

gwascat: structuring and querying the NHGRI GWAS catalog

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Contents

1	Introduction	2
1.1	Installation	2
1.2	Attachment and access to documentation	2
1.3	Illustrations: computing	2
2	Some visualizations	3
2.1	Basic Manhattan plot	3
2.2	Annotated Manhattan plot	4
2.3	Integrative view of potential genetic determinants	4
3	SNP sets and trait sets	5
3.1	SNPs by name	5
3.2	Traits by genomic location	7
4	Counting alleles associated with traits	9
5	Imputation to unobserved loci	11
6	Formal management of trait vocabularies	1480
6.1	Diseases: Disease Ontology	1480
6.2	Other phenotypic traits: Human Phenotype Ontology	1482
7	CADD scores	1483
8	Appendix: Adequacy of location annotation	1484

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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"	"getRsids"
[4] "getTraits"	"gwcex2gviz"	"ldtagr"
[7] "locs4trait"	"makeCurrentGwascats"	"metadata"
[10] "node2uri"	"obo2graphNEL"	"riskyAlleleCount"
[13] "show"	"subsetByChromosome"	"subsetByTraits"
[16] "topTraits"	"traitsManh"	"uri2node"

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(ebicats37)
```

To determine the most frequently occurring traits:

```
> topTraits(ebicats37)
```

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.

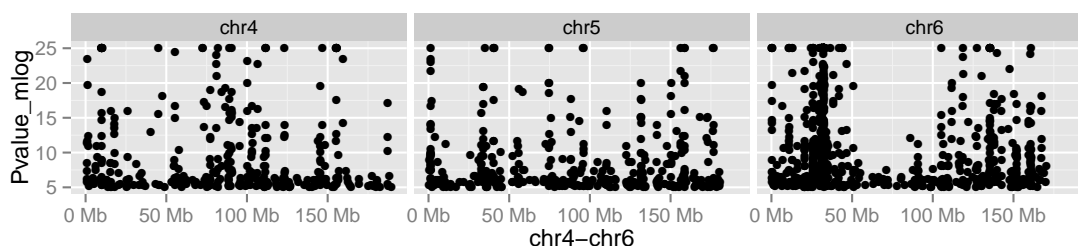
```
> gwtrunc = ebicat37
> requireNamespace("S4Vectors")
> mcols = S4Vectors::mcols
> mlpv = mcols(ebicat37)$PVALUE_MLOG
> mlpv = ifelse(mlpv > 25, 25, mlpv)
> mcols(gwtrunc)$PVALUE_MLOG = mlpv
> library(GenomeInfoDb)
> seqlevelsStyle(gwtrunc) = "UCSC"
```

```

> gwlit = gwtrunc[ which(as.character(seqnames(gwtrunc)) %in% c("chr4", "chr5", "chr6")) ]
> library(ggbio)
> mlpv = mcols(gwlit)$PVALUE_MLOG
> mlpv = ifelse(mlpv > 25, 25, mlpv)
> mcols(gwlit)$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="gwascats")
> library(rtracklayer)
> c17tg = import(gffpath)

```

We make a Gviz DataTrack of the dsQTL scores.

```
> c17td = c17tg[ which(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.

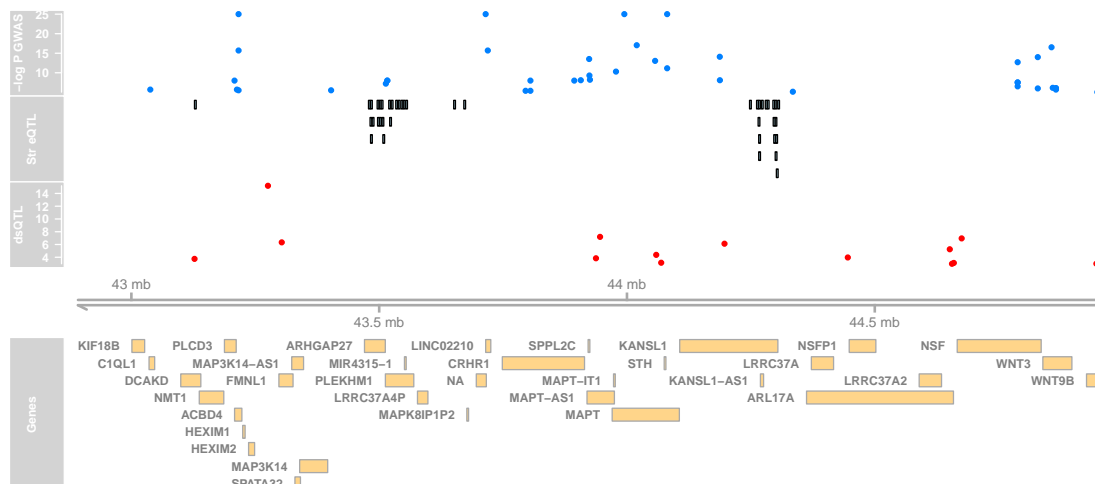
```
> g2 = GRanges(seqnames="chr17", IRanges(start=4.3e7, width=2e6))
> seqlevelsStyle(ebicat37) = "UCSC"
> basic = gwcex2gviz(basegr = ebicat37, contextGR=g2, plot.it=FALSE)
```

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

```
> c17ts = c17tg[ which(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` 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))
> 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 ± 500 bp.

```
> 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 <character>	P-VALUE <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 disor
[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),]
> 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
rs9747194 rs9747497 chr17:149349 rs9746989 chr17:149583 chr17:149593
chr17:149596 chr17:149615 rs12936405 rs56709577 chr17:150830
chr17:151137 chr17:151242 rs9285362 rs4286161 rs62053676 rs56117701
chr17:151951 rs4638649 chr17:152189 rs4313866 rs4354994 chr17:152522
chr17:152666 chr17:152735 rs9747475 chr17:153195 rs12453473 rs9747969
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chr17:78639011 chr17:78639143 chr17:78639702 chr17:78639933
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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
NA06985      03      02      03      02      02      01      01
      rs4890194 rs9674467 rs8075084 rs4890171 rs4890197 rs4890198 rs12941826
NA06985      03      02      03      01      01      01      01
      rs8073847 rs3923018 rs11651800 rs3923017 rs11654890 rs11652984

```

NA06985	02	01	03	03	02	01	
	rs11150893	rs11653255	rs12603796	rs12103587	rs4890172	rs8074031	
NA06985	02	01	01	03	01	03	
	rs7213702	rs12449638	rs7217872	rs12937656	rs9908467	rs9896350	rs7207284
NA06985	03	01	01	03	02	03	02
	rs7222853	rs12602957	rs7223759	rs7221298	rs12452527	rs11150870	
NA06985	01	03	02	03	02	03	
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	rs11658347	rs11247583	rs11656031	rs4968185	rs9893026	rs11650714	
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	rs9894771	rs16943416	rs8070433	rs9890206	rs9890233	rs12601516	
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	rs12602997	rs11867310	rs7209568	rs16943458	rs4643388	rs9747012	
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	rs8077676	rs8078848	rs8072936	rs9893813	rs10401010	rs7211126	rs7214422
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	rs6502542	rs1472180	rs4790867	rs6502774	rs6502776	rs9893760	rs9898628
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	rs4790833	rs4790832	rs242120	rs2292236	rs4790290	rs4790289	rs1056292
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	rs11078622	rs4790823	rs11078629	rs9912549	rs9898672	rs4790288	rs9898694
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	rs7209162	rs7224935	rs7211521	rs2661720	rs12936071	rs11652378	
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	rs12935994	rs6503055	rs9303225	rs7208333	rs12601838	rs2361572	
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	rs7209096	rs4566239	rs12944784	rs8069030	rs1873826	rs902968	rs12232494
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	rs746145	rs902967	rs902966	rs12952369	rs12953162	rs12937460	rs7219763

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	rs10852932	rs6503356	rs216217	rs34166400	rs9892016	rs216219	rs11650903
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	rs216195	rs1885986	rs216193	rs216192	rs4523957	rs391300	rs8081273

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	rs16953580	rs12451331	rs9893372	rs16953582	rs917605	rs3084	rs887387
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	rs2285470	rs876660	rs876659	rs876658	rs876657	rs2016193	rs2285468
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	rs2097657	rs1989811	rs1989810	rs8067108	rs3785938	rs7209483	rs2285466
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	rs2285464	rs2285463	rs3815013	rs3815009	rs17817203	rs2239930	rs201616
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	rs6503317	rs201615	rs9915717	rs8069980	rs878186	rs201613	rs201612
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	rs1876726	rs201611	rs968292	rs3899045	rs9890830	rs201609	rs201608
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	rs8077090	rs201607	rs7220819	rs7221027	rs201606	rs201605	rs7210682
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	rs169313	rs4792010	rs201603	rs4792012	rs4791412	rs4791413	rs4791414
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	rs4791415	rs2662970	rs7210143	rs11868026	rs6503319	rs7221019	rs4792016
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	rs2662959	rs7512	rs2520195	rs2520194	rs2520191	rs11078857	rs2063269
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	rs2662948	rs2175040	rs2106400	rs7211630	rs2520185	rs2520184	rs7223486
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	rs2520173	rs2175039	rs1509112	rs3809732	rs2520166	rs2662975	rs2520162
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	rs9675007	rs9674970	rs365080	rs7502648	rs452038	rs369095	rs446432
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	rs11867626	rs4792105	rs11078887	rs2024135	rs2024134	rs11078888	
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	rs1860178	rs7214237	rs2159219	rs4573972	rs1860300	rs12453889	rs725924
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	rs725923	rs4352083	rs2191089	rs11653055	rs6503362	rs11078889	rs1558215
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	rs1558216	rs11867530	rs4792109	rs4792110	rs1558217	rs9895757	rs10521180
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	rs989170	rs7216976	rs989171	rs9913134	rs12941011	rs9907860	rs17510939
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	rs6502136	rs758429	rs9913500	rs758430	rs758431	rs758432	rs1541461
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	rs16944595	rs7225825	rs7225753	rs7225629	rs16944600	rs16944601	
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	rs2215081	rs16947175	rs16947179	rs16947180	rs12453710	rs7221702	
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	rs12602147	rs9915141	rs11650498	rs8066062	rs8067791	rs11652225	
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	rs11867181	rs2079627	rs8080210	rs11078169	rs11078170	rs11078171	
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	rs9913919	rs968026	rs17664268	rs11078172	rs12602056	rs10775375	
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	rs2322938	rs1013120	rs1013121	rs12952261	rs16948209	rs11654313	
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	rs12452400	rs16948213	rs2190855	rs4792386	rs16948215	rs9915235	
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	rs11651688	rs11651718	rs765475	rs765476	rs917388	rs7222364	rs7222105
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	rs4387631	rs2108701	rs2108702	rs7214210	rs4622548	rs12938631	rs2322954
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	rs11078176	rs9900362	rs7216617	rs2218343	rs2120187	rs11868265	
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	rs4792388	rs11654855	rs9896446	rs11867798	rs9896522	rs9904913	rs9905770
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	rs9906006	rs9912987	rs11078180	rs12942445	rs16948314	rs12940830	
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	rs7212552	rs2323049	rs2323050	rs2323051	rs4343324	rs12946441	rs12946451
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	rs2856185	rs16949118	rs2856147	rs3020869	rs12941439	rs2158978
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	rs17617684	rs7218697	rs7223903	rs17679866	rs4792453	rs4792454	rs2323221
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	rs7221273	rs11870395	rs12373159	rs12103925	rs7222205	rs4792471	
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	rs8078705	rs8080020	rs12944383	rs7215862	rs4792478	rs2086514	rs7207163
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	rs16949502	rs16949506	rs7222435	rs11652792	rs9908835	rs7225858	
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	rs7207501	rs4791610	rs4792570	rs8070377	rs2323554	rs6502414
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	rs1013191	rs1029757	rs16950886	rs9890420	rs2159316	rs2323555
						rs4792571

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	rs7210338	rs4523961	rs8182278	rs7215953	rs17647413	rs9890618	rs9891106
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	rs12709317	rs8081521	rs2098086	rs8081750	rs16950897	rs2098087	rs9905175
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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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	rs8080796	rs6502428	rs8080912	rs12940885	rs8067996	rs2058178	rs8076577
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	rs8082023	rs9906584	rs9889270	rs9896057	rs11078276	rs16950936	rs7216290
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	rs17771065	rs11653659	rs12451281	rs9912965	rs10852828	rs10852829
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	rs9906227	rs8064964	rs4636946	rs9912273	rs9635691	rs9892430	rs9892849
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	rs4791615	rs4792582	rs4239132	rs7215417	rs4356515	rs11658122	rs11658156
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	rs1459096	rs9916167	rs12604074	rs11078284	rs12938757	rs12938764	
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	rs230925	rs230926	rs9909980	rs230927	rs12450668	rs1006978	rs230929
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	rs2531952	rs230930	rs12938289	rs230934	rs192046	rs7207069	rs9916786
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	rs230936	rs4555188	rs9895080	rs230937	rs230938	rs1993614	rs917517
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	rs11654383	rs13027	rs7538	rs13422	rs230941	rs230943	rs9912998
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	rs230945	rs230946	rs230947	rs16951239	rs230948	rs3785654	rs3785653
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	rs7215851	rs17773165	rs12938773	rs3744333	rs11545341	rs230950	rs9899103
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	rs12453838	rs3785652	rs3785651	rs230911	rs3826362	rs231030	rs231029

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	rs981251	rs981250	rs7212138	rs2006787	rs973761	rs8079693	rs9896534
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	rs230964	rs13961	rs230966	rs7224677	rs230967	rs8074324	rs230893
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	rs230897	rs230898	rs16951335	rs2531950	rs4589600	rs957300	rs11871526
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	rs11654114	rs1903112	rs11651313	rs16951345	rs230889	rs1014027	rs230888
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	rs2610065	rs433993	rs414494	rs433068	rs432432	rs446597	rs417637
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	rs230986	rs230985	rs230984	rs17701187	rs230983	rs230982	rs230981
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	rs6502461	rs17702771	rs2654282	rs8064896	rs16940991	rs917567	rs9912642
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	rs2938158	rs9894170	rs2938171	rs6502463	rs7217356	rs236809	rs236807
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	rs7207037	rs3760304	rs3760303	rs3760302	rs642537	rs7223879	rs7213245
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	rs2601988	rs163383	rs163384	rs3865262	rs17776733	rs7217484	rs8074851

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	rs3865264	rs2530068	rs2530064	rs9905520	rs2240596	rs2240594	rs12600853
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	rs8069776	rs4349187	rs2529988	rs2529972	rs11650318	rs2003515	rs2240593
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	rs1057430	rs2529963	rs2323803	rs3966994	rs7217219	rs558767	rs2955833
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	rs13380858	rs9914346	rs7208480	rs4436816	rs1971159	rs1443427	rs2324027
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	rs7226023	rs10852832	rs2228045	rs4792677	rs533242	rs517905	rs488561
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	rs2586557	rs8082656	rs7208654	rs11658871	rs11872072	rs8079686	rs8080194
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	rs859235	rs859237	rs12381131	rs1622059	rs1622062	rs859241	rs12942819
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	rs7208308	rs859243	rs859244	rs3900639	rs859245	rs3922810	rs859247
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	rs859248	rs859250	rs859251	rs859252	rs859253	rs7208549	rs7208915
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	rs859254	rs859256	rs708591	rs17776817	rs859263	rs859264	rs859265
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	rs859266	rs859267	rs12603728	rs2535600	rs9909446	rs9889801	rs9907878
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	rs7225585	rs11657647	rs2779193	rs2779194	rs2779195	rs2228101	rs2041456
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	rs8069362	rs2324082	rs16959491	rs12602291	rs8068607	rs17715109	
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	rs8070859	rs4792709	rs6502482	rs7211756	rs758853	rs3760298	rs11554353
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	rs8072652	rs8076538	rs2302416	rs8077373	rs6502483	rs2041460	rs718884
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	rs7212804	rs7213125	rs3826360	rs7220790	rs9891938	rs8070719	rs8074888
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	rs8071733	rs4792715	rs11078324	rs2301652	rs2157992	rs3744328	rs7217896
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	rs3760295	rs7222645	rs7214695	rs7504016	rs2051736	rs1125156	rs11872032
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	rs178659	rs178657	rs16959542	rs16959544	rs16959547	rs7219062	rs178654

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	rs12937149	rs12937716	rs178810	rs178809	rs178805	rs8071774	rs178802
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	rs2272775	rs8075655	rs178791	rs1018364	rs7212650	rs178785	rs5015580
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	rs17779879	rs3785624	rs4792731	rs11871194	rs11654658	rs3112511	
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	rs3112513	rs11078338	rs9944524	rs6502499	rs764984	rs3785621	rs9908081
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	rs12951442	rs1005380	rs2074995	rs9890539	rs15739	rs2302314	rs9890867
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	rs3095169	rs1476810	rs11650438	rs7210068	rs12945877	rs3112518	rs3112521
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	rs1009715	rs2286666	rs3112528	rs11653585	rs3095173	rs3095172	rs7224259
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	rs7224180	rs7224604	rs11868473	rs6502508	rs7216088	rs12451262	
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	rs9905479	rs7503412	rs28392580	rs7502225	rs11653100	rs11653209	
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	rs8073842	rs8073851	rs11658762	rs4452010	rs4985779	rs4985780	rs4278804
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	rs11078366	rs6502556	rs8068587	rs4985714	rs8066877	rs8070944	rs16961288
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	rs7220492	rs7221842	rs7216176	rs7216705	rs11654562	rs7223686	rs6502557
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	rs8080972	rs4985715	rs11658533	rs6502558	rs6502559	rs7207187	rs11658084
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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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	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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	rs12453474	rs11658227	rs8081130	rs16960349	rs8064572	rs8079625	
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	rs12602374	rs4925042	rs16960357	rs12942065	rs4925043	rs11657623	
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	rs7214841	rs4924793	rs1006553	rs12948881	rs11650088	rs2108967	rs1006556
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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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	rs16960386	rs11204415	rs9898251	rs17793620	rs2052052	rs7225305	
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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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	rs379703	rs9892995	rs17794370	rs166841	rs157386	rs192511	rs4462660
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	rs157387	rs157388	rs157389	rs157390	rs157391	rs157393	rs7216958
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	rs11204416	rs157394	rs12602779	rs157405	rs157406	rs150122	rs157407
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	rs157408	rs157409	rs11204417	rs157401	rs157402	rs16960454	rs16960456
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	rs157397	rs157398	rs169513	rs205103	rs205104	rs9905538	rs8064549
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	rs9903586	rs281334	rs281333	rs394008	rs9897053	rs4586510	rs281364
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	rs281363	rs281362	rs11654515	rs281366	rs9899357	rs4925054	rs9914273
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	rs119672	rs7224713	rs203450	rs11871326	rs175922	rs4476228	rs203481
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	rs203480	rs203479	rs2891912	rs2891911	rs203478	rs16960545	rs850623
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	rs6587207	rs8080190	rs7224567	rs7224875	rs9915039	rs4925067	rs8079093
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	rs17759041	rs9892588	rs8068440	rs17759083	rs9915758	rs16960660	
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	rs4588033	rs1812934	rs7223505	rs9897168	rs9893832	rs17686839	rs1971044
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	rs11869959	rs11658722	rs9895618	rs9896109	rs11650623	rs4073723	
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	rs1585743	rs4889771	rs6565466	rs1585740	rs4522456	rs1600263	rs4889773
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	rs8076832	rs7359574	rs1121327	rs2169915	rs7502023	rs8079247	rs1842110
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	rs1076066	rs899416	rs2880231	rs17052381	rs2342045	rs9892857	rs11871441
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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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	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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	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
NA06985	03	03	03	01	02	01	01
	rs1518050	rs4547384	rs4547385	rs4589611	rs4325621	rs11150721	rs2221893
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	rs4989218	rs4989217	rs4989216	rs4989215	rs11650384	rs2048584	rs8075299
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	rs7213111	rs12941214	rs8072114	rs8068515	rs9895515	rs4263002	rs8078516
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	rs7215275	rs12940712	rs4889733	rs17808614	rs11150722	rs9891438	
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	rs7220748	rs17808656	rs7223844	rs12150287	rs1512845	rs907705	rs907706
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	rs12946383	rs1512844	rs1914613	rs17808708	rs1878659	rs2089962	rs7207851
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	rs8072903	rs1518054	rs7211548	rs2037270	rs7502250	rs11656011	rs11868258
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	rs4889705	rs2681323	rs17808964	rs2738971	rs17735945	rs2681322	
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	rs17736008	rs12452777	rs11658166	rs2341271	rs11651702	rs2341266	
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	rs2879991	rs8072503	rs11654965	rs8182322	rs4243239	rs7221013	rs13353197
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	rs9904279	rs1850917	rs9904608	rs7502677	rs1850918	rs8067434	rs4889741
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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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	rs11868335	rs2203931	rs7222514	rs8070275	rs8066332	rs11658968	
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	rs12952805	rs1606914	rs9893002	rs7502976	rs4889748	rs2340410	rs7210668
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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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	rs4889755	rs4889756	rs7211286	rs11867939	rs8075304	rs12325748	
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	rs11080080	rs16972768	rs8082664	rs8064338	rs9709033	rs3932342	
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	rs11080119	rs8079454	rs7503713	rs3930206	rs9748137	rs9748024	rs9893017
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	rs11655572	rs9903867	rs9904110	rs4988873	rs7211389	rs11657089	rs9911680
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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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	rs11080053	rs12451926	rs17702342	rs16972674	rs660344	rs16964160	
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	rs1975980	rs1402726	rs2061893	rs8074736	rs1851267	rs16972661	rs16972676
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	rs16964174	rs11867986	rs7210518	rs7211074	rs8072882	rs1521560	rs9909708
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	rs4795428	rs1829662	rs1829663	rs11080056	rs665910	rs3933803	rs9902684
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	rs8073417	rs1402724	rs11652017	rs11650889	rs11658450	rs11653183	
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	rs2169956	rs1824900	rs1824901	rs6505104	rs8182310	rs12449549	rs4795494
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	rs7220921	rs8077978	rs1123926	rs12453002	rs2012468	rs11871886	
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	rs16965240	rs8075356	rs3762811	rs17776355	rs7209815	rs8079002	
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	rs11080110	rs2270759	rs2270758	rs2270757	rs6505149	rs6505150	rs6505151
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	rs4794872	rs4344800	rs11869594	rs4795552	rs1909472	rs12602174	rs1875043
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	rs11550663	rs7212516	rs12306	rs7221912	rs11871012	rs7213143	rs4795560
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	rs322178	rs8075253	rs322179	rs322180	rs11871339	rs322182	rs322183
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	rs322188	rs322190	rs7209640	rs7222157	rs4795609	rs4794888	rs9989470
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	rs7217148	rs9989456	rs2086033	rs2100894	rs2100895	rs10853139	rs10853140
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	rs940012	rs2945395	rs940013	rs9905586	rs2945397	rs12103787	rs2948525
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	rs745221	rs12150143	rs11080226	rs1403320	rs1403321	rs2278624	rs2278625
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	rs4795628	rs4795629	rs315431	rs315433	rs8065531	rs315437	rs429276
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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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	rs315481	rs7213584	rs7219254	rs9895962	rs11650856	rs395438	rs9905204
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	rs9807050	rs9807054	rs416206	rs12936363	rs12936664	rs447750	rs425809

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	rs9905799	rs7210624	rs9915184	rs9893718	rs395613	rs9893975	rs453365
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	rs8072636	rs425083	rs398061	rs8082682	rs427272	rs11080165	rs7214705
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	rs7210009	rs7210175	rs420799	rs9891408	rs9890552	rs1979207	rs373242
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	rs417042	rs404849	rs447366	rs417178	rs386583	rs404918	rs12325970
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	rs420546	rs412820	rs9896104	rs1631252	rs391287	rs413155	rs419358
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	rs400459	rs401781	rs9635765	rs376517	rs425967	rs385559	rs6505256
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	rs412107	rs432414	rs417156	rs421875	rs412018	rs315497	rs315498
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	rs11655497	rs12937437	rs315499	rs10512437	rs7209149	rs315500	rs16966823
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	rs7219892	rs11658518	rs315501	rs770505	rs397729	rs315506	rs12103874
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	rs315509	rs11080166	rs12945272	rs417702	rs12949285	rs9900159	rs1551355
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	rs8077893	rs7222438	rs10853143	rs770510	rs1670694	rs12602686	rs7223262
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	rs315492	rs16966833	rs16966835	rs315495	rs315496	rs9916296	rs9897220
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	rs9890373	rs9890598	rs9889619	rs9898609	rs8072792	rs315502	rs7223829
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	rs449331	rs7210226	rs11654750	rs450735	rs447241	rs442939	rs399414
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	rs392669	rs770512	rs17182071	rs17182078	rs884351	rs8066501	rs12939349
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	rs10512436	rs16966855	rs17827108	rs16966858	rs17246714	rs365112	
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	rs17779853	rs397503	rs386811	rs11870496	rs9914500	rs9915265	rs7211595
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	rs11659123	rs11650648	rs8074803	rs8078853	rs2880709	rs11871038	
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	rs1477201	rs2111665	rs2111666	rs1106262	rs9905818	rs4795639	rs7212433

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	rs220441	rs220443	rs9906818	rs7215931	rs220447	rs220448	rs220451
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	rs220452	rs220453	rs9912356	rs220456	rs9889483	rs220457	rs220458
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	rs16966876	rs9913053	rs7220518	rs9893130	rs16966878	rs9893595	
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	rs9899799	rs9902451	rs9303646	rs9902100	rs9903176	rs13380827	rs9902817
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	rs9903046	rs16966900	rs13380855	rs12325969	rs9910876	rs9911317	
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	rs8064507	rs8081344	rs16963625	rs9889558	rs4624243	rs4795653	rs8071544
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	rs6505263	rs11657397	rs11080171	rs8068039	rs8074024	rs11080172	
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	rs8073620	rs4795657	rs4795658	rs8082200	rs9889291	rs11649786	rs8080314
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	rs8078471	rs6505265	rs7223225	rs16967012	rs11649876	rs7217004	rs8074383
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	rs9909478	rs2344310	rs8068049	rs12941700	rs9906443	rs4795659	rs739799
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	rs739800	rs16967028	rs9899093	rs10491099	rs16967029	rs2051810	
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	rs3744613	rs1978116	rs3760454	rs7222814	rs10468585	rs16967042	rs2074101

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	rs8064843	rs9891114	rs7225901	rs8066335	rs7216102	rs7210970	rs9913796
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	rs7225398	rs5019565	rs7218986	rs9911264	rs9912129	rs8066558	rs5003283
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	rs5003287	rs2627070	rs11870077	rs2627066	rs9901121	rs7405579	rs9899054
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	rs2627145	rs8077092	rs8071694	rs506766	rs11871335	rs508566	rs578635
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	rs2470243	rs559228	rs521919	rs2428338	rs2470250	rs473342	rs548957
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	rs16967101	rs17182434	rs7503360	rs3925748	rs9903408	rs2930267	rs2627171
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	rs1020901	rs1020902	rs4633763	rs2344620	rs9915569	rs7217747	rs12942624
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	rs7221734	rs9911706	rs6505286	rs301348	rs8076166	rs9911425	rs8080615
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	rs16967129	rs16967132	rs12948310	rs11868374	rs9903284	rs733674	rs733675
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	rs9902253	rs17182658	rs16967194	rs301342	rs12953030	rs16967197	
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	rs3948664	rs9900089	rs9889352	rs9894550	rs9910731	rs9889607	rs9913984
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	rs2543968	rs2543969	rs7208878	rs2543970	rs17247848	rs11868702	rs2543971
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	rs12601970	rs7215958	rs7209106	rs2253180	rs2291636	rs2729338	rs2640837
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	rs12603703	rs2640838	rs2640839	rs11869369	rs2543977	rs7209587	rs7210072
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	rs4530182	rs12947682	rs2032753	rs8068418	rs17780664	rs8073415	rs8073565
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	rs2521980	rs1859076	rs7222467	rs6505314	rs6505315	rs3025286	rs28980
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	rs1394395	rs6505337	rs7220131	rs11652103	rs11656759	rs7215745	rs8074678
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	rs867132	rs867133	rs159280	rs159284	rs159285	rs159286	rs159288
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	rs10853173	rs8066240	rs11080302	rs6505432	rs6505433	rs7213106	
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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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	rs17544975	rs8081228	rs234822	rs1005596	rs53782	rs11652355	rs4796009
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	rs12938847	rs11869882	rs11652634	rs11656251	rs11656105	rs11080306	
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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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	rs382861	rs12453198	rs11654954	rs272157	rs7502356	rs371957	rs7504080
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	rs2429549	rs16966134	rs2462961	rs12946793	rs12945784	rs8068810	
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	rs7221263	rs1662750	rs16970538	rs1731893	rs16940397	rs12103761	
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	rs1642603	rs151196	rs151195	rs1662754	rs149422	rs7222905	rs9899906
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	rs467148	rs186691	rs2070592	rs8067852	rs231462	rs231461	rs11651138
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	rs3744758	rs3744759	rs3744760	rs3744761	rs4362432	rs12603813	rs7215546
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	rs7217321	rs7221649	rs2129732	rs2129731	rs9894306	rs6503423	rs7207047
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	rs9895377	rs11653145	rs11652187	rs12944434	rs8075440	rs8073737	
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	rs9303454	rs9890150	rs7223320	rs7224944	rs12603905	rs9913579	rs9893672
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	rs901754	rs1542688	rs8065916	rs4986172	rs16939879	rs9898309	rs1053578
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	rs9897116	rs3744411	rs3809745	rs1801921	rs8070447	rs7217422	rs9894024
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	rs4383190	rs1105858	rs16939893	rs8074032	rs11657325	rs4627401	rs8070221
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	rs4792819	rs12450321	rs4401082	rs9912995	rs9901692	rs9899470	rs11651809
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	rs17630064	rs9897711	rs16939911	rs8068730	rs9901986	rs11869039	
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	rs1552458	rs7221388	rs8065387	rs12449792	rs1906342	rs4316799	rs9916564
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	rs8182370	rs1801353	rs9901406	rs12450278	rs8065345	rs2291448	rs11651968
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	rs7212560	rs11652120	rs9908267	rs9909939	rs9889279	rs4248280	rs7342962
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	rs4248914	rs4986168	rs4247364	rs11867409	rs11656414	rs7215764	rs7217153
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	rs11574835	rs3744410	rs1047833	rs2285674	rs8076520	rs16939926	
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	rs11574834	rs2074293	rs11867907	rs11574832	rs4792809	rs3178151	
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	rs4792811	rs11574831	rs7213493	rs9635724	rs11079501	rs7214657	rs9911183
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	rs16939943	rs7222751	rs16939948	rs7207549	rs3785803	rs2074292	
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	rs12449740	rs17686001	rs4792848	rs7216796	rs4792849	rs2106721	
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	rs11870853	rs16939958	rs4328483	rs16939961	rs4792814	rs8081107	
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	rs9891633	rs9905902	rs1000354	rs8079270	rs10451274	rs17686238	rs8066224
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	rs12452717	rs1230072	rs1230073	rs1230090	rs1230091	rs1237651	rs1230094
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	rs732589	rs2905454	rs1059504	rs8327	rs2903703	rs2905455	rs17630836
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	rs1230106	rs9916694	rs12947718	rs11654226	rs1230079	rs12942666	
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	rs7222389	rs7215693	rs11012	rs9730	rs3186976	rs17631303	rs6503437
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	rs2077606	rs2521840	rs7212764	rs3946526	rs9891390	rs2078200	rs9905465

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	rs2684623	rs2947573	rs8076773	rs9914198	rs2696638	rs2696641	rs2696642
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	rs2696645	rs3859266	rs1852269	rs17642476	rs2458221	rs2950657	rs2463519
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	rs1724411	rs7502280	rs440778	rs2259932	rs418891	rs2462840	rs647838
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	rs241023	rs241022	rs7208489	rs16940858	rs241021	rs241020	rs1358072
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	rs7214503	rs12600777	rs1724409	rs17760577	rs12601866	rs16940884	
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	rs17760631	rs1635299	rs12452462	rs1635298	rs1724408	rs17687462	
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	rs1631850	rs1635295	rs17687571	rs1630095	rs17687625	rs1635291	
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	rs17687667	rs9892505	rs1635289	rs7221025	rs1724401	rs1724400	rs17687740
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	rs16941035	rs16941038	rs2049515	rs2158474	rs17761207	rs17688002	
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	rs1078830	rs753235	rs34097347	rs2106784	rs2158072	rs10491140	rs2055794
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	rs12938245	rs17651549	rs1529534	rs2435211	rs17572795	rs17572823	
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	rs2440123	rs8078918	rs2049675	rs11650396	rs7212732	rs1881139	rs4794123
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	rs2302254	rs16949654	rs11556834	rs11868380	rs2041296	rs2159359	
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	rs7223690	rs12949330	rs8073586	rs11651110	rs1860574	rs12943887	
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	rs7212007	rs9905051	rs12453596	rs11079947	rs8076111	rs12950750	
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	rs9897386	rs6504698	rs11657310	rs2286760	rs2286761	rs11868199	rs9898969

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	rs6504700	rs7350913	rs7216962	rs9893865	rs11079949	rs9902908	rs4794214
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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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	rs10853118	rs16949739	rs2318788	rs4794218	rs8077559	rs4448992	rs8076189
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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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	rs17575864	rs8077970	rs9902070	rs9894576	rs9906643	rs11655149	rs4794229
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	rs4794230	rs1034922	rs1034923	rs8082469	rs8074198	rs8078014	rs9904925
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	rs4794234	rs11079956	rs8067194	rs8070067	rs8073974	rs6504708	rs7207505
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	rs9914877	rs8066624	rs7215513	rs9910203	rs8064322	rs8068355	rs9807015
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	rs2013281	rs4630593	rs9903614	rs8070189	rs2191151	rs8070200	rs8071443
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	rs1501266	rs9894061	rs16950685	rs7220627	rs8068272	rs8073930	rs10153251
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	rs11868731	rs967676	rs16950698	rs2523005	rs12149982	rs12149983	
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	rs9890997	rs7217610	rs9904666	rs16950700	rs7208129	rs13380825	
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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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	rs11870623	rs11652834	rs2319455	rs16950715	rs2107114	rs11654419	
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	rs11870299	rs9675273	rs7218104	rs9674802	rs7220115	rs12150424	
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	rs35773539	rs10451287	rs9675183	rs9675108	rs9890328	rs11869742	rs64636
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	rs11870328	rs9914746	rs202128	rs16950751	rs202127	rs202124	rs202123
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	rs202122	rs8082027	rs17590785	rs202121	rs202120	rs202119	rs202118

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	rs12940120	rs203065	rs203066	rs12601939	rs11653979	rs203067	rs11658752
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	rs9895834	rs203084	rs203087	rs7225987	rs203089	rs203090	rs203092
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	rs203093	rs203094	rs203095	rs203096	rs69178	rs4094323	rs169388
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	rs4141124	rs203104	rs7225947	rs9907586	rs183248	rs203105	rs203004
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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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	rs12602734	rs2191400	rs11652898	rs8076677	rs11079989	rs9895521	
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	rs2319989	rs1492201	rs9897475	rs1388730	rs1492198	rs9901790	rs9904661
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	rs2452222	rs2452223	rs1388728	rs12946442	rs7220350	rs2467482	rs2467483
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	rs2467484	rs902770	rs883737	rs2087742	rs2087741	rs902769	rs870045
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	rs4794366	rs2467515	rs1492219	rs17622497	rs9303603	rs11080012	rs2452243
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	rs1907667	rs2467509	rs2452249	rs2452250	rs4794369	rs9910728	rs1492222
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	rs4794466	rs9900857	rs8073810	rs9909370	rs11869663	rs16953835	rs4578709
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	rs12449689	rs9898127	rs4794468	rs4794469	rs2331798	rs2331864	rs12603369
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	rs4591189	rs4344797	rs9900247	rs10515050	rs9899290	rs3966061	rs7220285
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	rs12451457	rs12603921	rs9915338	rs11654487	rs4283265	rs9897039	
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	rs16953922	rs9906958	rs16953923	rs4306565	rs12602488	rs9913928	
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	rs11655410	rs9899343	rs7224938	rs9915430	rs12942705	rs4349192	
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	rs12942489	rs12942314	rs11079105	rs12601165	rs9674910	rs9674925	
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	rs4793771	rs4793772	rs4793773	rs9916837	rs8069183	rs11868487	rs10438751
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	rs10468505	rs1530382	rs13342522	rs1443493	rs10468538	rs4794520	
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	rs12946688	rs12948883	rs12948899	rs9913816	rs4794711	rs9894031	
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	rs7207598	rs7206986	rs12939981	rs7212897	rs17833855	rs12946796	
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	rs12949128	rs3916160	rs10468553	rs7208395	rs12953169	rs8068108	
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	rs8073909	rs16958126	rs7214294	rs950608	rs950607	rs9789042	rs7225872
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	rs9905382	rs9893283	rs3744086	rs12943166	rs11649815	rs8071182	rs8071058

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	rs17220805	rs17833884	rs12452040	rs16958130	rs9895389	rs16958134	
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	rs16958138	rs9902023	rs7223919	rs9911796	rs6503800	rs6503801	rs6503802
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	rs16958184	rs12602160	rs7223884	rs7208507	rs6503803	rs7213498	
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	rs10515137	rs17761226	rs9912288	rs1815198	rs4341799	rs4528641	
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	rs16958190	rs4794716	rs16958191	rs868740	rs9907152	rs13353194	rs3803757
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	rs11654429	rs4794717	rs9895523	rs7214706	rs9904236	rs4794718	rs6503806
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	rs8071867	rs11079287	rs2280713	rs9894487	rs2332902	rs12453840	
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	rs17833955	rs7207879	rs12450328	rs7218459	rs12937169	rs7215734	
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	rs792393	rs792392	rs16958244	rs792391	rs16958250	rs16958255	rs7226136
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	rs2695348	rs1982268	rs8080443	rs4793851	rs8066677	rs7342859	rs11657462
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	rs17834277	rs10852999	rs12603207	rs10853000	rs11079300	rs11652711	
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	rs10083861	rs1476730	rs1476729	rs11871658	rs16942358	rs7210646	
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	rs12709430	rs1987693					
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	rs1395826	rs1395825	rs17713225	rs11870521	rs9899635	rs7221351	rs740804
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	rs4791005	rs12943286	rs4791004	rs4791003	rs6504477	rs7223743	rs7209184
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	rs882704	rs2363246	rs2363247	rs4791002	rs4536507	rs17713442	rs9904944

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	rs16960477	rs6504485	rs9905988	rs1019105	rs16960478	rs16960481	
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	rs12943291	rs9901798	rs1507504	rs12602616	rs3785581	rs7215034	rs7220486
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	rs7221048	rs872719	rs2363838	rs740558	rs740557	rs740556	rs8070371
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	rs2108823	rs2108822	rs2159211	rs12948055	rs9913820	rs9892547	rs9892388
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	rs3760259	rs3760258	rs11650711	rs17699284	rs16960487	rs3785579	
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	rs9903282	rs9904079	rs4790992	rs7210865	rs9891796	rs11651301	rs2363843
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	rs16960497	rs3785578	rs16960501	rs11079678	rs2270084	rs2363844	
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	rs11653532	rs11867533	rs8081791	rs1035176	rs2287127	rs12103643	
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	rs8068558	rs8073568	rs9908482	rs9903876	rs8067363	rs8067446	rs9891520
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	rs9891840	rs7221557	rs16960635	rs8076238	rs8076243	rs12601957	rs6504491
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	rs9908264	rs1547438	rs9303516	rs16960709	rs16960711	rs9902671	rs4791307
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	rs10512514	rs8080100	rs2302669	rs9903264	rs16960718	rs12185246	
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	rs12936992	rs9900598	rs12950532	rs9899805	rs12948427	rs11657175	
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	rs9903701	rs9902703	rs12944519	rs9891956	rs12601376	rs7221844	rs9894480
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	rs12944878	rs11079688	rs10853079	rs12945225	rs8066176	rs10432042	
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	rs12453759	rs12951876	rs12936722	rs3935732	rs6504499	rs8064921	
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	rs11867328	rs11870490	rs9897693	rs4408579	rs12325820	rs16960829	
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	rs9903680	rs7221926	rs11079690	rs12601131	rs7207020	rs7208394	rs7207190
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	rs4791285	rs7224073	rs7210323	rs7209236	rs2949928	rs7209778	rs11657188
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	rs4496197	rs11652682	rs4496198	rs4496196	rs7215161	rs6504520	rs11657839
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	rs11658303	rs2083790	rs4968967	rs1443261	rs4148007	rs8075332	rs4148006
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	rs2218350	rs9892535	rs991209	rs991210	rs4246431	rs1373066	rs4147998

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	rs16973416	rs4968972	rs8076099	rs4968824	rs4968973	rs4968826	rs8066738
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	rs8068204	rs12952511	rs12945133	rs12945184	rs7211979	rs4147997	
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	rs9907353	rs16973430	rs4147989	rs7221939	rs4147988	rs12150510	
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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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	rs16973450	rs3744497	rs16973452	rs3744498	rs3744499	rs4147970	rs4147969
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	rs4147968	rs10438702	rs9893051	rs9909773	rs10438703	rs4147967	
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	rs10512521	rs4147962	rs4147961	rs4147957	rs4147956	rs887380	rs4147953
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	rs4147951	rs8065139	rs4147948	rs7208717	rs4147944	rs7502027	rs9897075
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	rs12950368	rs8076973	rs6501916	rs8070045	rs7210891	rs10852773	
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	rs8080055	rs8076776	rs9891295	rs1558289	rs6501920	rs764425	rs1344055
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	rs16973495	rs16973499	rs1984722	rs2159435	rs11650611	rs7217379	
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	rs12162136	rs740516	rs740517	rs758255	rs9892445	rs7209351	rs8077252
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	rs16973562	rs12602396	rs12453921	rs11077942	rs11656320	rs1860120	
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	rs6502001	rs16973567	rs7214079	rs1468514	rs6502002	rs2364315	rs4141177

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	rs1974575	rs9282553	rs9889289	rs9895546	rs736528	rs2058128	rs11659091
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	rs7504026	rs9282554	rs5025273	rs9914407	rs10512524	rs10512525	rs8080508
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	rs7208586	rs12952117	rs7213831	rs8079981	rs9909516	rs9896564	rs4968839
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	rs12941842	rs9907847	rs11654323	rs2542215	rs817126	rs9889277	rs16973883
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	rs9894141	rs531586	rs564426	rs9898003	rs1550828	rs4553686	rs7223000
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	rs12450743	rs481876	rs12450952	rs568536	rs476677	rs9912134	rs534645
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	rs1011548	rs4310935	rs4310936	rs494946	rs509830	rs568354	rs16973895
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	rs11652207	rs4968854	rs520389	rs11871086	rs16973904	rs16973905	
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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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	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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	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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	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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	rs11650517	rs12950334	rs12936002	rs12943426	rs7214110	rs12943751	
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	rs9892141	rs9909427	rs9646390	rs8080719	rs8068409	rs11077467	rs714768
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	rs179922	rs179921	rs179920	rs179919	rs9635665	rs9635666	rs179918
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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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	rs9904038	rs180072	rs9913799	rs12948136	rs180068	rs180067	rs180066
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	rs236511	rs4968887	rs16975398	rs2529681	rs16975401	rs5014129	rs236499
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	rs17715333	rs312725	rs312726	rs312727	rs11077488	rs6501384	rs411079
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	rs16975529	rs9901891	rs7208007	rs312707	rs8080802	rs7225313	rs7224535
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	rs7209611	rs10163526	rs312729	rs312732	rs17778044	rs312733	rs312734

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	rs11868369	rs17715938	rs312739	rs16975549	rs16975551	rs11653587	
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	rs7207089	rs312740	rs312741	rs17716015	rs312742	rs17716021	rs312743
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	rs7209774	rs16975575	rs8072128	rs312688	rs11653931	rs312690	rs10775360
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	rs17763583	rs312691	rs16975583	rs4462644	rs312677	rs12947451	rs11654895
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	rs17175927	rs8064240	rs312747	rs16975594	rs16975596	rs312749	rs12603464
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	rs312762	rs312763	rs312764	rs312768	rs3915641	rs312770	rs9911531
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	rs312771	rs312772	rs16975645	rs16975648	rs312773	rs3914424	rs141155
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	rs12938026	rs9911671	rs7220885	rs601297	rs601656	rs418402	rs9894881
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	rs4793513	rs4793514	rs9908854	rs4570897	rs9901138	rs11077530	rs35205675
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	rs1014216	rs1014217	rs11870515	rs9899958	rs11870467	rs7212475	rs7211437

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	rs9907236	rs2215059	rs4793355	rs8076723	rs17179656	rs16976696	
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	rs12936656	rs6501490	rs12945062	rs6501492	rs7219970	rs17179684	
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	rs11655127	rs8069860	rs9901464	rs12935876	rs16976701	rs11653238	
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	rs16976703	rs16976704	rs16976707	rs17766905	rs16976709	rs12449752	
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	rs11655308	rs12150490	rs9902920	rs887704	rs17766911	rs16976713	
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	rs9893232	rs12941721	rs17226067	rs17825774	rs17825799	rs7224905	
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	rs12939014	rs12940661	rs12949295	rs12941681	rs9635667	rs9635668	
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	rs11653590	rs8077419	rs17766990	rs12940397	rs12452395	rs17825805	
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	rs16976726	rs4793358	rs7224274	rs9897758	rs9904024	rs8071904	rs7359605
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	rs4793361	rs917802	rs17226165	rs16976730	rs9901407	rs16976732	

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	rs8071921	rs965693	rs16976761	rs16976762	rs12603245	rs12601992	
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	rs17825883	rs16976766	rs9915016	rs9895912	rs7503210	rs4480853	rs4519368
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	rs7217501	rs9907606	rs8073528	rs9900249	rs9907166	rs4447470	rs4499283
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	rs741348	rs759500	rs918082	rs2193059	rs16977131	rs4793274	rs8082370
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	rs12601883	rs17181232	rs4793405	rs17181246	rs8078957	rs2159010	
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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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	rs9892238	rs11077599	rs12941103	rs8079928	rs4793421	rs16977166	
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	rs12600868	rs10221244	rs1870319	rs1047743	rs12601949	rs8081539		
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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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	rs2290769	rs2290768	rs17496835	rs7212635	rs10401023	rs17581728		
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	rs6501838	rs8067076	rs3744007	rs9904366	rs3744011	rs3744012	rs2290771	
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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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	rs8081004	rs7218498	rs16968330	rs8072095	rs2608882	rs2608881	rs3744002	
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	rs11650151	rs535136	rs745464	rs510629	rs510599	rs600212	rs3803742
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	rs16969661	rs1662356	rs12600361	rs16969668	rs17611415	rs3744062	
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	rs16970252	rs3826290	rs3826291	rs2410426	rs2410427	rs3916018	rs9891343
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	rs4889884	rs9907193	rs9906827	rs12938812	rs9905909	rs4889783	rs4889784
NA06985	02	03	01	03	03	02	03
	rs9889315	rs11869453	rs884204	rs11655435	rs9909177	rs9902891	rs8079708
NA06985	03	03	03	03	03	01	03
	rs7208502	rs12603215	rs9911171	rs1471788	rs12948054	rs7211095	rs9894952
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	rs9894978	rs9895186	rs4062178	rs11867785	rs2315924	rs9652896	rs8065598
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	rs9898952	rs12948040	rs11150739	rs12939413	rs9900445	rs8081444	
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	rs12450876	rs12453034	rs8068064	rs1564868	rs4889888	rs12936287	
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	rs7211818	rs12453718	rs12944407	rs6565478	rs4889889	rs9896820	rs2315923
NA06985	01	03	01	03	01	01	02
	rs7503911	rs2315922	rs9913162	rs7359591	rs8072229	rs8072355	rs7359577
NA06985	02	02	03	01	01	01	03
	rs8072836	rs9899843	rs12941958	rs8069295	rs12951944	rs12941790	
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	rs9902376	rs9896771	rs12946115	rs12603074	rs10401045	rs2315921	
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	rs9915378	rs9891160	rs12940631	rs7503394	rs6565479	rs7406799	rs4889786
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	rs9674559	rs12941240	rs3764371	rs7213696	rs4602089	rs12942526	
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	rs12601089	rs9899782	rs4396582	rs9902639	rs4969230	rs3898096	rs2291359
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	rs4969235	rs9895584	rs7217825	rs12950541	rs7223405	rs8078829	rs8080789
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	rs12450464	rs7215564	rs9913009	rs10871488	rs9901049	rs9900687	
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	rs12943552	rs9915518	rs7213638	rs9890313	rs9891139	rs9894401	rs9897830
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	rs4969388	rs9895847	rs9989484	rs4380096	rs2340773	rs7208831	rs9989446
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	rs7216268	rs7216295	rs4969404	rs12947507	rs7221492	rs12941973	rs9900956
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	rs4969411	rs12452243	rs8064506	rs7221178	rs8077901	rs7208971	rs7208536

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	rs2589138	rs8064563	rs908238	rs11654508	rs9889802	rs9897026	rs7224354
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	rs7206983	rs7225574	rs9893956	rs9908495	rs11651724	rs4969443	rs4969277
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	rs4969444	rs4969445	rs9890578	rs9915738	rs2672886	rs2672887	rs734338
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	rs2090204	rs9904138	rs11658248	rs9915426	rs2333990	rs9894955	rs9893383
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	rs2672903	rs7212411	rs8065995	rs8065459	rs7212127	rs2138125	rs2048753
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	rs12600434	rs4969456	rs9898554	rs9893314	rs11150748	rs9912928	rs1567961
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	rs9907099	rs9893680	rs2589133	rs7221948	rs7217174	rs9895510	rs7221214
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	rs11653207	rs9908195	rs9911574	rs12103708	rs2672901	rs9895174	rs9899844
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	rs2672871	rs7212468	rs2589143	rs2589144	rs7212174	rs746405	rs9897826
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	rs7219745	rs2672900	rs2589158	rs7226021	rs7226025	rs4969219	rs2589157
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	rs3829572	rs3751945	rs2589156	rs2333988	rs7217580	rs2248502	rs2589155
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	rs2589153	rs2589152	rs2589151	rs8065471	rs2589150	rs1040127	rs7220765
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	rs7217623	rs7208264	rs2280146	rs11869745	rs2280147	rs9909086	rs8075013
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	rs9908270	rs2271602	rs2271603	rs2271604	rs2271606	rs7212666	rs3817292
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	rs6565491	rs908236	rs6565494	rs6565495	rs2271608	rs3817293	rs7502001
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	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 getopt("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 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 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="gwascatalog"), 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, Lihua 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>.