

gwascat: structuring and querying the NHGRI GWAS catalog

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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 `ebicats38`).

```
> 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.

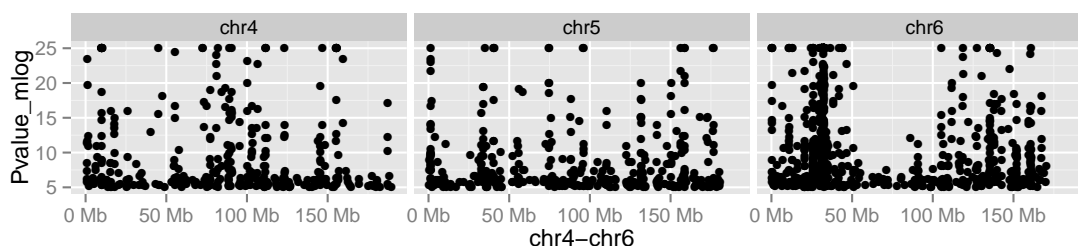
```
> gwtrunc = ebicat37
> requireNamespace("S4Vectors")
> mcols = S4Vectors::mcols
> mlpv = mcols(ebicat37)$PVALUE_MLOG
> mlpv = ifelse(mlpv > 25, 25, mlpv)
> mcols(gwtrunc)$PVALUE_MLOG = mlpv
> library(GenomeInfoDb)
> seqlevelsStyle(gwtrunc) = "UCSC"
```

```

> 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="gwascat")
> 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.

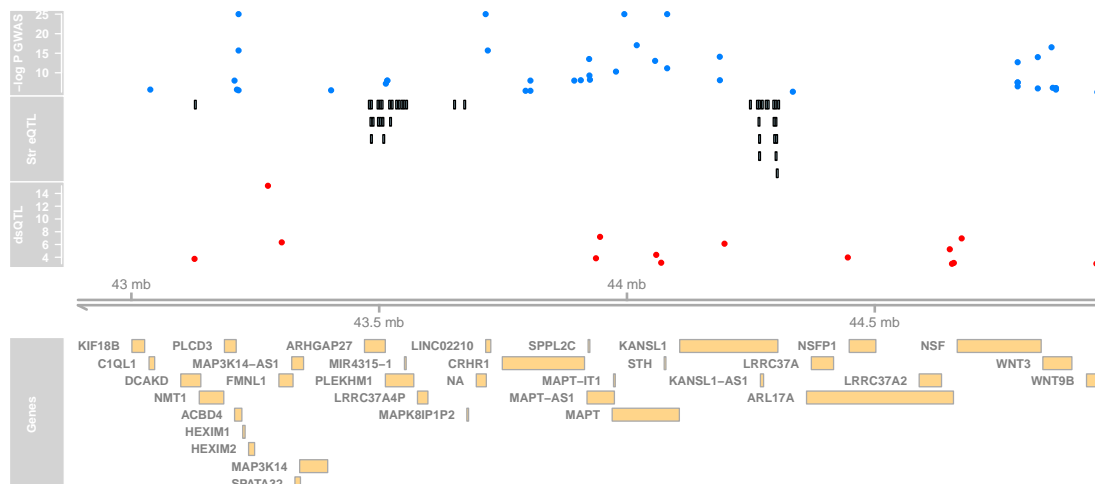
```
> g2 = GRanges(seqnames="chr17", IRanges(start=4.3e7, width=2e6))
> seqlevelsStyle(ebicat37) = "UCSC"
> basic = gwcex2gviz(basegr = ebicat37, contextGR=g2, plot.it=FALSE)
```

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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	rs16958287	rs16958291	rs11871067	rs16958295	rs8080385	rs16958298	
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	rs16958324	rs8064229	rs17809138	rs729162	rs7214499	rs10521158	rs8077489
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	rs9913255	rs9892809	rs3786095	rs3786094	rs3786093	rs3786092	rs6503276
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	rs7216708	rs12952654	rs12949586	rs2058173	rs7208058	rs16959151	
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	rs12373138	rs3786076	rs3786075	rs11654135	rs9910357	rs9915662	
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	rs17208275	rs9896675	rs16959231	rs9905876	rs9906715	rs9901298	rs3786074
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	rs11867626	rs4792105	rs11078887	rs2024135	rs2024134	rs11078888	
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	rs2321578	rs12452905	rs9898243	rs9899265	rs12452954	rs2190964	rs9902841
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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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	rs12604042	rs16944481	rs1558218	rs1558219	rs7211030	rs7215155	rs7216441
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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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	rs11650237	rs9892139	rs9893055	rs9898629	rs11656384	rs11870790	rs717985
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	rs11870262	rs9903128	rs4792125	rs11868682	rs1990286	rs9913953	rs4791463
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	rs1546560	rs6502140	rs205027	rs8078341	rs11868892	rs6502141	rs6502142
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	rs16944595	rs7225825	rs7225753	rs7225629	rs16944600	rs16944601	
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	rs2429374	rs11868587	rs8072140	rs8072158	rs205048	rs8072919	rs8072822
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	rs205053	rs205054	rs205059	rs205060	rs16944657	rs205061	rs205062

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	rs7218691	rs7223512	rs7208665	rs7208960	rs7209893	rs4293419	rs7210236
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	rs1513744	rs1513743	rs1034899	rs1034900	rs1034901	rs7214336	rs17745012
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	rs2969232	rs7210815	rs7210720	rs8068309	rs8069608	rs1513742	rs8069749
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	rs9906083	rs9904264	rs16945275	rs4792164	rs9892290	rs3744577	rs3744578
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	rs11650739	rs11650740	rs3744581	rs3744582	rs17603240	rs12943947	
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	rs237332	rs237336	rs237340	rs184678	rs237270	rs237274	rs237278
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	rs237364	rs12600924	rs237363	rs237362	rs4791499	rs9915351	rs237360
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	rs8073382	rs9905776	rs11657441	rs16949080	rs6502337	rs8065848 rs3785681
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	rs8073984	rs12449610	rs12937279	rs12939377	rs2323095	rs2323096
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	rs2323097	rs2874958	rs1990234	rs9303100	rs16949103	rs7212977 rs8070339
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	rs8075612	rs8079642	rs8081414	rs12936411	rs2530377	rs12453546 rs2856183
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	rs2530376	rs2530375	rs9913639	rs2530373	rs2530370	rs2530368 rs2259118
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	rs2856185	rs16949118	rs2856147	rs3020869	rs12941439	rs2158978
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	rs16949234	rs12449595	rs2529629	rs12453877	rs2529627	rs2856177

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	rs2529625	rs3826366	rs917308	rs9901549	rs12452172	rs3785662	rs3785659
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	rs12601148	rs4792446	rs1050214	rs2230355	rs11078233	rs11078234	
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	rs7214082	rs1802618	rs2071245	rs1050216	rs1050223	rs11869719	rs11869759
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	rs11869709	rs4792447	rs7211577	rs7212116	rs12951559	rs12944270	
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	rs12945766	rs12150130	rs12150136	rs4792448	rs11871019	rs8080585	
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	rs16949277	rs11656595	rs8065030	rs4792449	rs11655445	rs12946884	
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	rs4792450	rs8066913	rs17679758	rs9891187	rs726729	rs7213012	rs7214697
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	rs17617684	rs7218697	rs7223903	rs17679866	rs4792453	rs4792454	rs2323221
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	rs8077212	rs988489	rs7207687	rs7207431	rs983424	rs1859909	rs1859907
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	rs11653991	rs11654370	rs9895549	rs9897617	rs9896249	rs11655666	
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	rs9903896	rs8067063	rs1859905	rs1859904	rs17680043	rs2874993	rs7503943
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	rs12452465	rs2097970	rs12453154	rs12453232	rs12453201	rs12941860	
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	rs12453856	rs12453899	rs11078236	rs11078237	rs12450424	rs16949314	
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	rs11868525	rs16949319	rs7214616	rs4792461	rs9911711	rs960296	rs3815271
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	rs4284690	rs4303583	rs4303584	rs4303585	rs4303586	rs1465243	rs1465242
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	rs9908703	rs9908513	rs11868964	rs11078238	rs17680211	rs2874994	
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	rs1107828	rs9913734	rs9913735	rs7502686	rs886865	rs9914886	rs960361
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	rs10521265	rs7223442	rs7226172	rs4281772	rs12942622	rs9909592	rs9889484
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	rs11869567	rs11869643	rs764428	rs7214941	rs17680283	rs4792462	rs7214696

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	rs7220012	rs755732	rs755730	rs733769	rs12942020	rs7223714	rs2190626
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	rs4792467	rs4791571	rs886862	rs9890556	rs4791573	rs16949371	rs4791574
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	rs2323174	rs9907589	rs9908363	rs3785658	rs9303102	rs1005322	rs1005321
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	rs740379	rs11078240	rs4792468	rs4792469	rs3826365	rs9890648	rs758049
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	rs7221273	rs11870395	rs12373159	rs12103925	rs7222205	rs4792471	
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	rs8080590	rs726942	rs7211702	rs2108461	rs9900779	rs1015663	rs2058044
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	rs9890916	rs9891555	rs740376	rs6502345	rs11870724	rs9909862	rs720873
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	rs7220003	rs4792473	rs1990203	rs3785655	rs8078587	rs11078241	rs2200000
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	rs7222164	rs1859906	rs917310	rs1871784	rs7217818	rs11552190	rs1053326
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	rs2291208	rs2086515	rs6502346	rs2199998	rs7225272	rs7226075	rs2127998
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	rs9909578	rs9912871	rs4792477	rs9905394	rs12450665	rs11869433	rs9944399
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	rs8078705	rs8080020	rs12944383	rs7215862	rs4792478	rs2086514	rs7207163
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	rs16949420	rs1994029	rs8069341	rs17619418	rs17619424	rs11078245	
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	rs7209627	rs8066595	rs7214411	rs7220093	rs7220276	rs16949423	rs7220344
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	rs16949426	rs8077326	rs17692591	rs11657444	rs17692633	rs17619645	
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	rs9914530	rs3912261	rs3912262	rs3912263	rs3912264	rs11651598	rs11651699

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	rs16949443	rs12453007	rs16949449	rs2127994	rs11658470	rs11658502	
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	rs12951864	rs12941224	rs12943137	rs2323178	rs16949456	rs11656638	
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	rs2323180	rs2323181	rs9903191	rs9909373	rs8071588	rs8071460	rs2874982
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	rs2323182	rs9913173	rs9913599	rs2323183	rs9913728	rs8074962	rs9915002
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	rs9906816	rs7212410	rs12941577	rs7359614	rs9916615	rs7223120	rs8065351
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	rs9902989	rs7359531	rs9896612	rs9903741	rs16949482	rs16949487	
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	rs2022234	rs2022235	rs7503671	rs2022237	rs4792482	rs8068166	rs17693422
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	rs16949502	rs16949506	rs7222435	rs11652792	rs9908835	rs7225858	
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	rs17620524	rs9891190	rs7219645	rs3859257	rs4054644	rs9905271	rs10521269
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	rs3967057	rs11869441	rs13341754	rs7221370	rs16949529	rs2127995	
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	rs8066199	rs11652133	rs8066803	rs8072456	rs2022242	rs2022241	rs17620735

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	rs8072828	rs7215419	rs7216735	rs9912653	rs17621552	rs7220278	rs9896798
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	rs665248	rs8079813	rs10521272	rs9303106	rs8079300	rs4791580	rs4792484
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	rs11650346	rs9891291	rs8070110	rs12603558	rs985401	rs9807111	rs2022243
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	rs4541117	rs2323291	rs11871514	rs2022248	rs2022247	rs2022246	rs1073086
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	rs16950131	rs12940255	rs9899511	rs2323455	rs987189	rs12942331	rs8073806
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	rs12941773	rs12936630	rs9890349	rs12602267	rs12602281	rs9899112	
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	rs9914939	rs1558271	rs1558272	rs9914043	rs9914639	rs12950816	rs12950593
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						rs7214520

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	rs859254	rs859256	rs708591	rs17776817	rs859263	rs859264	rs859265
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	rs7212804	rs7213125	rs3826360	rs7220790	rs9891938	rs8070719	rs8074888
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	rs12937149	rs12937716	rs178810	rs178809	rs178805	rs8071774	rs178802
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	rs11871259	rs2440153	rs2453580	rs751259	rs894680	rs12943918	rs8080953
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	rs2018675	rs2453583	rs735579	rs2453584	rs9905246	rs2440154	rs12451696
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	rs2440155	rs2453585	rs2453576	rs1808941	rs2014082	rs2453574	rs2453573
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	rs7219149	rs11650156	rs2247518	rs2289668	rs8076893	rs9909350	rs16960201

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	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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	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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	rs9905570	rs205094	rs1662214	rs1638522	rs205093	rs205090	rs176098
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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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	rs119672	rs7224713	rs203450	rs11871326	rs175922	rs4476228	rs203481
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	rs203480	rs203479	rs2891912	rs2891911	rs203478	rs16960545	rs850623
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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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	rs899414	rs11871520	rs755583	rs755584	rs2199698	rs4993505	rs12949684
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	rs4993506	rs4993507	rs4993511	rs981637	rs12051613	rs12601480	rs8069077

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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
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	rs1518050	rs4547384	rs4547385	rs4589611	rs4325621	rs11150721	rs2221893
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	rs7220748	rs17808656	rs7223844	rs12150287	rs1512845	rs907705	rs907706
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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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	rs8080725	rs7225129	rs12942556	rs11868559	rs12150105	rs12944067	
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	rs1850005	rs1515750	rs1973661	rs2292697	rs2292698	rs9807046	rs12453646
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	rs11080119	rs8079454	rs7503713	rs3930206	rs9748137	rs9748024	rs9893017
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	rs4302084	rs7213094	rs1976838	rs5015403	rs4795878	rs11868485	rs11653494
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	rs9910343	rs16966494	rs11867343	rs7218531	rs11656707	rs11871417	
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	rs2313050	rs4795077	rs7215009	rs4796099	rs1851271	rs7226210	rs7221571
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	rs1969373	rs1521563	rs12103473	rs11657456	rs7225143	rs12453728	
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	rs11080053	rs12451926	rs17702342	rs16972674	rs660344	rs16964160	
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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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	rs16965240	rs8075356	rs3762811	rs17776355	rs7209815	rs8079002	
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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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	rs8077749	rs9900797	rs315444	rs8064545	rs315445	rs770520	rs770521
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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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	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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	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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	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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	rs6505263	rs11657397	rs11080171	rs8068039	rs8074024	rs11080172	
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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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	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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	rs2470243	rs559228	rs521919	rs2428338	rs2470250	rs473342	rs548957
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	rs1979706	rs1602886	rs2080739	rs2080740	rs1493596	rs2249638	rs2543967
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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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	rs7501865	rs2729336	rs321180	rs11867826	rs2640829	rs9911168	rs9912761
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	rs2466862	rs2466861	rs2470230	rs12950239	rs9891861	rs9904988	rs11656181
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	rs2188947	rs2188946	rs9912569	rs2521984	rs2521983	rs12947866	rs10512442
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	rs2470205	rs2726131	rs2726132	rs2079040	rs28988	rs1989894	rs7225406
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	rs2521980	rs1859076	rs7222467	rs6505314	rs6505315	rs3025286	rs28980
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	rs7221771	rs8066827	rs16967818	rs11080200	rs1859079	rs1859078	
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	rs9892452	rs28929	rs3025250	rs12602141	rs28927	rs3025249	rs2074215
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	rs16554	rs16553	rs7502414	rs16552	rs7218428	rs11871864	rs7225507
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	rs1994660	rs6505378	rs9630746	rs2087633	rs11657171	rs1994661	rs9903823
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	rs12603776	rs2172091	rs2130818	rs923633	rs17836945	rs10512456	
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	rs2220613	rs1907398	rs317415	rs222491	rs317416	rs317418	rs16968962
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	rs7221263	rs1662750	rs16970538	rs1731893	rs16940397	rs12103761	
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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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	rs11574834	rs2074293	rs11867907	rs11574832	rs4792809	rs3178151	
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	rs12449740	rs17686001	rs4792848	rs7216796	rs4792849	rs2106721	
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	rs1230106	rs9916694	rs12947718	rs11654226	rs1230079	rs12942666	
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	rs241023	rs241022	rs7208489	rs16940858	rs241021	rs241020	rs1358072
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	rs2318786	rs12452050	rs8076679	rs7222463	rs7221093	rs4273084	rs7213406
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	rs16949683	rs17574235	rs7342961	rs3815411	rs4793687	rs12450473	
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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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	rs1019195	rs4793692	rs7210107	rs7210300	rs9893889	rs4794220	rs7215691
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	rs12941969	rs12948421	rs9893020	rs17575641	rs917654	rs11867403	
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	rs12453696	rs731591	rs175388	rs7225064	rs7226332	rs175391	rs6504707
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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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	rs8080797	rs11868760	rs9907687	rs9906422	rs7211912	rs6504716	rs16949818
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	rs12453925	rs1468553	rs1468554	rs11656830	rs11650643	rs9897182	
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	rs16950626	rs7222418	rs11655338	rs202132	rs9303593	rs11651107	rs7219047
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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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	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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	rs203005	rs203007	rs12386069	rs10514990	rs203008	rs203009	rs203010
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	rs16950872	rs203016	rs203017	rs169385	rs9896830	rs203018	rs203020
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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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	rs9906815	rs9893317	rs9902317	rs9903361	rs4556834	rs9889332	rs9910452
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	rs12453099	rs12601384	rs16951004	rs1503060	rs2221331	rs1542907	
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	rs1027679	rs12937546	rs4362437	rs996346	rs1393731	rs9898442	rs2938133
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	rs16953922	rs9906958	rs16953923	rs4306565	rs12602488	rs9913928	
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	rs4793771	rs4793772	rs4793773	rs9916837	rs8069183	rs11868487	rs10438751
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	rs1443489	rs1443490	rs1443491	rs7207718	rs1348397	rs1822430	rs9912982
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	rs7502152	rs16954723	rs1443496	rs1443495	rs1443494	rs1561979	rs1561977
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	rs2120292	rs3948169	rs2197267	rs1158261	rs4794519	rs9894172	rs3919720
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	rs10468505	rs1530382	rs13342522	rs1443493	rs10468538	rs4794520	
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	rs4793776	rs2218362	rs1373159	rs12936021	rs1443492	rs12946074	
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	rs16954908	rs10468512	rs7211119	rs7210585	rs10468548	rs16954924	
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	rs17213411	rs4360992	rs17820396	rs9910714	rs9910441	rs7218500	rs2215758
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	rs6505060	rs12940466	rs7218559	rs7223494	rs16957271	rs1442831	rs8070836

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	rs12449510	rs10852986	rs11654979	rs16957312	rs764583	rs4794642	
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	rs1372855	rs1372856	rs12450244	rs10515129	rs10515130	rs9895965	
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	rs768758	rs1372858	rs12450049	rs9891583	rs2028593	rs4794643	rs4794644
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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>.