs159317	rs159318
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	rs867132	rs867133	rs159280	rs159284	rs159285	rs159286	rs159288
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	rs7502772	rs12603353	rs12603965	rs17653433	rs17574949	rs159289	rs159290
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	rs159305	rs159306	rs159307	rs4552064	rs1347000	rs1367954	rs159308
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	rs212462	rs212463	rs212464	rs212465	rs212466	rs169862	rs167171
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	rs159247	rs150509	rs150511	rs150512	rs150514	rs2118232	rs150516
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	rs159245	rs150521	rs4795917	rs7217062	rs159244	rs16969797	rs17577327
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	rs159236	rs210812	rs159237	rs1036494	rs1036492	rs11080273	rs159240
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	rs9907428	rs11658990	rs9916329	rs1978685	rs4041613	rs4795921	rs159242
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	rs159243	rs183309	rs12603249	rs4795923	rs9912429	rs1431994	rs969979
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	rs210832	rs210833	rs210834	rs1030603	rs12950822	rs212448	rs191931
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	rs176931	rs8065093	rs295066	rs295067	rs8076080	rs12602394	rs12951119
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	rs17614930	rs12947419	rs1431993	rs295094	rs7214235	rs11651716	rs7216203
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	rs213136	rs12952020	rs8064381	rs213137	rs213138	rs9916697	rs213139
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	rs213140	rs172482	rs1437214	rs190038	rs4306569	rs169889	rs11653563
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	rs213141	rs213142	rs7214683	rs4795929	rs9898608	rs4795004	rs9899090
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	rs887229	rs887228	rs4996565	rs16970084	rs11654085	rs11080285	rs7215934
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	rs12938657	rs12950814	rs968891	rs9916771	rs16970282	rs9896407	rs8074211
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	rs17666879	rs4795998	rs8067477	rs4795999	rs12451550	rs11080297	rs723704

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	rs2159223	rs9898213	rs9899592	rs887081	rs12453075	rs4795044	rs12951090
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	rs11655495	rs4796000	rs12451007	rs758302	rs16970352	rs758301	rs7207633
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	rs7214396	rs11871853	rs8076256	rs9893071	rs16970359	rs11080299	
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	rs8082403	rs740569	rs740055	rs17603809	rs7216020	rs4796002	rs16970375
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	rs16970378	rs9652888	rs16970379	rs7225050	rs7225391	rs714895	rs11080300
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	rs9892982	rs2339211	rs9898801	rs11652524	rs9674621	rs11652046	rs9894585
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	rs730547	rs12051815	rs2009052	rs11080301	rs1008094	rs7222275	rs4616327
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	rs10853173	rs8066240	rs11080302	rs6505432	rs6505433	rs7213106	
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	rs11080303	rs10512465	rs4796004	rs11080304	rs17544779	rs11656880	
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	rs11653855	rs8072551	rs715111	rs11654328	rs7208329	rs11655777	
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	rs11655780	rs1860199	rs1860198	rs1153926	rs16970398	rs8068834	rs8069018
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	rs11080305	rs7221264	rs11650778	rs16970400	rs234808	rs11650925	
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	rs12936984	rs17627603	rs1482102	rs16970402	rs11657254	rs734612	rs758299
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	rs17544975	rs8081228	rs234822	rs1005596	rs53782	rs11652355	rs4796009
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	rs12938847	rs11869882	rs11652634	rs11656251	rs11656105	rs11080306	
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	rs4796010	rs9895219	rs12150271	rs12150241	rs234824	rs17627806	
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	rs12941800	rs11080308	rs9674871	rs714666	rs739741	rs744298	rs11080309
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	rs9675202	rs1564562	rs7216238	rs12948069	rs12938711	rs2840067	
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	rs11651360	rs7359659	rs7359660	rs12942949	rs17545366	rs234828	
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	rs10445389	rs12601965	rs12600682	rs234829	rs8067780	rs4796011	rs170923
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	rs12945685	rs12945921	rs234831	rs11652590	rs17545471	rs9893892	

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	rs234835	rs11658261	rs11871805	rs17146	rs16970422	rs4796012	rs11080311
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	rs234818	rs234819	rs17545903	rs2339116	rs11658047	rs4796013	rs7223630
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	rs7211280	rs7210677	rs900206	rs11080312	rs900207	rs754791	rs12601180
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	rs12953044	rs12452723	rs7213591	rs7211660	rs7213451	rs11651066	
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	rs12449962	rs7220083	rs7213132	rs975126	rs6505435	rs11653582	rs12451451
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	rs4796014	rs12945282	rs1482104	rs9910965	rs4280300	rs7209401	rs11655339
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	rs4796020	rs16970461	rs11868737	rs12937810	rs11868554	rs2062101	
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	rs8249	rs7208342	rs8075549	rs8076878	rs4041564	rs2339120	rs1351554
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	rs3135991	rs3135992	rs3135993	rs3135996	rs3135997	rs3135998	rs3136000
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	rs3136021	rs3136022	rs3136023	rs3136025	rs3136026	rs4986974	rs3136028
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	rs9913773	rs9892424	rs6505438	rs8067493	rs2240074	rs10853174	rs3926358
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	rs9914089	rs16970607	rs10491117	rs16970611	rs3937429	rs11868399	
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	rs11080320	rs9891230	rs11650161	rs12947947	rs9914109	rs4796032	
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	rs2622524	rs9893542	rs16970808	rs2671822	rs2622525	rs2671820	rs11080335
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	rs17550632	rs12452797	rs17637907	rs2840044	rs321601	rs9891887	
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	rs17550716	rs11653310	rs16971128	rs11655098	rs9891563	rs12600662	
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	rs183435	rs2604845	rs16971207	rs2604844	rs225249	rs17669281	rs17606150
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	rs8065607	rs8069816	rs4794762	rs4794763	rs7212656	rs4794764	rs9904684
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	rs11653037	rs17138919	rs2176395	rs4794766	rs2138733	rs8080584	rs1914365
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	rs7222985	rs8068600	rs11867558	rs8070847	rs9900623	rs9895316	rs8074124
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	rs3803749	rs2471623	rs3902482	rs2471624	rs3884068	rs8070036	rs2429994
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	rs11079059	rs7219106	rs12450778	rs12949337	rs12942093	rs7221033	
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	rs228274	rs4907	rs228275	rs668461	rs9903126	rs11656344	rs2306882
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	rs228286	rs3744070	rs2241014	rs228287	rs228288	rs228289	rs228290
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	rs16531	rs16534	rs2240083	rs16537	rs521633	rs16530	rs3025213	rs559502
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	rs9908131	rs8069194	rs7223438	rs6503507	rs4511574	rs11078898	rs7221875
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	rs7208487	rs8065896	rs7215002	rs8073144	rs9906612	rs8077629	rs8077259
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	rs10491128	rs12600751	rs8076546	rs9904919	rs6503512	rs3814885	rs6503513
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	rs7211837	rs1139825	rs4795357	rs4795358	rs11656614	rs7501488	rs7226222
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	rs4795369	rs11655550	rs4533315	rs12938099	rs4611492	rs9896487	
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	rs11654535	rs4390625	rs12940881	rs11078901	rs11078902	rs11078903	
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	rs12449852	rs4426376	rs9893757	rs9894037	rs12948906	rs11870631	
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	rs8077658	rs2018026	rs6503518	rs12943456	rs11078907	rs7225096	
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	rs12936996	rs12937013	rs8069155	rs11868837	rs7503705	rs11078912	
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	rs11078913	rs2303315	rs4795379	rs9916852	rs11658678	rs8065963	rs4404103
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	rs7226073	rs4795380	rs8069074	rs12450559	rs4239222	rs7503069	rs16965156
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	rs11657058	rs11657153	rs11654018	rs2303316	rs12947506	rs7503377	
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	rs7216086	rs7342947	rs9972899	rs17604809	rs11078915	rs6503521	
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	rs12938115	rs4795384	rs4488484	rs12602067	rs12944298	rs7503195	
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	rs8081144	rs7218361	rs903507	rs8182252	rs7224759	rs1874226	rs11653404
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	rs4795385	rs11657812	rs9909879	rs412430	rs1619021	rs1877030	rs388548
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	rs3907837	rs998480	rs9916503	rs9889354	rs380373	rs12453736	rs12453682
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	rs14050	rs2952151	rs2941503	rs907087	rs2247862	rs903502	rs2941504
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	rs1565922	rs2934955	rs2934954	rs2934953	rs2934952	rs2941505	rs2941506
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	rs9892376	rs2517954	rs2517955	rs2517956	rs2517961	rs12601489	rs8182267
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	rs9911069	rs9908983	rs8076347	rs12942660	rs2060941	rs9910852	rs9911017
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	rs12946188	rs12946792	rs16965360	rs3816470	rs9913769	rs12945253	
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	rs3169572	rs2278894	rs7942	rs4378650	rs8076131	rs9910635	rs12603332
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	rs9916279	rs17855429	rs8066582	rs8080546	rs11652139	rs11658328	
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	rs25645	rs2227331	rs12602956	rs2827	rs1042657	rs2227332	rs1042658
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	rs2227334	rs1045929	rs12309	rs709592	rs709591	rs16965540	rs2270401
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	rs9915684	rs7503939	rs9916158	rs2302775	rs2302774	rs8071421	rs9709063
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	rs16965916	rs9902392	rs3136695	rs3136694	rs2229095	rs2023906	rs3136689
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	rs588019	rs2290065	rs3136688	rs16965949	rs3136687	rs11574664	rs11574663
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	rs11078949	rs1018953	rs3136686	rs3136685	rs7218603	rs12453886	
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	rs12603336	rs7221109	rs8074179	rs803129	rs9895632	rs9894823	rs757411
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	rs2429549	rs16966134	rs2462961	rs12946793	rs12945784	rs8068810	
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	rs17574228	rs7521	rs10445372	rs7502673	rs11870461	rs7350928	rs17574361
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	rs17652961	rs17574425	rs7220988	rs1076222	rs1078997	rs7212164	rs7350980
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	rs4597358	rs17574604	rs17653162	rs16940834	rs17653193	rs17653211	
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	rs12185243	rs8077487	rs11079729	rs12150542	rs12150090	rs7221390	
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	rs1102461	rs858677	rs701982	rs11570480	rs221605	rs11570475	rs11570466
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	rs2734274	rs2277633	rs2696245	rs2277634	rs2586488	rs1800215	rs2075559
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	rs16948767	rs8179178	rs2696249	rs2696250	rs2586495	rs2586498	rs1057297
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	rs2696298	rs11652870	rs12150329	rs7223741	rs11079902	rs9903154	
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	rs12938283	rs1881141	rs1881140	rs10853113	rs2586440	rs2463496	
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	rs12941381	rs12951961	rs8067128	rs2696280	rs9911114	rs8082231	rs2920417
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	rs4794124	rs2586458	rs2696261	rs9913213	rs4994726	rs11079905	rs2246629
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	rs12948932	rs1881138	rs4793645	rs2141280	rs2696259	rs2250422	rs7221964
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	rs12601268	rs12326011	rs11650280	rs12945508	rs17572837	rs12150297	
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	rs17651736	rs9890652	rs9894096	rs11870110	rs12450083	rs12947199	
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	rs7226059	rs9911801	rs12947122	rs17651875	rs7223917	rs8080761	rs1001475
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	rs1005513	rs12952336	rs9909668	rs1558252	rs11650085	rs11651252	
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	rs7207090	rs8078191	rs1558253	rs17651988	rs9303572	rs880178	rs4793683
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	rs10514981	rs16949637	rs12939771	rs9914104	rs11652793	rs2215290	
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	rs16949644	rs9909686	rs2318782	rs16949649	rs3760467	rs3760468	rs3760469
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	rs2302254	rs16949654	rs11556834	rs11868380	rs2041296	rs2159359	
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	rs2318784	rs2318785	rs12941593	rs4605213	rs3744659	rs8073005	rs3515
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	rs16949672	rs9894098	rs4793686	rs929482	rs8069453	rs11652695	rs11653287
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	rs12946936	rs16949702	rs9915099	rs9910086	rs9789064	rs2079883	rs9910220
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	rs7212007	rs9905051	rs12453596	rs11079947	rs8076111	rs12950750	
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	rs12950137	rs12943424	rs12943742	rs12951858	rs9896627	rs4793689	
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	rs12937069	rs12938251	rs11079950	rs16949732	rs2191443	rs11653126	
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	rs16949734	rs8076463	rs7211731	rs9911123	rs9897204	rs8080145	rs9906719
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	rs10514982	rs7213331	rs7502980	rs9889715	rs3786007	rs8067441	rs6504702
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	rs12941969	rs12948421	rs9893020	rs17575641	rs917654	rs11867403	
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	rs4794230	rs1034922	rs1034923	rs8082469	rs8074198	rs8078014	rs9904925
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	rs9910669	rs11868907	rs9889963	rs9905355	rs9897304	rs2017945	rs9906328
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	rs9892205	rs1005676	rs1005677	rs16949860	rs740704	rs9916205	rs758522
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	rs16950626	rs7222418	rs11655338	rs202132	rs9303593	rs11651107	rs7219047
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	rs7215018	rs16950631	rs7225179	rs7219262	rs7207077	rs7216689	rs9906977
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	rs202139	rs7219884	rs9907127	rs6504751	rs11655258	rs9915777	rs11658806
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	rs11650453	rs11659117	rs11649760	rs8077830	rs8082059	rs7221231	
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	rs1501268	rs16950712	rs878435	rs8075251	rs8071064	rs17666563	rs8071898

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	rs11870299	rs9675273	rs7218104	rs9674802	rs7220115	rs12150424	
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	rs202122	rs8082027	rs17590785	rs202121	rs202120	rs202119	rs202118
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	rs172107	rs188028	rs9916828	rs2109453	rs2109454	rs183246	rs7503693
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	rs12940614	rs203022	rs7502229	rs203025	rs203026	rs11871480	rs6504753
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	rs203043	rs203044	rs203045	rs385940	rs4262991	rs1501252	rs7215008
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	rs203049	rs4794315	rs4794316	rs1501253	rs203050	rs7350958	rs7350960
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	rs16957225	rs16957230	rs11654202	rs9915352	rs17820342	rs7208145
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	rs987313	rs1014267	rs11650061	rs7224952	rs16957237	rs9899492 rs8082082
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	rs12453043	rs11079482	rs758519	rs8069431	rs16946370	rs8073744	
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	rs17746094	rs17746153	rs1005062	rs1985394	rs1003783	rs2286568	rs2286566
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	rs1860339	rs9910639	rs16946471	rs1860336	rs3901444	rs6504124	rs7504097
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	rs7216408	rs3999623	rs4968744	rs6504134	rs9903993	rs7224903	rs7226117
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	rs12709426						
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	rs12709430	rs1987693					
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	rs3020619	rs4080076	rs5388	rs6174	rs3744287	rs4341800	rs2001344
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	rs2005132	rs2320125	rs2003549	rs2286565	rs16947270	rs9911257	rs1860334
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	rs196909	rs196910	rs196911	rs196912	rs8077780	rs196913	rs196914
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	rs9897942	rs196915	rs196917	rs2302238	rs196918	rs196919	rs196920
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	rs9912097	rs196922	rs196923	rs196924	rs77684	rs9908611	rs123206
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	rs9890717	rs196929	rs9914491	rs2021746	rs196933	rs17688830	rs9904640
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	rs7222333	rs11655941	rs9899048	rs7208168	rs7208494	rs1833344	rs17621950
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	rs7211481	rs7212901	rs1421033	rs6416948	rs7212898	rs6416949	rs8074158
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	rs2318868	rs1592658	rs1592659	rs2318869	rs7218844	rs2024275	rs2024274

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	rs1395826	rs1395825	rs17713225	rs11870521	rs9899635	rs7221351	rs740804
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	rs2218352	rs2197245	rs7222793	rs1443263	rs2165840	rs4968965	rs8078168
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	rs17744276	rs980423	rs17682084	rs1470286	rs17682138	rs9905404	rs1470294
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	rs1838101	rs12451154	rs16973376	rs11652518	rs7218957	rs4148012	
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	rs3826429	rs9896422	rs3744491	rs2120193	rs6501834	rs8070768	rs8078836

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	rs4148009	rs8068987	rs16973400	rs894594	rs4968966	rs6501835	rs4148008
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	rs8068204	rs12952511	rs12945133	rs12945184	rs7211979	rs4147997	
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	rs3744494	rs3744495	rs3744496	rs11653438	rs4147996	rs1373068	rs1373067
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	rs6501851	rs9302995	rs7209220	rs4147994	rs4147993	rs4147992	rs16973424
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	rs9907353	rs16973430	rs4147989	rs7221939	rs4147988	rs12150510	
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	rs12149992	rs4147983	rs9893781	rs6501870	rs12149981	rs4147982	rs4147981
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	rs6501873	rs7212686	rs1344213	rs767690	rs4147980	rs4147979	rs4147978
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	rs4147977	rs4147976	rs4147975	rs4147973	rs11656365	rs3826430	rs16973446
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	rs10512521	rs4147962	rs4147961	rs4147957	rs4147956	rs887380	rs4147953
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	rs10852774	rs9905330	rs7207730	rs7207748	rs9896819	rs1121077	rs8080973

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	rs16973495	rs16973499	rs1984722	rs2159435	rs11650611	rs7217379	
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	rs12941842	rs9907847	rs11654323	rs2542215	rs817126	rs9889277	rs16973883
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	rs1011548	rs4310935	rs4310936	rs494946	rs509830	rs568354	rs16973895
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	rs16974195	rs3952613	rs12601271	rs9674886	rs929212	rs9892801	rs9892002
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NA06985	02	03	03	02	01	03	03
	rs12936389	rs9897858	rs2158039	rs11077453	rs7217139	rs2947866	rs2947865
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	rs2947864	rs8081060	rs8067819	rs2905447	rs2078968	rs7208930	rs4556831
NA06985	02	01	03	02	02	02	01
	rs2947863	rs2009910	rs2188782	rs8074895	rs2905443	rs2905442	rs763698
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	rs2947862	rs10445226	rs10445206	rs10445207	rs9903306	rs2947887	
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	rs16974253	rs2905439	rs1121381	rs2428347	rs7214397	rs17762511	rs7224395

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	rs2947885	rs7211272	rs7502523	rs9913573	rs2365776	rs2905438	rs7502851
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	rs6501341	rs16974265	rs4381637	rs4381638	rs12937601	rs17762595	
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	rs8064791	rs2905370	rs543279	rs2214207	rs2188783	rs4506945	rs471194
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	rs4019941	rs7502257	rs4307918	rs1079767	rs8066963	rs8071684	rs11868456
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	rs2188698	rs12949316	rs2947879	rs1157845	rs12942463	rs16974282	
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	rs16974286	rs7208359	rs7208086	rs7226266	rs16974294	rs2905364	rs8070789
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	rs2905363	rs17689719	rs2905362	rs7209163	rs7214418	rs2214169	rs12944247
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	rs2157988	rs2051734	rs2285572	rs10512528	rs2947872	rs16974315	
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	rs12951576	rs9895917	rs8182257	rs2947871	rs2947870	rs1858969	rs2947869
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	rs1119753	rs1119752	rs16966924	rs2947868	rs2012628	rs2012061	rs2947883
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	rs12451012	rs2189757	rs2947876	rs2189756	rs3919477	rs2906086	rs2947880
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	rs12601748	rs1967299	rs1859426	rs12947839	rs8078070	rs11077460	rs956255
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	rs4488494	rs12939860	rs7222686	rs16974335	rs16974337	rs10445208	
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	rs8071754	rs8070733	rs2189755	rs4141190	rs4141192	rs8077406	rs2107606
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	rs4968863	rs1473120	rs2057823	rs2057822	rs16974356	rs12452498	
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	rs11868063	rs757531	rs757530	rs11652982	rs11654389	rs8066785	rs8066367
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	rs8071337	rs12453583	rs2366015	rs12452449	rs2366016	rs7225725	rs9900638
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	rs7209503	rs4968867	rs9891669	rs12450634	rs12451817	rs8074145	rs9901947
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	rs17690625	rs8077452	rs12941653	rs997095	rs16974368	rs8068410	rs8068479
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	rs8074261	rs11077463	rs9913873	rs7210514	rs9911208	rs12600841	rs8068581

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	rs12150482	rs4561512	rs997284	rs16974375	rs11870477	rs8072462	rs1468322
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	rs1987598	rs970561	rs12602917	rs16974392	rs7212316	rs7213660	rs6501346
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	rs8074693	rs6501347	rs9916704	rs11867679	rs8081453	rs8064482	rs990766
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	rs9915293	rs9907055	rs7214875	rs7221122	rs16974415	rs9900551	rs2214160
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	rs16974417	rs1029413	rs9895820	rs12940437	rs9911585	rs8079773	
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	rs12949999	rs9909198	rs6501349	rs11077465	rs9897717	rs9897738	rs9896923
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	rs8068469	rs9302904	rs9898541	rs9898758	rs11871026	rs10512530	rs7222397
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	rs11650517	rs12950334	rs12936002	rs12943426	rs7214110	rs12943751	
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	rs7219650	rs12601403	rs16974435	rs8077738	rs12949859	rs9892111	
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	rs9892141	rs9909427	rs9646390	rs8080719	rs8068409	rs11077467	rs714768
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	rs714770	rs9909532	rs16974450	rs974654	rs7210327	rs9898430	rs9891878
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	rs972846	rs9915890	rs9915283	rs12943826	rs2106608	rs2157981	rs12103827
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	rs739551	rs739550	rs6501354	rs6501355	rs9902593	rs9896999	rs1024422
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	rs1024421	rs1024420	rs2886549	rs4459587	rs1468165	rs7220240	rs7219349
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	rs7220878	rs2366021	rs9890257	rs1018883	rs1018882	rs9302905	rs6501356
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	rs9302906	rs9302909	rs2188661	rs2188660	rs7224273	rs7223426	rs12601734
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	rs3744488	rs747886	rs739549	rs739548	rs9899484	rs2106607	rs10512532
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	rs179929	rs179928	rs12948375	rs179927	rs179925	rs8066344	rs8066497

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	rs179922	rs179921	rs179920	rs179919	rs9635665	rs9635666	rs179918
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	rs179915	rs179913	rs9674477	rs6360	rs8078617	rs179903	rs180145 rs180144
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	rs180142	rs180139	rs180138	rs180135	rs8067741	rs8077328	rs180134
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	rs180133	rs180117	rs9909431	rs180116	rs9896083	rs180113	rs9898445
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	rs9897084	rs9898891	rs9897472	rs180112	rs16974626	rs7217278	rs180110
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	rs8071763	rs180109	rs180108	rs180107	rs8071899	rs12944193	rs16974638
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	rs16974642	rs7220016	rs4322711	rs9911187	rs9890562	rs180106	rs714272
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	rs7211227	rs7350969	rs7350970	rs13342174	rs180103	rs180102	rs16974658
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	rs16974662	rs13342669	rs13342680	rs8066354	rs7222428	rs2106611	rs180100
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	rs9891420	rs180076	rs9895362	rs180074	rs9896571	rs180073	rs9904930
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	rs9904038	rs180072	rs9913799	rs12948136	rs180068	rs180067	rs180066
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	rs9896547	rs118774	rs1024423	rs7214067	rs6501357	rs180061	rs2106610
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	rs1978104	rs8065941	rs180055	rs1106977	rs16974724	rs180054	rs2214161
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	rs8073347	rs9892612	rs9891051	rs10512533	rs1987916	rs180053	rs16974737
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	rs9907896	rs180052	rs12453357	rs8080450	rs9895890	rs8079591	rs17699266
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	rs17699296	rs180051	rs180050	rs16966966	rs390094	rs3815180	rs10512534
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	rs142464	rs1079965	rs142463	rs180160	rs6364	rs8077917	rs10451223
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	rs180162	rs16974854	rs180163	rs180165	rs180167	rs180168	rs180170
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	rs180171	rs180172	rs180181	rs180184	rs16974855	rs11871263	rs180186
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	rs12600653	rs11077470	rs11656883	rs9910533	rs11652259	rs2215006	
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	rs4519370	rs1013996	rs7223525	rs1013995	rs7209397	rs2190605	rs917299
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	rs2108437	rs4141238	rs8070382	rs3760394	rs3760393	rs11656778	rs1990197
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	rs9916313	rs9907952	rs8080326	rs8076244	rs2886630	rs8081626	rs8080091
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	rs1024574	rs968231	rs968232	rs7210827	rs8068029	rs7216332	rs4436822
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	rs9905061	rs8075605	rs9910249	rs8077601	rs8077604	rs8080332	rs8082049
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	rs8067556	rs8081648	rs8068539	rs8068704	rs2024053	rs6501363	rs4246424
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	rs12709250	rs4433847	rs9892289	rs2886632	rs7207387	rs7207528	rs6501367
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	rs7222323	rs7222352	rs7223856	rs11077473	rs11077474	rs11077475	
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	rs7209456	rs6501377	rs7212038	rs8073266	rs8077783	rs9906269	rs9913034
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	rs9892291	rs9892758	rs3922321	rs9895243	rs8074090	rs8079768	rs9909905
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	rs17775002	rs8069323	rs8069098	rs9907022	rs8078612	rs12943869	
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	rs16975204	rs9909756	rs9902217	rs11651001	rs1978209	rs16975212	
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	rs7209041	rs6788	rs3744487	rs7225830	rs8078418	rs2366489	rs2158967
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	rs17702078	rs758036	rs12949270	rs7217293	rs7217947	rs4405595	rs4497742
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	rs11077477	rs11077478	rs8066863	rs9889883	rs9897832	rs236512	rs993242
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	rs236513	rs1468472	rs7221086	rs173135	rs9302914	rs9302915	rs9895478
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	rs9894661	rs3815306	rs643637	rs1544489	rs1544490	rs4328485	rs236518
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	rs236523	rs1514235	rs236524	rs236525	rs11077480	rs9898954	rs236527
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	rs236528	rs638538	rs236529	rs12944409	rs236530	rs9902679	rs236531
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	rs9895144	rs9914814	rs236533	rs657282	rs656918	rs656367	rs9913208
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	rs7217871	rs7218404	rs7210918	rs7210740	rs11077483	rs236597	rs8077356
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	rs6501382	rs9912955	rs236564	rs236565	rs10512538	rs12150626	rs11868788
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	rs12936484	rs12943968	rs8064542	rs8064570	rs9896020	rs11870865	rs999978
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	rs236567	rs9916584	rs1969242	rs1019064	rs236549	rs9905182	rs9914801
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	rs236550	rs4538053	rs236551	rs236552	rs236553	rs236554	rs236555
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	rs236556	rs9896235	rs236557	rs236558	rs236559	rs9891872	rs7213181
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	rs9908872	rs9914455	rs236561	rs236562	rs12942828	rs4346246	rs12943216
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	rs236563	rs9905884	rs11652180	rs9903628	rs992072	rs7502061	rs9899175
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	rs236511	rs4968887	rs16975398	rs2529681	rs16975401	rs5014129	rs236499
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	rs236504	rs236505	rs7223705	rs171036	rs9894659	rs1399185	rs1355915
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	rs8075271	rs8076950	rs631407	rs17714860	rs17777095	rs7210212	rs11650230
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	rs1014216	rs1014217	rs11870515	rs9899958	rs11870467	rs7212475
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	rs9907236	rs2215059	rs4793355	rs8076723	rs17179656	rs16976696
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	rs10512569	rs10512570	rs10512571	rs11654195	rs12945199	rs12943436
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	rs16976703	rs16976704	rs16976707	rs17766905	rs16976709	rs12449752
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	rs9893232	rs12941721	rs17226067	rs17825774	rs17825799	rs7224905
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	rs12939014	rs12940661	rs12949295	rs12941681	rs9635667	rs9635668
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	rs16977095	rs8076087	rs9909461	rs8075603	rs8079403	rs4422015	rs16977101

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	rs17181304	rs17779161	rs2159009	rs4793406	rs4793407	rs4793408	rs4793409
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	rs8068580	rs1859929	rs1859928	rs4793276	rs7220150	rs4793277	rs12451603
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	rs2713973	rs2567544	rs9709284	rs16977367	rs8077412	rs2713974	rs962572

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	rs2713980	rs7224611	rs16977369	rs9891327	rs11651312	rs8073197	rs9906450
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	rs16977376	rs2435984	rs9906808	rs2859523	rs2915446	rs1864682	rs2567538
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	rs7226195	rs16977377	rs7211612	rs2567533	rs6501565	rs934341	rs1864681
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	rs12942980	rs12450445	rs11077634	rs2567524	rs2060097	rs9907286	
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	rs2567517	rs2714016	rs2714017	rs2714018	rs2567515	rs2714019	rs2567514
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	rs7405952	rs2345421	rs6501634	rs8070326	rs6501635	rs8070370	rs8070503
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	rs7225634	rs7221985	rs12939296	rs12937218	rs12449408	rs4789619	
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	rs7213751	rs9908733	rs9909121	rs7218487	rs7219778	rs7222528	rs12950389
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	rs4789621	rs4789622	rs7224502	rs4789623	rs7208214	rs7208526	rs11871493
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	rs12950851	rs17185021	rs9893938	rs11870889	rs7213360	rs4789638	
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	rs12452761	rs9891430	rs7222264	rs11651551	rs7501578	rs12940715	
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	rs748872	rs2101224	rs2101223	rs12939511	rs9914644	rs11868900	rs1564732
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	rs9899590	rs3853368	rs11656163	rs16977868	rs949628	rs9908672	rs1319805
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	rs10468449	rs2169628	rs12950777	rs12602594	rs5021043	rs4239007	
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	rs12453337	rs12602757	rs9302974	rs9302975	rs4789631	rs4563067	rs7219987
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	rs4789632	rs746397	rs729191	rs1870988	rs4789633	rs4393601	rs3892366
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	rs2382841	rs4435291	rs9893810	rs4789634	rs4789635	rs8070845	rs7219464
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	rs4789641	rs4789642	rs8081928	rs9899862	rs9900778	rs9906888	rs8069056
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	rs9897994	rs820227	rs4789225	rs12453828	rs7208296	rs820164	rs7216509	

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	rs2584104	rs2857582	rs8079267	rs8079424	rs8079901	rs820172	rs8064336
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	rs11657833	rs11759	rs8669	rs743685	rs1008177	rs1051486	rs871443
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	rs743554	rs12602523	rs820386	rs7209235	rs11649838	rs4485425	rs12450349
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	rs3687	rs7342	rs1060120	rs10338	rs1060113	rs2410866	rs2071654
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	rs12600868	rs10221244	rs1870319	rs1047743	rs12601949	rs8081539	
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	rs8069105	rs10512604	rs17581498	rs4789229	rs1113758	rs7214214	rs7214701
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	rs9910273	rs4318268	rs1531268	rs3803733	rs9908146	rs8074216	rs11868471
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	rs11868566	rs878371	rs8077170	rs3744003	rs1106344	rs1106343	rs8078452
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	rs8078208	rs9675230	rs7207208	rs2305912	rs2898587	rs9916685	rs7210574
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	rs6501838	rs8067076	rs3744007	rs9904366	rs3744011	rs3744012	rs2290771
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	rs936393	rs936391	rs1463485	rs11869977	rs11870121	rs9894383	rs3744017
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	rs1055129	rs1551619	rs3760128	rs3744028	rs7370	rs1046446	rs8079113
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	rs8065264	rs3785437	rs9302994	rs8065151	rs9895947	rs3826274	rs9891076
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	rs3643	rs12430	rs3682	rs3785436	rs8064613	rs8082018	rs8069565
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	rs8065946	rs7217955	rs9909589	rs10163493	rs16968345	rs2467099	rs8064955
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	rs12325804	rs16968347	rs8080880	rs1137582	rs8076960	rs6501843	rs8076106
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	rs10852766	rs4267337	rs7222393	rs17855420	rs11077799	rs12603572	
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	rs9914319	rs3744034	rs3744035	rs9915998	rs11867946	rs4561495	rs6501847
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	rs8082573	rs11654948	rs12051605	rs12945114	rs12945400	rs12602750	
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	rs363796	rs9902405	rs2069534	rs2069535	rs2069536	rs2069538	rs2069539
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	rs2290251	rs2665993	rs2598420	rs2071195	rs2071194	rs2071192	rs2244377
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	rs2665964	rs7224702	rs7207515	rs12951986	rs16968411	rs7224593	rs7223631
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	rs11649993	rs16968417	rs8077135	rs16968425	rs17498898	rs7409	rs16968440
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	rs1530834	rs2305345	rs6501850	rs2665979	rs8081829	rs2598434	rs7210777
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	rs2598435	rs2665972	rs12949265	rs12943034	rs8071975	rs7219845	rs2665995
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	rs2665983	rs2246999	rs2247007	rs2598412	rs2665981	rs2250054	rs2243536
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	rs2250081	rs2457693	rs2457692	rs7501512	rs7208391	rs2666009	rs2666011
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	rs9895541	rs2290245	rs2666013	rs1979132	rs8069139	rs4442850	rs9895276
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	rs1868826	rs2002987	rs881564	rs1868824	rs2585739	rs16968595	rs880212
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	rs1465960	rs3744036	rs2598425	rs7208373	rs2585738	rs2585737	rs7359559
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	rs7359560	rs2585736	rs2598424	rs2585735	rs1868821	rs754708	rs754706
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	rs754707	rs894544	rs881502	rs16968610	rs4789246	rs12165062	rs1947284
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	rs9904343	rs2289606	rs2289604	rs8072857	rs2290244	rs4788915	rs3816427
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	rs9893558	rs16968642	rs1376356	rs11539879	rs2278826	rs1551104	rs2278825
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	rs8071198	rs10512608	rs4143087	rs4789248	rs12937813	rs920713	rs1868827
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	rs9912355	rs2585734	rs2598449	rs9899673	rs9908949	rs9909652	rs16968692
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	rs16968696	rs11077807	rs12938489	rs16968702	rs12602521	rs12604011	
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	rs12453778	rs12952480	rs12945842	rs9911832	rs9914821	rs8077453	
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	rs16968719	rs12051808	rs8068421	rs8067947	rs4789251	rs1108127	
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	rs12453112	rs4505373	rs12950642	rs12601803	rs9911122	rs9912975	
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	rs6501862	rs10512607	rs10512606	rs9302997	rs9302998	rs9916150	
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	rs4789261	rs8071545	rs9910028	rs8182357	rs385377	rs8079062	rs11651645
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	rs8901	rs71815	rs11871165	rs347675	rs347674	rs7342820	rs7342824
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	rs10459	rs447294	rs2279057	rs2279056	rs2279055	rs9904844	rs16968822
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	rs407281	rs16968826	rs8078771	rs419793	rs421578	rs8079633	rs410384
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	rs346794	rs4789279	rs12453347	rs171135	rs449114	rs399029	rs382008
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	rs383048	rs2305936	rs7503030	rs385689	rs12937319	rs402273	rs374313
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	rs4788922	rs6501893	rs6501895	rs4789284	rs7217626	rs9909931	rs9910399
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	rs377253	rs372126	rs394873	rs7207108	rs443112	rs389809	rs404014
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	rs567009	rs12602544	rs1466003	rs669228	rs17596582	rs579983	rs694251
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	rs12051905	rs12936288	rs16969019	rs7219889	rs895160	rs752049	rs3744049
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	rs8070864	rs9890158	rs9892510	rs4788931	rs11077835	rs10852771	
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	rs10775368	rs10852772	rs3809700	rs3809702	rs4471711	rs868406	rs9892912
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	rs9893133	rs4788932	rs4789318	rs3940647	rs4788933	rs4238998	rs4575559
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	rs4633757	rs8070870	rs7212413	rs7214155	rs7212569	rs2532443	rs11654499
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	rs2410994	rs1117060	rs1117059	rs4788937	rs2098092	rs7223597	rs7210275
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	rs11867820	rs11867985	rs4788941	rs8068105	rs12950065	rs11077850	
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	rs2240774	rs2240773	rs2240772	rs2286585	rs1014390	rs7224225	rs2240769
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	rs12165027	rs4788943	rs8066239	rs2058215	rs4789351	rs12602772	rs15184
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	rs8073856	rs9914076	rs8080079	rs2429452	rs16969259	rs9916811	rs116719
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	rs7212157	rs16969262	rs8070803	rs8075207	rs16969272	rs2456784	rs2456783
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	rs16969273	rs12945957	rs13380809	rs11868654	rs9303005	rs10438704	
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	rs9889562	rs685441	rs8068021	rs11077862	rs7221130	rs8065907	rs8080150
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	rs11658794	rs7208060	rs925046	rs9900513	rs7208733	rs4789355	rs7220971
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	rs1507072	rs1532200	rs2411036	rs9905129	rs11077863	rs401299	rs4789359
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	rs11656467	rs402399	rs11868247	rs8075683	rs8076858	rs12449391	
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	rs12452874	rs11653831	rs11077869	rs8074553	rs8073017	rs8078747	
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	rs894952	rs894953	rs11869166	rs7225404	rs10468454	rs7213521	rs7216903
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	rs11650151	rs535136	rs745464	rs510629	rs510599	rs600212	rs3803742
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	rs9897357	rs448203	rs9038	rs3826284	rs368116	rs448767	rs2627222
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	rs445507	rs12946947	rs8080509	rs16970176	rs395857	rs407408	rs409081
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	rs9913591	rs445571	rs440582	rs435814	rs9894773	rs3744067	rs8077939
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	rs9897960	rs12949460	rs401510	rs12942318	rs2574861	rs449988	rs416544
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	rs408659	rs312813	rs312812	rs12952105	rs7212731	rs2574856	rs1865740
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	rs11650965	rs12937112	rs16970220	rs7219060	rs12947286	rs11871706	
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	rs4789462	rs9912867	rs12601962	rs16970224	rs12940892	rs7226077	
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	rs2411124	rs4294874	rs4296316	rs4586516	rs8076139	rs16970238	rs11650295
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	rs7219083	rs4789464	rs12103923	rs9915353	rs9913695	rs8082294	rs9892692
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	rs16970252	rs3826290	rs3826291	rs2410426	rs2410427	rs3916018	rs9891343
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	rs7503911	rs2315922	rs9913162	rs7359591	rs8072229	rs8072355	rs7359577
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	rs12449697	rs12449703	rs9319620	rs9674879	rs9709386	rs1799919	rs2070871
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	rs9896263	rs1065144	rs898097	rs898098	rs7225887	rs3744157	rs3744158
NA06985	02	00	02	02	01	03	01
	rs7222745	rs7222773	rs8079082	rs6502021	rs9906163	rs12949939	rs2380173
NA06985	02	02	01	02	02	01	02
	rs8074284	rs12937252	rs9916545	rs2380176	rs4271625	rs1531281	rs1001865
NA06985	02	01	01	01	01	03	01
	rs8078866	rs11077951	rs12942128	rs7215871	rs12449872	rs12947014	
NA06985	03	01	03	02	01	01	
	rs11868453	rs6502026	rs9747676	rs12952892	rs8065638	rs4986144	rs9303015
NA06985	01	02	02	03	01	01	03
	rs9303016	rs7209936	rs4986137	rs12936476	rs4986089	rs11650407	
NA06985	03	02	03	03	02	03	
	rs10775371	rs1551628	rs4986090	rs6416855	rs9898649	rs9890216	rs7503536
NA06985	02	02	03	02	03	03	02
	rs7503605	rs7503408	rs9891371	rs7405583	rs7405607	rs12603409	rs9905027
NA06985	02	02	03	02	02	01	02
	rs12603456	rs9906258	rs9907989	rs7214627	rs12943585	rs7406895	rs7406865
NA06985	01	02	02	02	03	03	02
	rs9893833	rs4986146	rs11870793	rs11870684	rs11656634	rs9911294	
NA06985	03	03	02	03	02	02	
	rs9912207	rs9910113	rs9911830	rs731447	rs9916813	rs9897919	rs6502033
NA06985	02	02	02	03	03	03	03
	rs7406848	rs12936735	rs7226076	rs7221410	rs7221423	rs12601298	rs9901757
NA06985	02	03	02	01	02	02	02
	rs9915799	rs751409	rs8068883	rs11658065	rs12939139	rs7405903	rs2168935
NA06985	02	02	02	01	02	03	01
	rs9893868	rs12603171	rs12946056	rs9892565	rs11650383	rs9899748	
NA06985	02	01	03	01	01	03	
	rs9899884	rs7213238	rs11868851	rs9915904	rs898099	rs7212102	rs12948347
NA06985	03	03	01	01	01	02	02
	rs9907767	rs7208987	rs7222550	rs9915460	rs7210722	rs9899855	rs9897674
NA06985	01	03	01	03	01	01	01
	rs7406067	rs8072951	rs8078193	rs4986140	rs898105	rs7405957	rs8081673
NA06985	02	01	01	02	01	02	01
	rs16940609	rs9889817	rs9890099	rs11656152	rs1471196	rs8065396	rs9908845
NA06985	01	03	02	01	01	03	02
	rs9894730	rs9903292	rs9903731	rs967825	rs9890149	rs12453381	rs9908243
NA06985	01	02	02	01	02	03	03
	rs7224733	rs10852789	rs1143006	rs7406119	rs9890743	rs7405834	rs6502040

```

NA06985      01      01      03      01      03      03      02
      rs3935099 rs12103530 rs4986100 rs4986075 rs4986103 rs7503665 rs7503547
NA06985      01      03      03      01      03      01      01
      rs9893153 rs4073038 rs9911217 rs12602181 rs8072482 rs11652770 rs9896583
NA06985      03      00      02      02      02      02      03
      rs8072895 rs6416856 rs7501672 rs9675039 rs6502043 rs10432005 rs12449903
NA06985      02      03      03      02      02      01      03
      rs7406561 rs8077967 rs7502145 rs4986109
NA06985      01      02      01      02
[ reached getOption("max.print") -- omitted 89 rows ]

```

For a realistic demonstration, we use the subset of these loci that are present on the Affy 6.0 SNP array.

```

> data(gw6.rs_17)
> g17SM = g17SM[, intersect(colnames(g17SM), gw6.rs_17)]
> dim(g17SM)

```

```
[1] 90 20359
```

The base data were used to create a set of rules allowing imputation from genotypes in the sparse set to the richer set. Some rules involve only a single locus, some as many as 4. The construction of rules involves tuning of modeling parameters. See `snp.imputation` in `snpStats` for details.

```

> if (!exists("rules_6.0_1kg_17")) data(rules_6.0_1kg_17)
> rules_6.0_1kg_17[1:5,]

```

```

chr17:1869 ~ rs9915268+rs11247571+rs9895105+rs6598837 (MAF = 0.06666667, R-squared = 
chr17:2220 ~ rs4790867+rs10454094+rs2586238+rs7207284 (MAF = 0.125, R-squared = 0.706
chr17:6689 ~ rs4424950+rs4790867+rs7225087+rs11658347 (MAF = 0.125, R-squared = 0.592
rs34663111 ~ rs11658079+rs1609550+rs4985594+rs9788983 (MAF = 0.1166667, R-squared = 0
rs62054999 ~ rs17609440+rs2740351+rs2589492+rs16956017 (MAF = 0.125, R-squared = 0.26

```

The summary of rules shows the degree of association between the predictors and predictands in terms of R^2 . Many potential targets are not imputed.

```
> summary(rules_6.0_1kg_17)
```

	SNPs used				
R-squared	1 tags	2 tags	3 tags	4 tags	<NA>
[0,0.1)	655	785	276	56	0
[0.1,0.2)	7	664	926	868	0
[0.2,0.3)	0	158	916	3054	0

[0.3,0.4)	0	28	411	5104	0
[0.4,0.5)	0	20	203	6365	0
[0.5,0.6)	0	21	121	6052	0
[0.6,0.7)	0	29	104	5623	0
[0.7,0.8)	0	54	108	6330	0
[0.8,0.9)	0	141	225	9506	0
[0.9,0.95)	652	700	572	8056	0
[0.95,0.99)	7274	1689	1388	6158	0
[0.99,1]	33660	1353	2326	10152	0
<NA>	0	0	0	0	53601

The overlap between the 6.0-resident g17SM loci and the catalog is

```
> length(intersect(colnames(g17SM), mcols(ebicat37)$SNPS))
```

```
[1] 184
```

The new expected B allele counts are

```
> exg17 = impute.snps(rules_6.0_1kg_17, g17SM)
```

The number of new loci that coincide with risk loci in the catalog is:

```
> length(intersect(colnames(exg17), mcols(ebicat37)$SNPS))
```

```
[1] 295
```

6 Formal management of trait vocabularies

6.1 Diseases: Disease Ontology

The Disease Ontology project Osborne et al. (2009) formalizes a vocabulary for human diseases. Bioconductor's DO.db package is a curated representation.

```
> library(DO.db)
> DO()
```

Quality control information for DO:

This package has the following mappings:

```
DOANCESTOR has 6569 mapped keys (of 6570 keys)
DOCHILDREN has 1811 mapped keys (of 6570 keys)
```



```

DOOBSOLETE has 2374 mapped keys (of 2374 keys)
DOOFFSPRING has 1811 mapped keys (of 6570 keys)
DOPARENTS has 6569 mapped keys (of 6570 keys)
DOTERM has 6570 mapped keys (of 6570 keys)

```

Additional Information about this package:

```

DB schema: DO_DB
DB schema version: 1.0

```

All tokens of the ontology are acquired via:

```

> alltob = unlist(mget(mappedkeys(DOTERM), DOTERM))
> allt = sapply(alltob, Term)
> allt[1:5]

```

```

                DOID:0001816                DOID:0002116
                "angiosarcoma"                "pterygium"
                DOID:0014667                DOID:0050004
"disease of metabolism" "seminal vesicle acute gonorrhea"
                DOID:0050012
                "chikungunya"

```

Direct mapping from disease trait tokens in the catalog to this vocabulary succeeds for a modest proportion of records.

```

> cattra = mcols(ebicat37)$Disease.Trait
> mat = match(tolower(cattra), tolower(allt))
> catDO = names(allt)[mat]
> na.omit(catDO)[1:50]

```

```

[1] NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA
[26] NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA NA

```

```

> mean(is.na(catDO))

```

```

[1] NaN

```

Approximate matching of unmatched tokens can proceed by various routes. Some traits are not diseases, and will not be mappable using Disease Ontology. However, consider

```

> unique(cattra[is.na(catDO)])[1:20]

```

NULL

```
> nomatch = cattra[is.na(catDO)]  
> unique(nomatch)[1:5]
```

NULL

Manual searching shows that a number of these have very close matches.

6.2 Other phenotypic traits: Human Phenotype Ontology

Bioconductor does not possess an annotation package for phenotype ontology, but the standardized OBO format can be parsed and modeled into a graph.

```
> hpobo = gzfile(dir(system.file("obo", package="gwascat"), pattern="hpo", full=TRUE)  
> HPOgraph = obo2graphNEL(hpobo)  
> close(hpobo)
```

The phenotypic terms are obtained via:

```
> requireNamespace("graph")  
> hpoterms = unlist(graph::nodeData(HPOgraph, graph::nodes(HPOgraph), "name"))  
> hpoterms[1:10]
```

```
HP:0000001  
  "All"  
HP:0000002  
  "Abnormality of body height"  
HP:0000003  
  "Multicystic kidney dysplasia"  
HP:0000004  
  "Onset and clinical course"  
HP:0000005  
  "Mode of inheritance"  
HP:0000006  
  "Autosomal dominant inheritance"  
HP:0000007  
  "Autosomal recessive inheritance"  
HP:0000008  
  "Abnormality of female internal genitalia"  
HP:0000009  
  "Functional abnormality of the bladder"  
HP:0000010  
  "Recurrent urinary tract infections"
```

Exact hits to unmatched GWAS catalog traits exist:

```
> intersect(tolower(nomatch), tolower(hpoterms))

character(0)
```

More work on formalization of trait terms is underway.

7 CADD scores

Kircher et al. (Kircher et al., 2014) define combined annotation-dependent depletion scores measuring variant pathogenicity in an integrative way. Small requests to bind scores for SNV to GRanges can be resolved through HTTP; large requests can be carried out on a local tabix-indexed selection from their archive.

```
> g3 = as(ebicat37, "GRanges")
> bg3 = bindcadd_snv( g3[which(seqnames(g3)=="chr3")][1:20] )
> inds = ncol(mcols(bg3))
> bg3[, (inds-3):inds]
```

This requires cooperation of network interface and server, so we don't evaluate in vignette build but on 1 Apr 2014 the response was:

GRanges with 20 ranges and 4 metadata columns:

	seqnames	ranges	strand		Ref	Alt
	<Rle>	<IRanges>	<Rle>		<character>	<character>
[1]	3	[109789570, 109789570]	*		A	G
[2]	3	[25922285, 25922285]	*		G	A
[3]	3	[109529550, 109529550]	*		T	C
[4]	3	[175055759, 175055759]	*		T	G
[5]	3	[191912870, 191912870]	*		C	T
...
[16]	3	[187716886, 187716886]	*		A	G
[17]	3	[160820524, 160820524]	*		G	C
[18]	3	[169518455, 169518455]	*		T	C
[19]	3	[179172979, 179172979]	*		G	T
[20]	3	[171785168, 171785168]	*		G	C

	CScore	PHRED
	<numeric>	<numeric>
[1]	-0.182763	3.110
[2]	-0.289708	2.616
[3]	0.225373	5.216
[4]	-0.205689	3.003

```

[5] -0.172189      3.161
...      ...      ...
[16] -0.019710      3.913
[17] -0.375183      2.235
[18] -0.695270      0.987
[19] -0.441673      1.949
[20]  0.231972      5.252
---
seqlengths:
      1          2          3          4 ...          21          22          X
249250621 243199373 198022430 191154276 ... 48129895 51304566 155270560

```

8 Appendix: Adequacy of location annotation

A basic question concerning the use of archived SNP identifiers is durability of the association between asserted location and SNP identifier. The `chklocs` function uses a current Bioconductor `SNPlocs` package to check this.

For example, to verify that locations asserted on chromosome 20 agree between the Bioconductor dbSNP image and the gwas catalog,

```

> if ("SNPlocs.Hsapiens.dbSNP144.GRCh37" %in% installed.packages()[,1]) {
+   library(SNPlocs.Hsapiens.dbSNP144.GRCh37)
+   chklocs("20", ebicat37)
+ }

[1] TRUE

```

This is not a fast procedure. As of March 2017, small numbers of catalog locations are found discrepant with dbSNP for GRCh37.

References

- Martin Kircher, Daniela M Witten, Preti Jain, Brian J O’Roak, Gregory M Cooper, and Jay Shendure. A general framework for estimating the relative pathogenicity of human genetic variants. *Nat Genet*, Feb 2014. doi: 10.1038/ng.2892.
- John D Osborne, Jared Flatow, Michelle Holko, Simon M Lin, Warren A Kibbe, Li-hua Julie Zhu, Maria I Danila, Gang Feng, and Rex L Chisholm. Annotating the human genome with disease ontology. *BMC Genomics*, 10 Suppl 1:S6, Jan 2009. doi: 10.1186/1471-2164-10-S1-S6. URL <http://www.biomedcentral.com/1471-2164/10/S1/S6>.