Discovery of Cancer Driver Long Noncoding RNAs across 1112 Tumour Genomes: New Candidates and Distinguishing Features.

Authors

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Supplementary Figure Legends

Supplementary Figure S1: Graphical representation of the ExInAtor workflow. The objective of this algorithm is the creation of a local background region with identical trinucleotide content to the exons of a given gene. As an example we take a hypothetical single-exon lncRNA gene. (A) Upstream and downstream regions within the window size are defined as background regions. All the trinucleotides in the exon region are counted. The mutations (indicated by *) in the central nucleotide positions of each trinucleotide are counted. Colours indicate the four nucleotides in the exon. Background region nucleotides are not coloured. For brevity, only four trinucleotide combinations are shown. (B) Next, an iterative sampling is performed. A set of trinucleotides, identical to the exonic trinucleotide set, are randomly sampled from the background region. This operation is repeated, without replacement of the central nucleotide (red "X"), until it is no longer possible to extract the appropriate set of trinucleotides. (C) The total number of nucleotide positions and mutations are counted for the exon region and the sampled background region. These values are used for the contingency table analysis shown in Figure 1.

Supplementary Figure S2: Ratio of exonic to background mutation density.

Supplementary Figure S3: Quantile-quantile ("QQ") plots for all analyses. Grey dots represent the P values obtained in the two simulations. The black and coloured dots correspond to the P values calculated in the real dataset.

Supplementary Figure S4: Histogram of predicted candidates in Breast across the 100 iterations of shuffling analysis. First, all lncRNAs randomly placed in a new position within the whole genome, while maintaining exon-intron structure. Then ExInAtor was run, with same settings as described, using real mutations from Breast. Shown are the number of predicted candidates at a cutoff of FDR<0.1. The number of predicted candidates using real gene locations is 3, greater than 97% of simulations.

Supplementary Figure S5: Quantile-quantile ("QQ") plot of "intronic gene" simulation in Breast. Artificial "intronic" gene models were constructed, where the exons of every gene were replaced by equally-sized, randomly-selected fragments of introns from the same gene. These genes were used as the input for ExInAtor and run (with same settings as for real data) on Breast samples.

Supplementary Figure S6: Expression of SAMMSON in Stomach (in which is detected by ExInAtor), and skin, sun-exposed or not (in which has been previously implicated in Melanoma).

Supplementary Figure S7: Exon-level mutational density of all lncRNAs candidates against the background regions.

Supplementary Figure S8: Intersection between ExInAtor, MiTranscriptome and Du et al candidates.

Supplementary Figure S9: Performance of ExInAtor compared MutSig, OncodriveFM and OncodriveClust in the Pancancer Alexandrov dataset. (A) Percentage of CGC candidates amongst predicted drivers for each method across different cutoffs (-log10 Q value) in all the Alexandrov cancer files. (B) As for (A), but displayed by ranked number of top predicted drivers.

Supplementary Figure S10: The overlap of predicted protein-coding drivers between methods. The percent of predicted drivers of each method on Pancancer Alexander mutations that are also predicted by at least one of the other methods displayed by (A) cutoff or by (B) ranked number of candidates.

Supplementary Figure S11: QQ plots of each method on the Pancancer Alexandrov dataset. Grey dots represent the P values obtained in a simulation. The black and coloured dots correspond to the P values calculated in the real dataset.

Supplementary Figure S12: Tumour specificity of lncRNA and protein coding genes. The figure shows the percent of genes of each biotype that are mutated in one or more distinct tumour samples.

Supplementary Figure S13: Screenshots of the 12 candidate's mutations analysed with IGV.

Supplementary Figure S14: Replication timing of cancer lncRNAs, ExInAtor predictions and other lncRNAs. Cumulative distribution are shown for S50 values in HeLa cells assigned to lncRNA gene sets. S50 ratio is defined as the fraction of the S phase at which 50% of the DNA is replicated (see Materials and Methods). Low ratios indicate early replication timing. Genes are grouped by: literature-reported cancer CRL lncRNAs; all ExInAtor candidates (both CRL and not); non-CRL novel ExInAtor candidates; non-CRL non-candidates, being all other GENCODE lincRNAs. Candidates here were defined at a threshold of $Q \leq 0.2$. Dashed vertical lines indicate the mean value of each group.

Supplementary File Legends

Supplementary File S1: CRL lncRNAs.

Supplementary File S2: Non-CRL lncRNAs.

Supplementary File S3: The full set of lncRNA drivers predicted by ExInAtor in CRL.

Supplementary File S4: The full set of lncRNA drivers predicted by ExInAtor in non-CRL.

Supplementary File S5: The full set of protein-coding drivers predicted by ExInAtor.

Supplementary File S6: The full set of results for lncRNAs and protein-coding genes described in this study.

Supplementary File S7: Candidates identified by Du et al. that are also considered in our study.

Supplementary File S8: Candidates identified by MiTranscriptome that are also considered in our study.

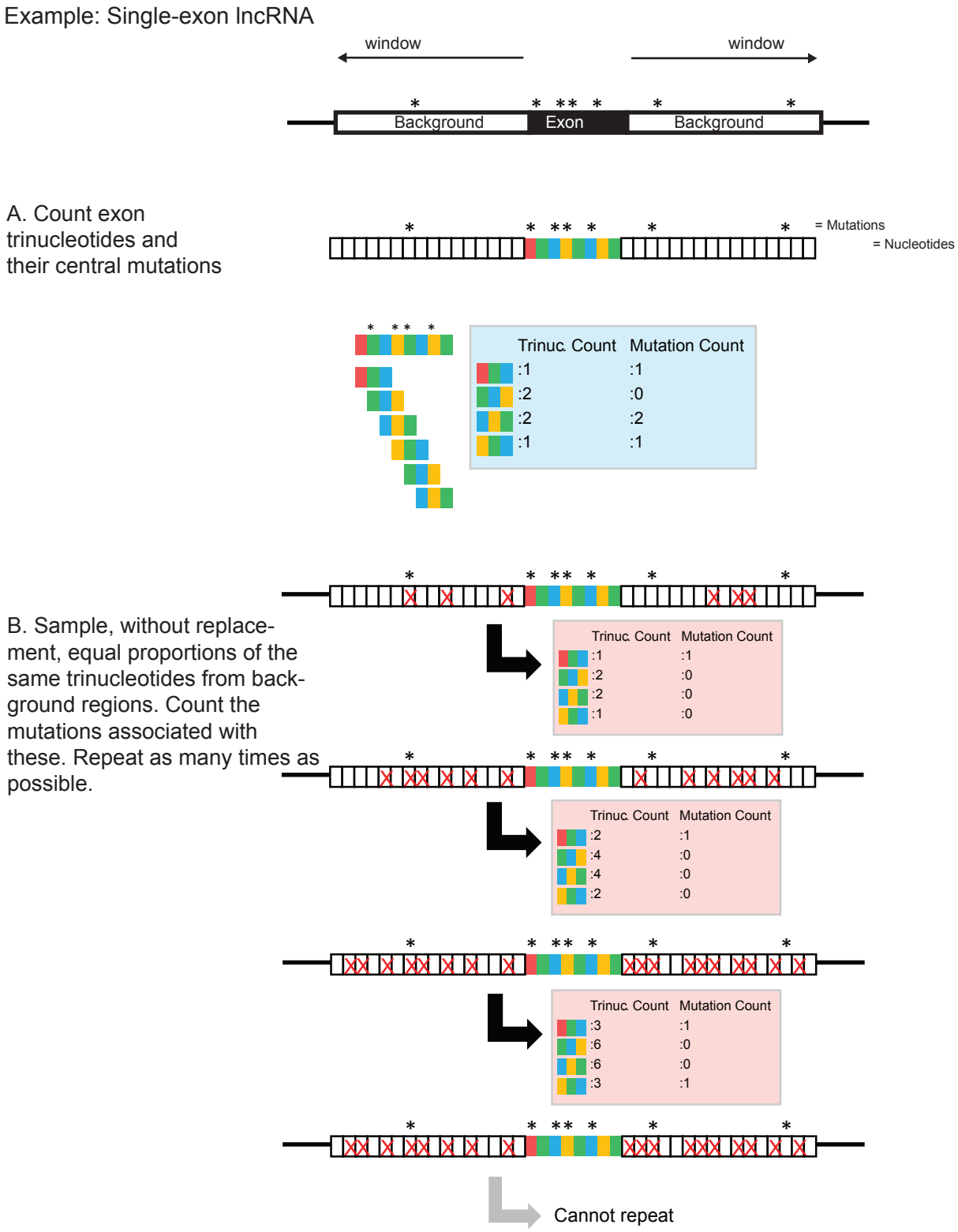
Supplementary File S9: The full set of CGC drivers analysed in this study.

Supplementary File S10: The set of IDs for protein-coding genes used in this study.

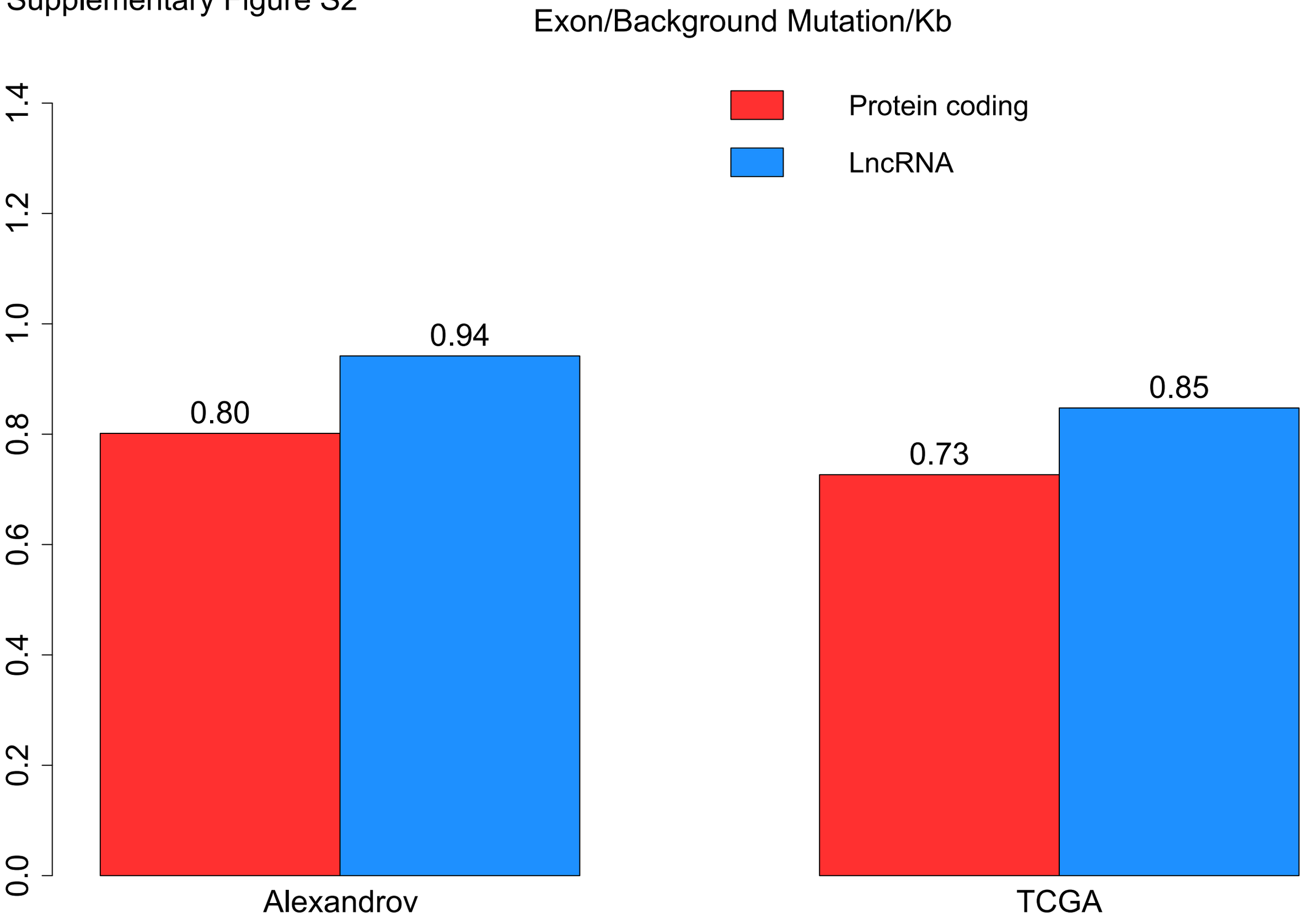
Supplementary File S11: Protein-coding overlap with CGC across all cancers and both datasets.

Supplementary File S12: Effects on ExInAtor predictions of various filtering schemes.

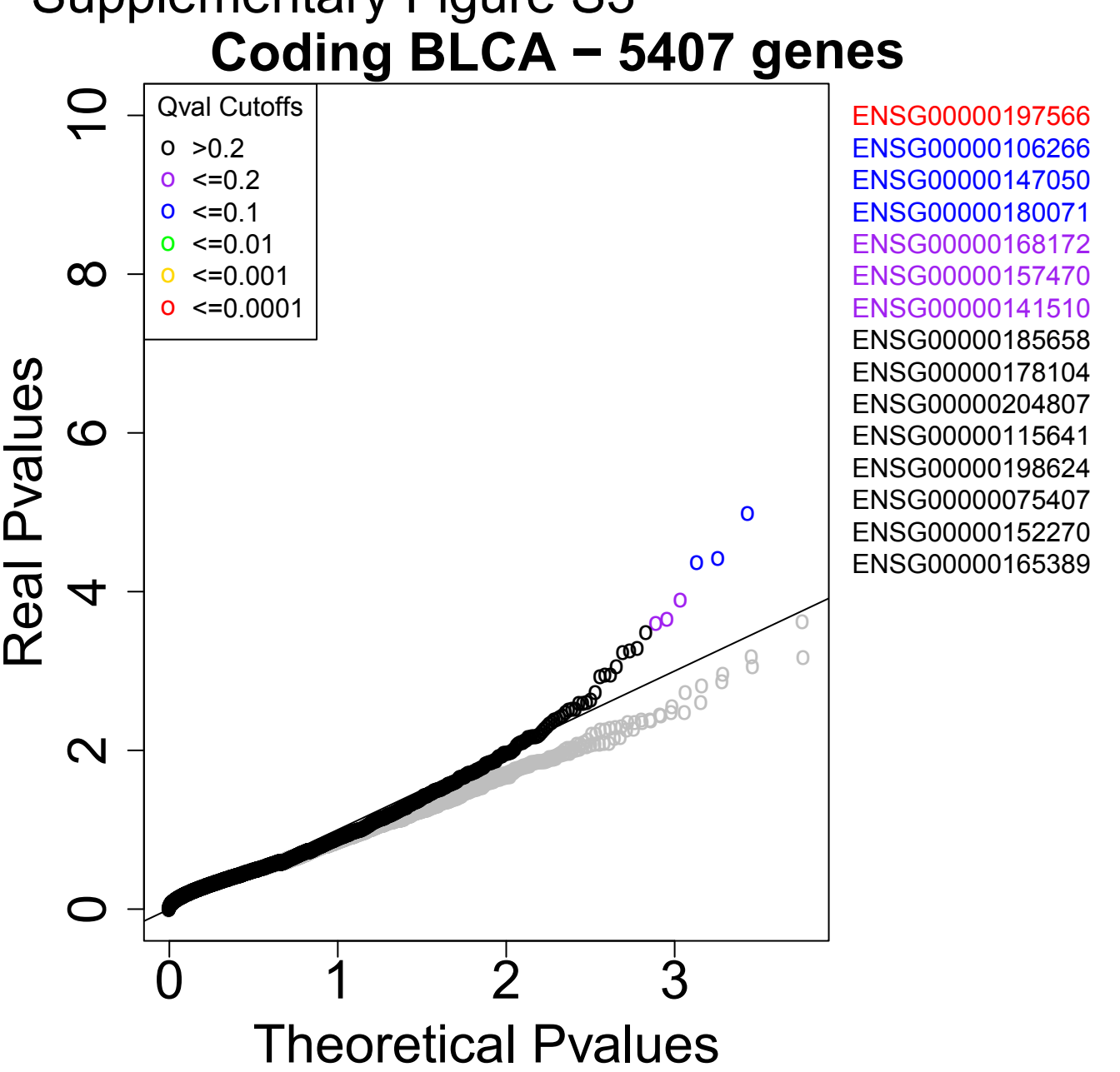
Supplementary Figure S1



Supplementary Figure S2



Supplementary Figure S3



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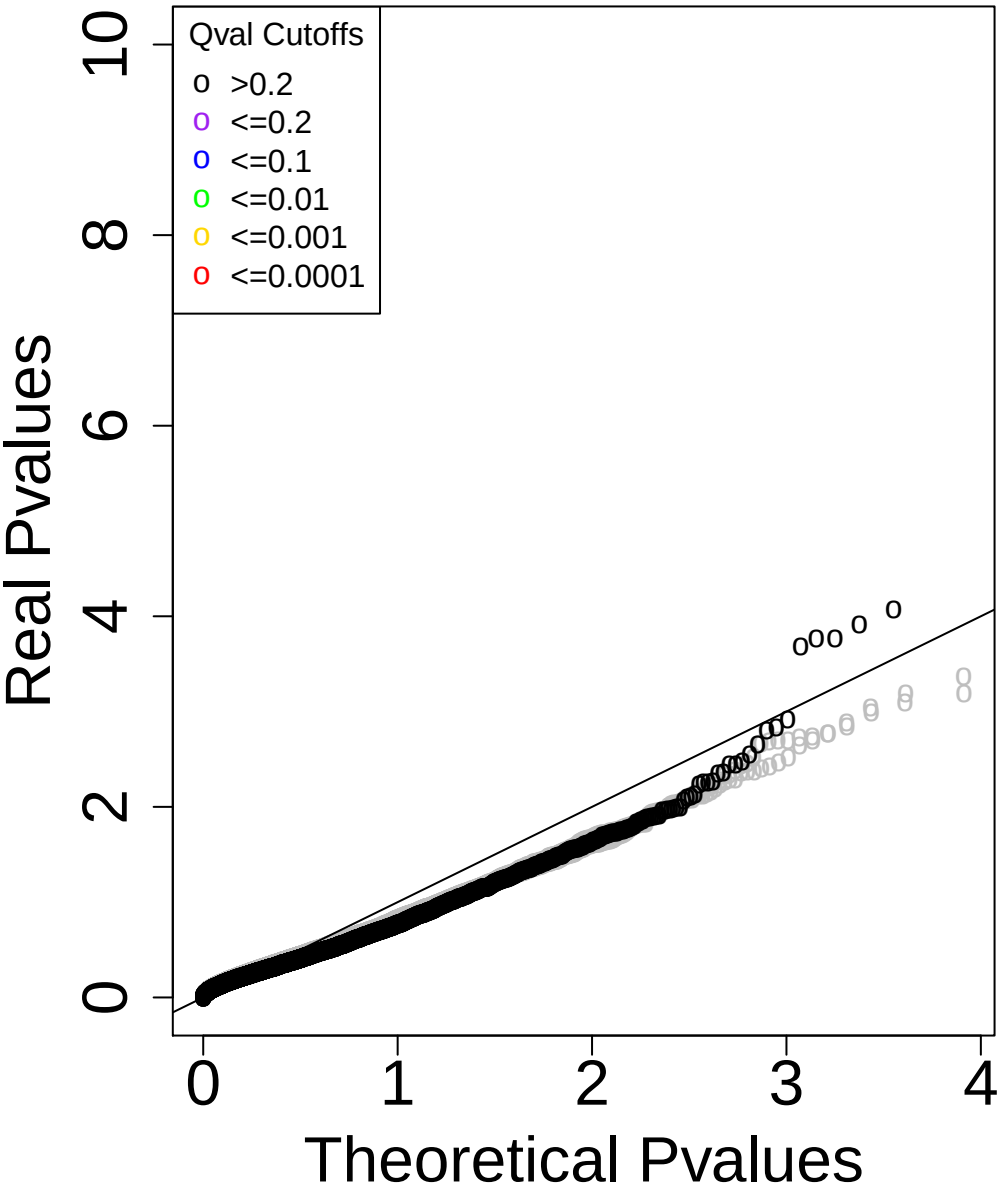

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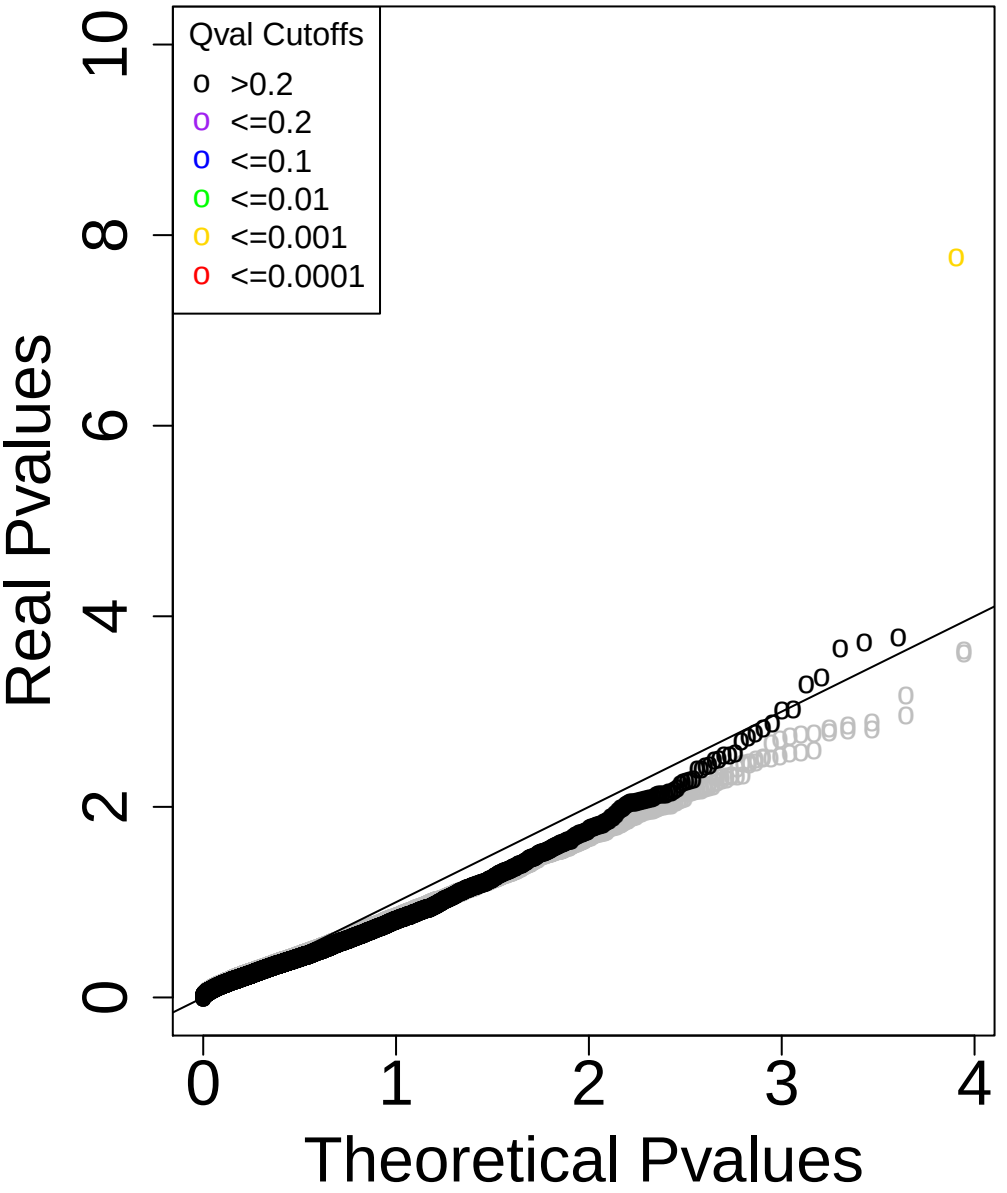

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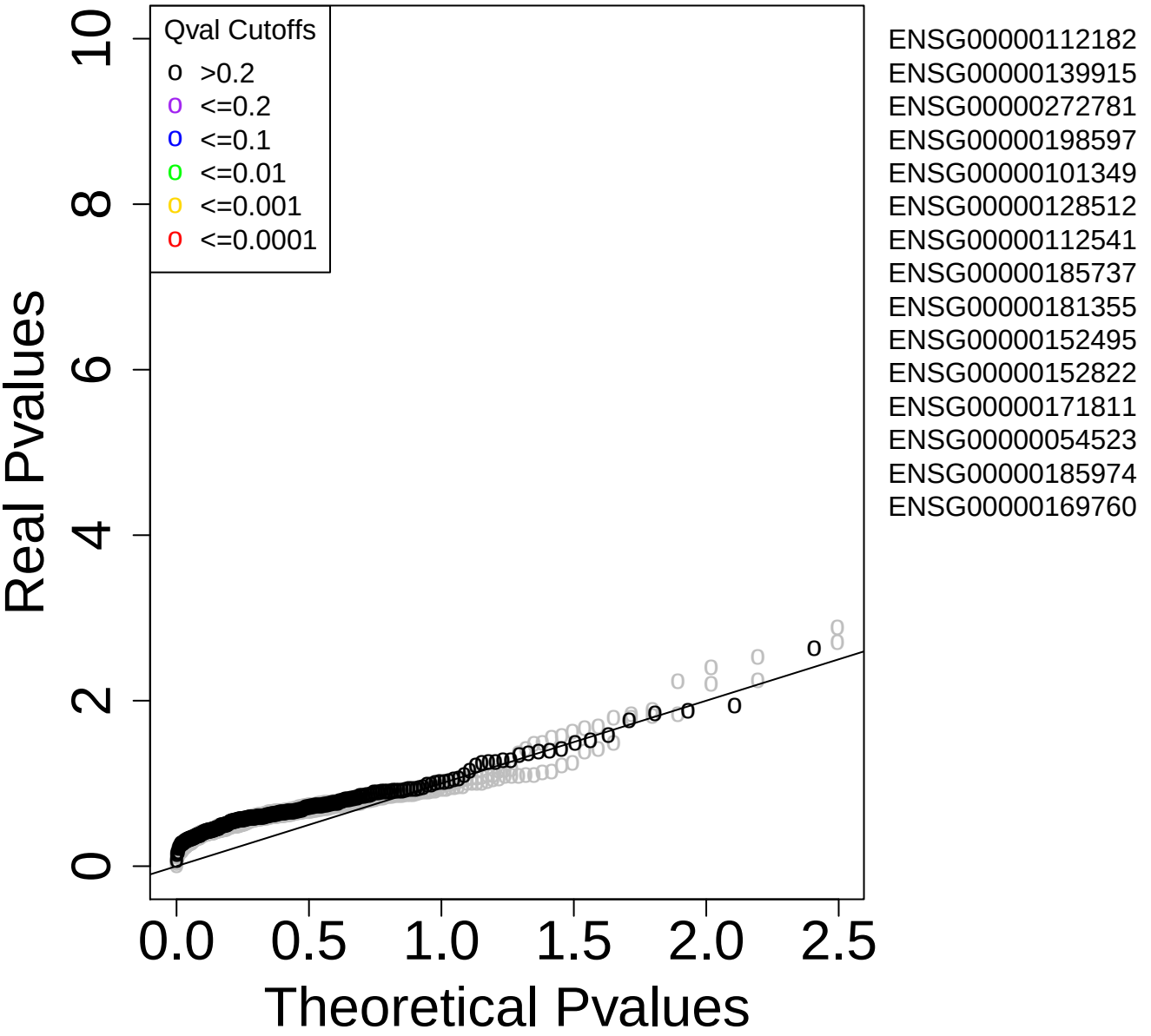
Coding CLL − 256 genes



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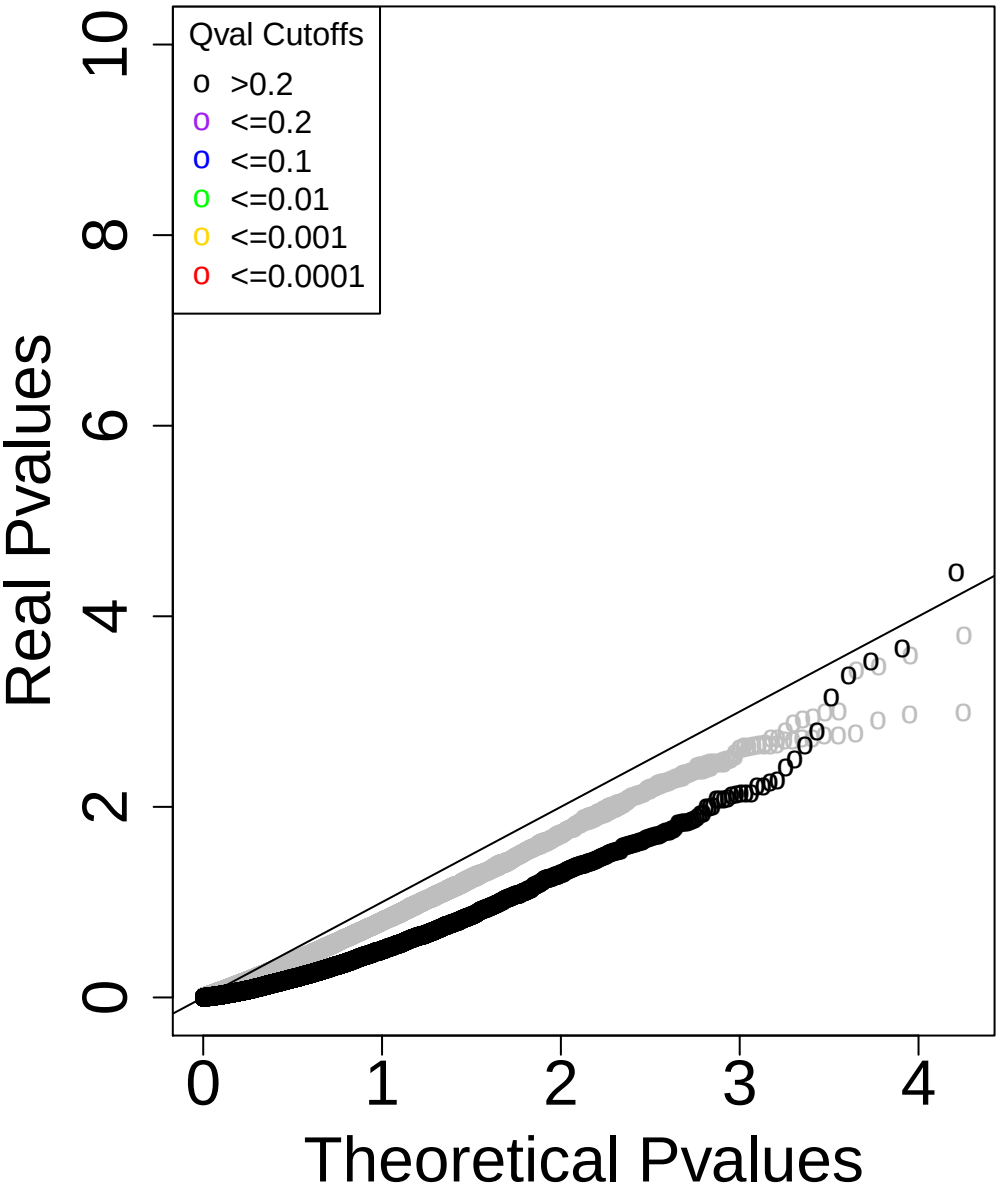
Coding CRC − 16265 genes



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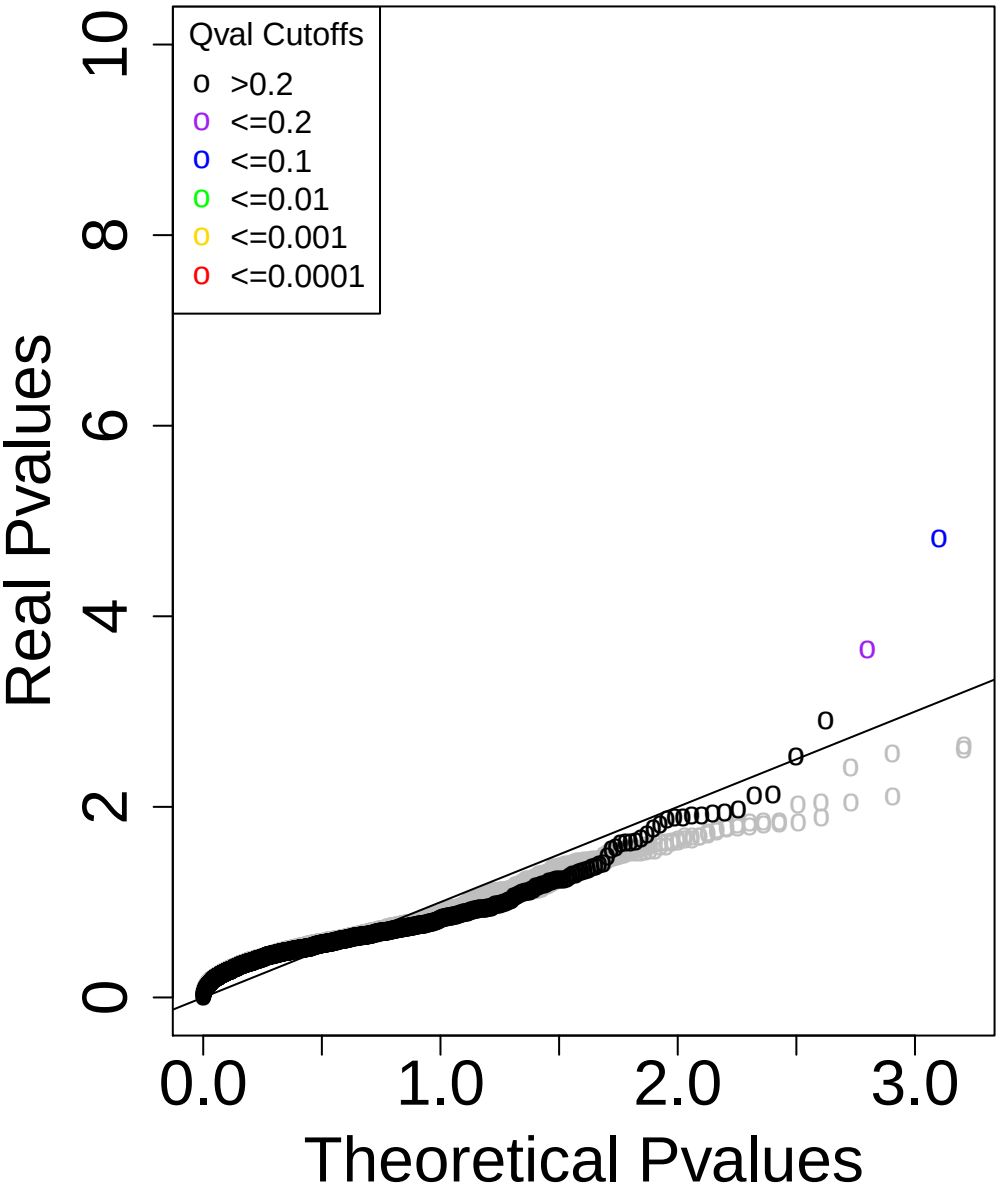
Coding GBM – 1262 genes



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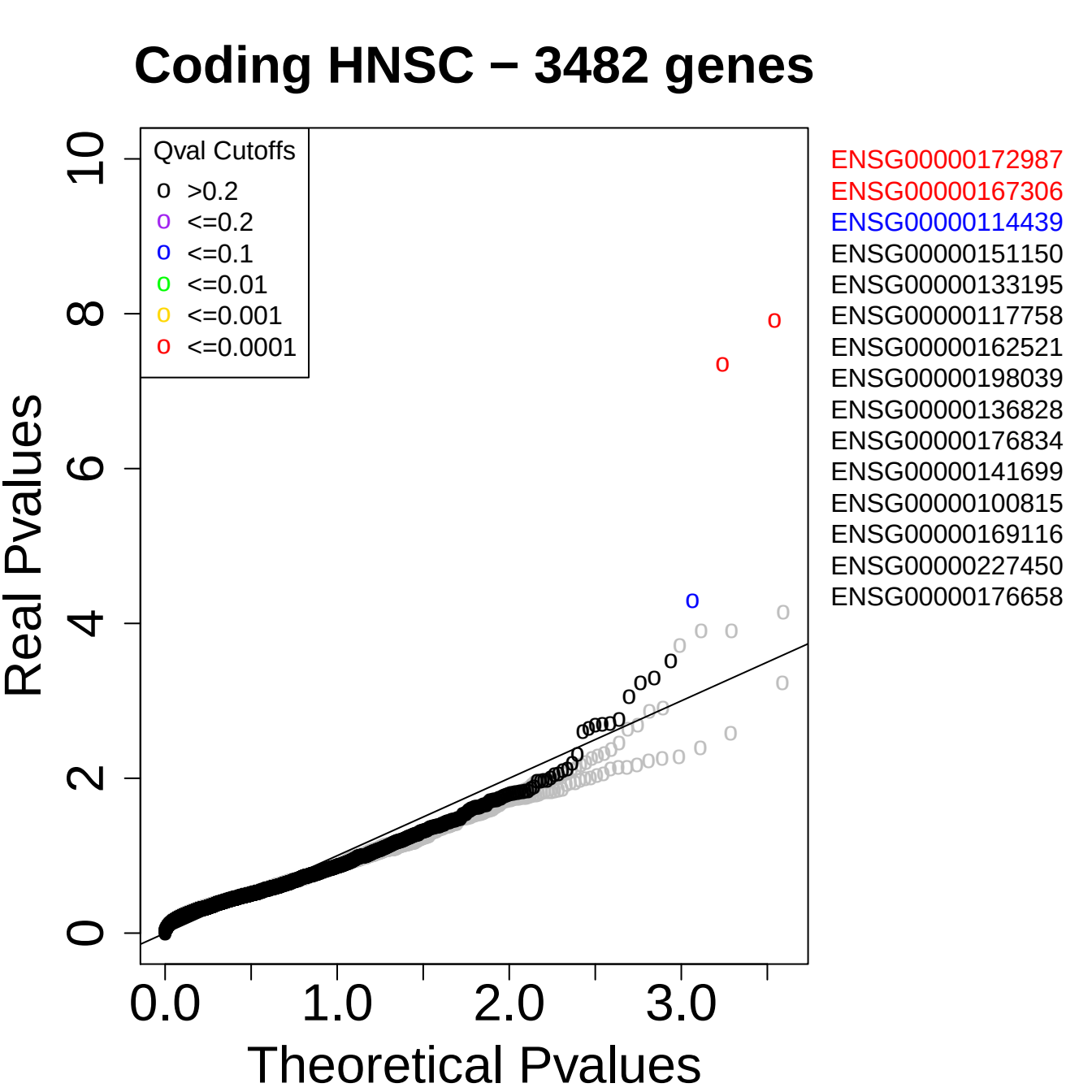
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<=0.1
<=0.01
<=0.001
<=0.0001
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2
4
6
8
10
0.0
1.0
2.0
3.0
Theoretical Pvalues
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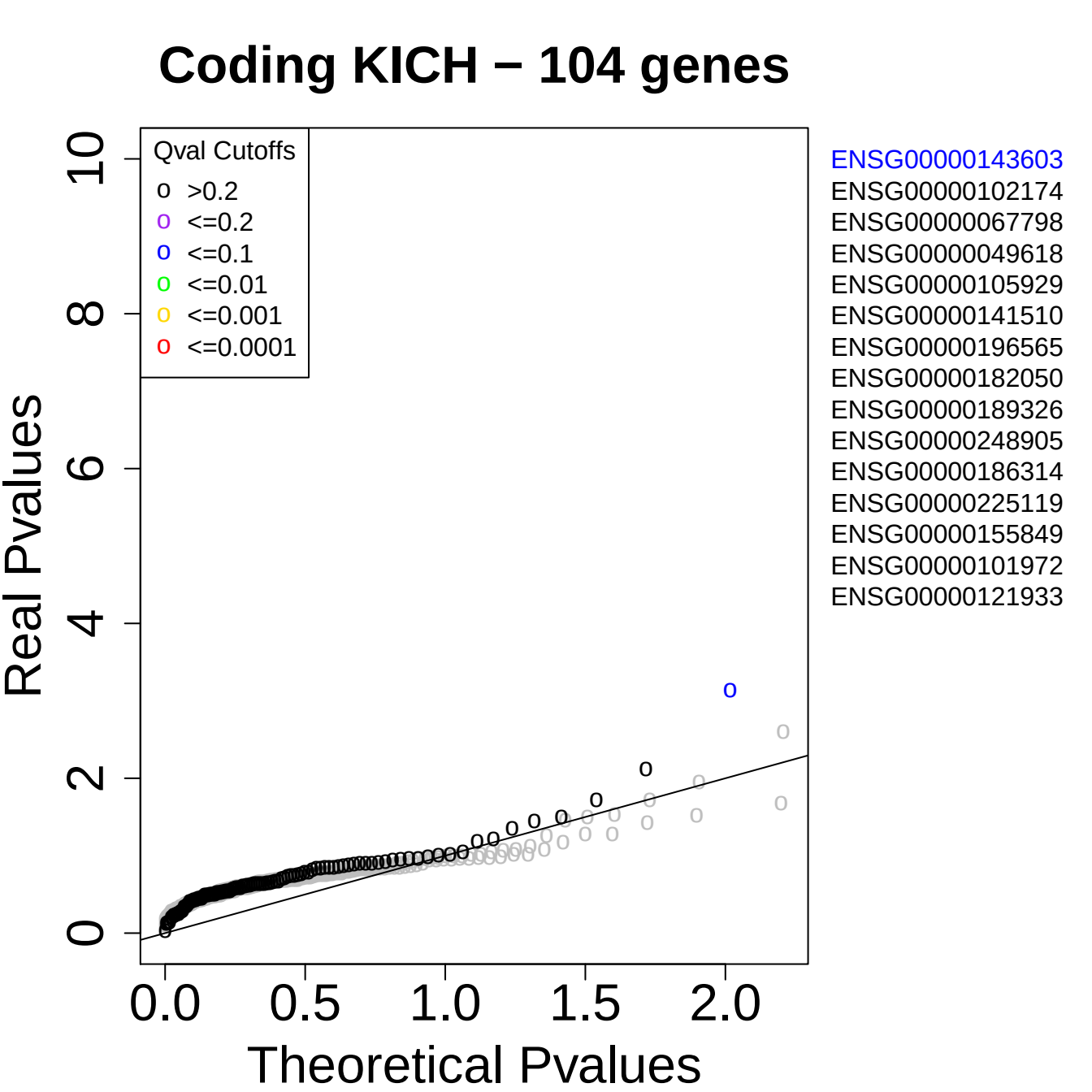
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Real Pvalues
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8
10
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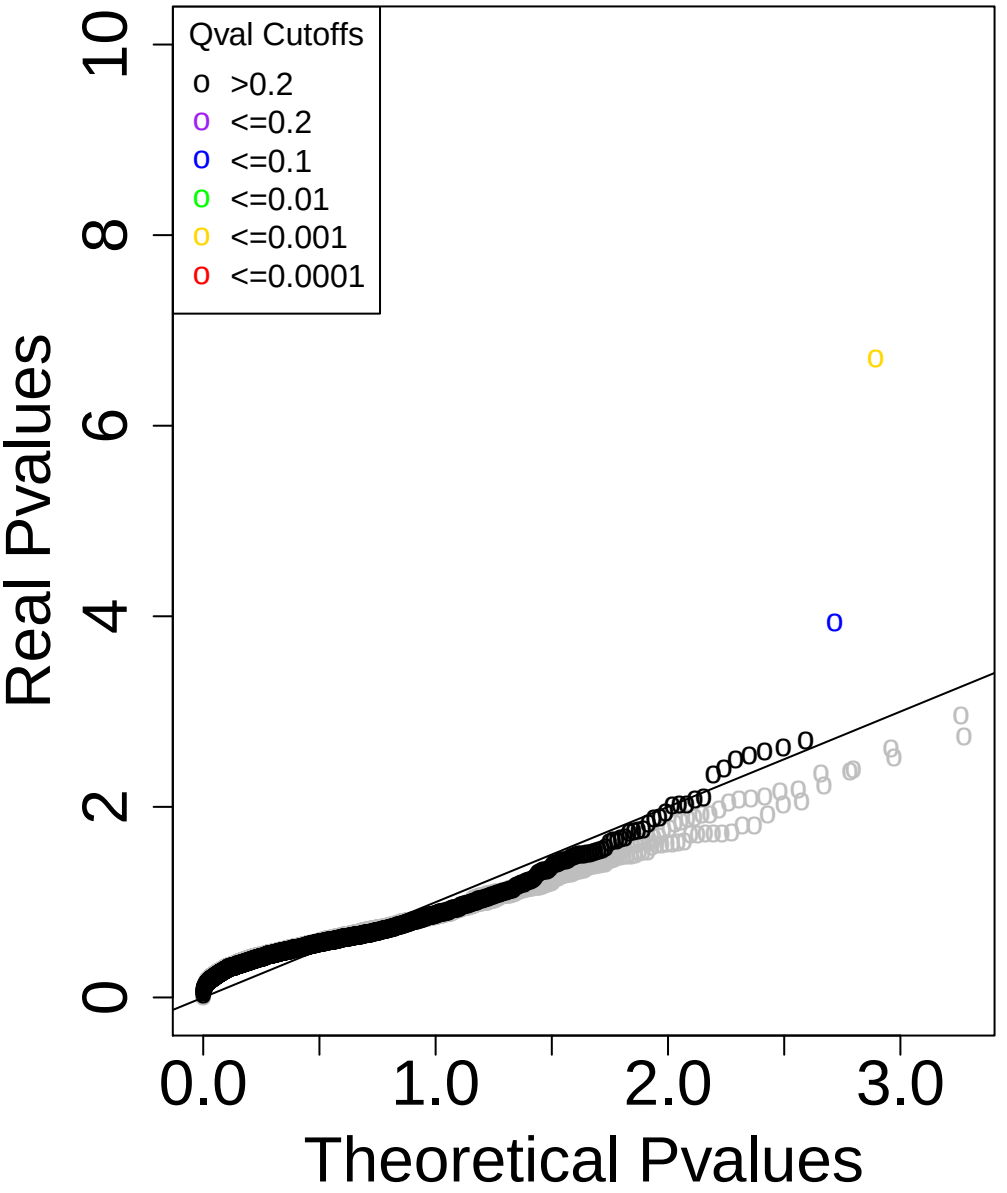
1.0
1.5
2.0
Theoretical Pvalues

Coding KIRC – 1566 genes



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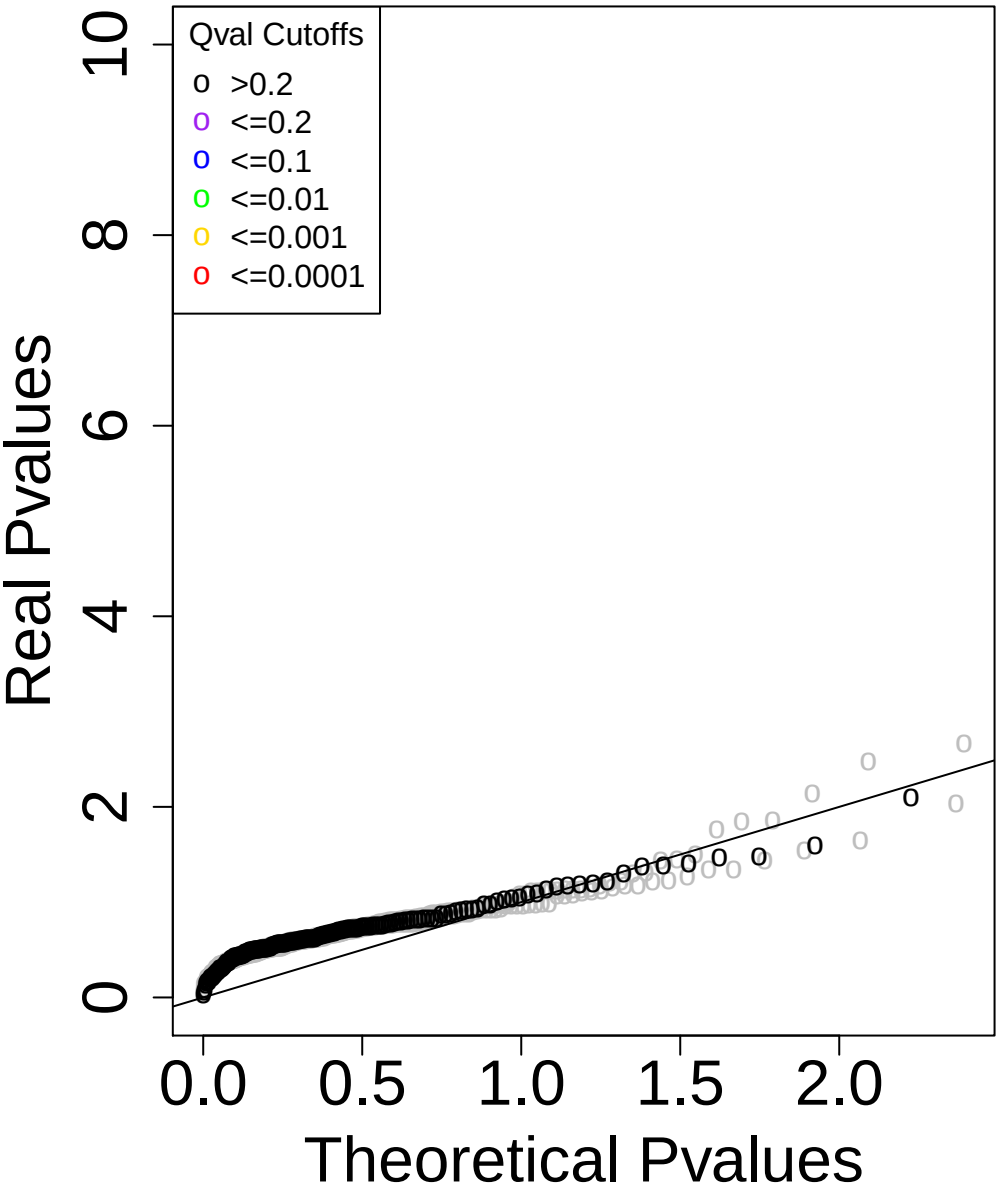
Coding LGG – 168 genes



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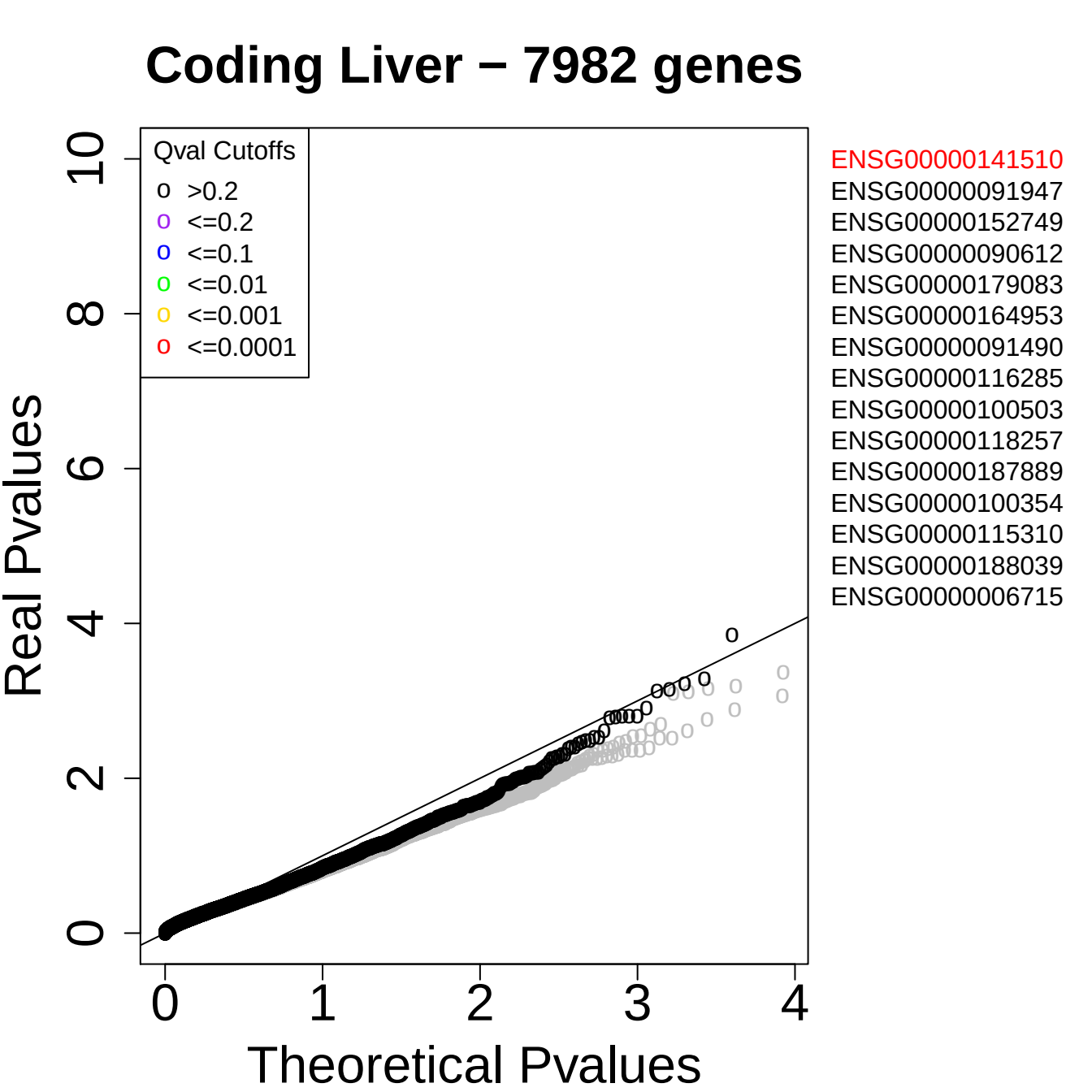
Coding Liver − 7982 genes
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<=0.1
<=0.01
<=0.001
<=0.0001
Real Pvalues
Theoretical Pvalues
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2
4
6
8
10
0
1
2
3
4
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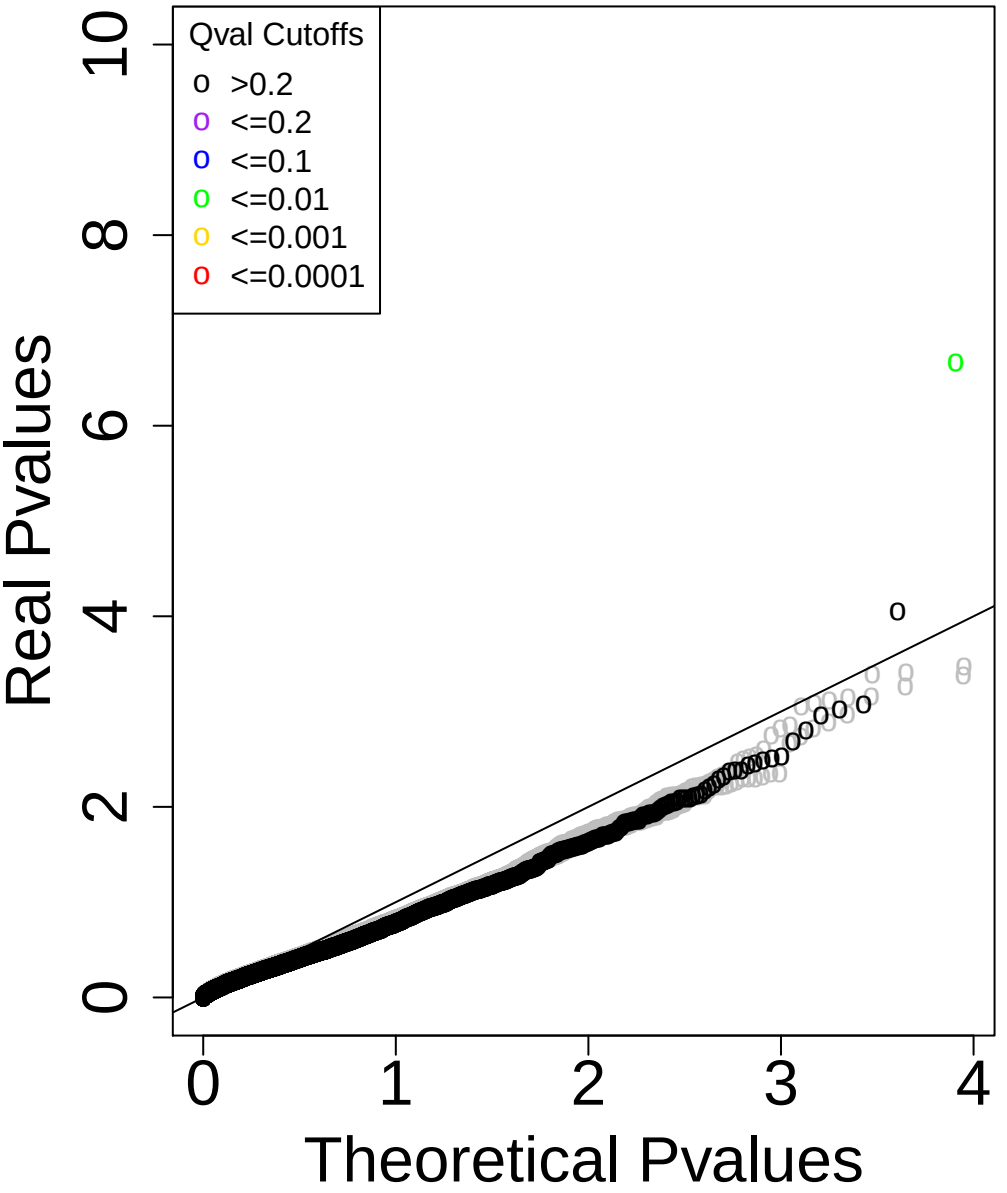
Coding LUAD – 8082 genes



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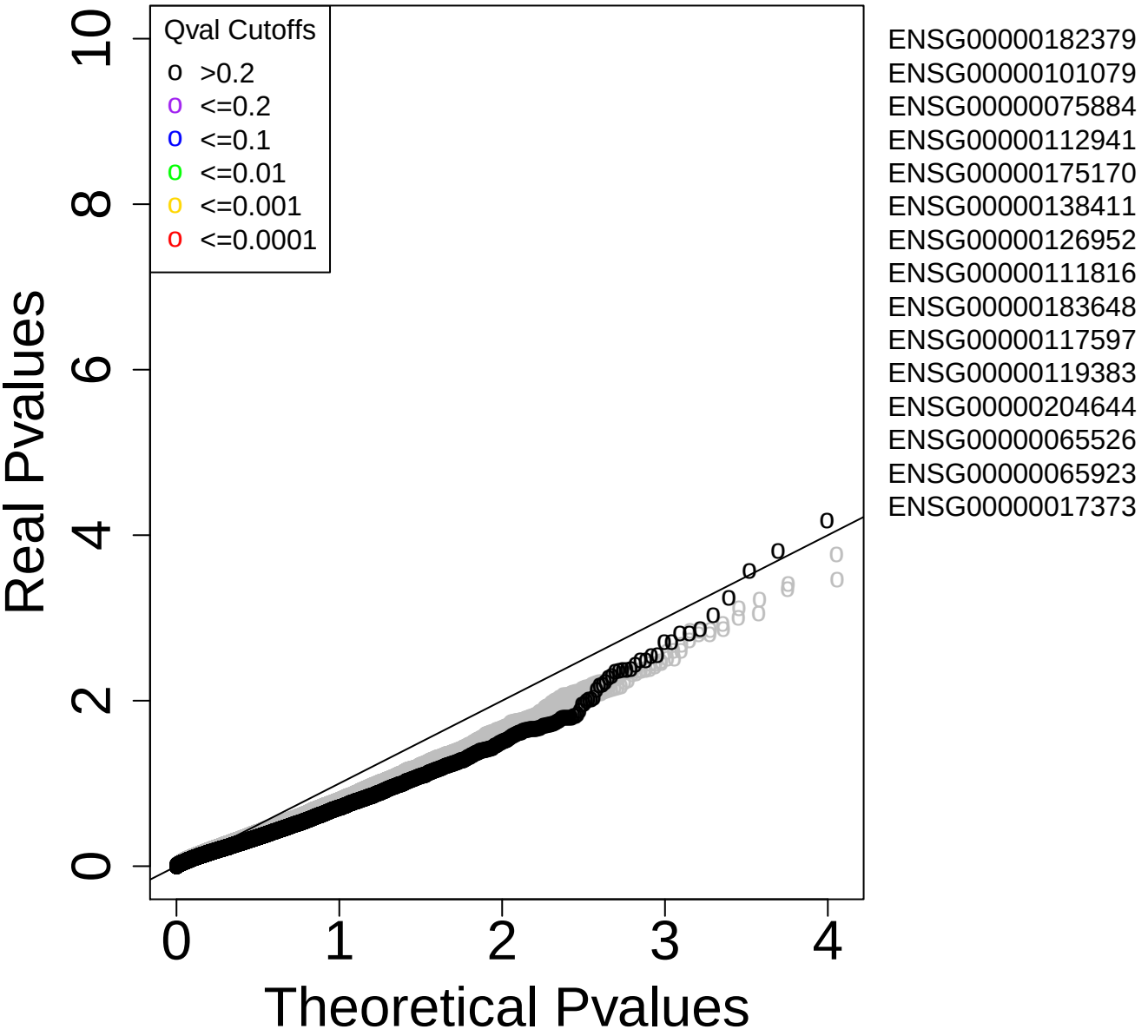
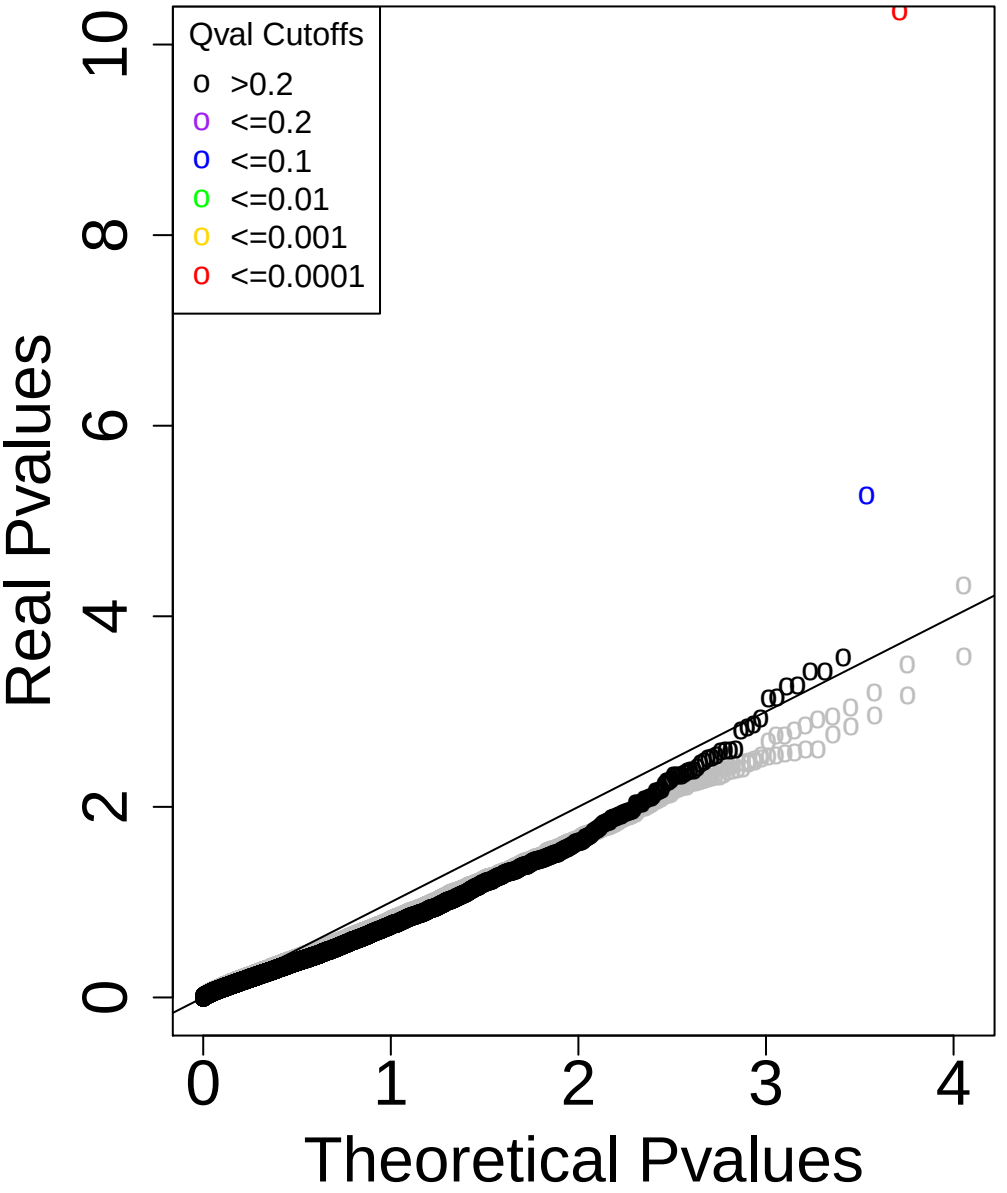
Coding Lung_adeno − 9893 genes



Coding LUSC – 10329 genes



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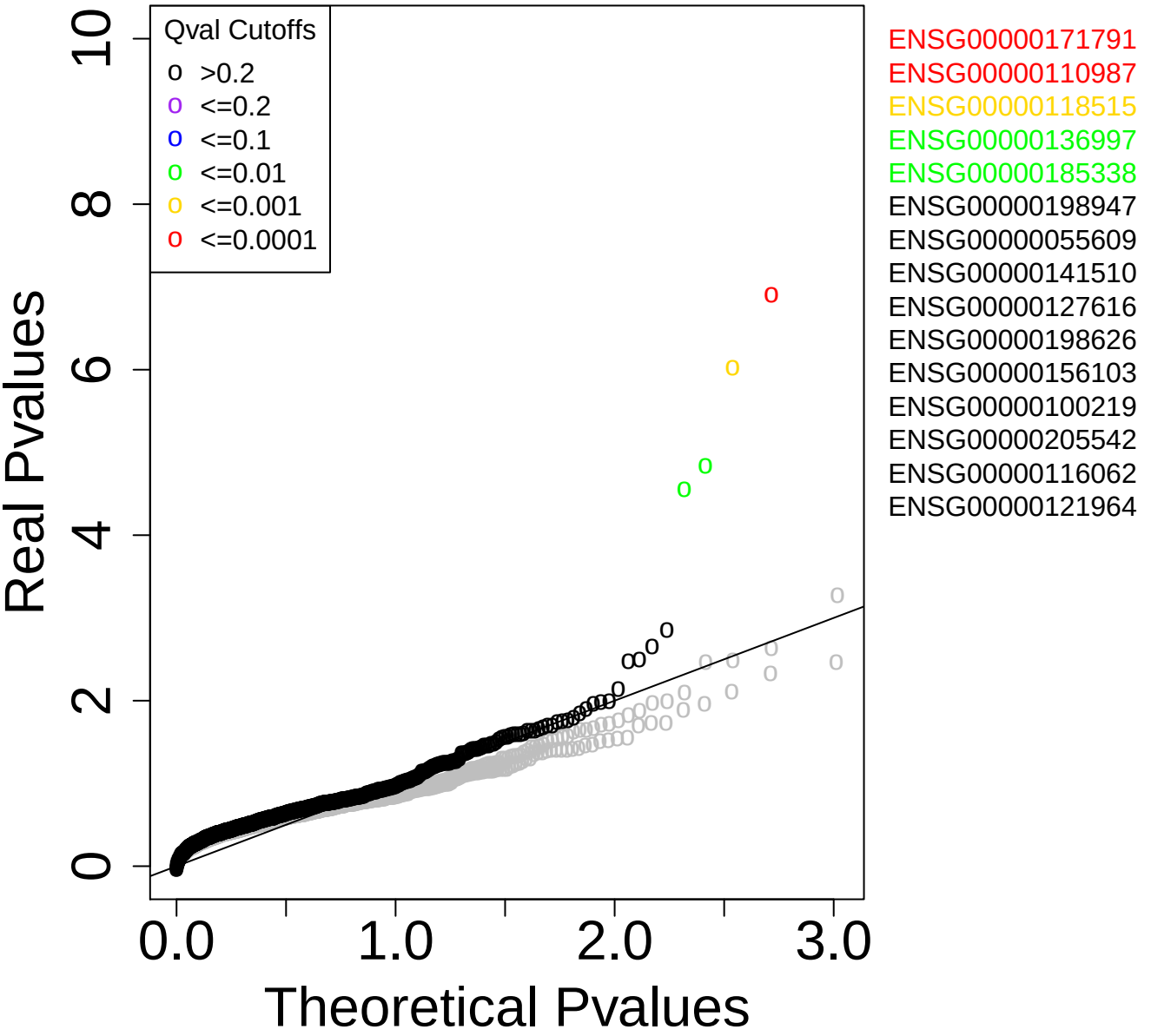
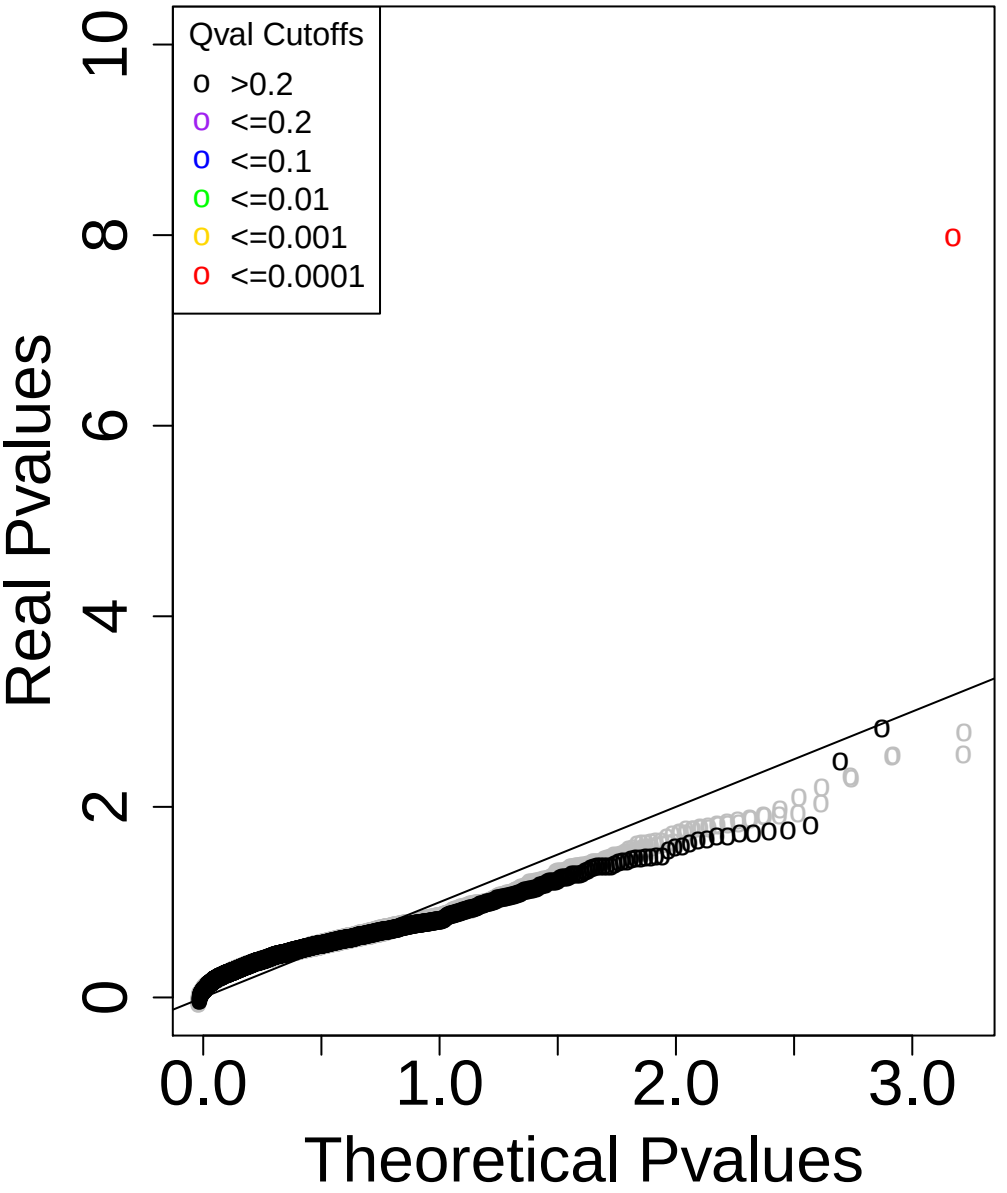
Coding Lymphoma_B−cell − 1038 genes



Coding Medulloblastoma − 1488 genes



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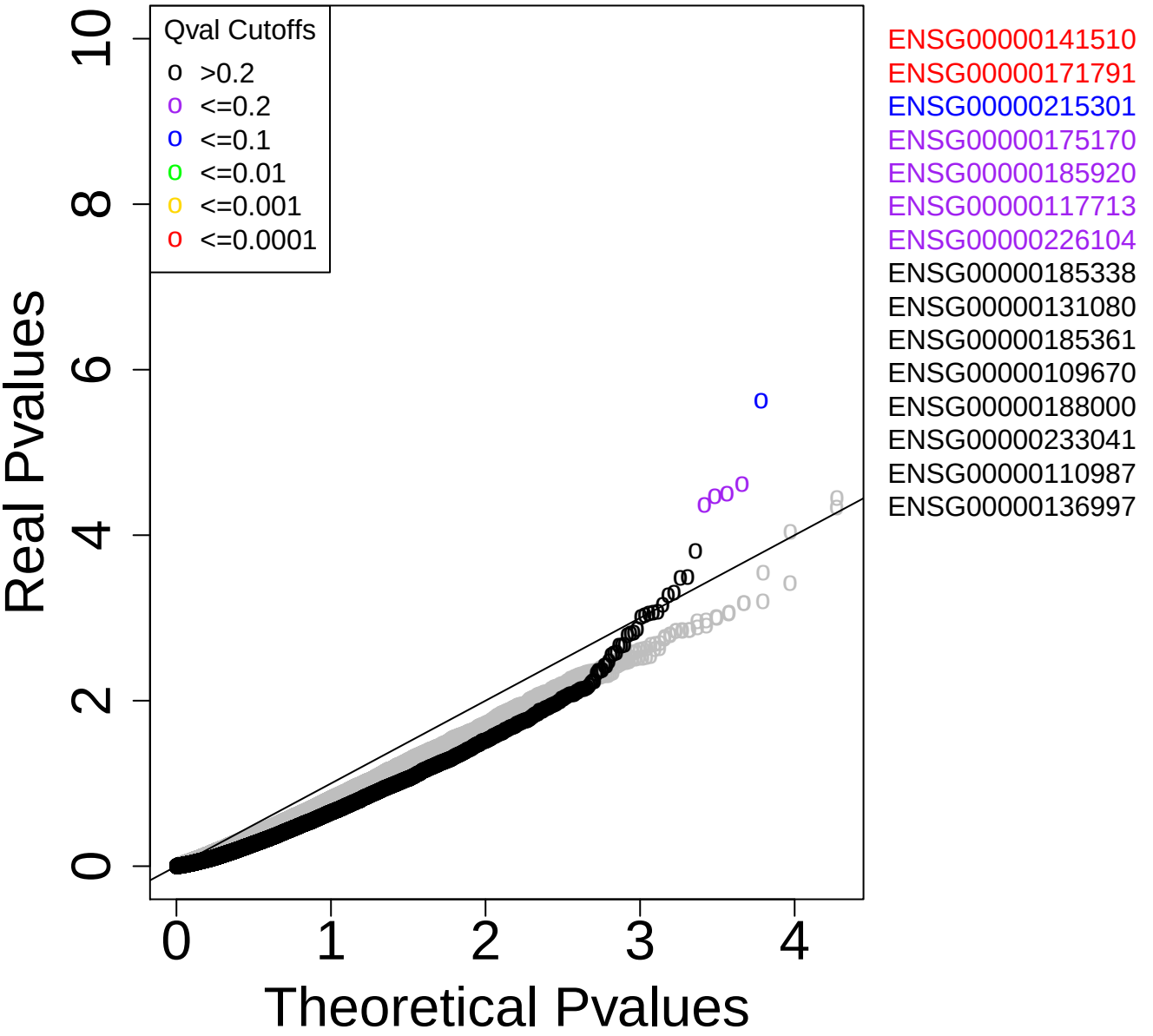
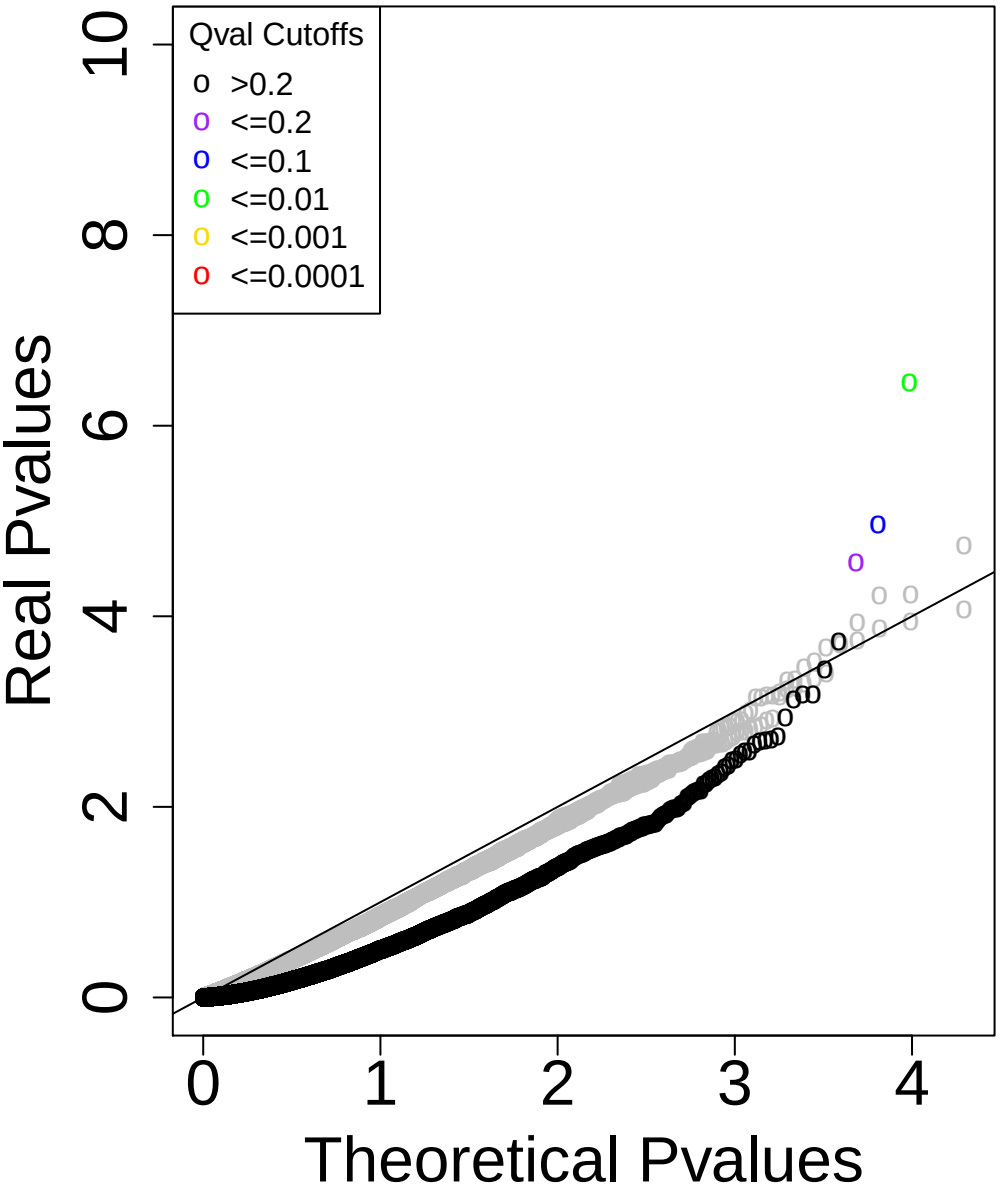
ling Pancancer_Alexandrov − 18261 genes



Coding Pancancer_TCGA − 19313 genes



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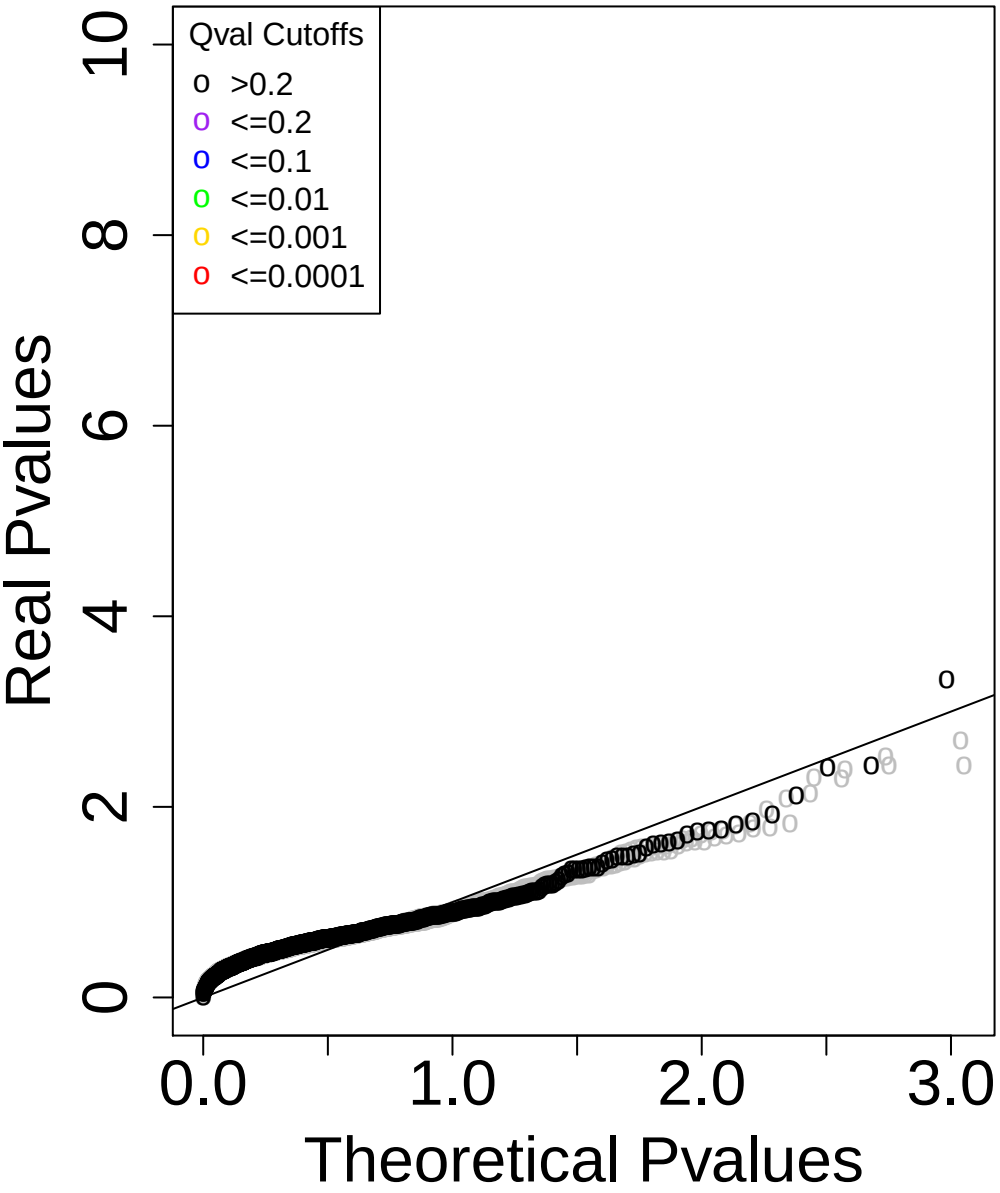
Coding Pancreas − 960 genes



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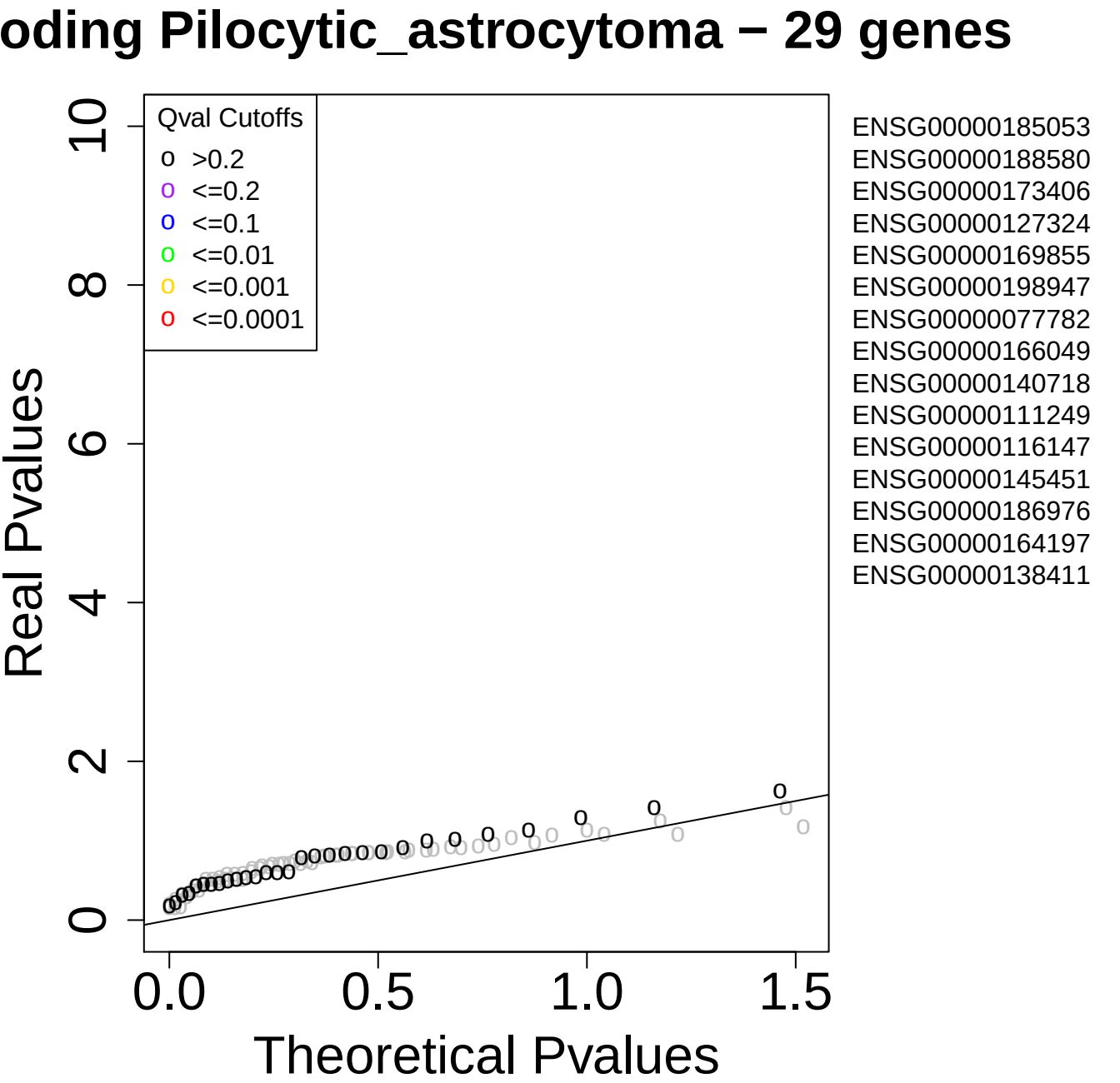
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Real Pvalues
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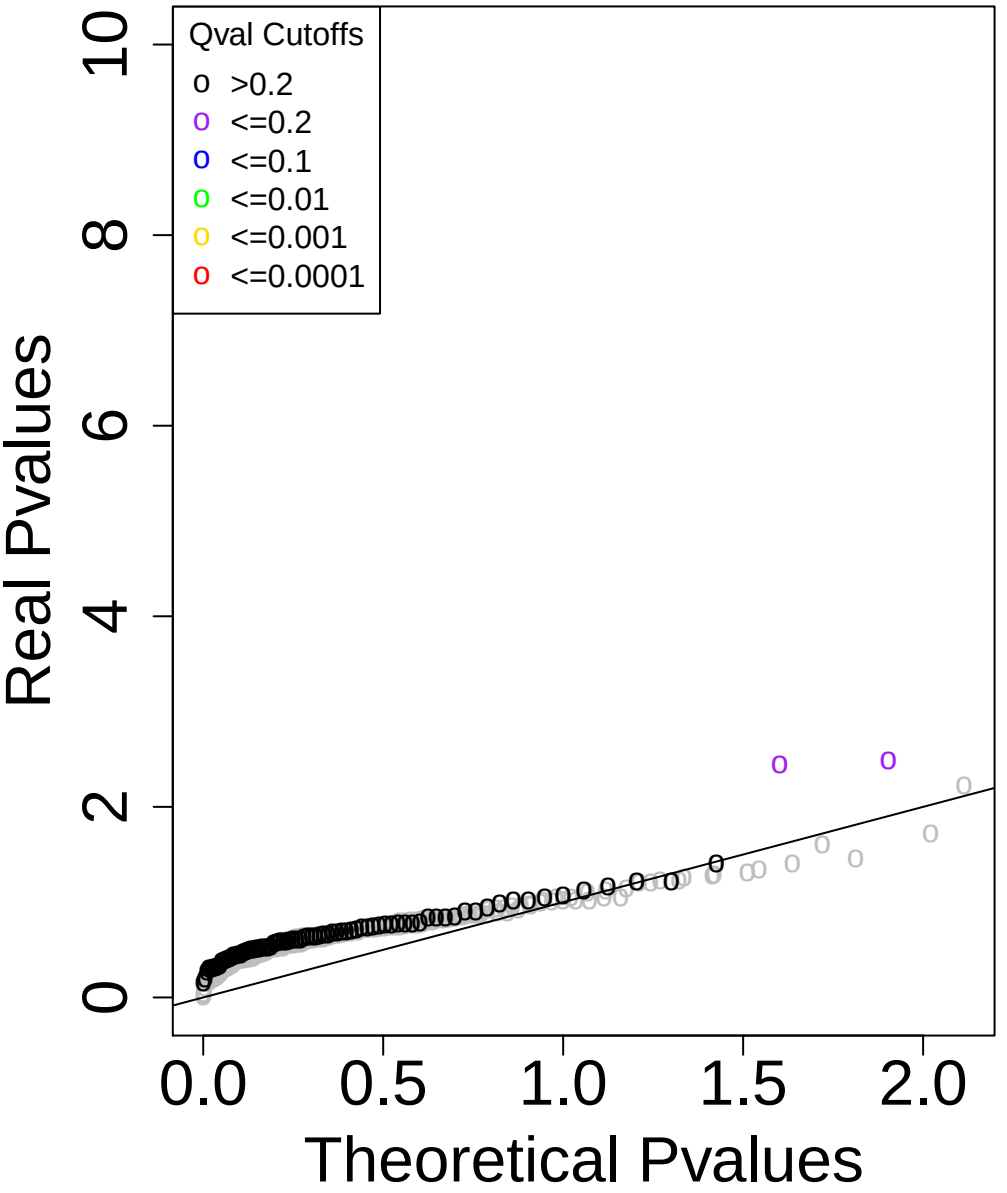
1.0
1.5
Theoretical Pvalues

Coding PRAD − 80 genes



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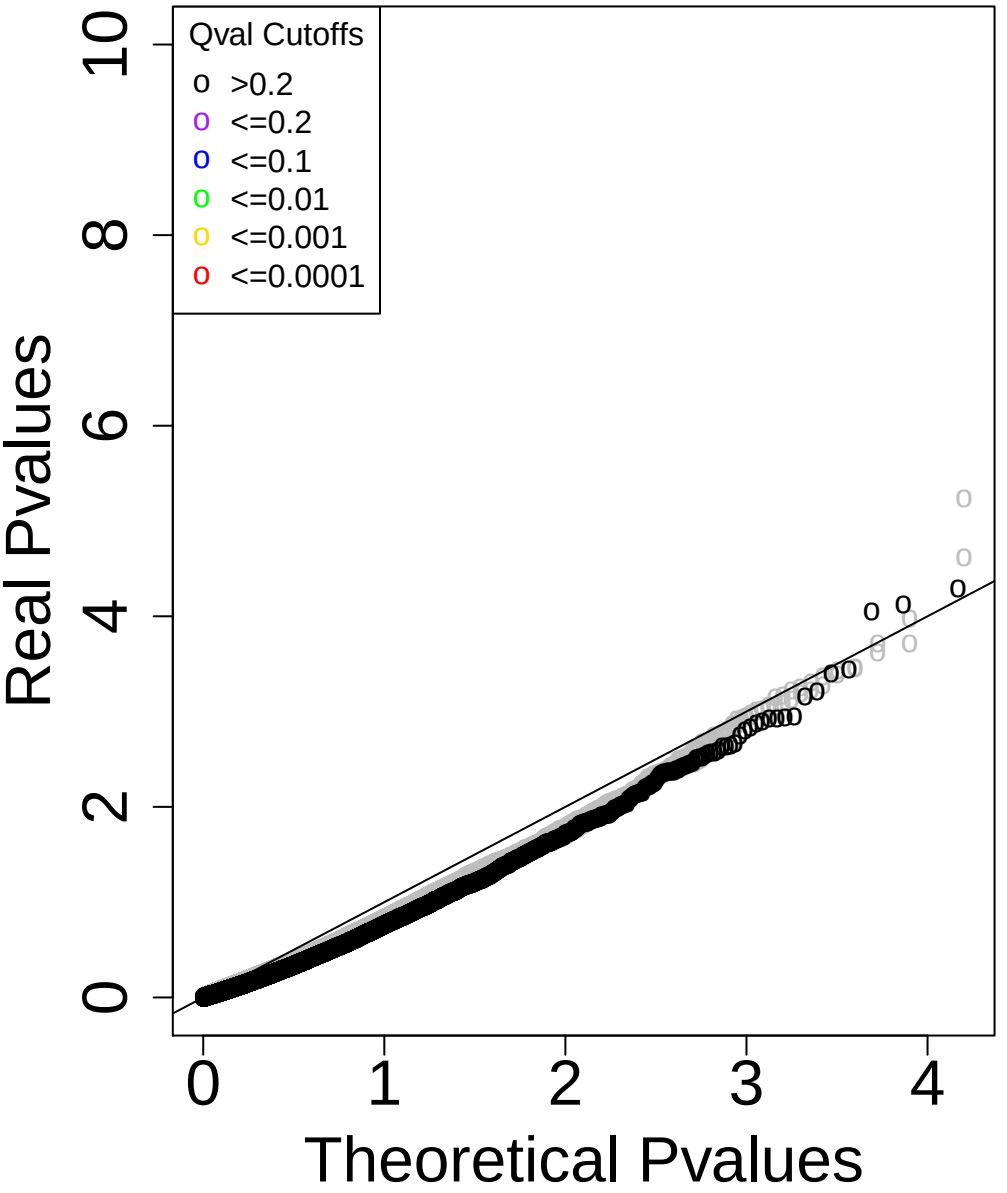
Coding SKCM – 14721 genes



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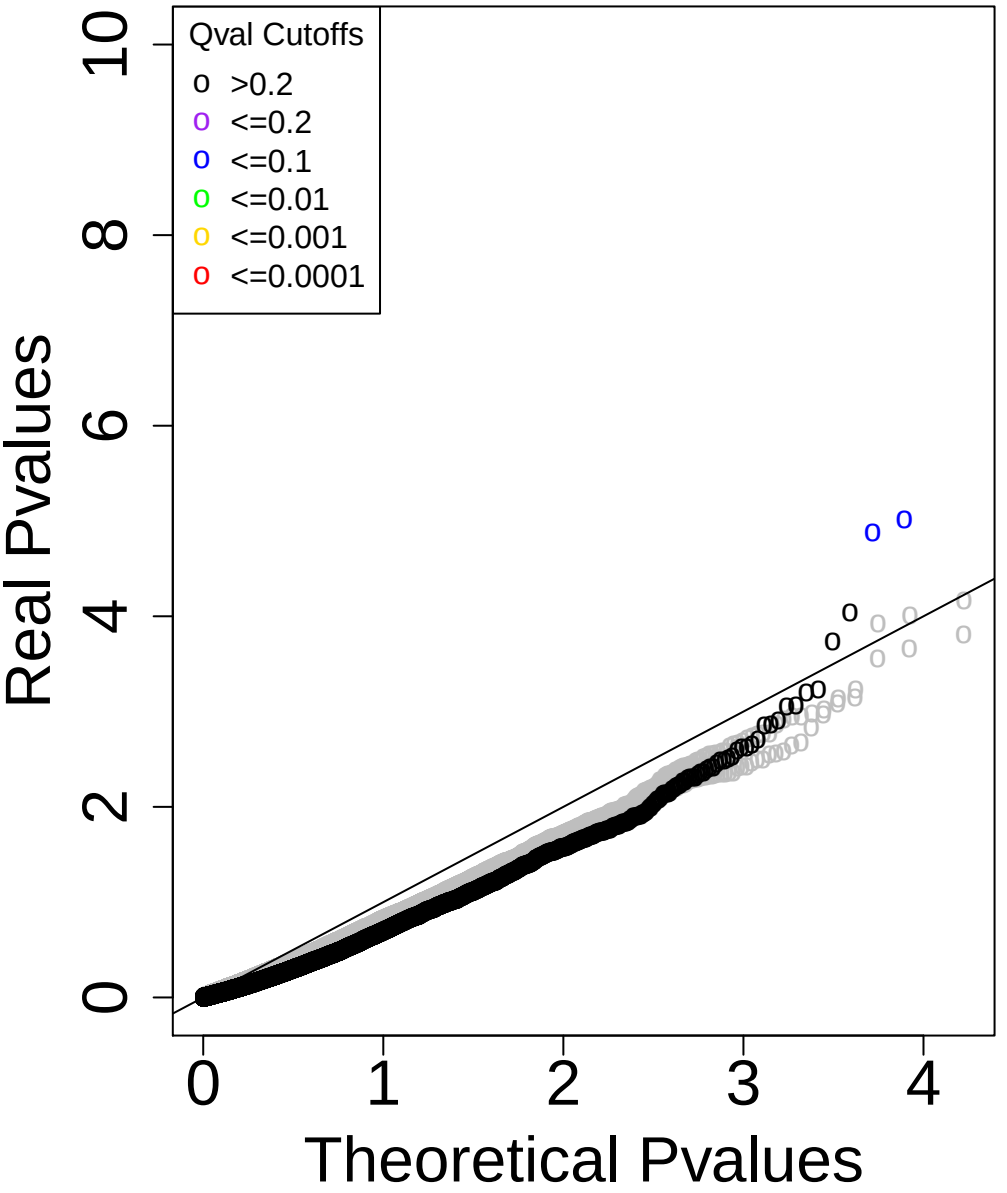
Coding Stad − 15662 genes



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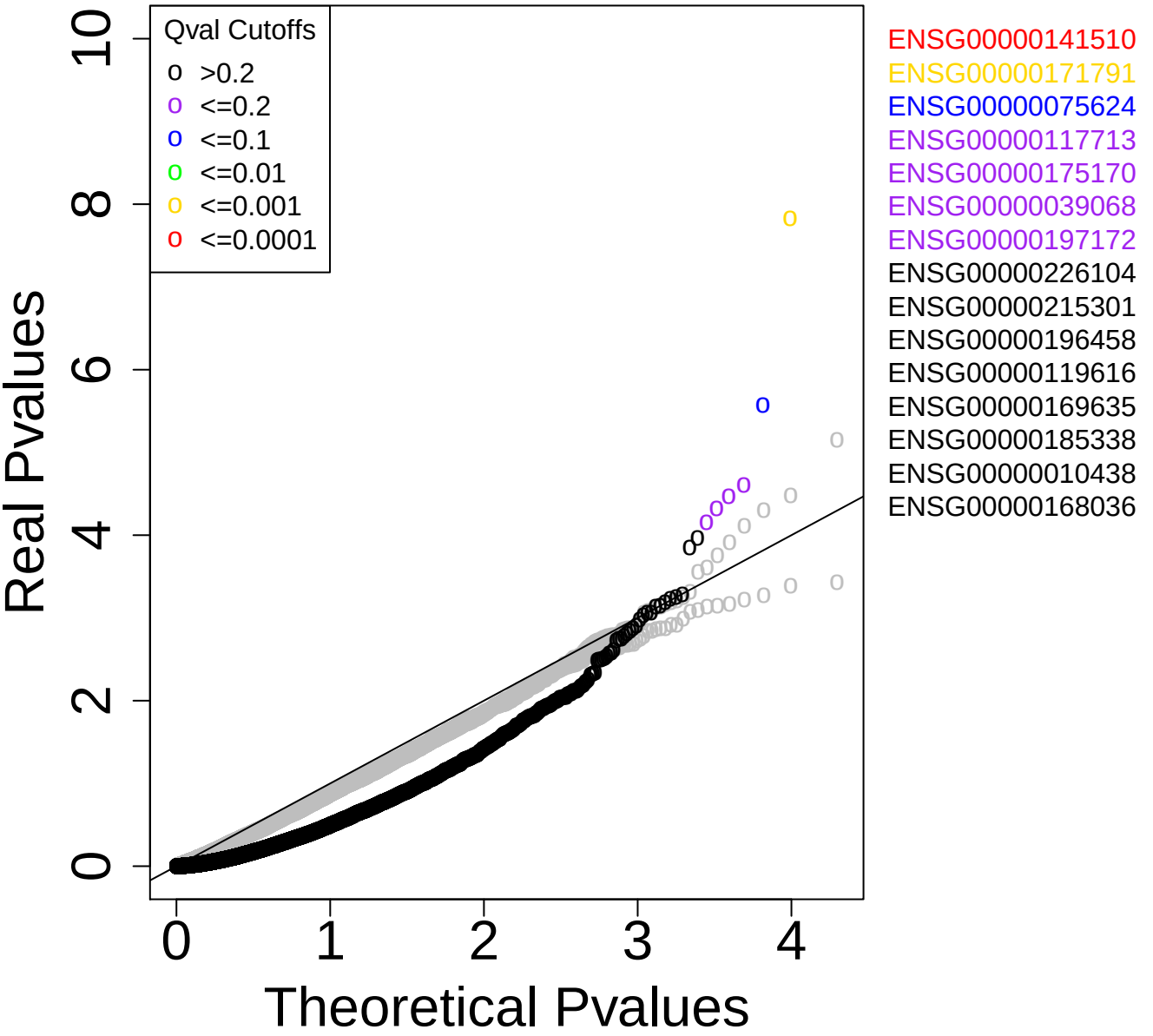
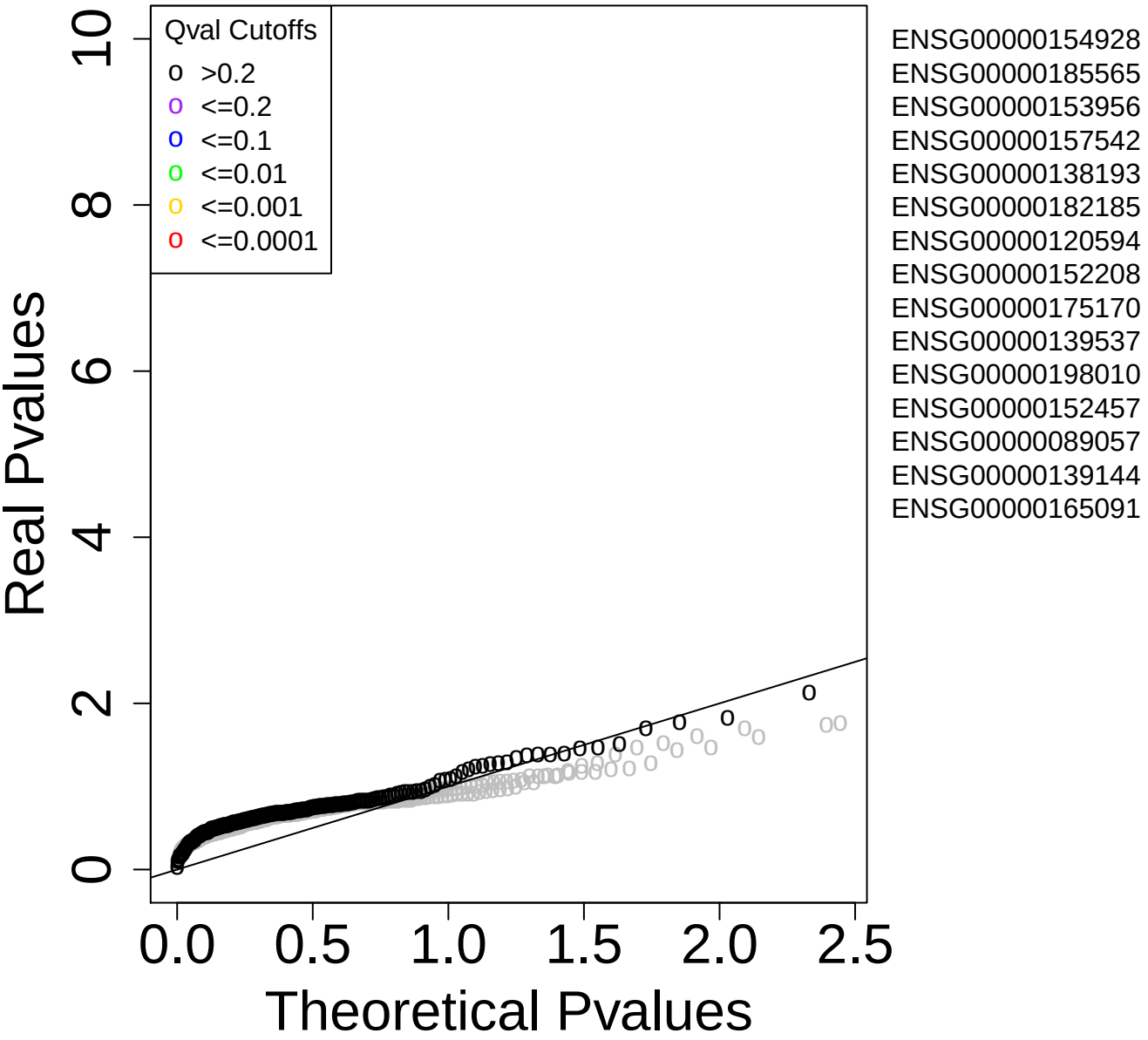
Coding Superpancancer – 19594 genes



Coding THCA – 214 genes



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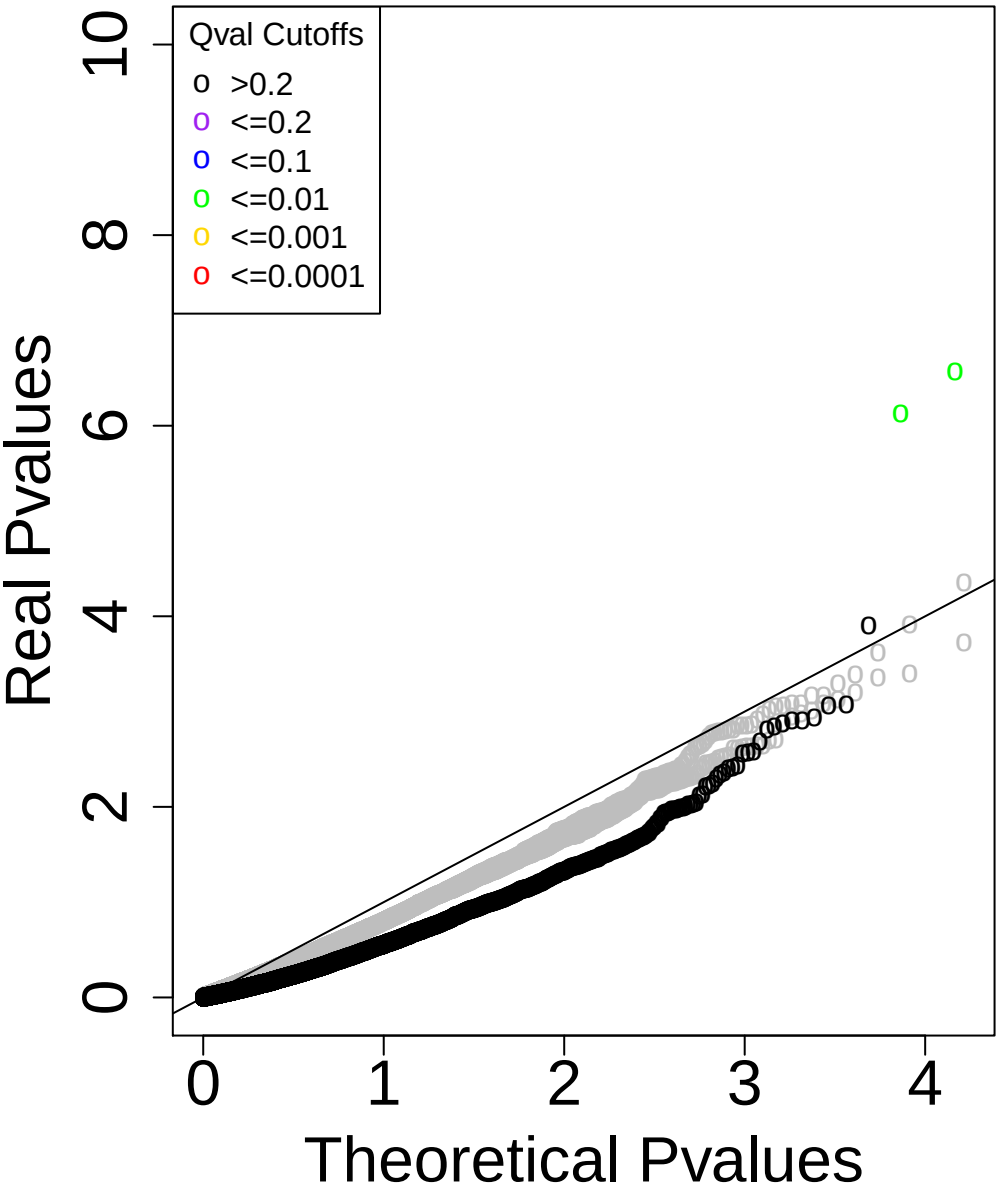
Coding UCEC – 14611 genes



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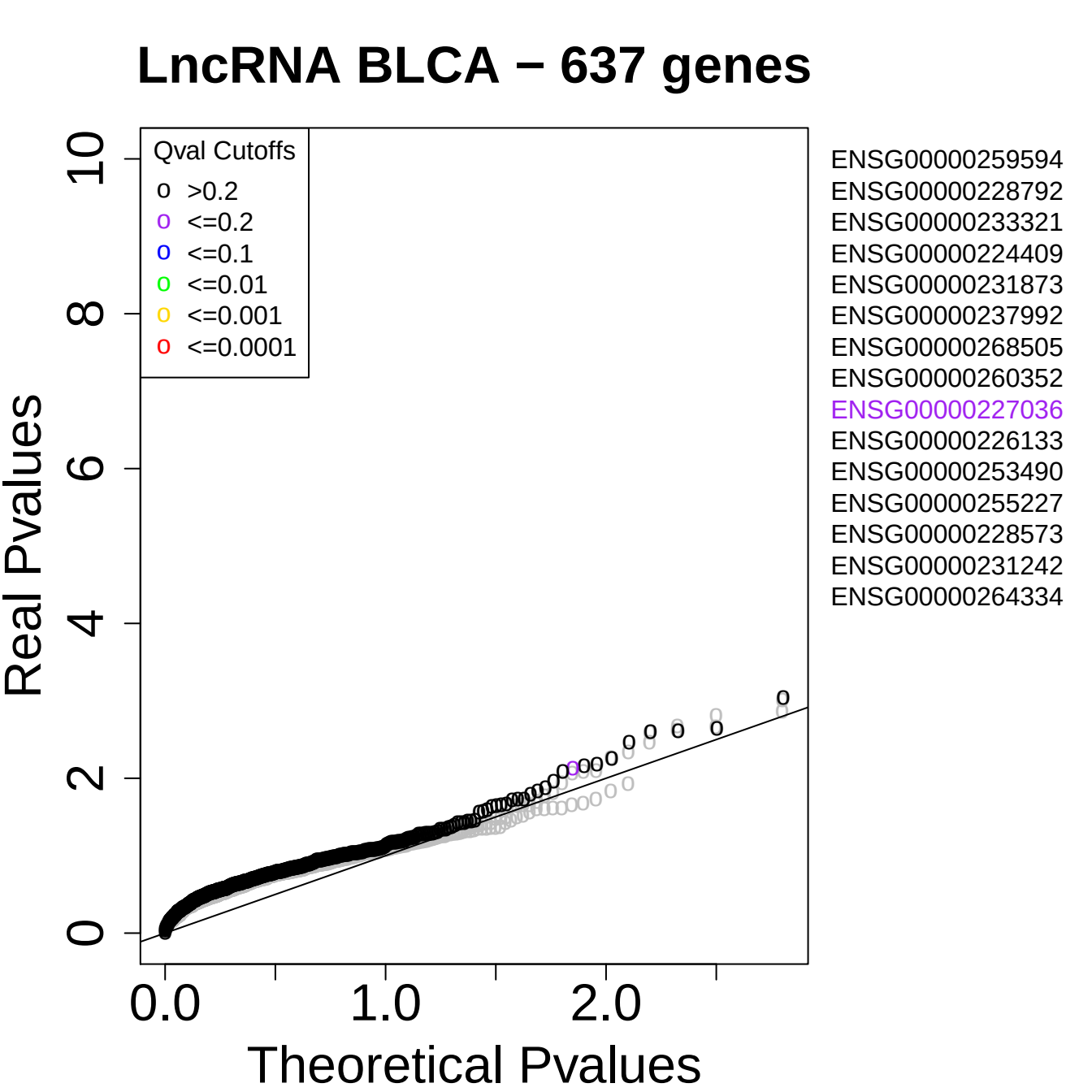
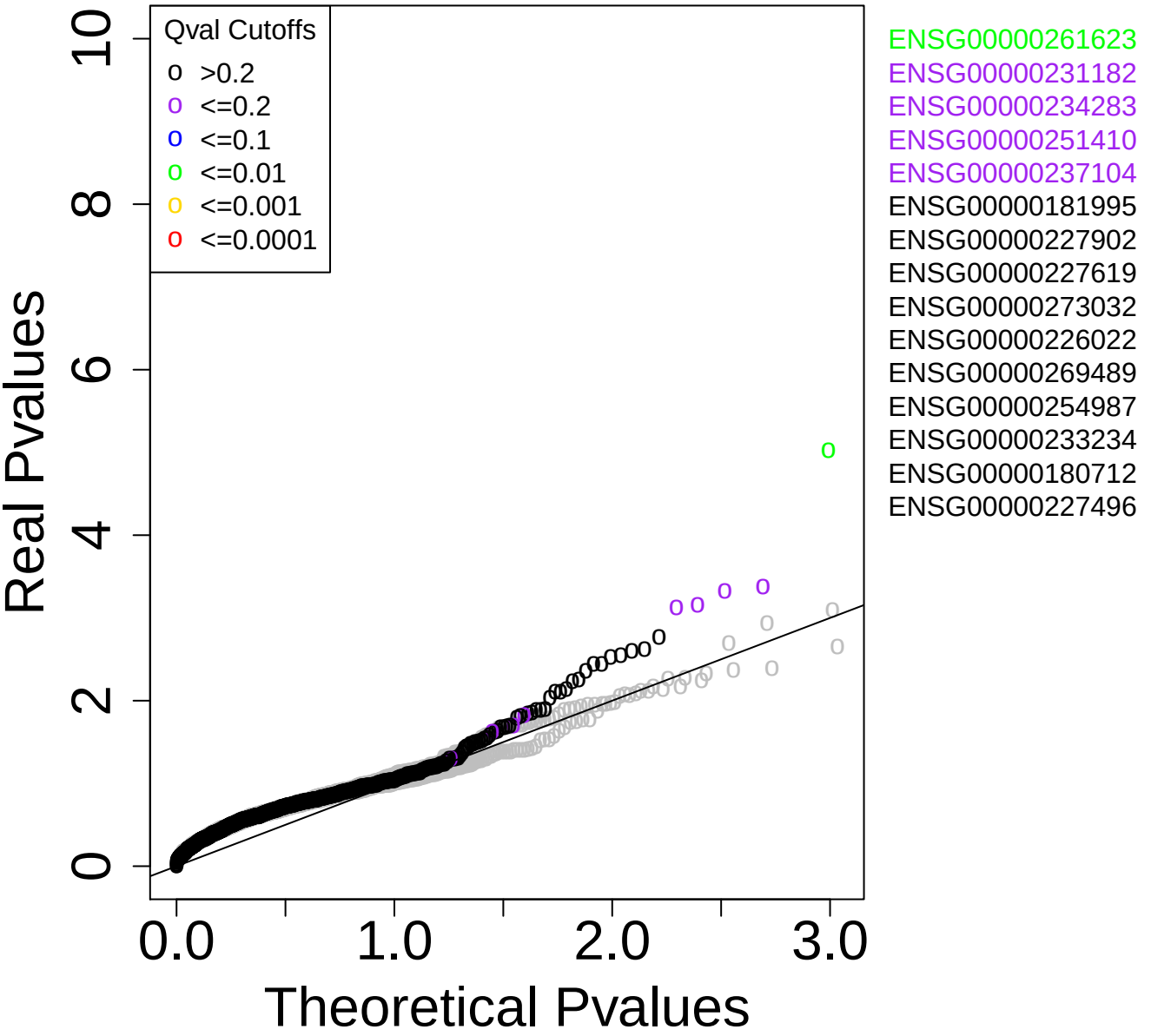
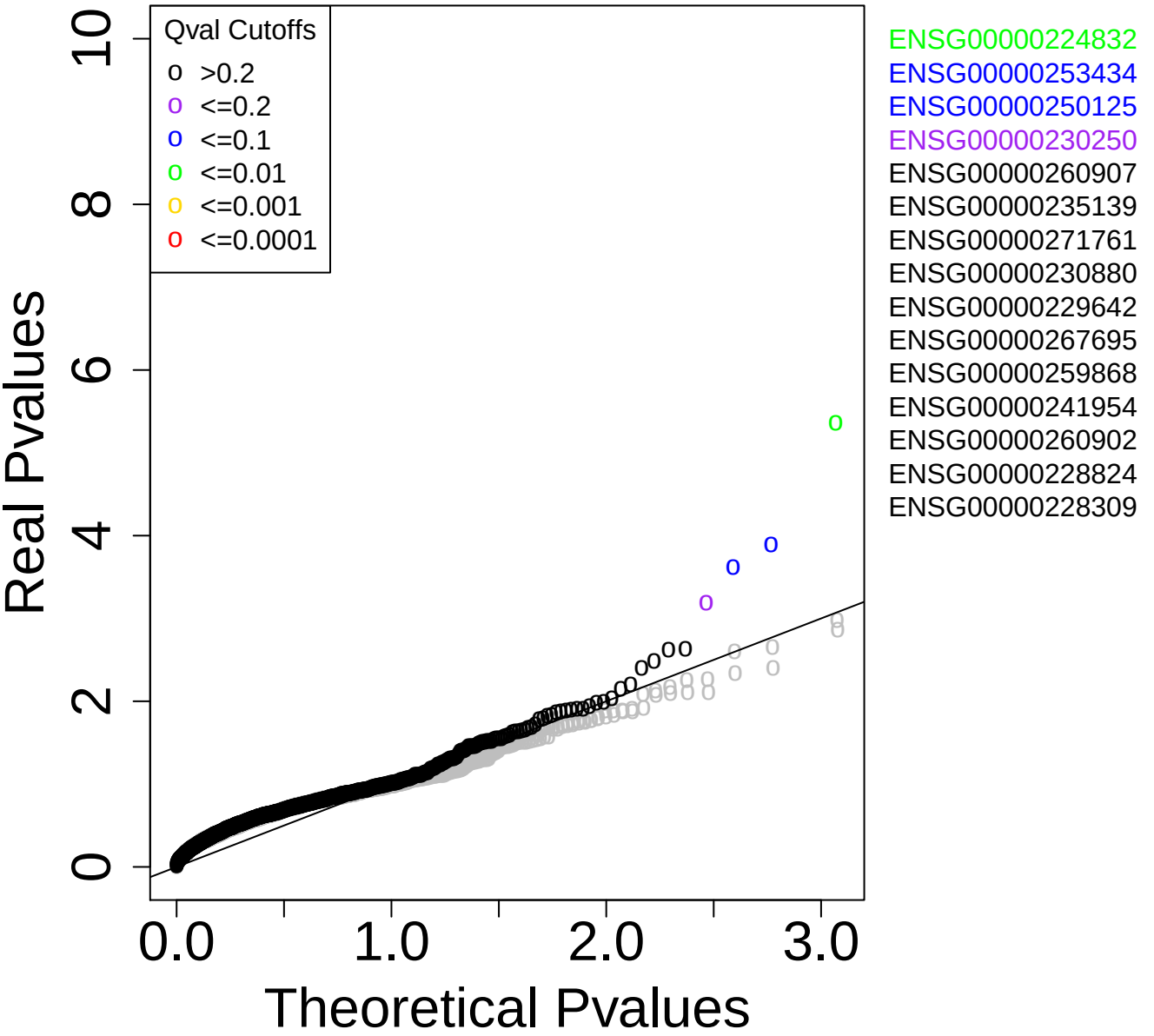

LncRNA BLCA − 637 genes
Qval Cutoffs
>0.2
<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
Real Pvalues
0
2
4
6
8
10
0.0
1.0
2.0
Theoretical Pvalues
ENSG00000259594
ENSG00000228792
ENSG00000233321
ENSG00000224409
ENSG00000231873
ENSG00000237992
ENSG00000268505
ENSG00000260352
ENSG00000227036
ENSG00000226133
ENSG00000253490
ENSG00000255227
ENSG00000228573
ENSG00000231242
ENSG00000264334

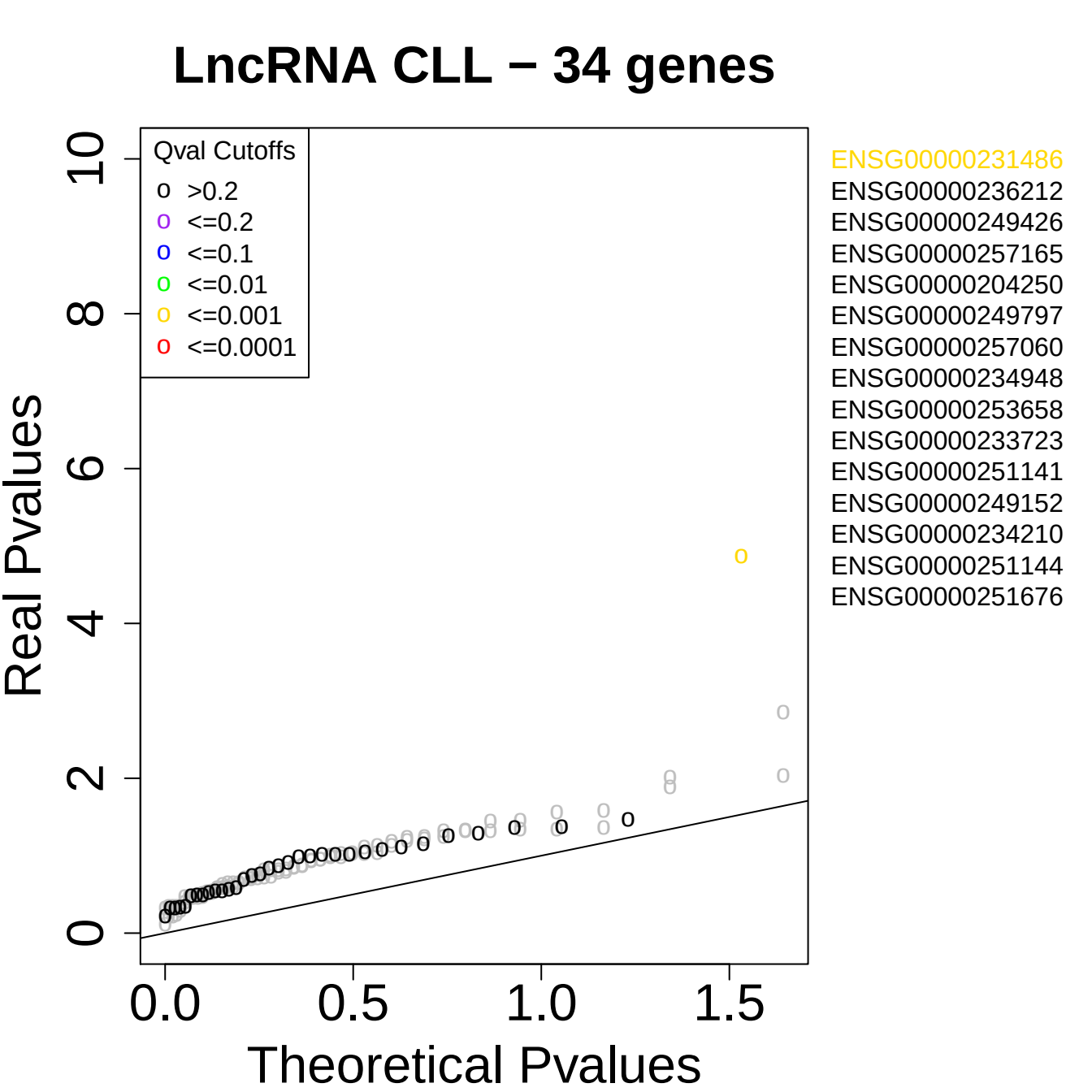
LncRNA BRCA − 985 genes



ENSG00000261623
ENSG00000231182
ENSG00000234283
ENSG00000251410
ENSG00000237104
ENSG00000181995
ENSG00000227902
ENSG00000227619
ENSG00000273032
ENSG00000226022
ENSG00000269489
ENSG00000254987
ENSG00000233234
ENSG00000180712
ENSG00000227496

LncRNA Breast − 1169 genes




LncRNA CLL − 34 genes
Qval Cutoffs
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<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
ENSG00000231486
ENSG00000236212
ENSG00000249426
ENSG00000257165
ENSG00000204250
ENSG00000249797
ENSG00000257060
ENSG00000234948
ENSG00000253658
ENSG00000233723
ENSG00000251141
ENSG00000249152
ENSG00000234210
ENSG00000251144
ENSG00000251676
Real Pvalues
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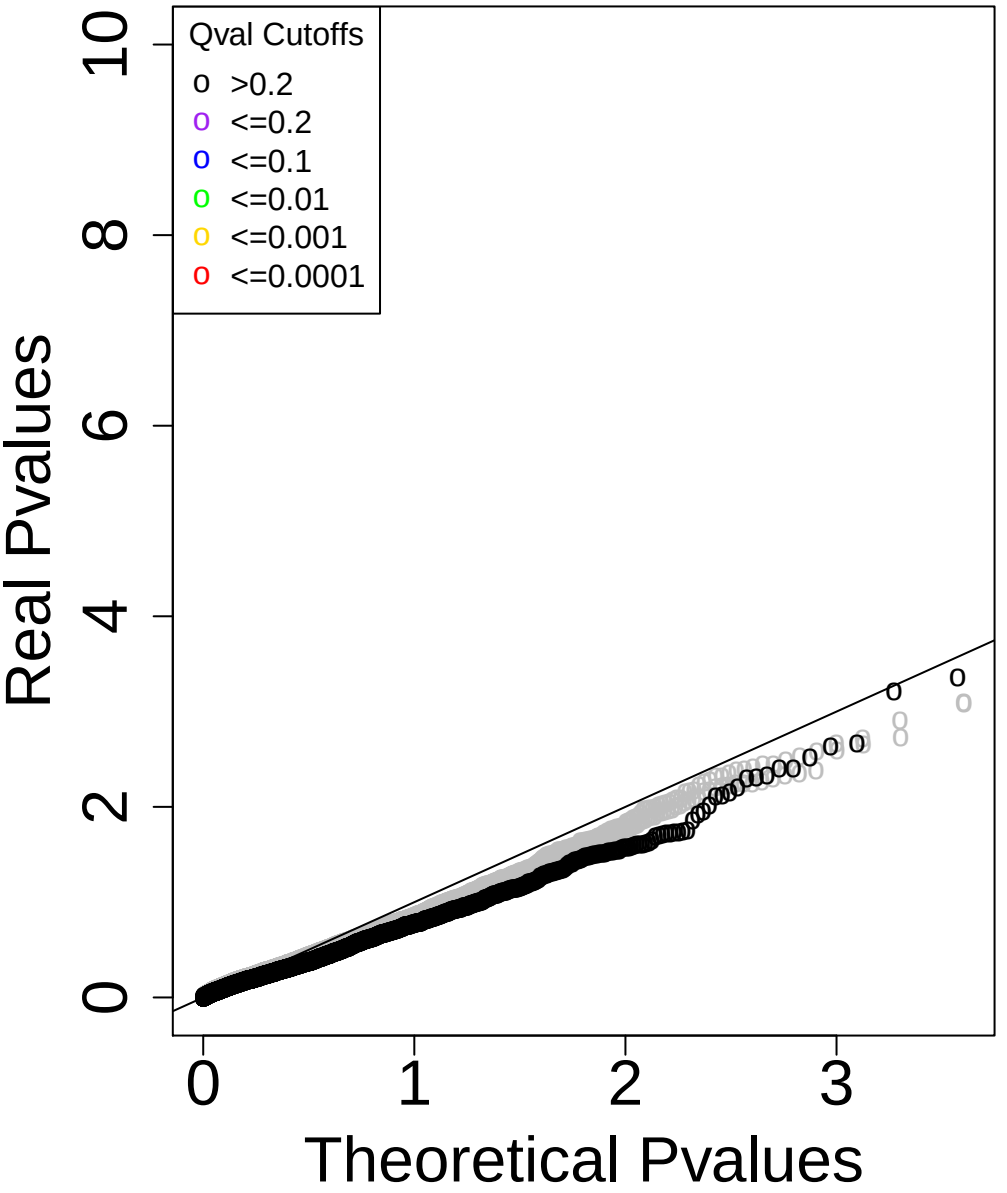
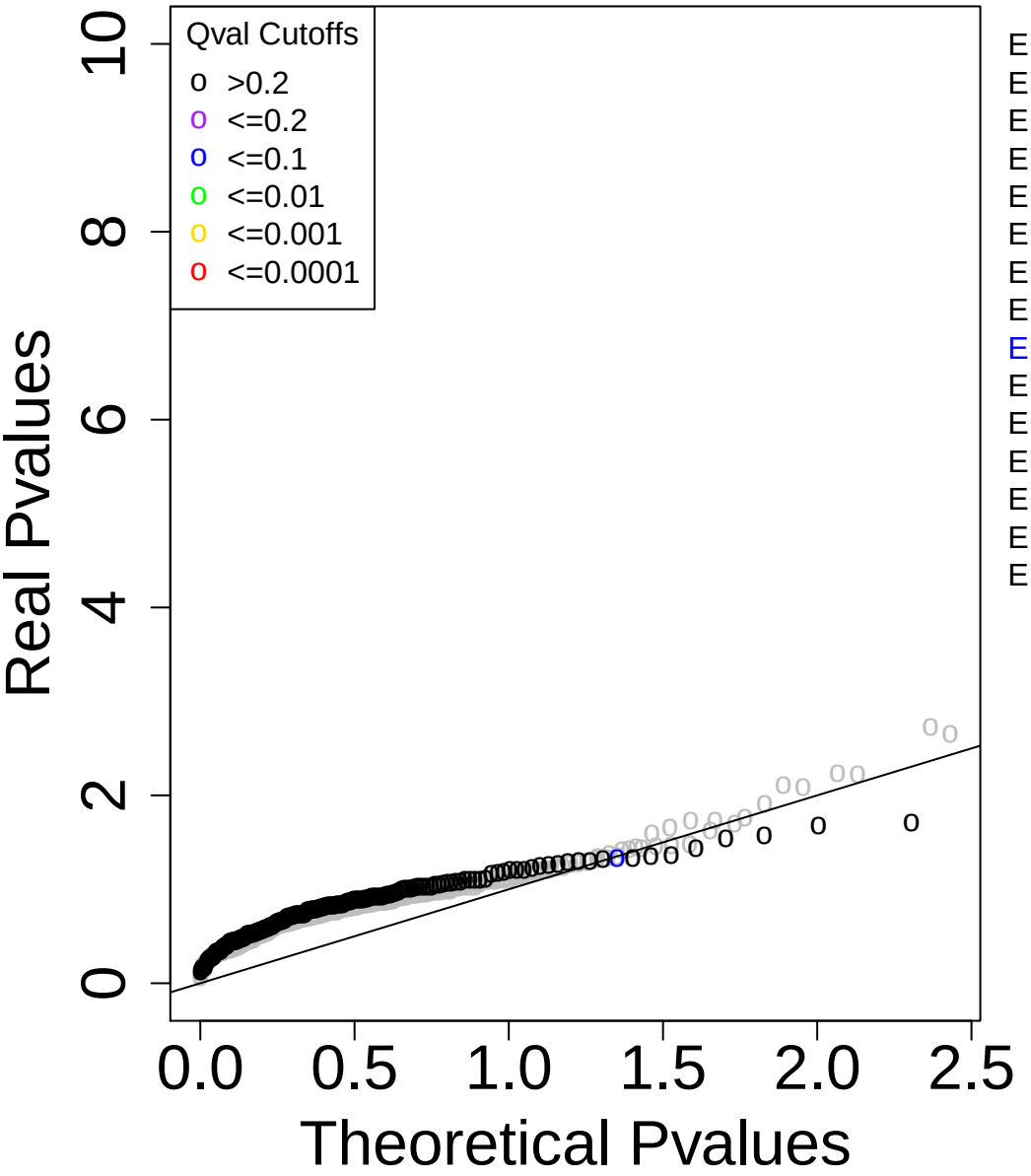
4
6
8
10
0.0
0.5
1.0
1.5
Theoretical Pvalues

LncRNA CRC − 3750 genes



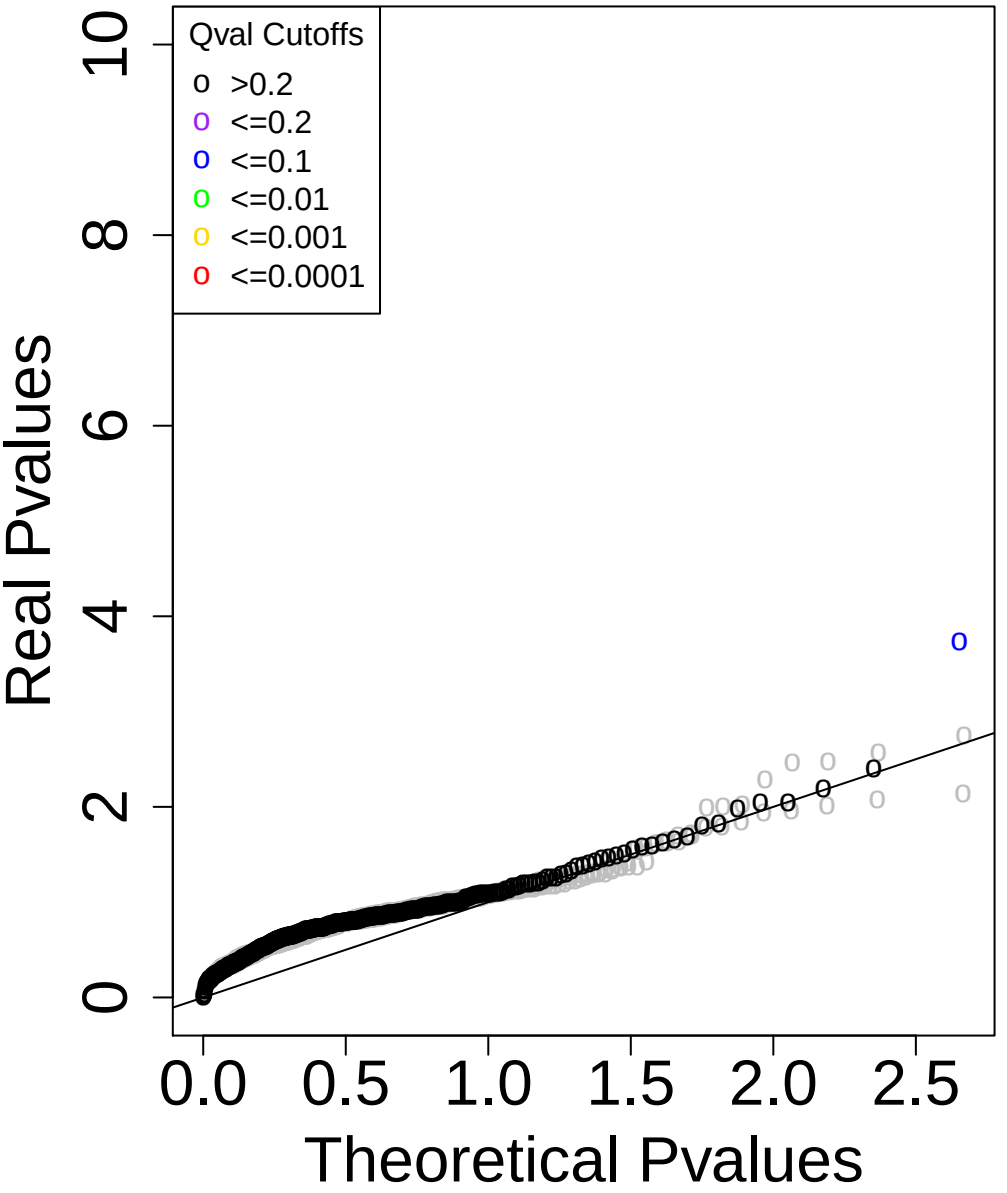
ENSG00000255087
ENSG00000246430
ENSG00000224077
ENSG00000258018
ENSG00000248329
ENSG00000258854
ENSG00000261598
ENSG00000258866
ENSG00000233349
ENSG00000236892
ENSG00000260585
ENSG00000228862
ENSG00000232931
ENSG00000259483
ENSG00000260941

LncRNA GBM − 202 genes

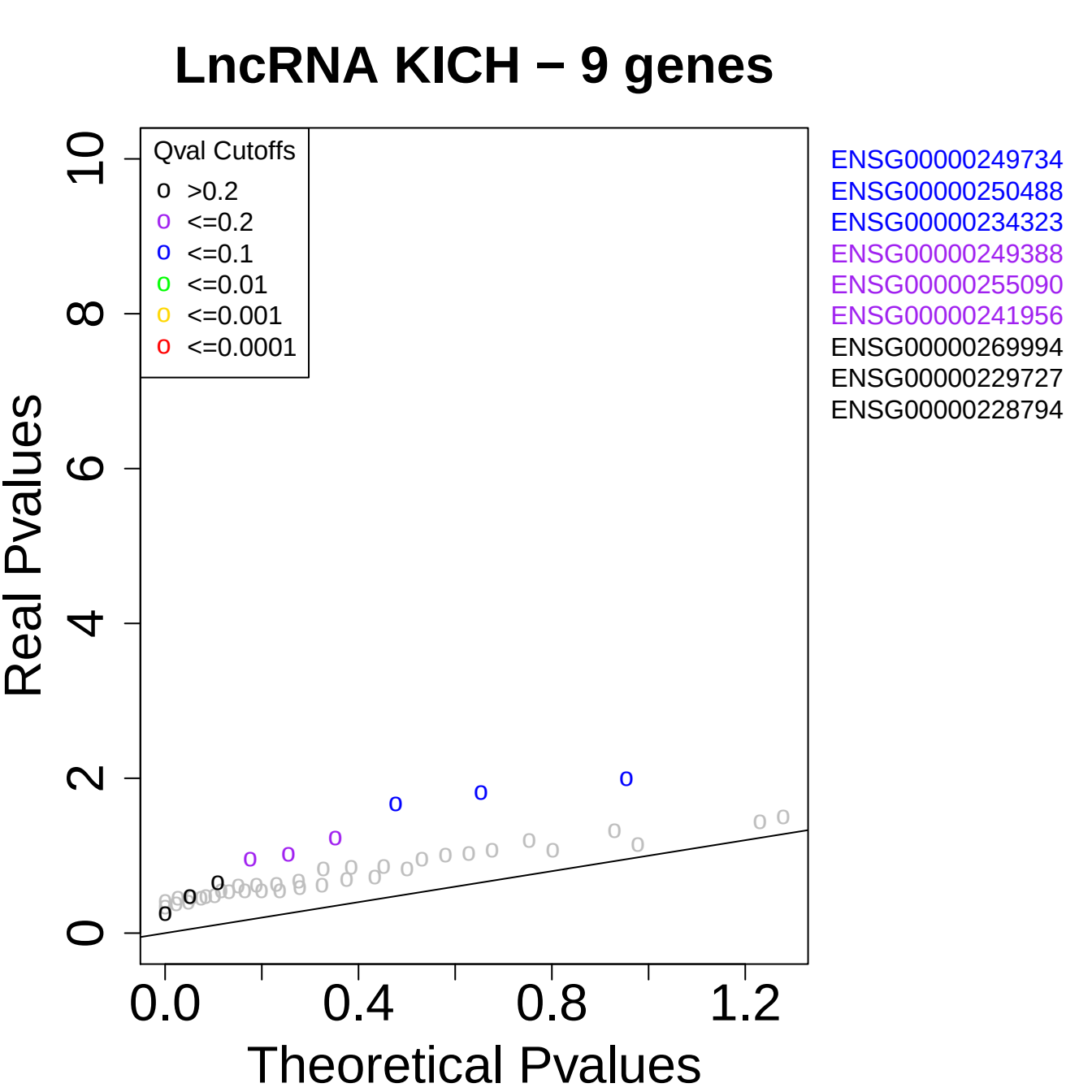


ENSG00000254130
ENSG00000231248
ENSG00000237019
ENSG00000260141
ENSG00000226829
ENSG00000249699
ENSG00000259149
ENSG00000253717
ENSG00000244306
ENSG00000231217
ENSG00000251170
ENSG00000258216
ENSG00000253561
ENSG00000241743
ENSG00000248646

LncRNA HNSC − 450 genes



ENSG00000254689
ENSG00000248973
ENSG00000219445
ENSG00000251129
ENSG00000226453
ENSG00000249547
ENSG00000227579
ENSG00000226833
ENSG00000260626
ENSG00000267014
ENSG00000223344
ENSG00000255109
ENSG00000236780
ENSG00000229140
ENSG00000251562


LncRNA KICH – 9 genes
Qval Cutoffs
>0.2
<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
ENSG00000249734
ENSG00000250488
ENSG00000234323
ENSG00000249388
ENSG00000255090
ENSG00000241956
ENSG00000269994
ENSG00000229727
ENSG00000228794
Real Pvalues
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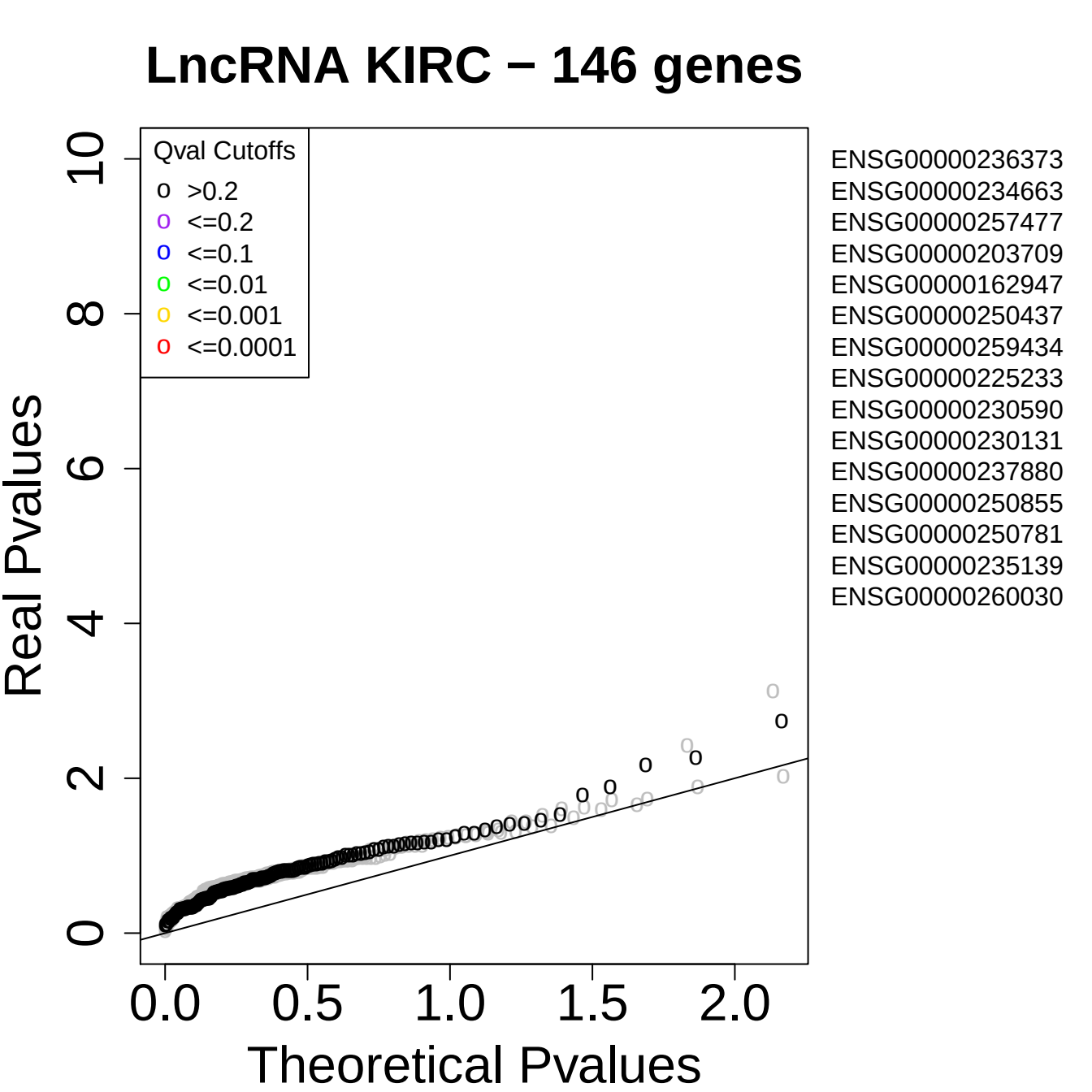
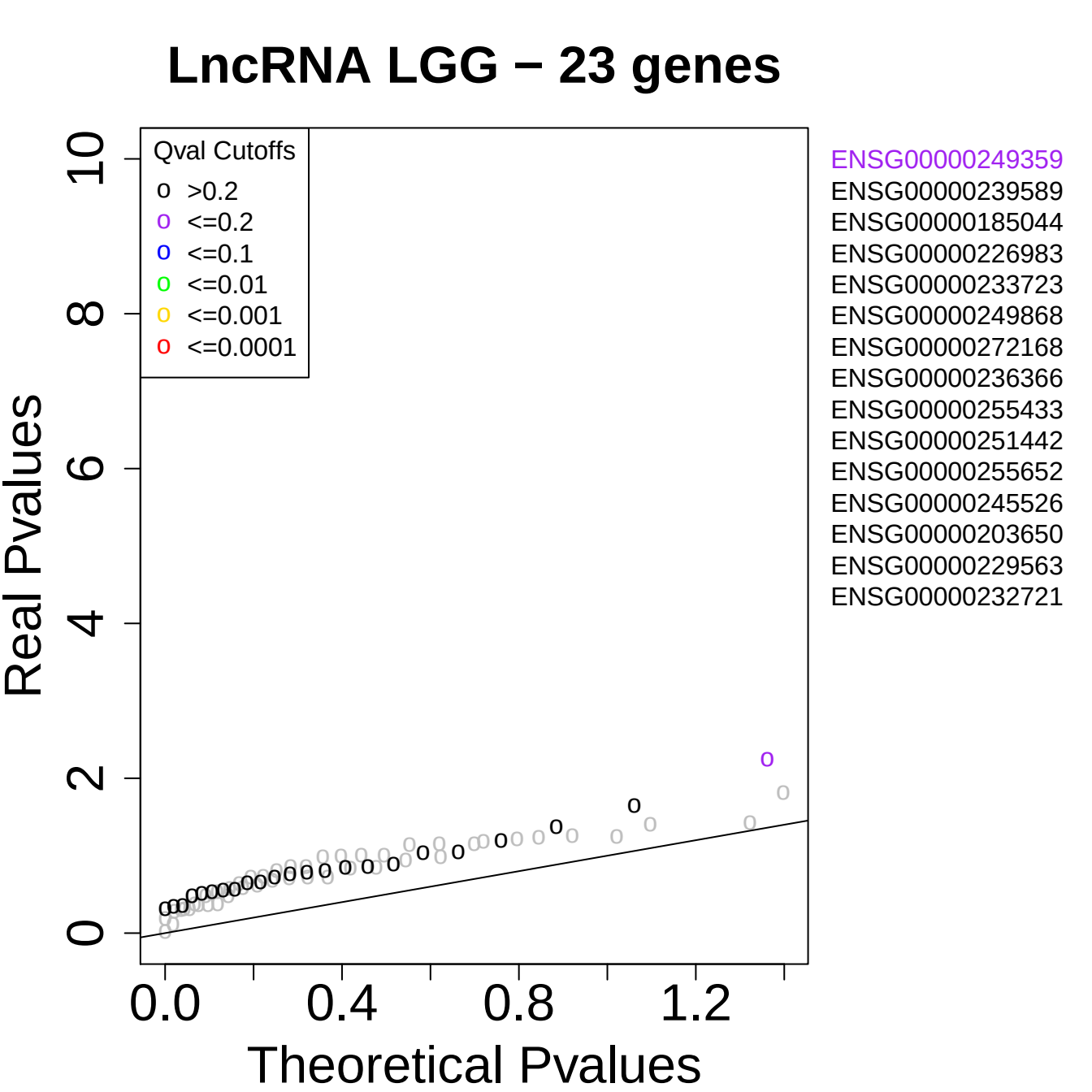
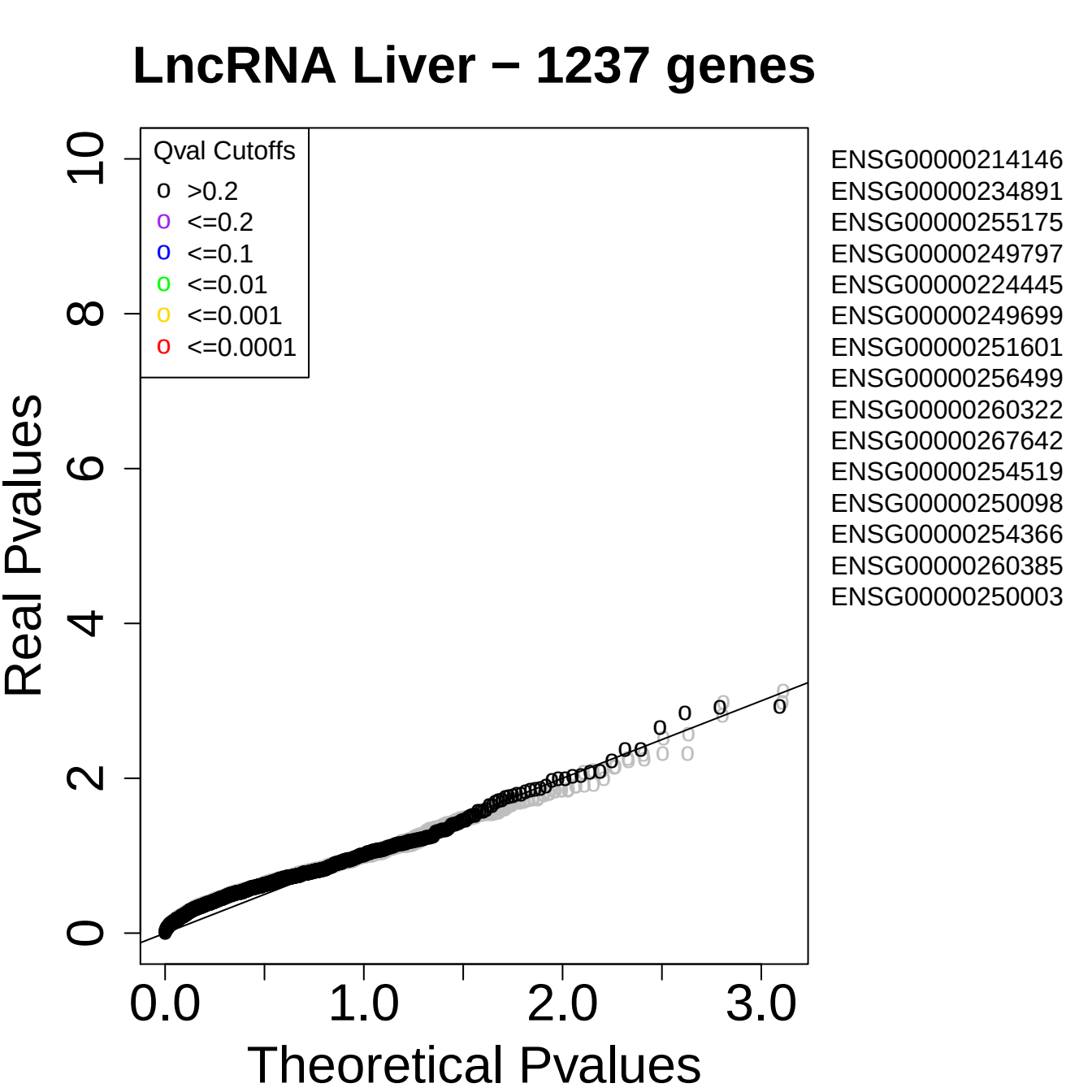
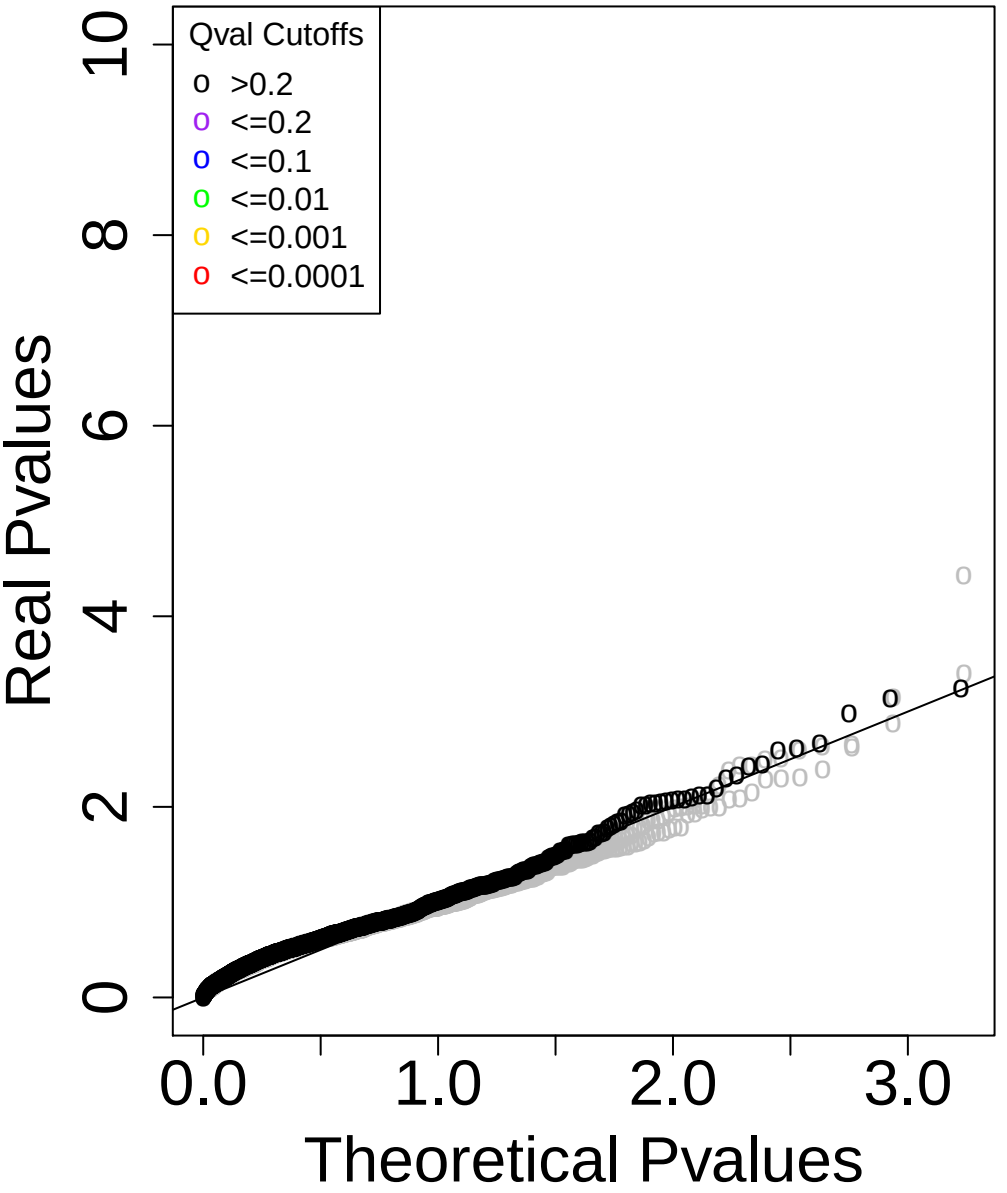
4
6
8
10
0.0
0.4
0.8
1.2
Theoretical Pvalues


LncRNA KIRC − 146 genes
Qval Cutoffs
>0.2
<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
ENSG00000236373
ENSG00000234663
ENSG00000257477
ENSG00000203709
ENSG00000162947
ENSG00000250437
ENSG00000259434
ENSG00000225233
ENSG00000230590
ENSG00000230131
ENSG00000237880
ENSG00000250855
ENSG00000250781
ENSG00000235139
ENSG00000260030
Real Pvalues
0
2
4
6
8
10
0.0
0.5
1.0
1.5
2.0
Theoretical Pvalues


LncRNA LGG − 23 genes
Qval Cutoffs
>0.2
<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
ENSG00000249359
ENSG00000239589
ENSG00000185044
ENSG00000226983
ENSG00000233723
ENSG00000249868
ENSG00000272168
ENSG00000236366
ENSG00000255433
ENSG00000251442
ENSG00000255652
ENSG00000245526
ENSG00000203650
ENSG00000229563
ENSG00000232721
Real Pvalues
0
2
4
6
8
10
0.0
0.4
0.8
1.2
Theoretical Pvalues

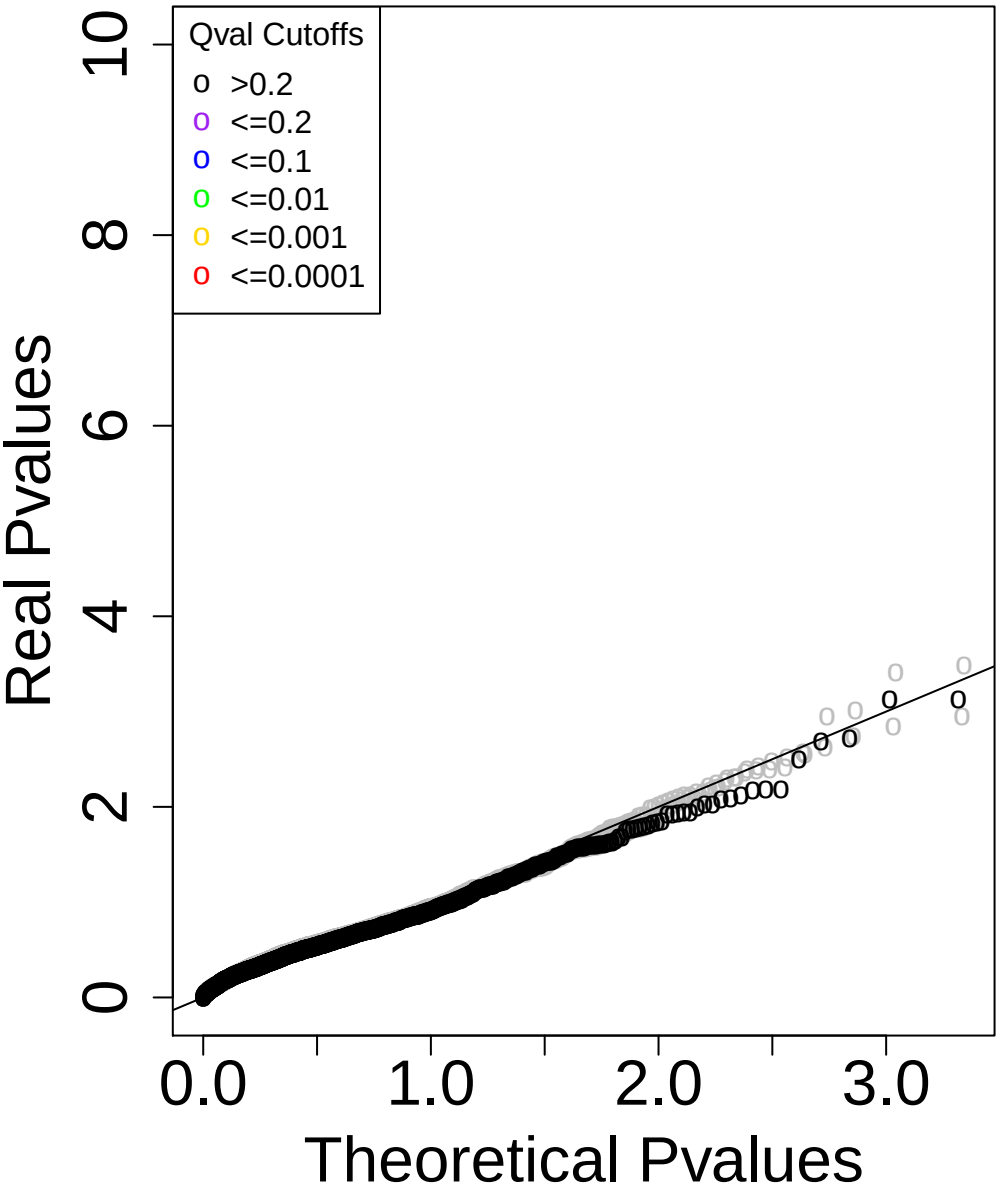

LncRNA Liver − 1237 genes
Qval Cutoffs
>0.2
<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
Real Pvalues
0
2
4
6
8
10
0.0
1.0
2.0
3.0
Theoretical Pvalues
ENSG00000214146
ENSG00000234891
ENSG00000255175
ENSG00000249797
ENSG00000224445
ENSG00000249699
ENSG00000251601
ENSG00000256499
ENSG00000260322
ENSG00000267642
ENSG00000254519
ENSG00000250098
ENSG00000254366
ENSG00000260385
ENSG00000250003

LncRNA LUAD – 1683 genes



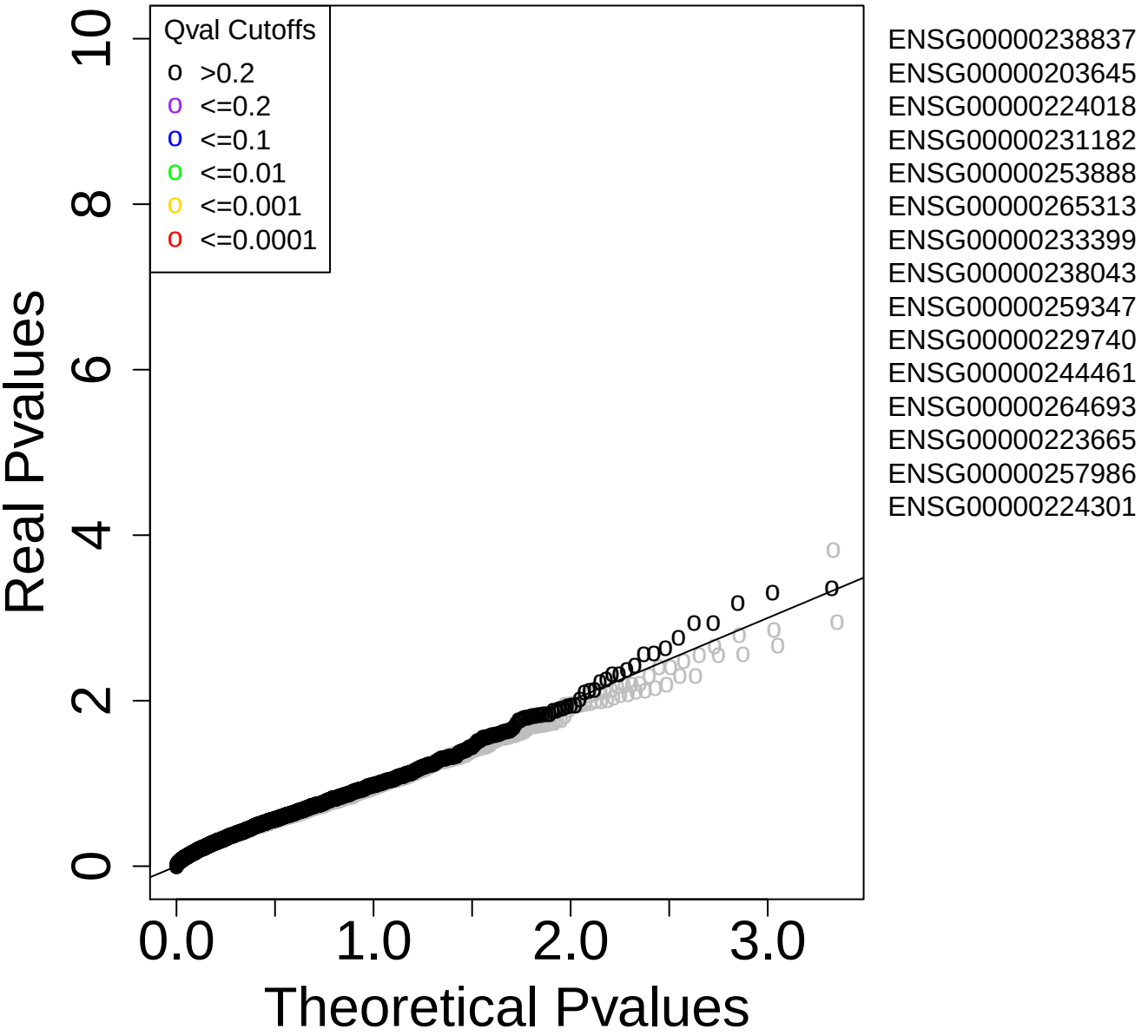
ENSG00000257683
ENSG00000248771
ENSG00000253524
ENSG00000227508
ENSG00000223883
ENSG00000241767
ENSG00000258418
ENSG00000236837
ENSG00000248717
ENSG00000250814
ENSG00000234710
ENSG00000228272
ENSG00000230647
ENSG00000249153
ENSG00000250256

LncRNA Lung_adeno − 2073 genes



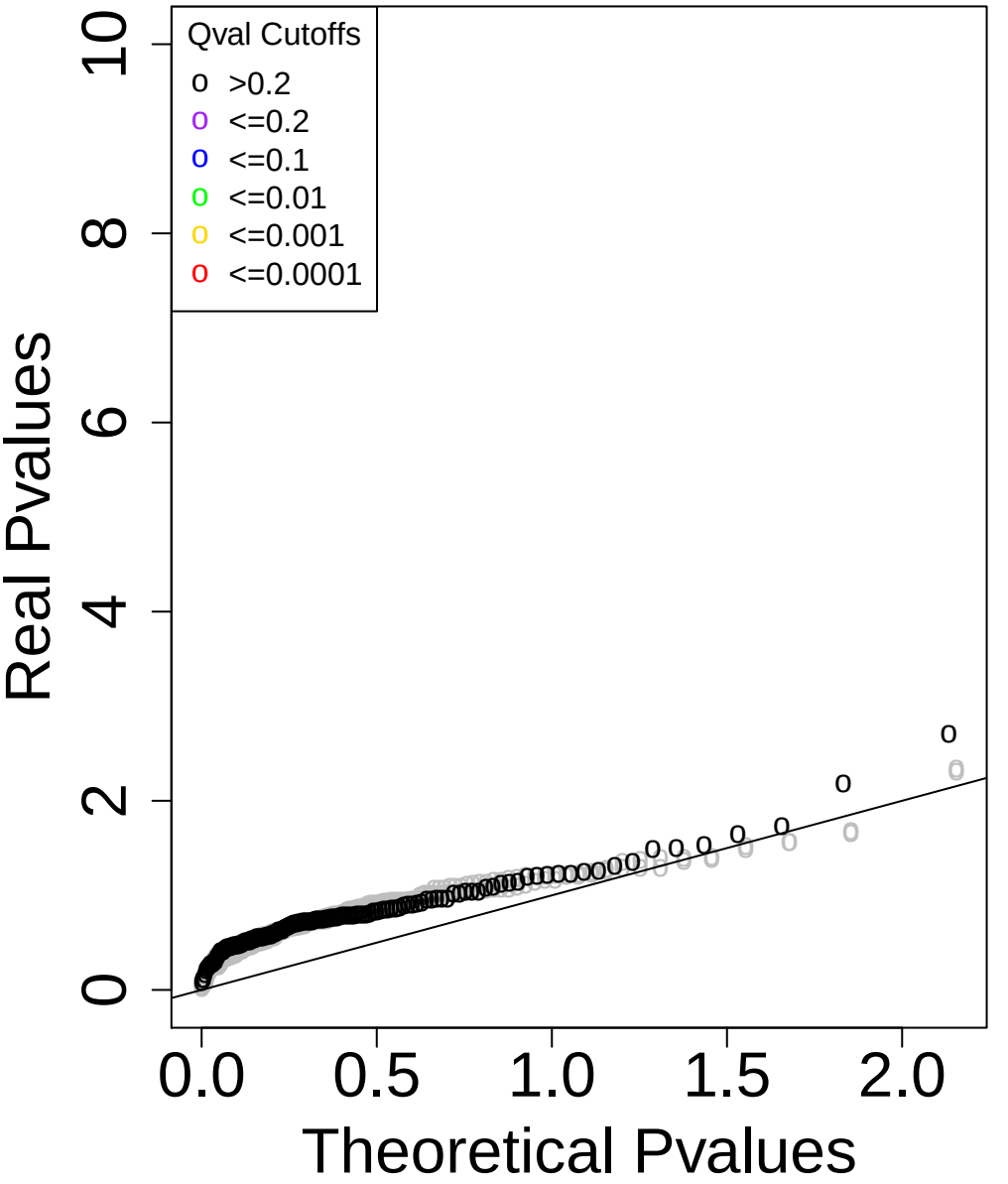
ENSG00000251218
ENSG00000266604
ENSG00000267537
ENSG00000260769
ENSG00000254001
ENSG00000259692
ENSG00000232591
ENSG00000271911
ENSG00000228235
ENSG00000235385
ENSG00000179219
ENSG00000224799
ENSG00000260959
ENSG00000228679
ENSG00000238198

LncRNA LUSC – 2117 genes



ENSG00000238837
ENSG00000203645
ENSG00000224018
ENSG00000231182
ENSG00000253888
ENSG00000265313
ENSG00000233399
ENSG00000238043
ENSG00000259347
ENSG00000229740
ENSG00000244461
ENSG00000264693
ENSG00000223665
ENSG00000257986
ENSG00000224301

LncRNA Lymphoma_B−cell − 136 genes



ENSG00000248174
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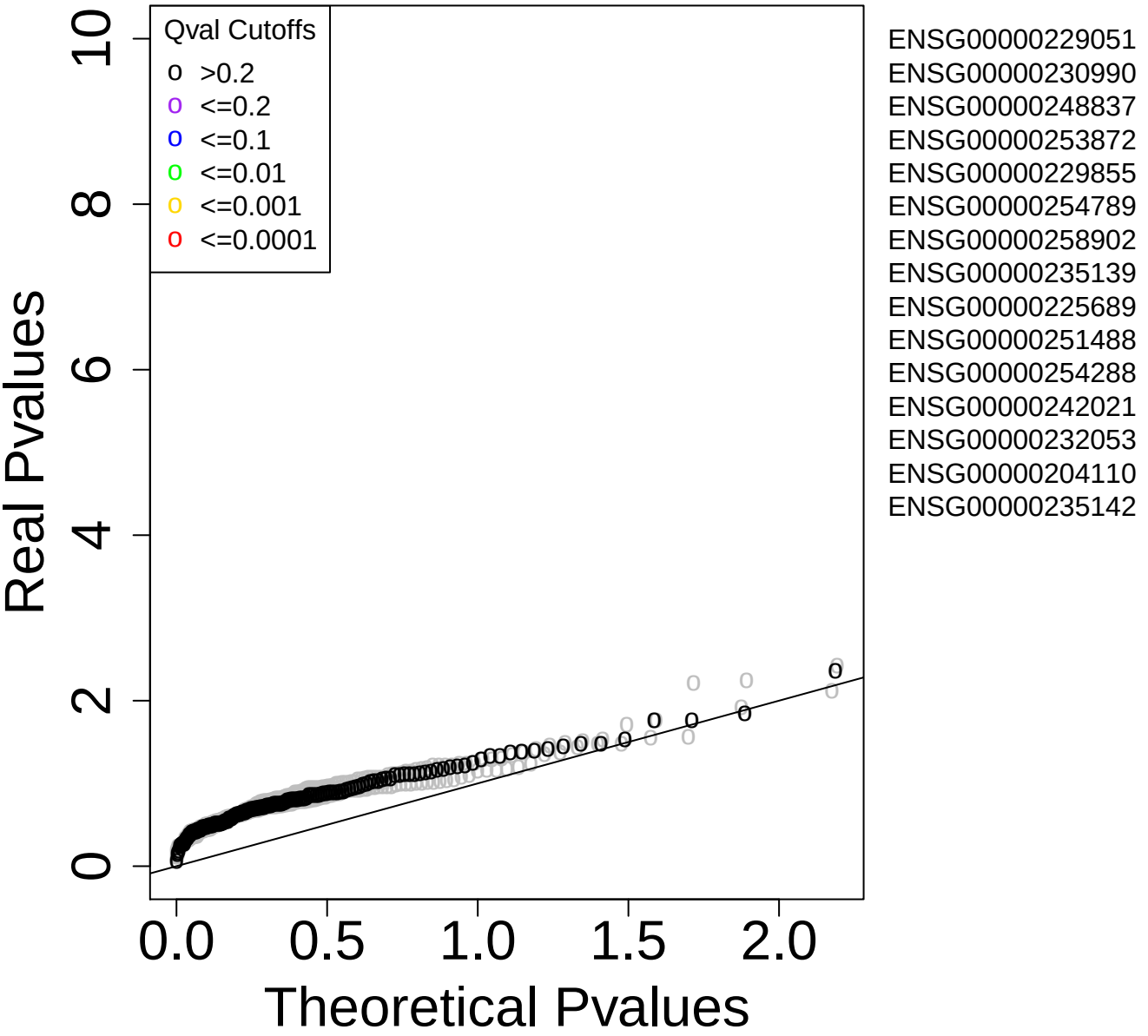
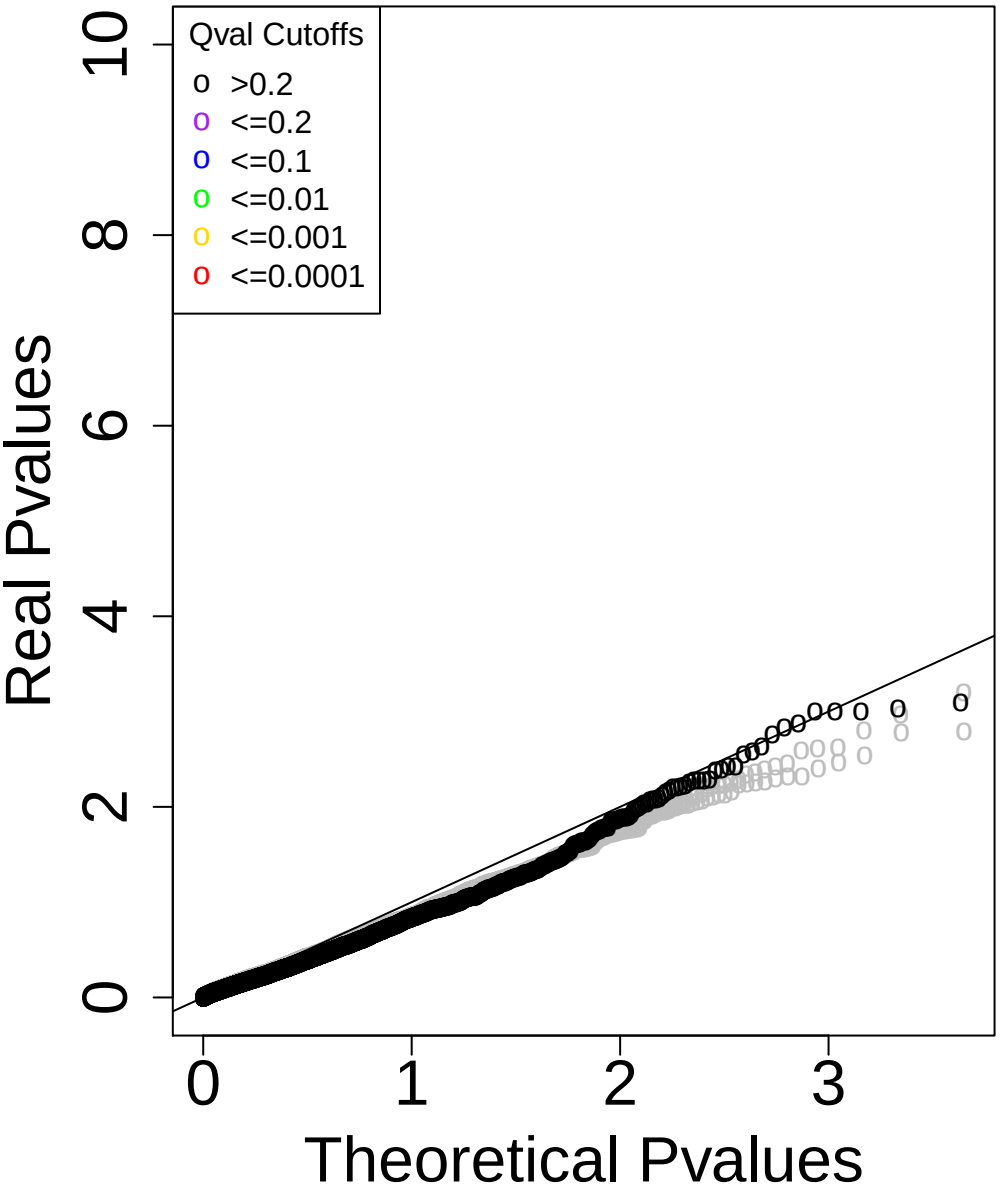
ENSG00000250049
ENSG00000258631
ENSG00000228065
ENSG00000226764
ENSG00000273143
ENSG00000242545
ENSG00000254269
ENSG00000231039
ENSG00000250064
ENSG00000224271
ENSG00000249797

LncRNA Medulloblastoma − 154 genes



ENSG00000229051
ENSG00000230990
ENSG00000248837
ENSG00000253872
ENSG00000229855
ENSG00000254789
ENSG00000258902
ENSG00000235139
ENSG00000225689
ENSG00000251488
ENSG00000254288
ENSG00000242021
ENSG00000232053
ENSG00000204110
ENSG00000235142

RNA Pancancer_Alexandrov – 4303 genes



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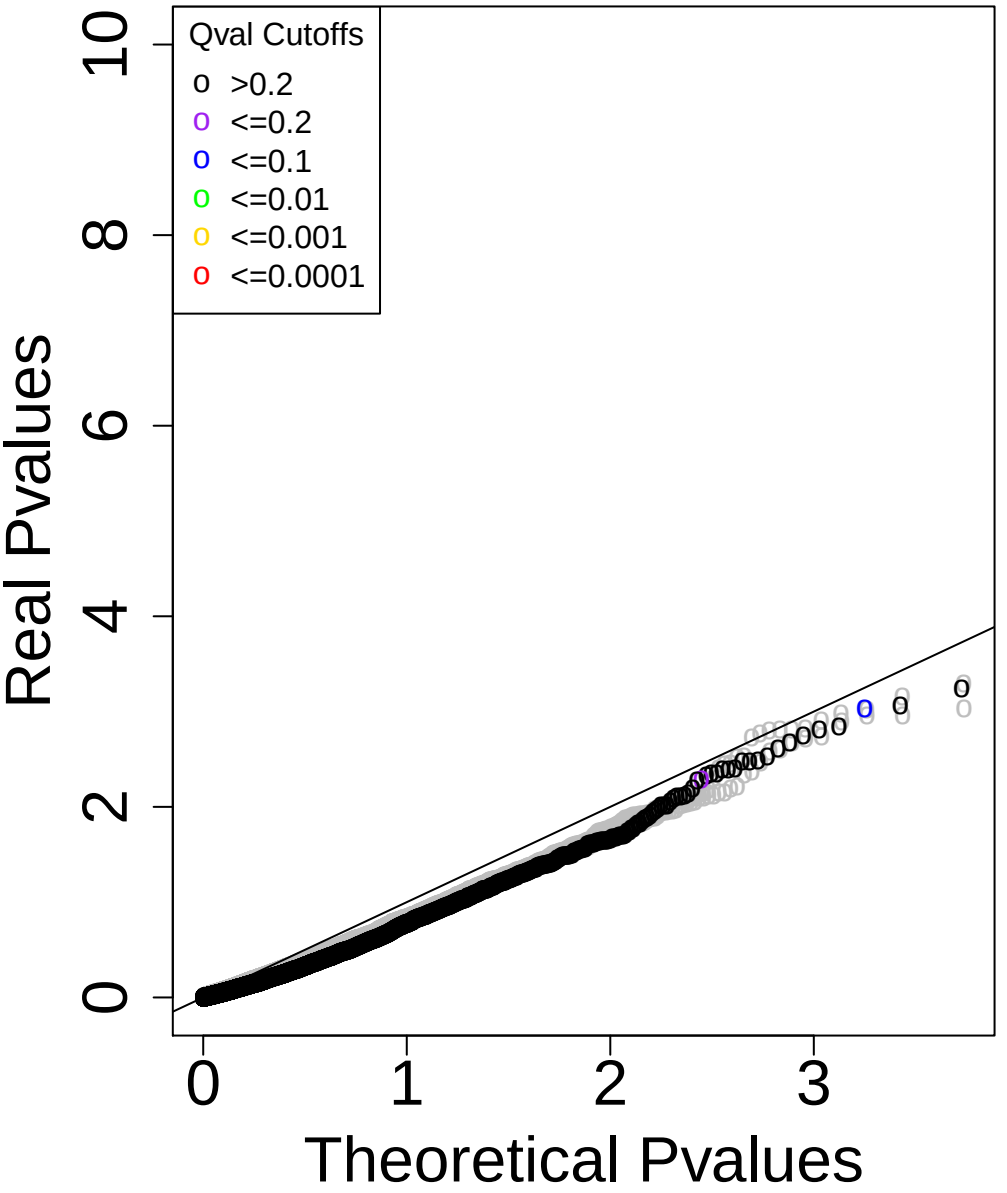
ENSG00000270069
ENSG00000261382
ENSG00000267537
ENSG00000246876
ENSG00000261584
ENSG00000260785
ENSG00000257612
ENSG00000266979
ENSG00000260402
ENSG00000237534
ENSG00000229308
ENSG00000247765
ENSG00000263547
ENSG00000253434

LncRNA Pancancer_TCGA − 5331 genes



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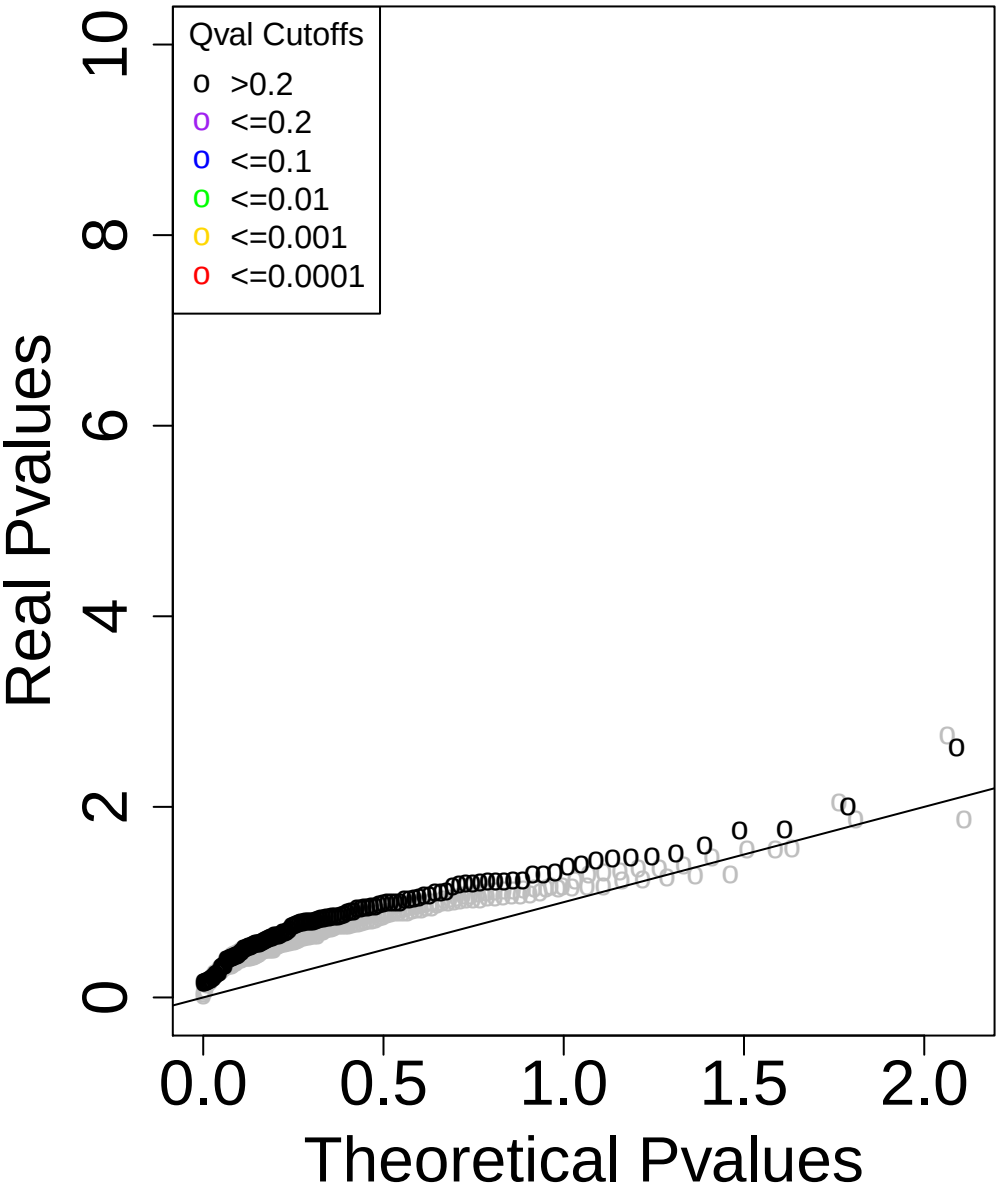
ENSG00000231182
ENSG00000245532
ENSG00000250754
ENSG00000249201
ENSG00000254830
ENSG00000230606
ENSG00000246430
ENSG00000241481
ENSG00000238277
ENSG00000219445
ENSG00000260738
ENSG00000248329
ENSG00000251372
ENSG00000223765

LncRNA Pancreas − 123 genes



ENSG00000266573
ENSG00000253434
ENSG00000215386
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ENSG00000250891
ENSG00000261307
ENSG00000237473
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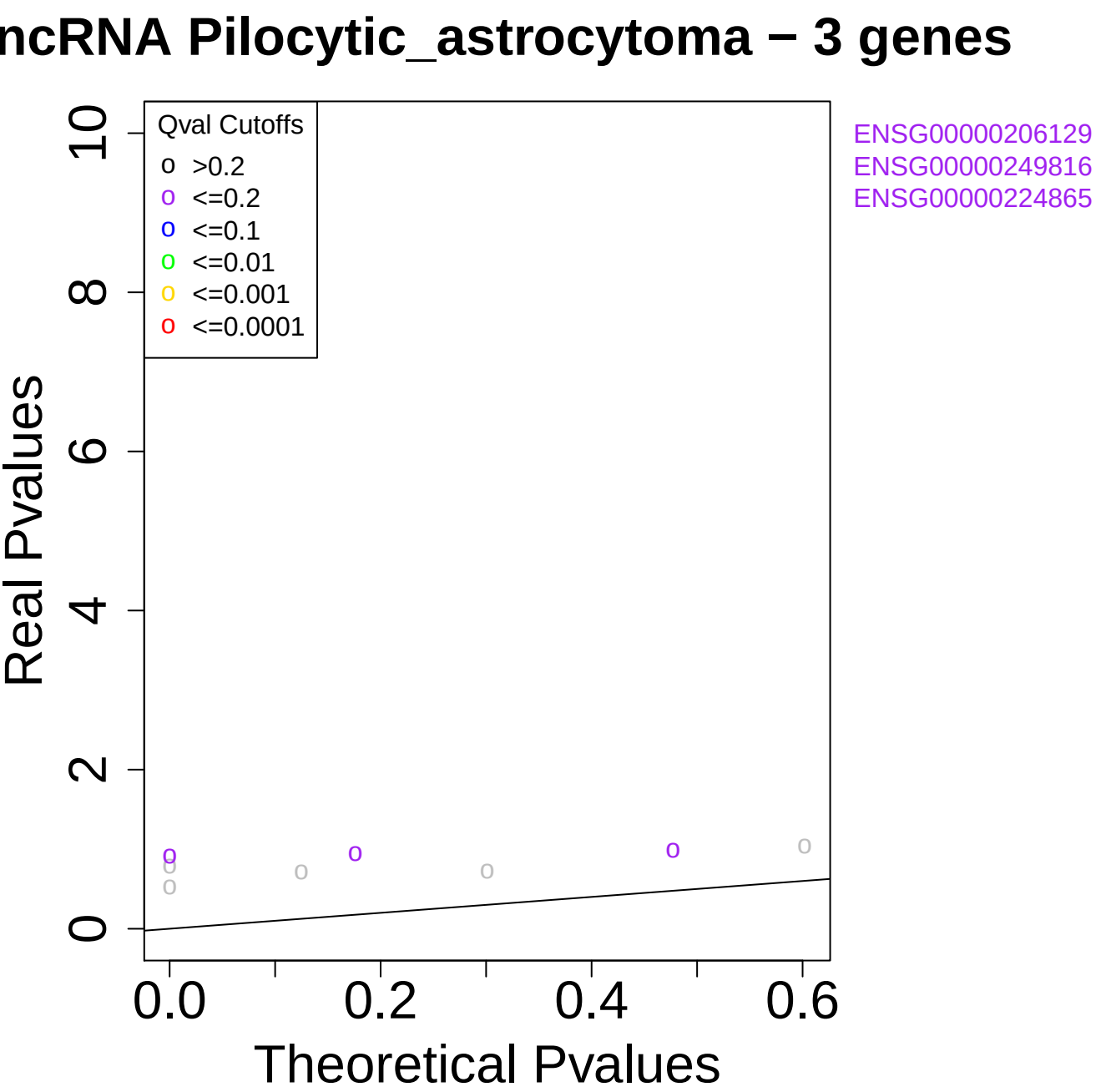
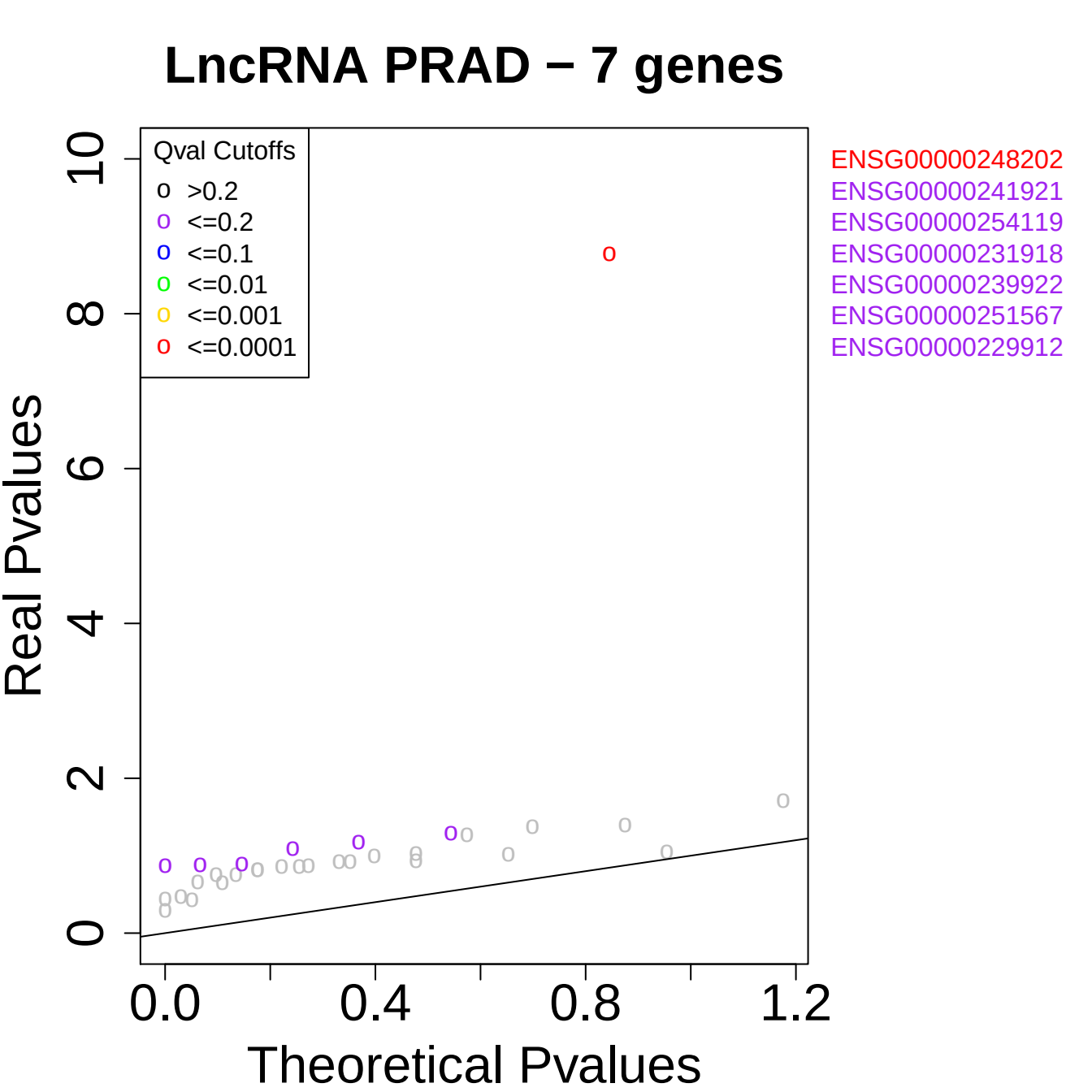
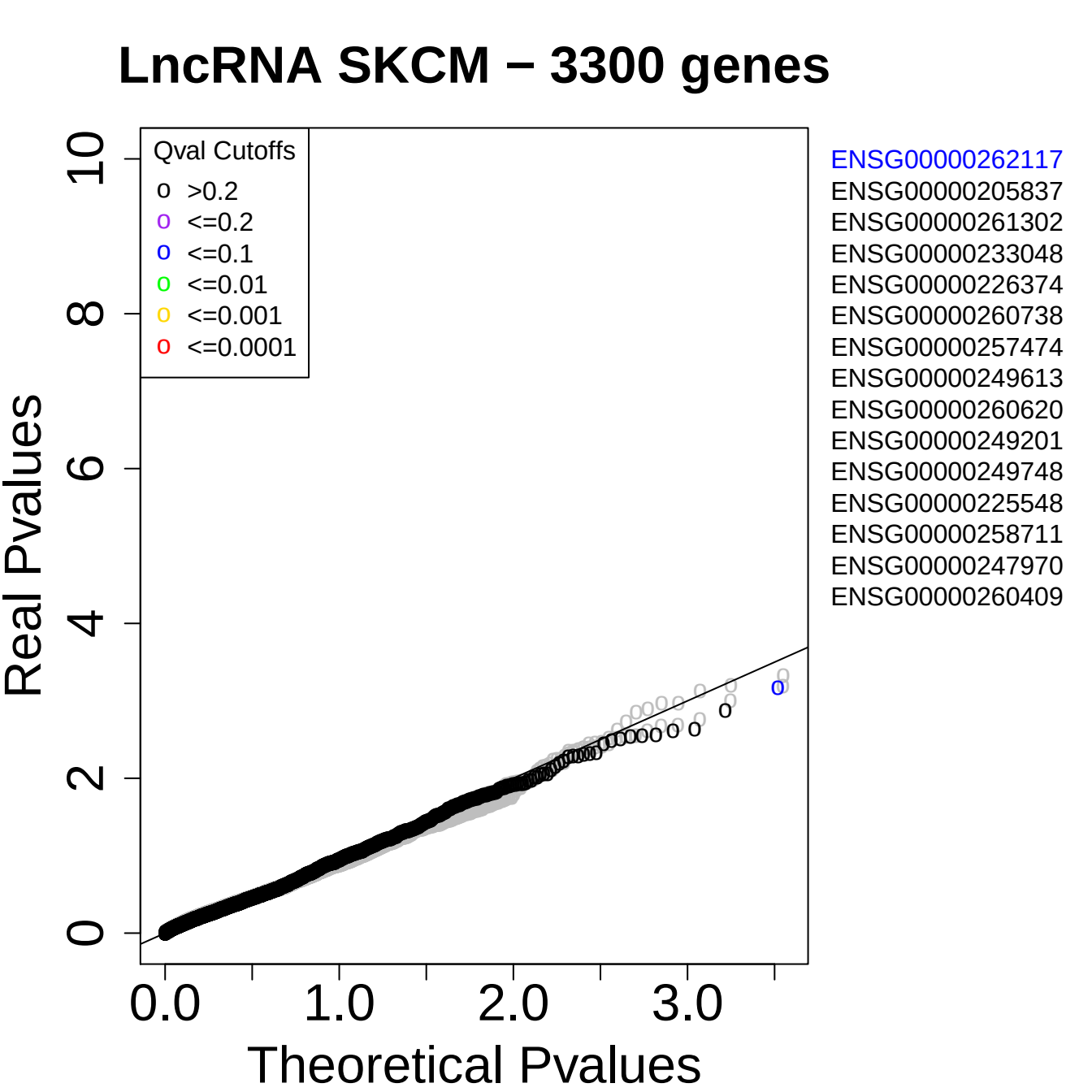

ncRNA Pilocytic_astrocytoma − 3 genes
Qval Cutoffs
>0.2
<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
ENSG00000206129
ENSG00000249816
ENSG00000224865
Real Pvalues
0
2
4
6
8
10
0.0
0.2
0.4
0.6
Theoretical Pvalues


LncRNA PRAD − 7 genes
Qval Cutoffs
>0.2
<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
ENSG00000248202
ENSG00000241921
ENSG00000254119
ENSG00000231918
ENSG00000239922
ENSG00000251567
ENSG00000229912
Real Pvalues
0
2
4
6
8
10
0.0
0.4
0.8
1.2
Theoretical Pvalues


LncRNA SKCM − 3300 genes
Qval Cutoffs
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<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
ENSG00000262117
ENSG00000205837
ENSG00000261302
ENSG00000233048
ENSG00000226374
ENSG00000260738
ENSG00000257474
ENSG00000249613
ENSG00000260620
ENSG00000249201
ENSG00000249748
ENSG00000225548
ENSG00000258711
ENSG00000247970
ENSG00000260409
Real Pvalues
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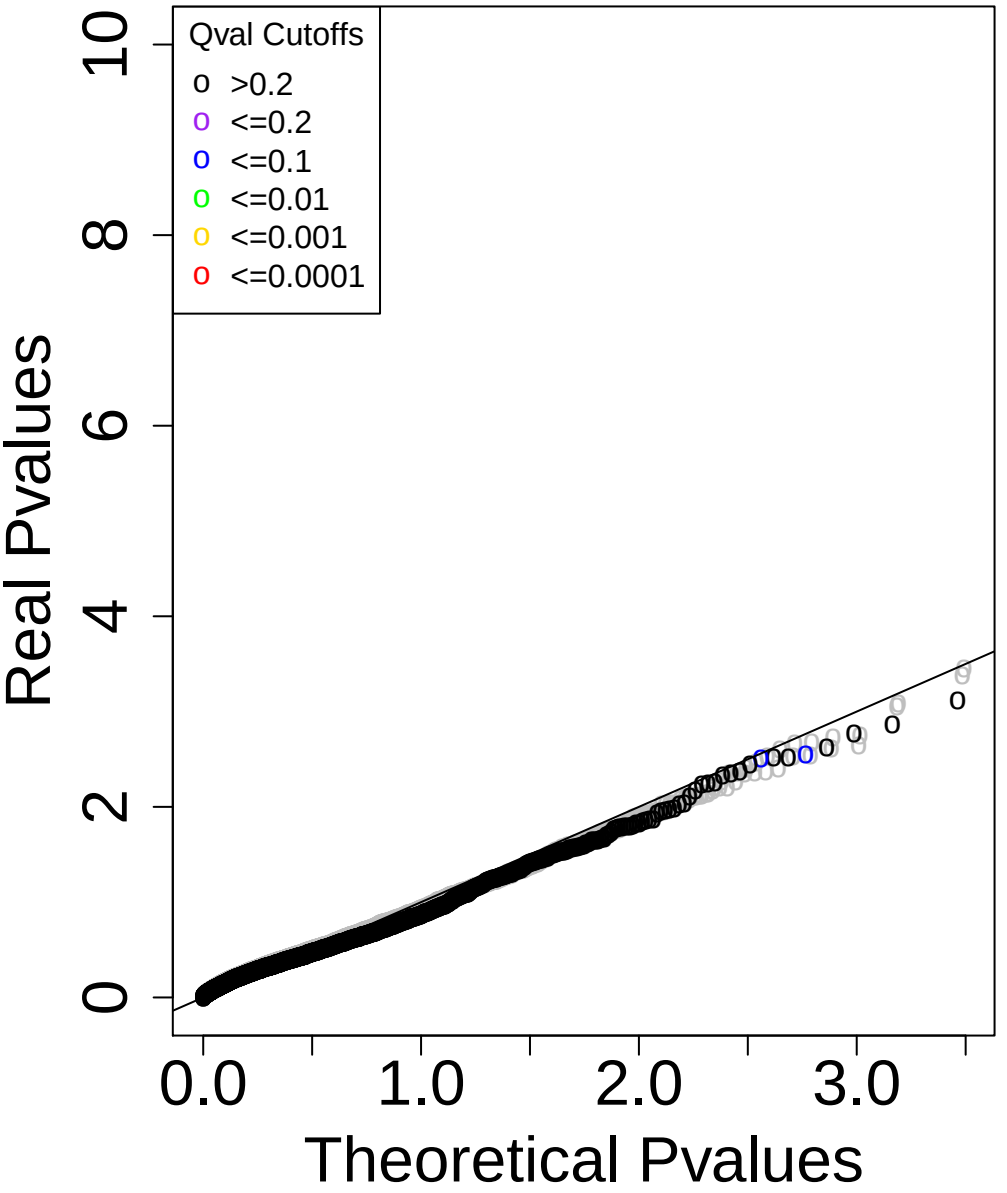
2
4
6
8
10
0.0
1.0
2.0
3.0
Theoretical Pvalues

LncRNA Stad − 2912 genes



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ENSG00000225937
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ENSG00000260402
ENSG00000240405
ENSG00000249694
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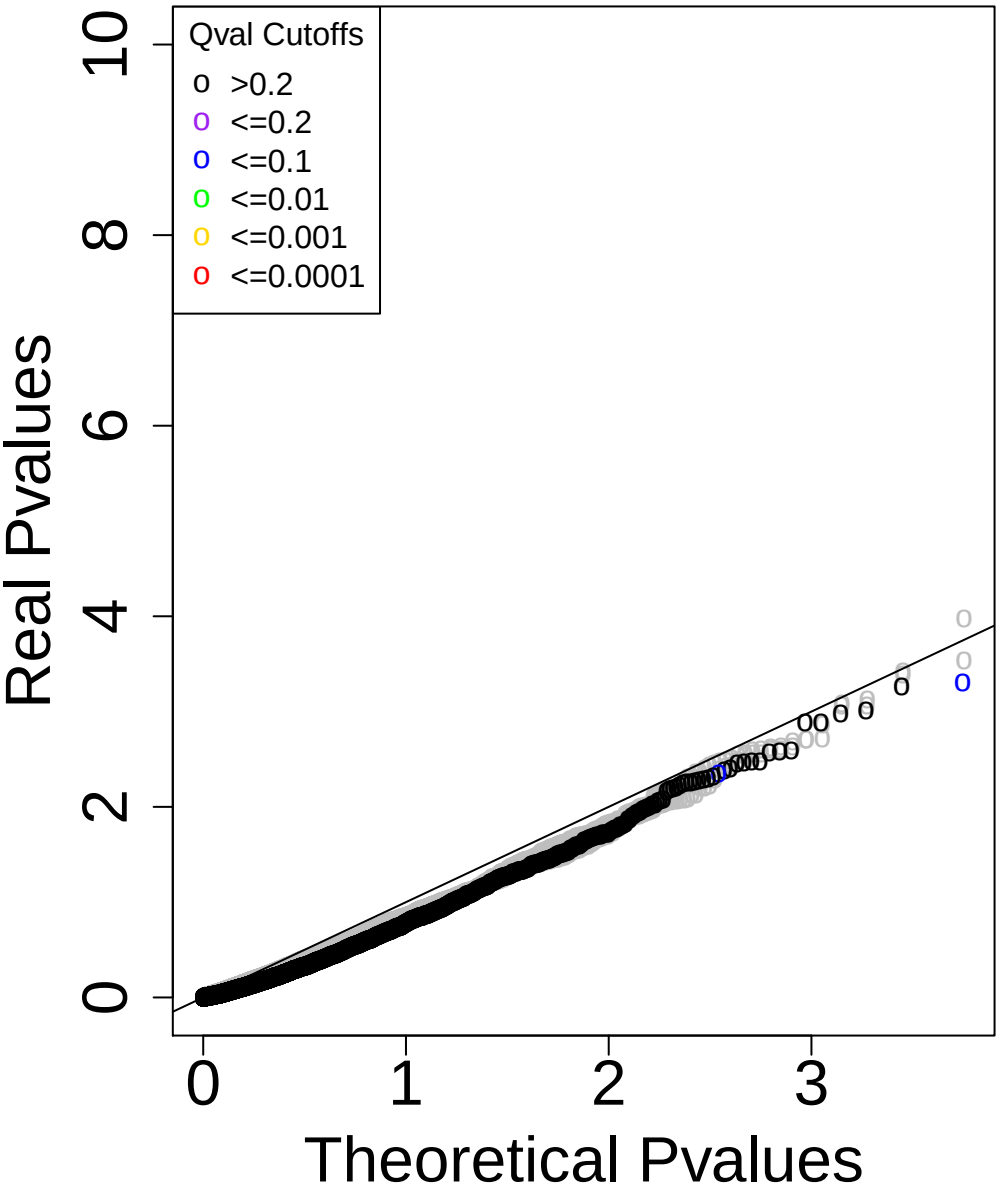
ENSG00000235198
ENSG00000238207
ENSG00000224413

LncRNA Superpancancer − 5583 genes



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ENSG00000263934
ENSG00000261584
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ENSG00000238837
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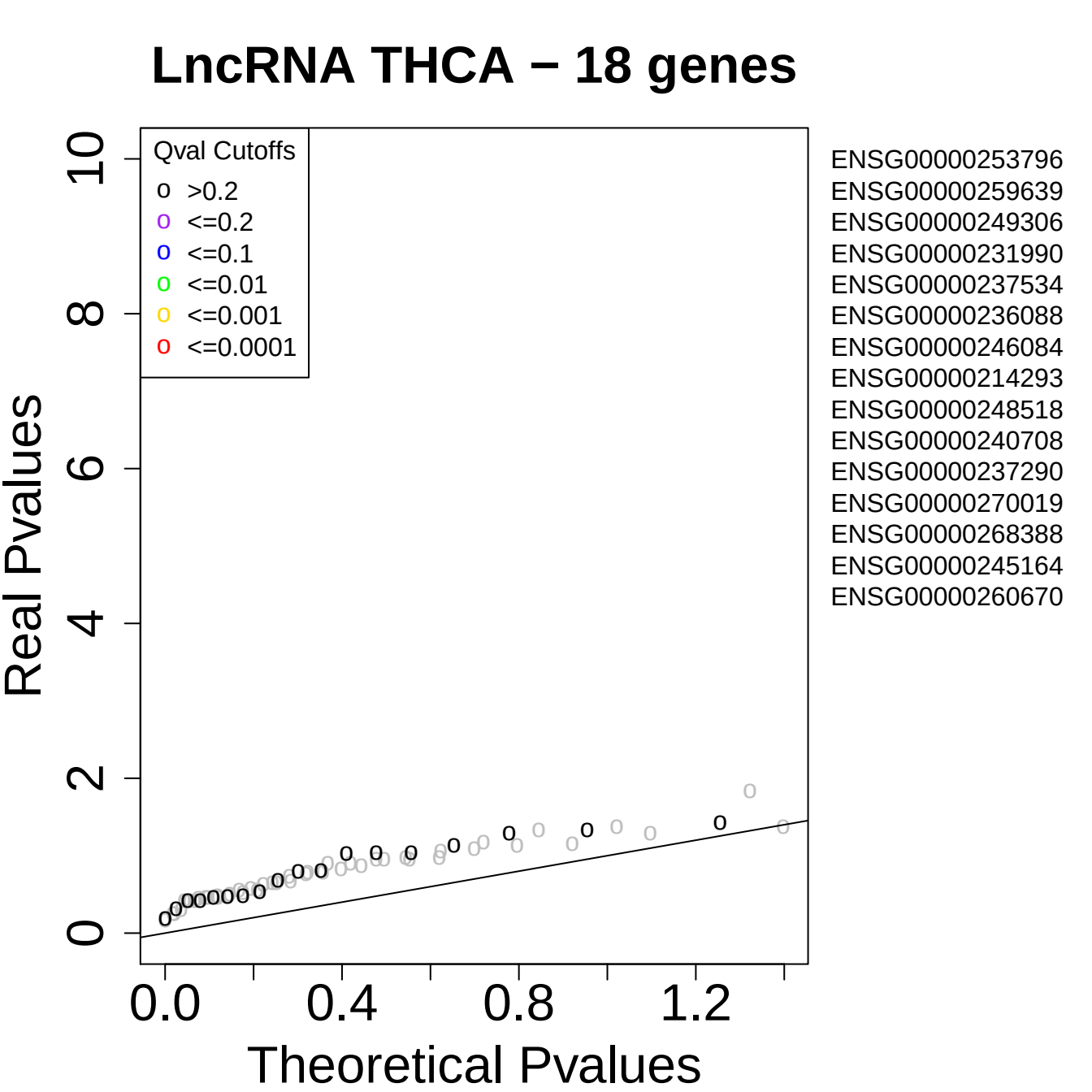
LncRNA THCA − 18 genes
Qval Cutoffs
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<=0.1
<=0.01
<=0.001
<=0.0001
ENSG00000253796
ENSG00000259639
ENSG00000249306
ENSG00000231990
ENSG00000237534
ENSG00000236088
ENSG00000246084
ENSG00000214293
ENSG00000248518
ENSG00000240708
ENSG00000237290
ENSG00000270019
ENSG00000268388
ENSG00000245164
ENSG00000260670
Real Pvalues
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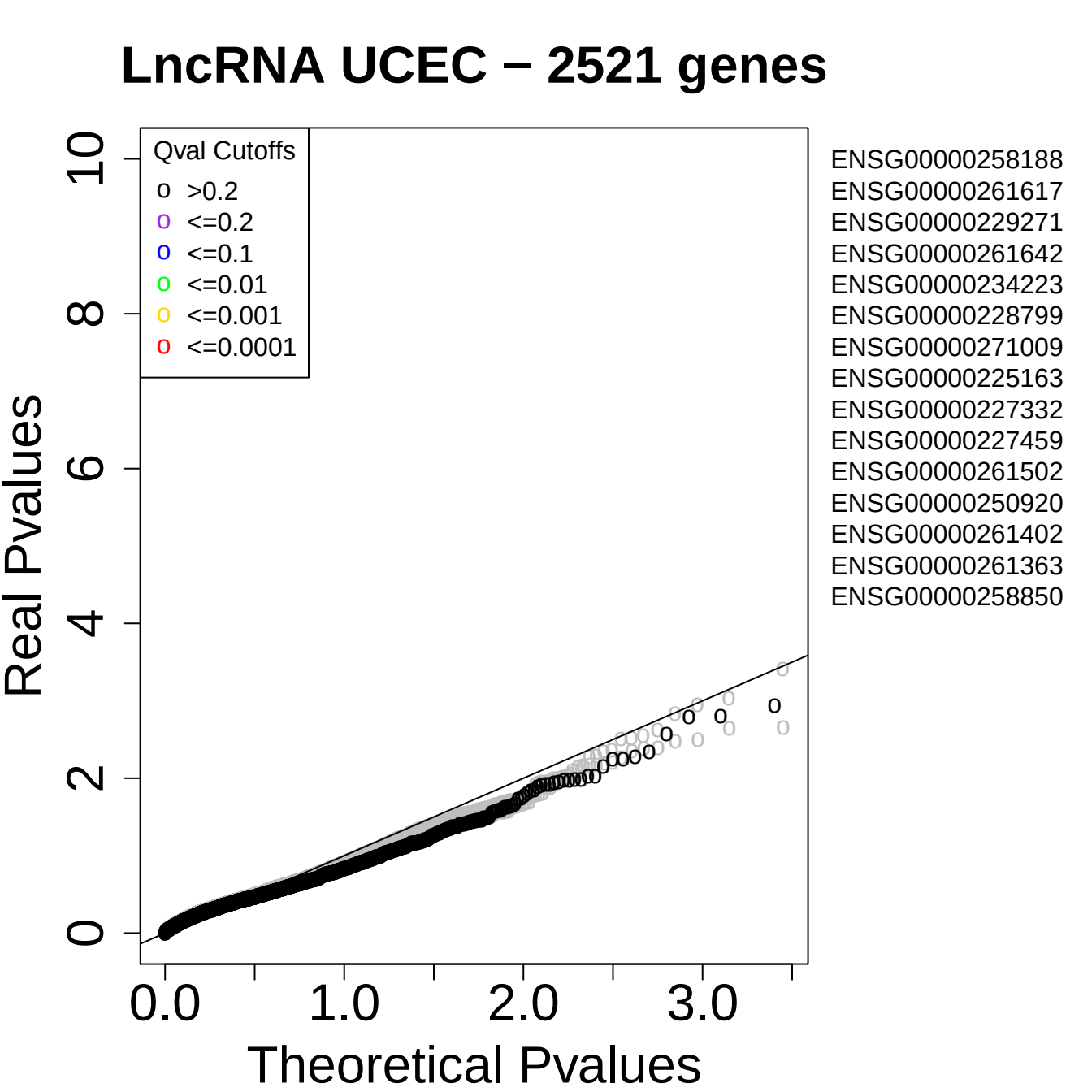
2
4
6
8
10
0.0
0.4
0.8
1.2
Theoretical Pvalues


LncRNA UCEC − 2521 genes
Qval Cutoffs
>0.2
<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
Real Pvalues
0
2
4
6
8
10
0.0
1.0
2.0
3.0
Theoretical Pvalues
ENSG00000258188
ENSG00000261617
ENSG00000229271
ENSG00000261642
ENSG00000234223
ENSG00000228799
ENSG00000271009
ENSG00000225163
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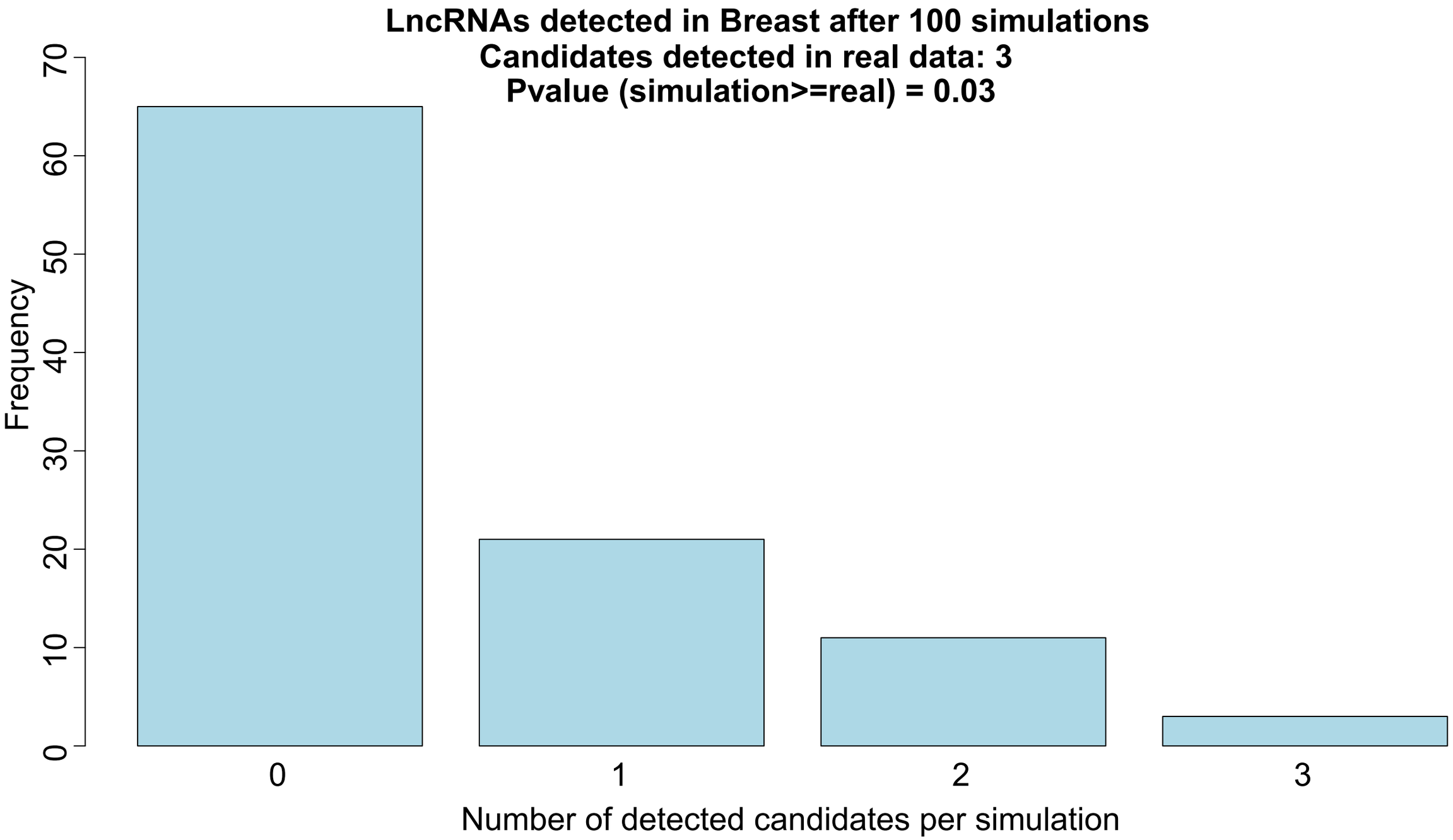
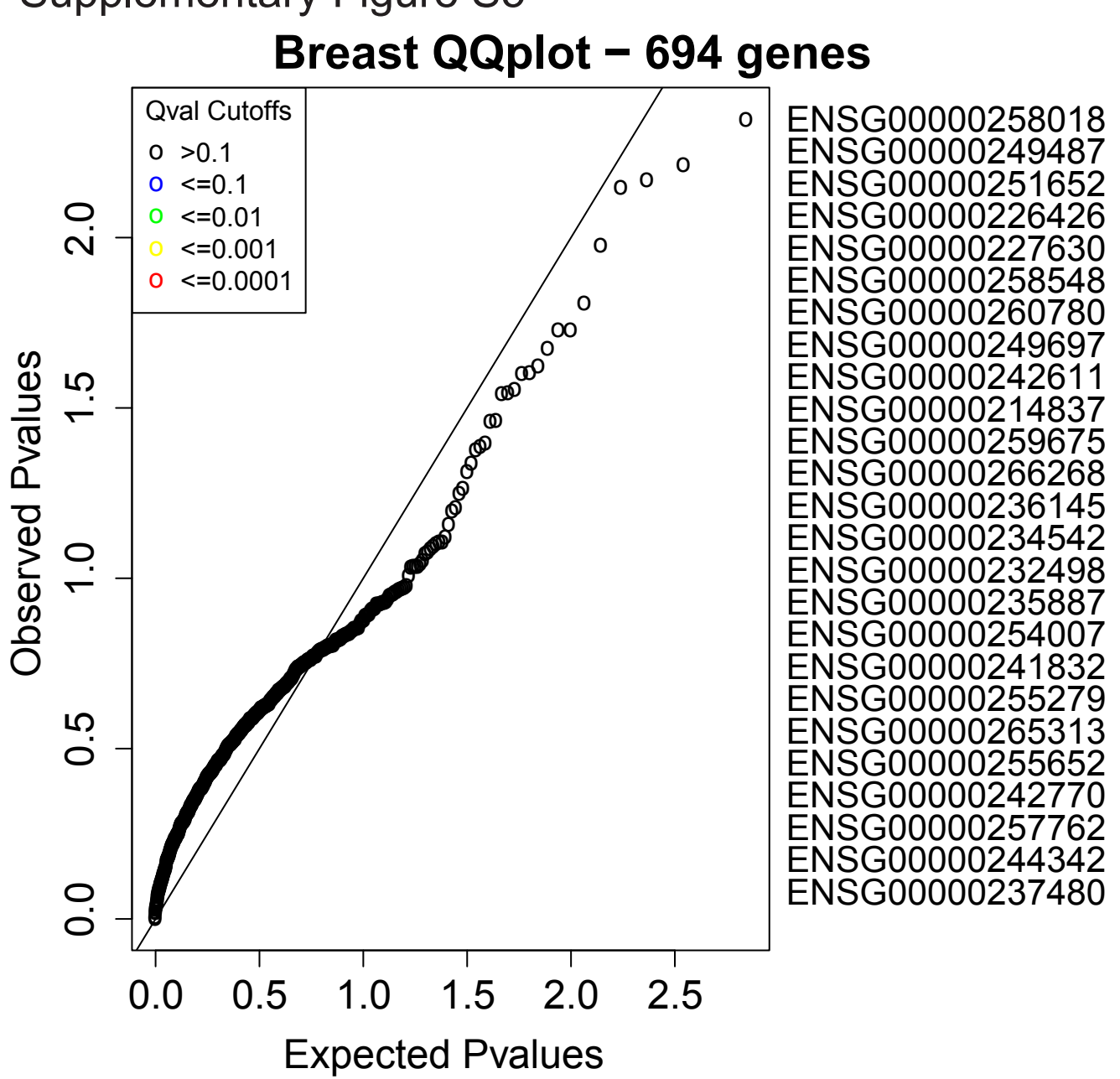
ENSG00000261363
ENSG00000258850

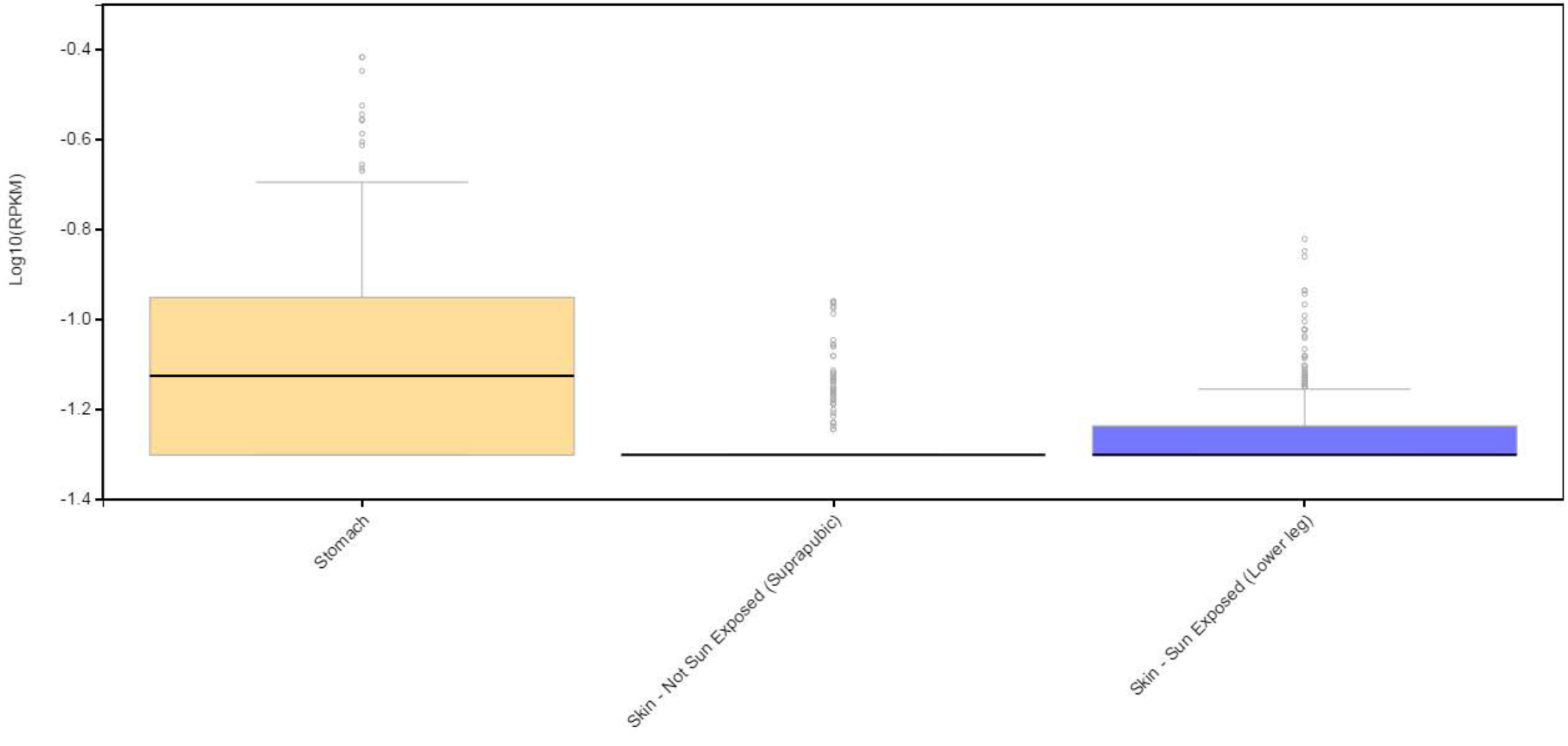
Supplementary Figure S4



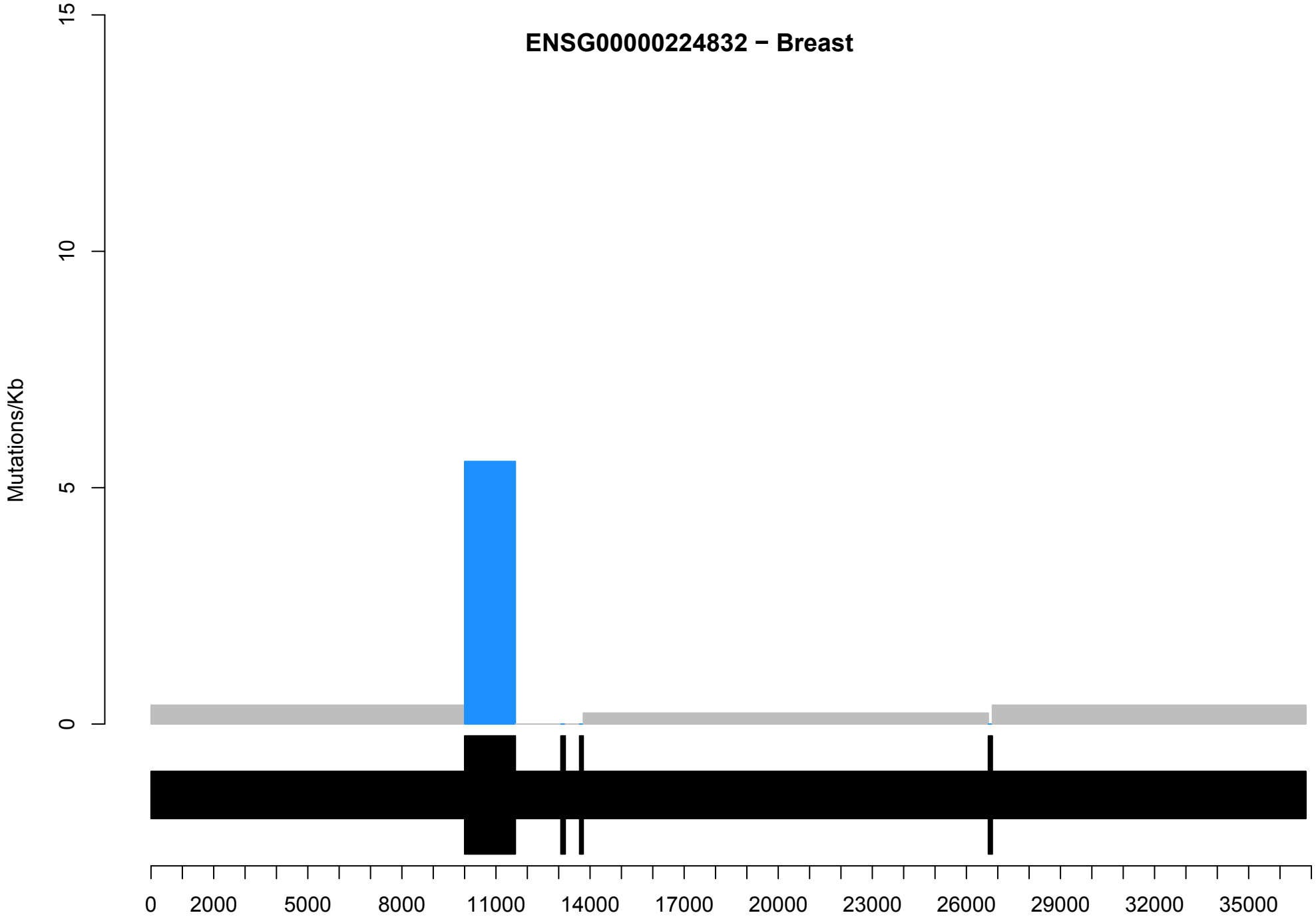
Supplementary Figure S5

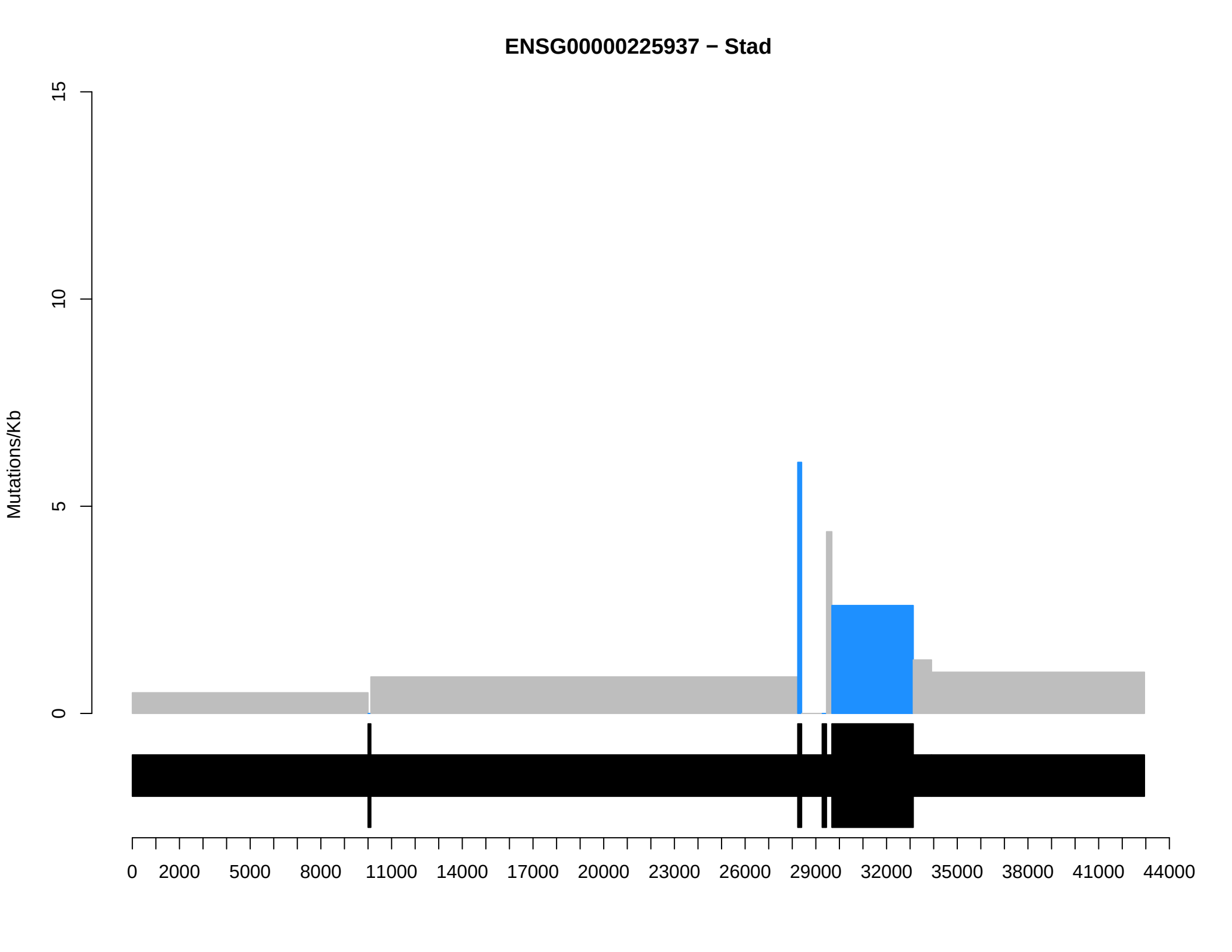


Supplementary Figure S6



Supplementary Figure S7




ENSG00000225937 − Stad
Mutations/Kb
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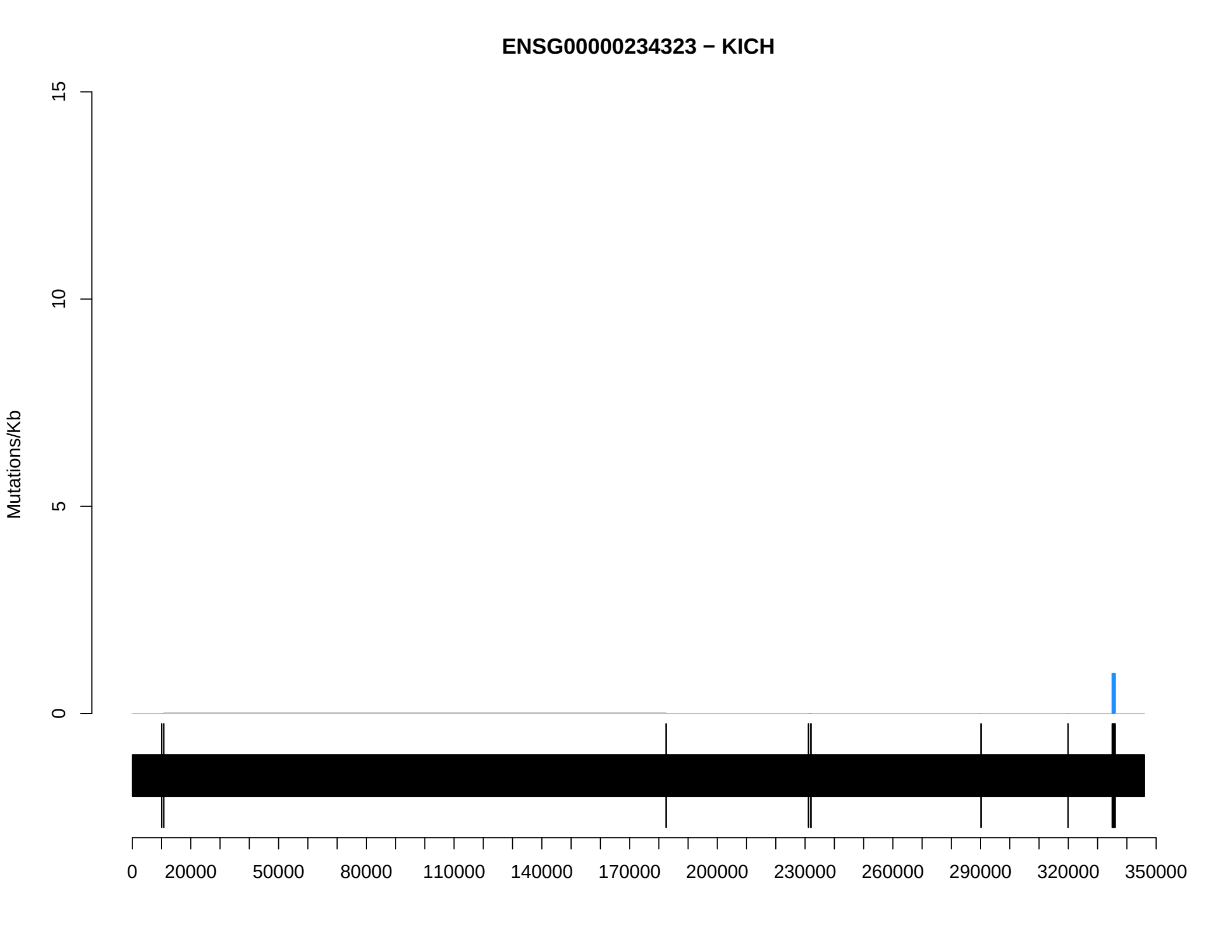
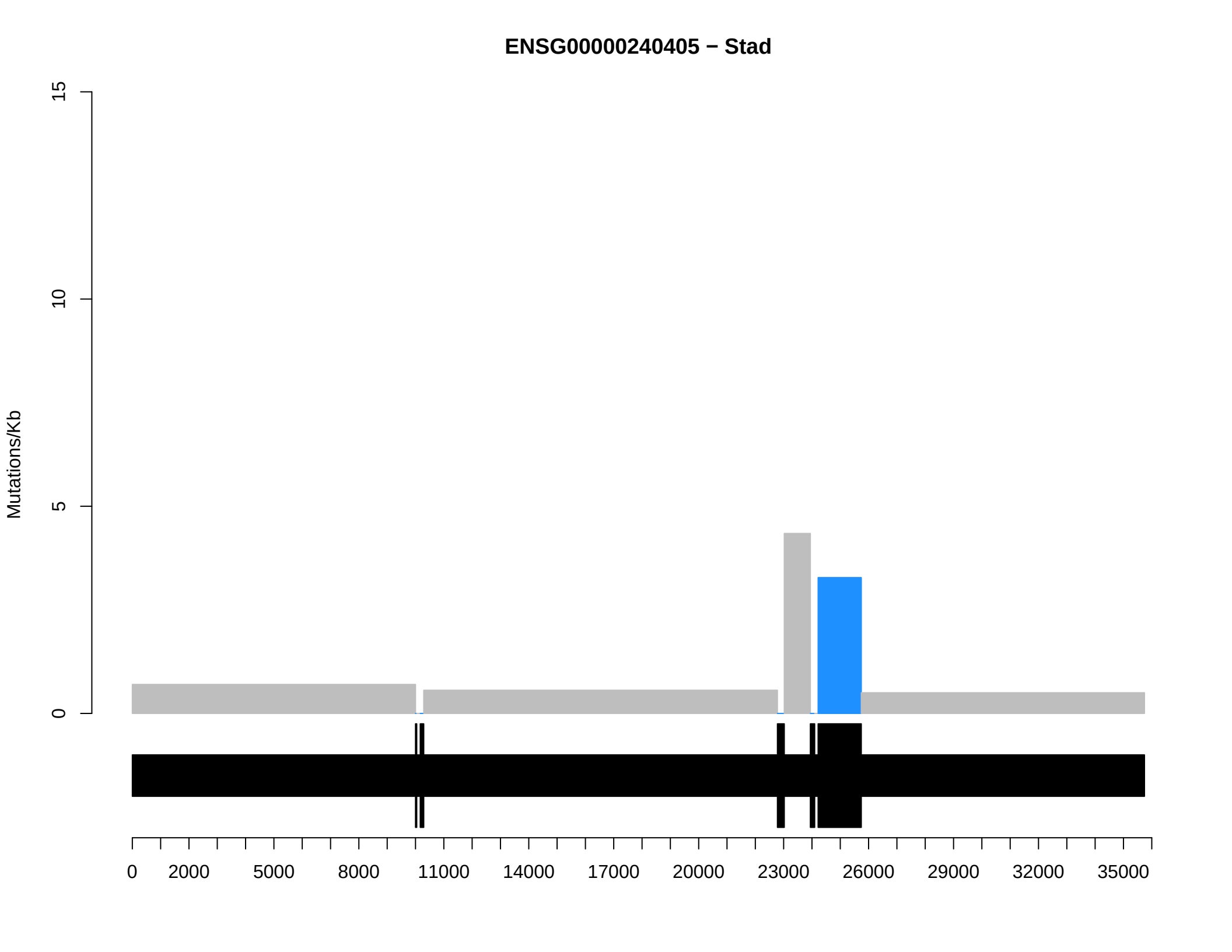
5
10
15
0
2000
5000
8000
11000
14000
17000
20000
23000
26000
29000
32000
35000
38000
41000
44000


ENSG00000234323 − KICH
Mutations/Kb
0
5
10
15
0
20000
50000
80000
110000
140000
170000
200000
230000
260000
290000
320000
350000


ENSG00000240405 − Stad
Mutations/Kb
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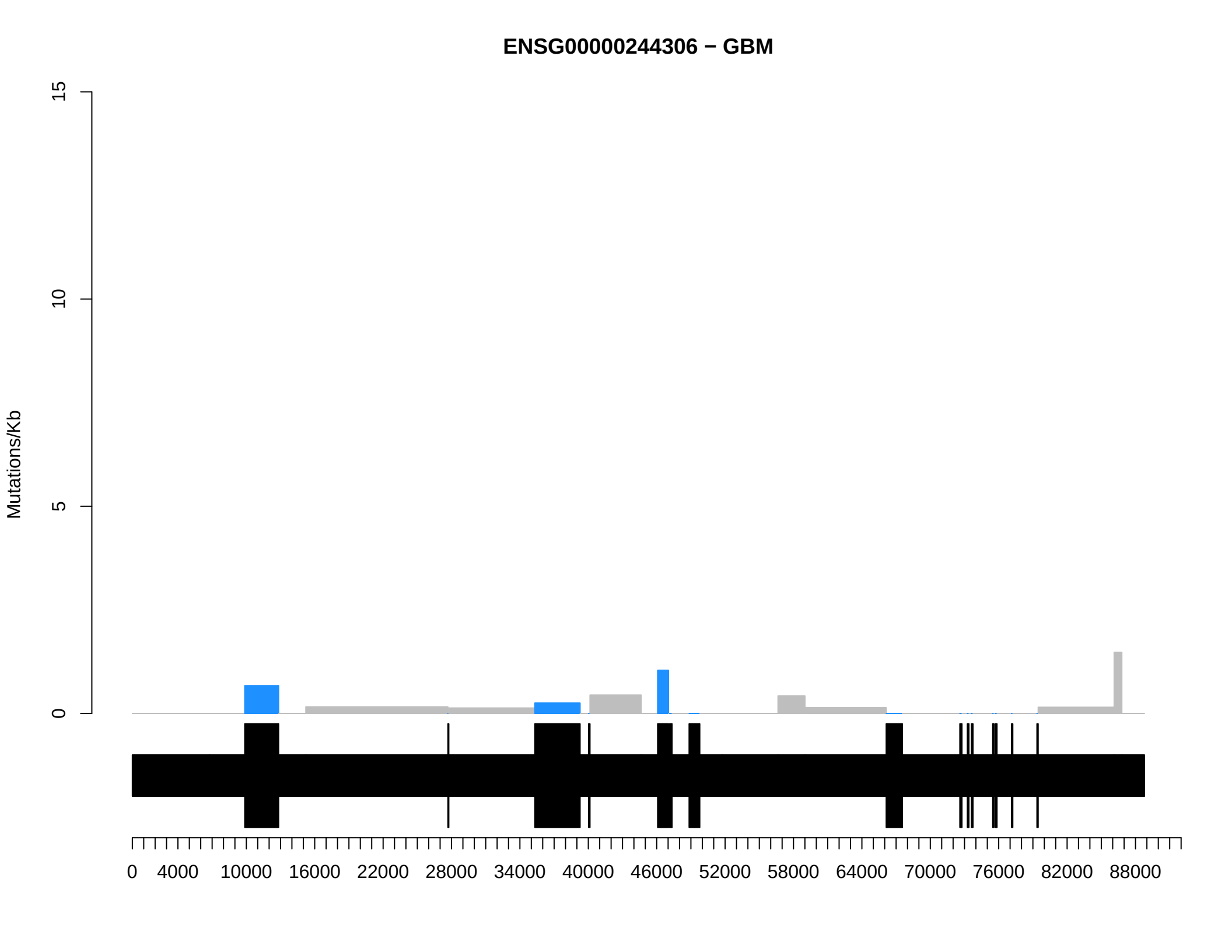
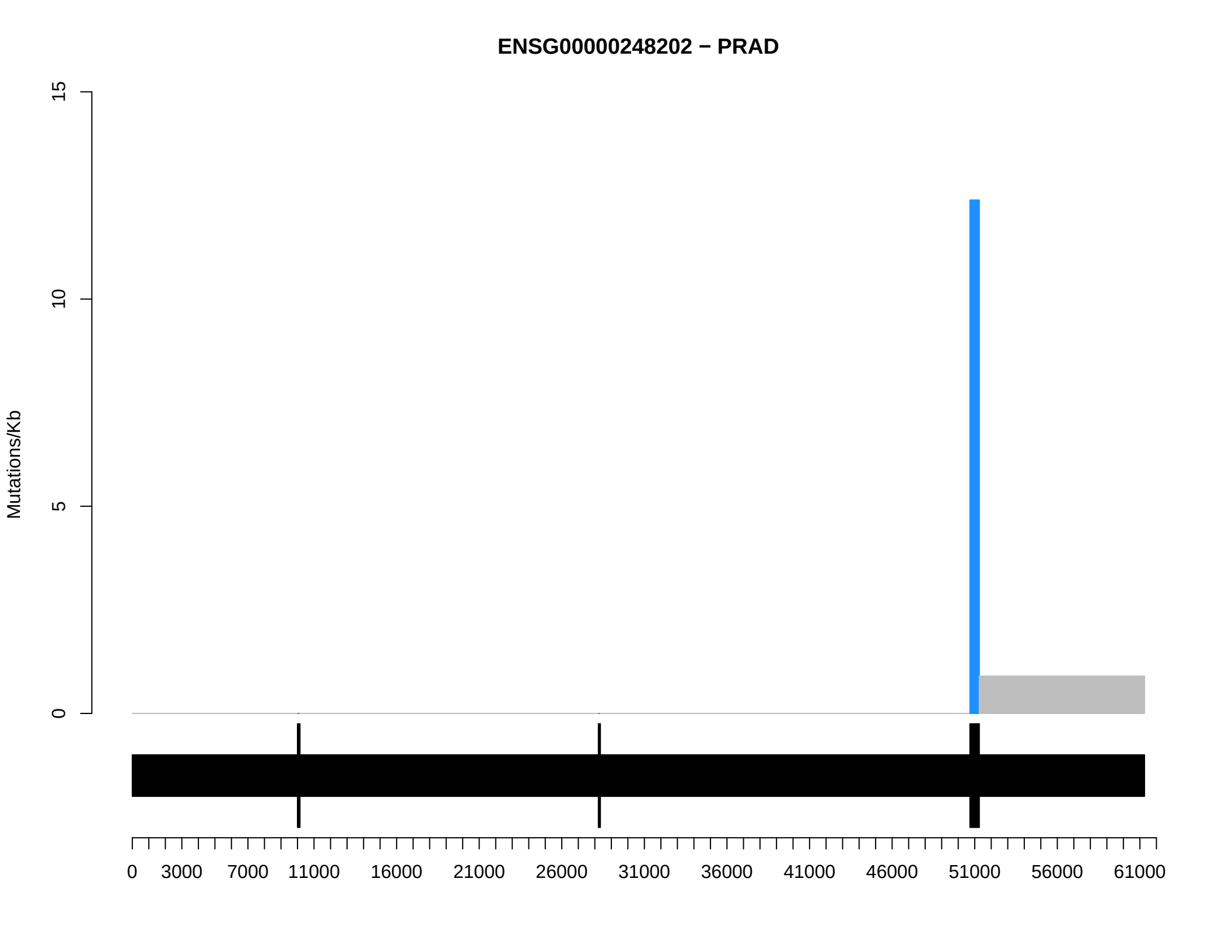
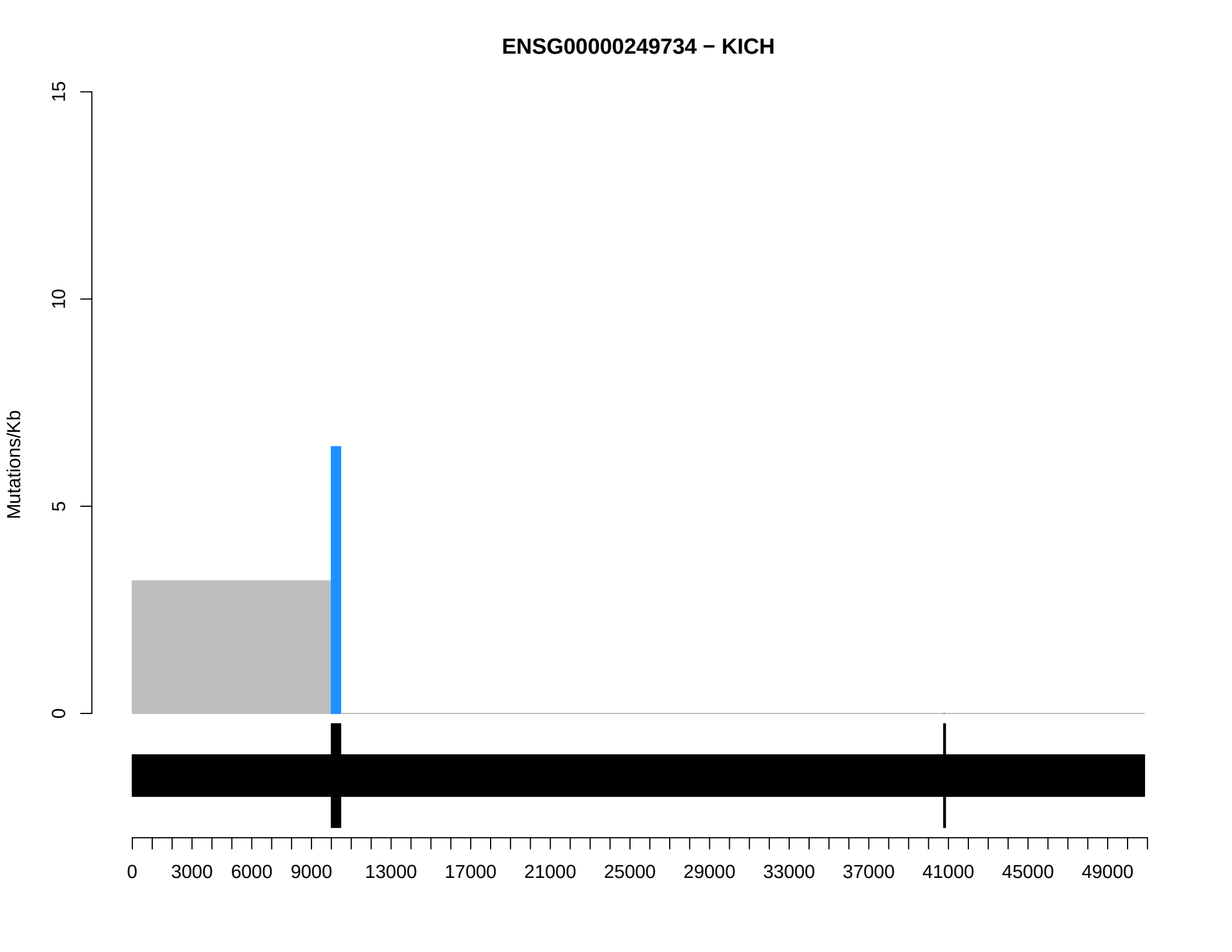
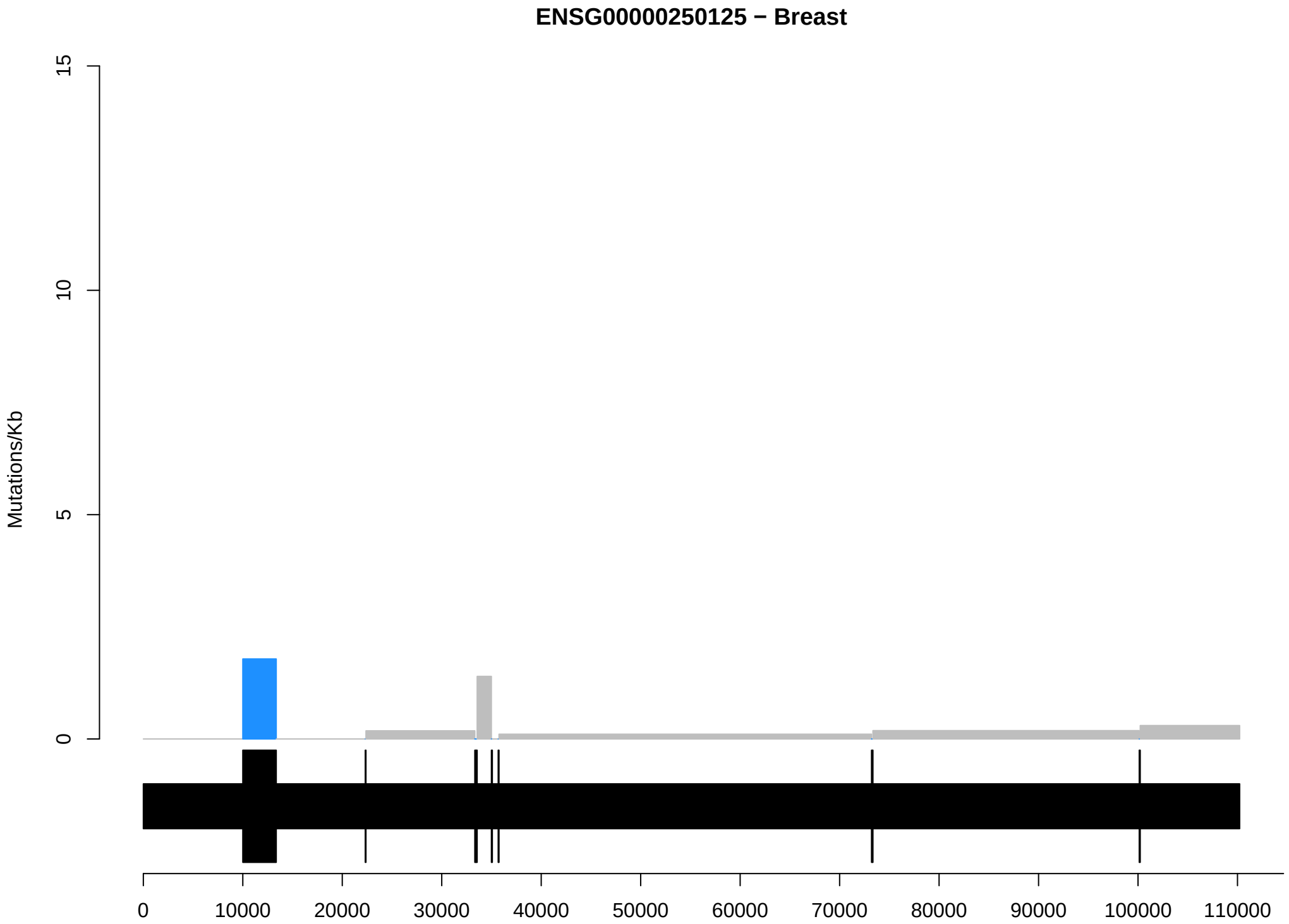
5
10
15
0
2000
5000
8000
11000
14000
17000
20000
23000
26000
29000
32000
35000


ENSG00000244306 − GBM
Mutations/Kb
15
10
5
0
0
4000
10000
16000
22000
28000
34000
40000
46000
52000
58000
64000
70000
76000
82000
88000


ENSG00000248202 − PRAD
Mutations/Kb
0
5
10
15
0
3000
7000
11000
16000
21000
26000
31000
36000
41000
46000
51000
56000
61000


ENSG00000249734 − KICH
Mutations/Kb
15
10
5
0
0
3000
6000
9000
13000
17000
21000
25000
29000
33000
37000
41000
45000
49000


ENSG00000250125 − Breast
Mutations/Kb
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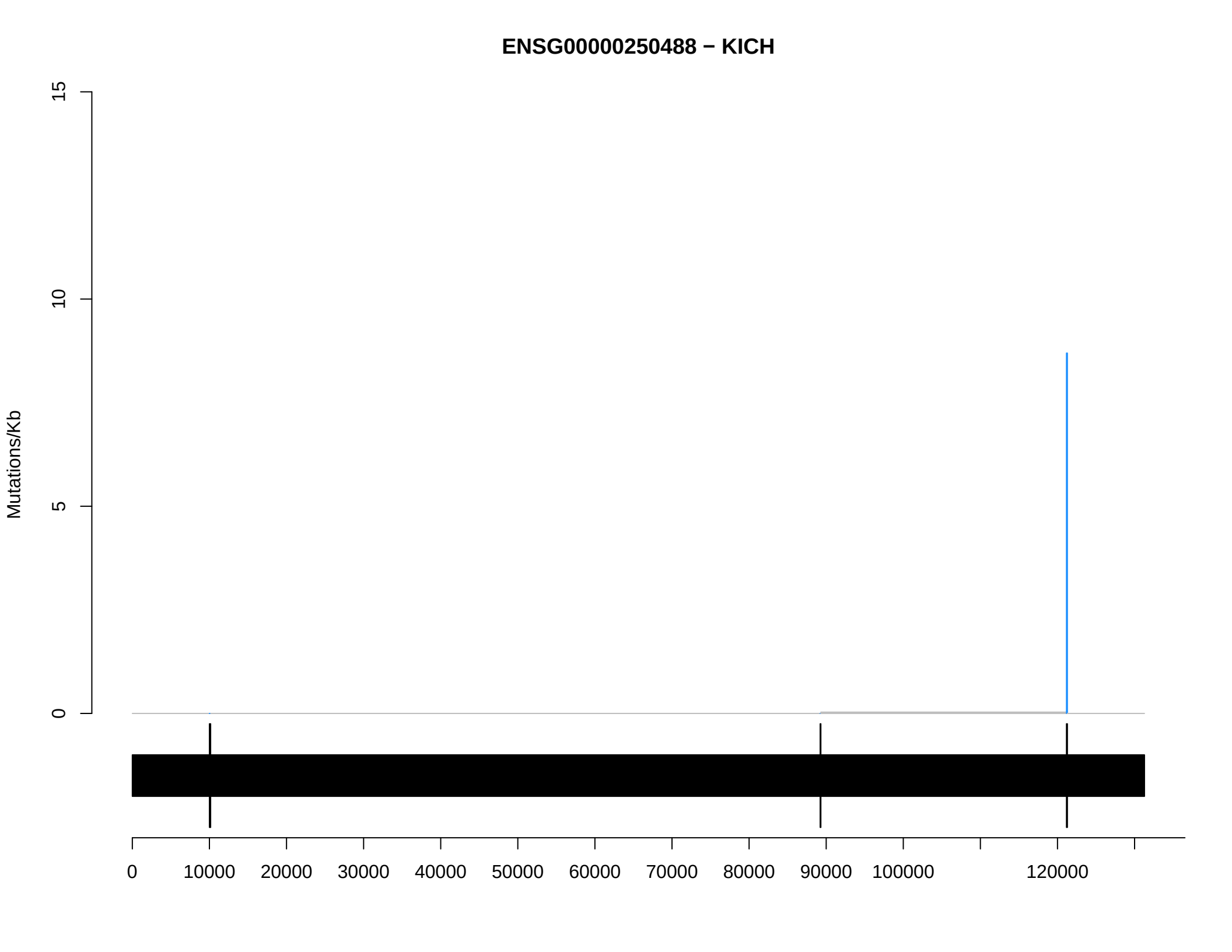
5
10
15
0
10000
20000
30000
40000
50000
60000
70000
80000
90000
100000
110000


ENSG00000250488 − KICH
Mutations/Kb
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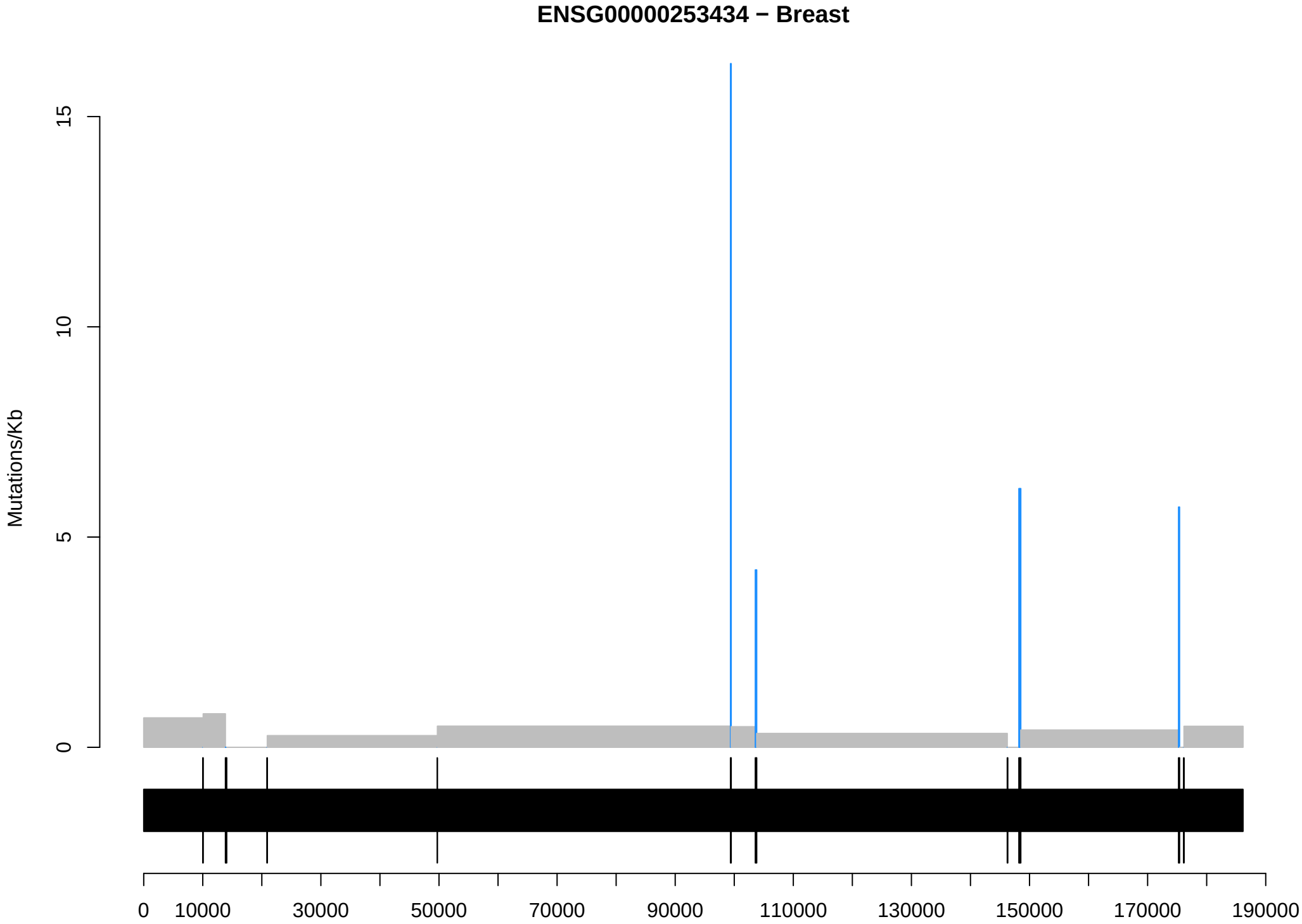
5
10
15
0
10000
20000
30000
40000
50000
60000
70000
80000
90000
100000
120000


ENSG00000253434 − Breast
Mutations/Kb
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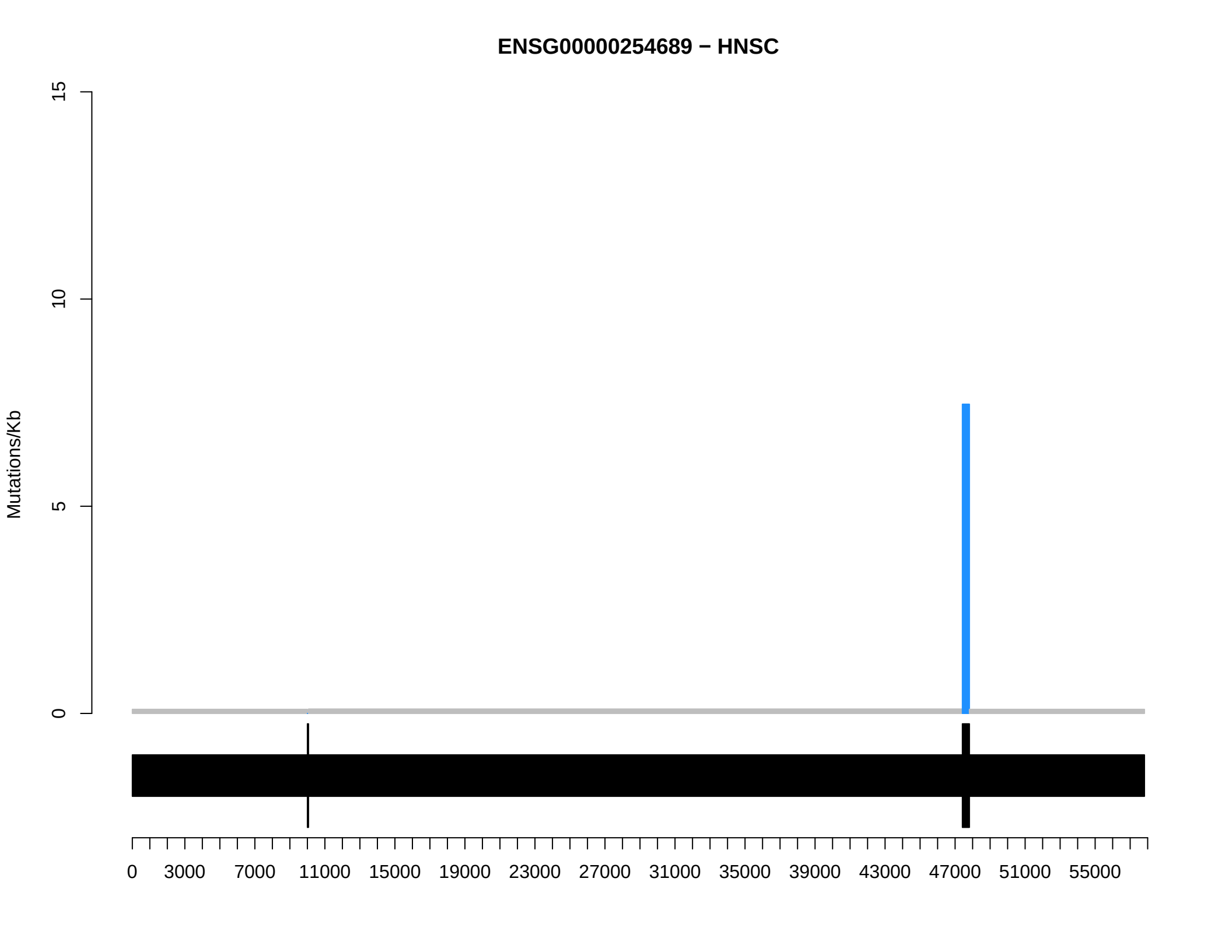
5
10
15
0
10000
30000
50000
70000
90000
110000
130000
150000
170000
190000


ENSG00000254689 − HNSC
Mutations/Kb
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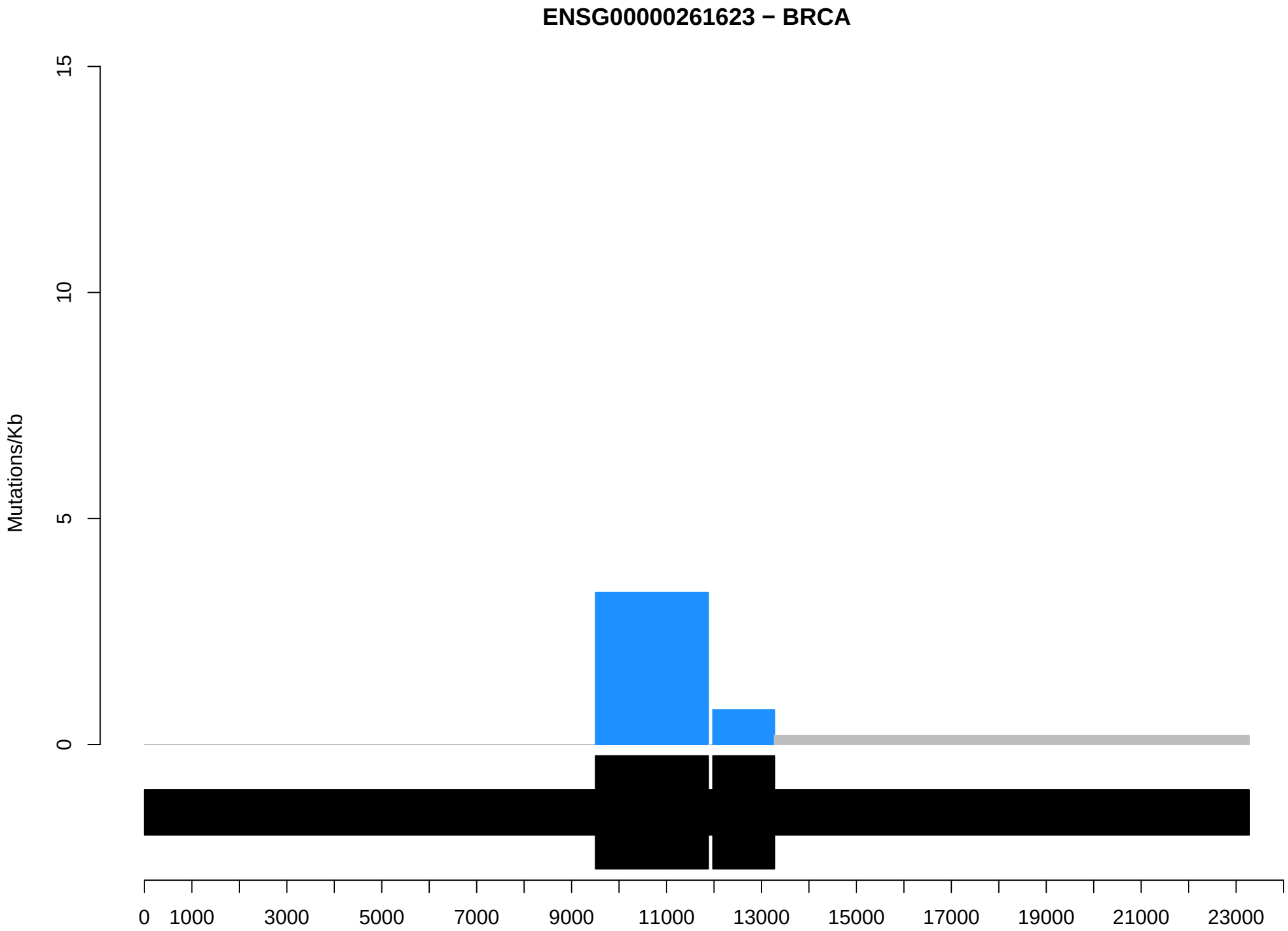
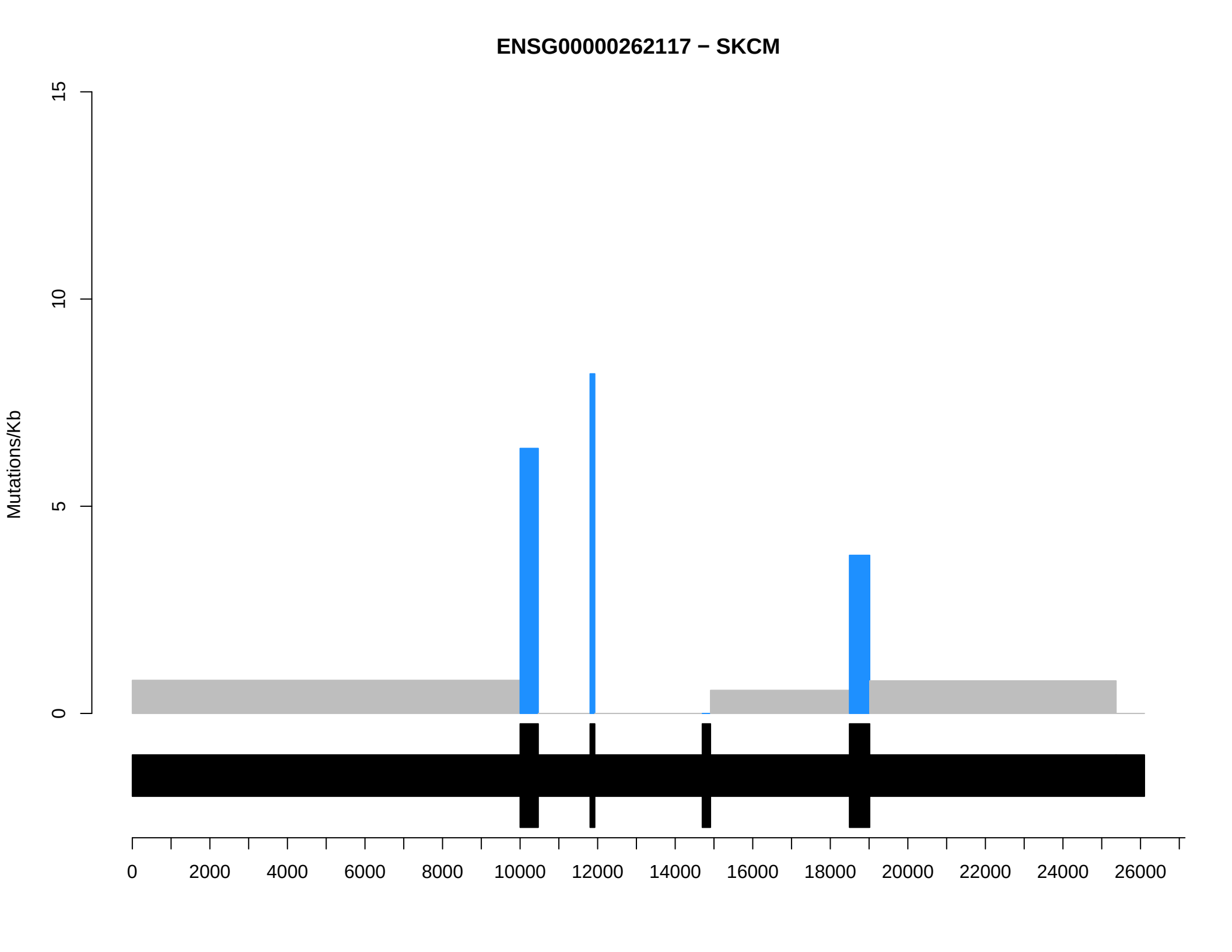
5
10
15
0
3000
7000
11000
15000
19000
23000
27000
31000
35000
39000
43000
47000
51000
55000


ENSG00000261623 − BRCA
Mutations/Kb
0
5
10
15
0
1000
3000
5000
7000
9000
11000
13000
15000
17000
19000
21000
23000


ENSG00000262117 − SKCM
Mutations/Kb
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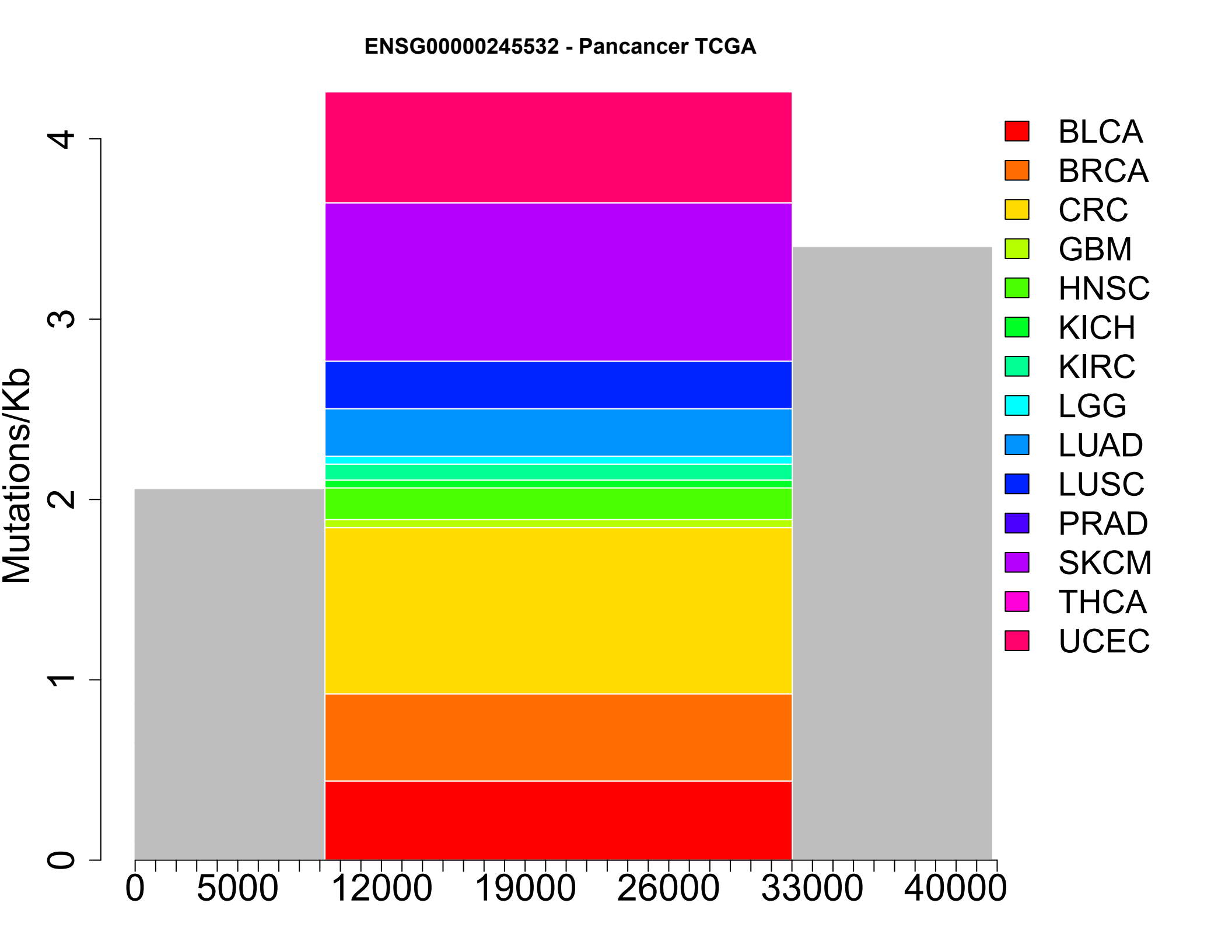
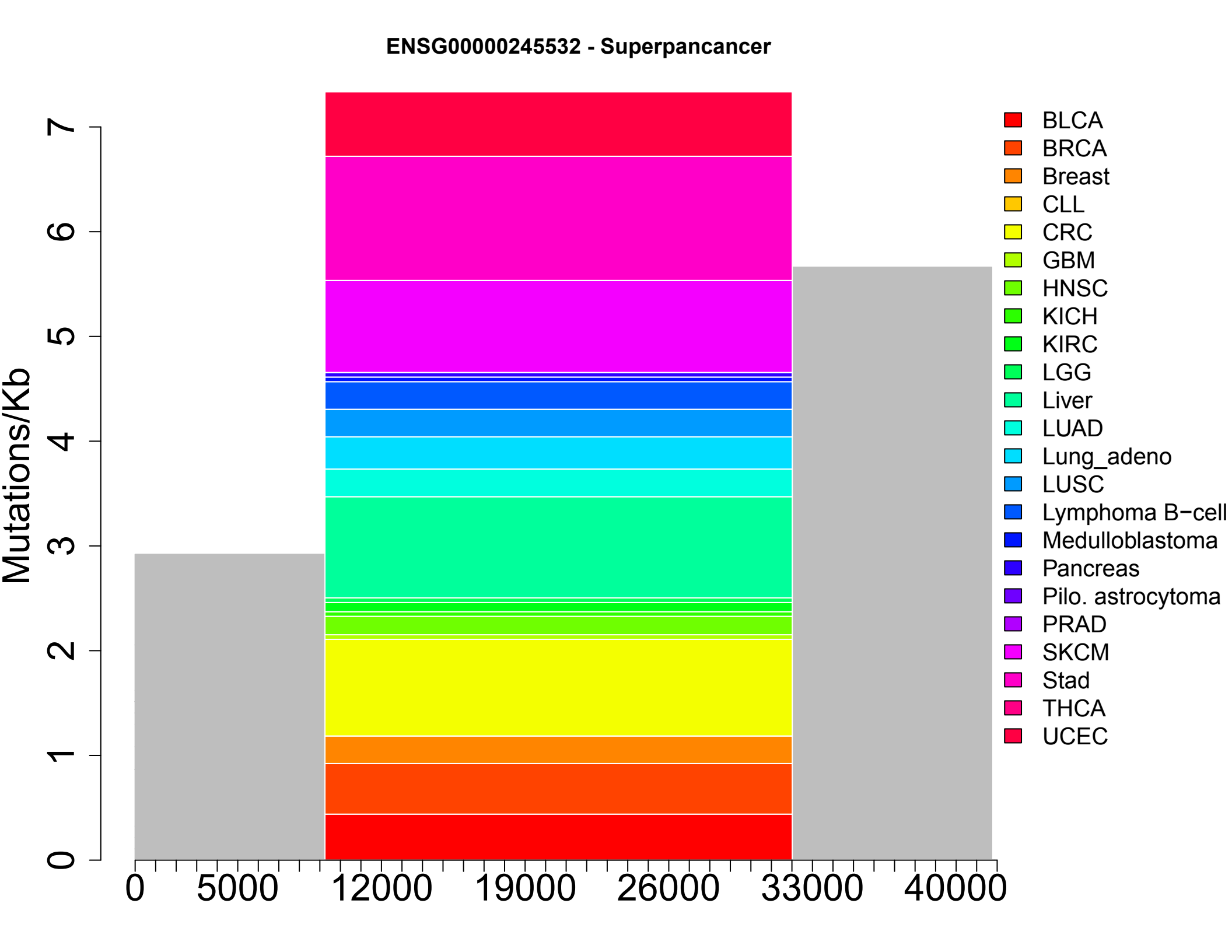
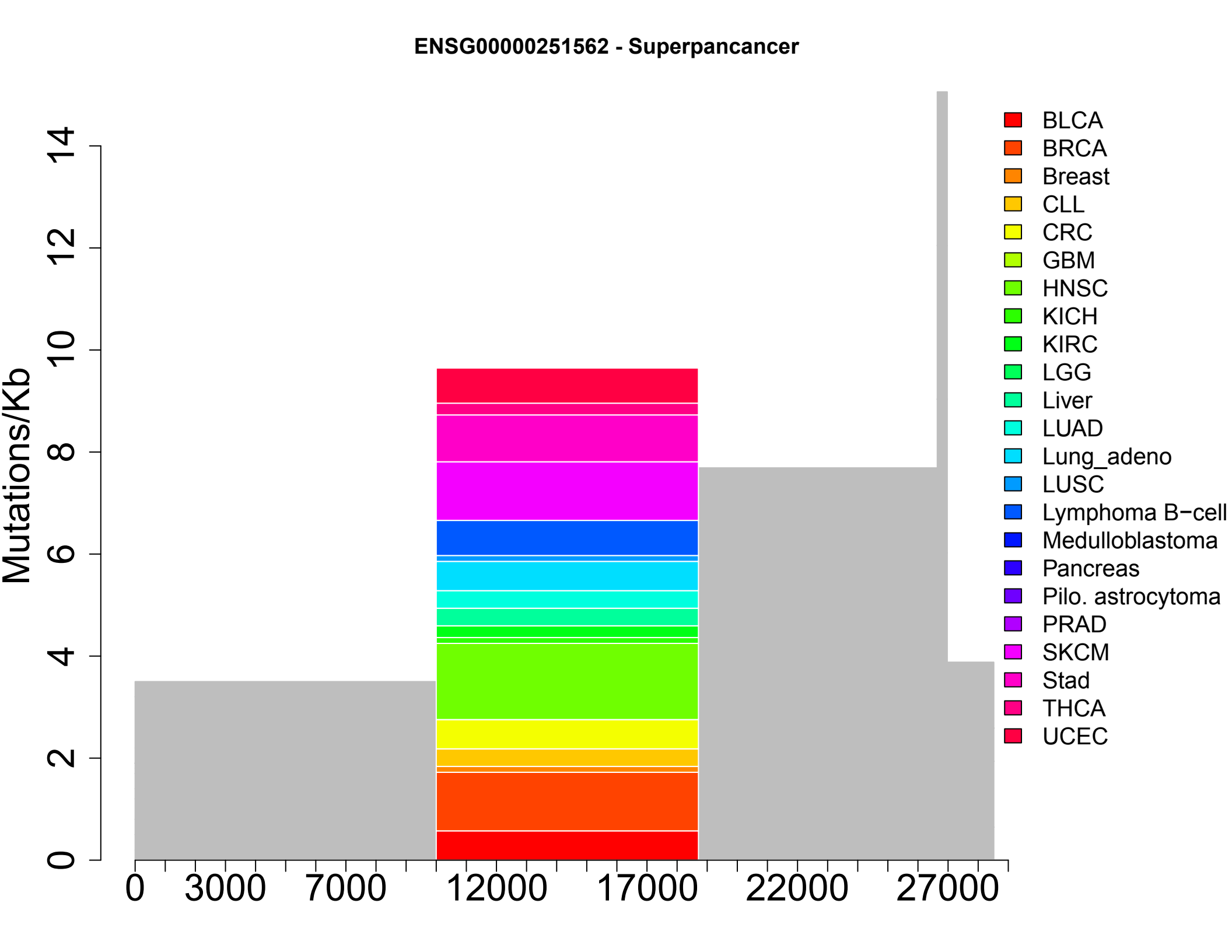
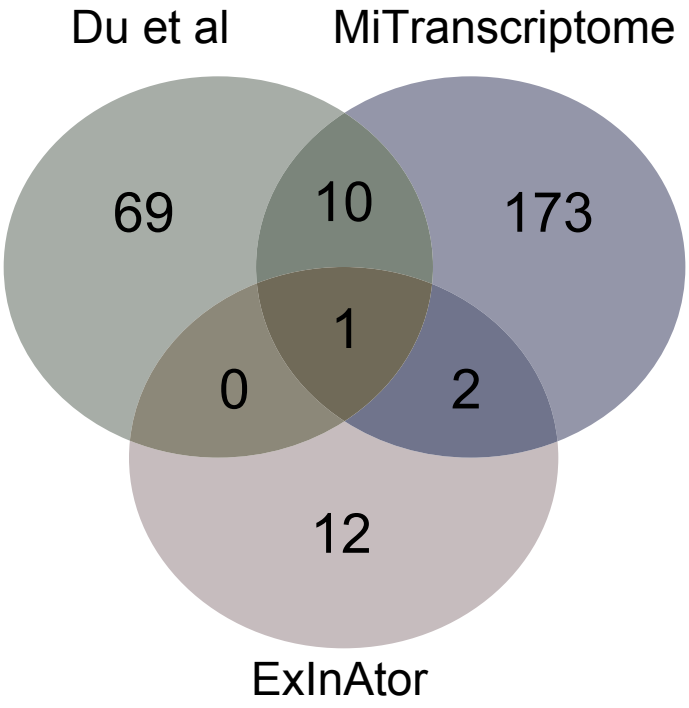
5
10
15
0
2000
4000
6000
8000
10000
12000
14000
16000
18000
20000
22000
24000
26000


ENSG00000245532 - Pancancer TCGA
Mutations/Kb
0
1
2
3
4
0
5000
12000
19000
26000
33000
40000
BLCA
BRCA
CRC
GBM
HNSC
KICH
KIRC
LGG
LUAD
LUSC
PRAD
SKCM
THCA
UCEC


ENSG00000245532 - Superpancancer
Mutations/Kb
0
1
2
3
4
5
6
7
0
5000
12000
19000
26000
33000
40000
BLCA
BRCA
Breast
CLL
CRC
GBM
HNSC
KICH
KIRC
LGG
Liver
LUAD
Lung_adeno
LUSC
Lymphoma B−cell
Medulloblastoma
Pancreas
Pilo. astrocytoma
PRAD
SKCM
Stad
THCA
UCEC

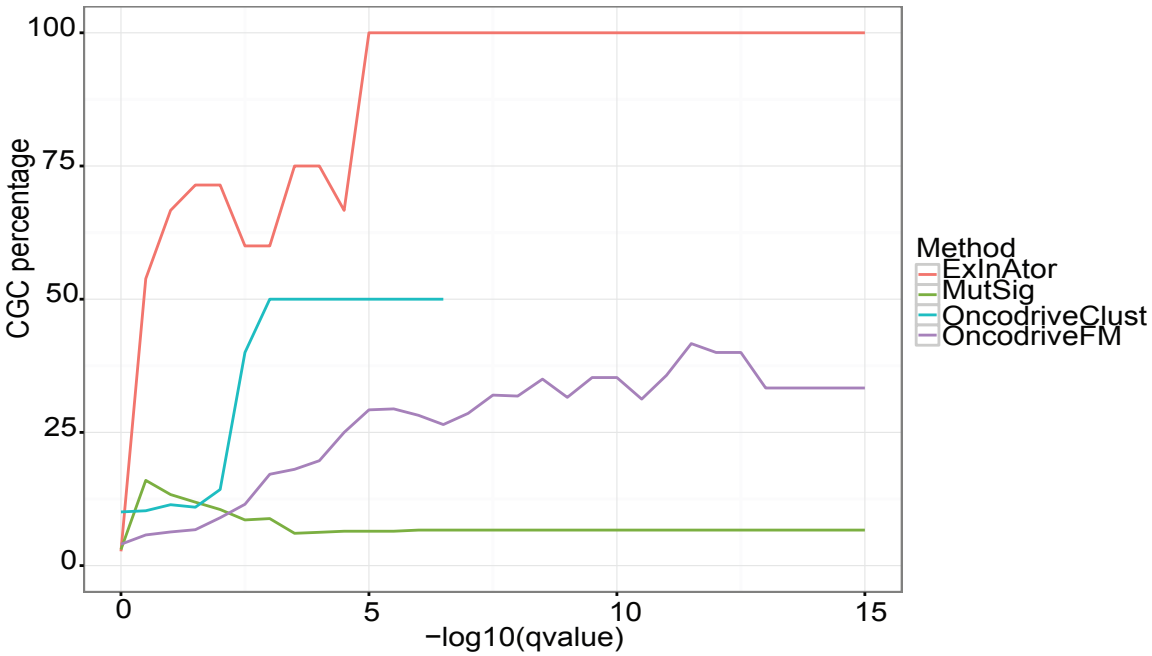

ENSG00000251562 - Superpancancer
Mutations/Kb
0
2
4
6
8
10
12
14
0
3000
7000
12000
17000
22000
27000
BLCA
BRCA
Breast
CLL
CRC
GBM
HNSC
KICH
KIRC
LGG
Liver
LUAD
Lung_adeno
LUSC
Lymphoma B−cell
Medulloblastoma
Pancreas
Pilo. astrocytoma
PRAD
SKCM
Stad
THCA
UCEC

Supplementary Figure S8

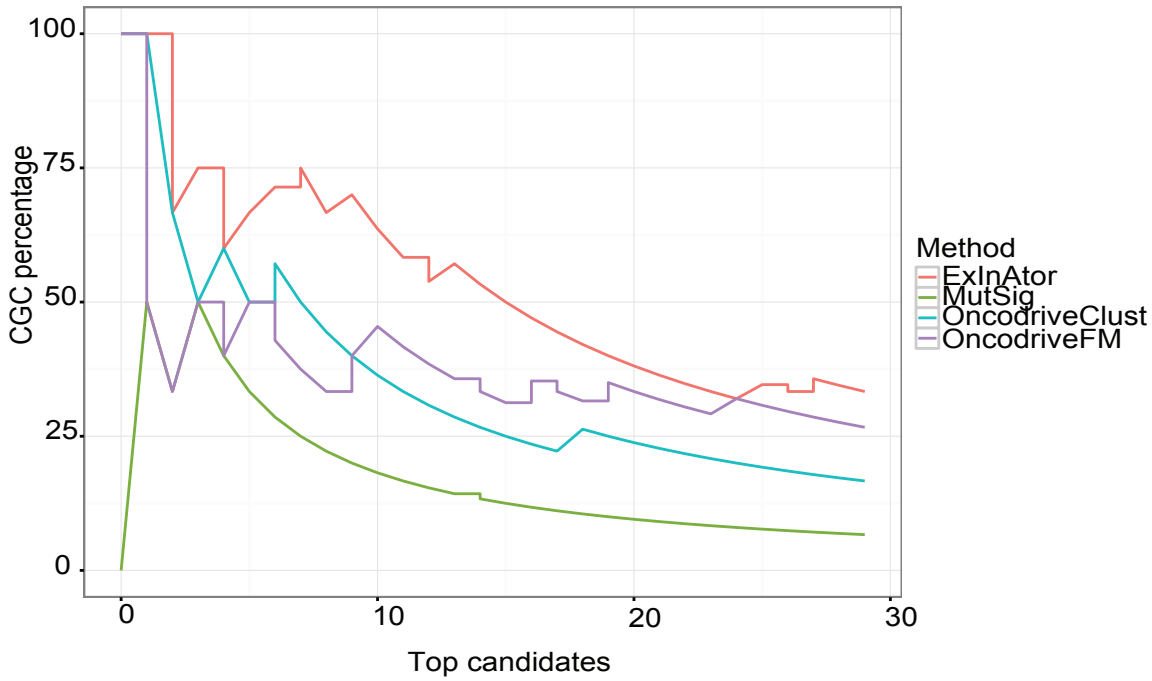


Supplementary Figure S9

A

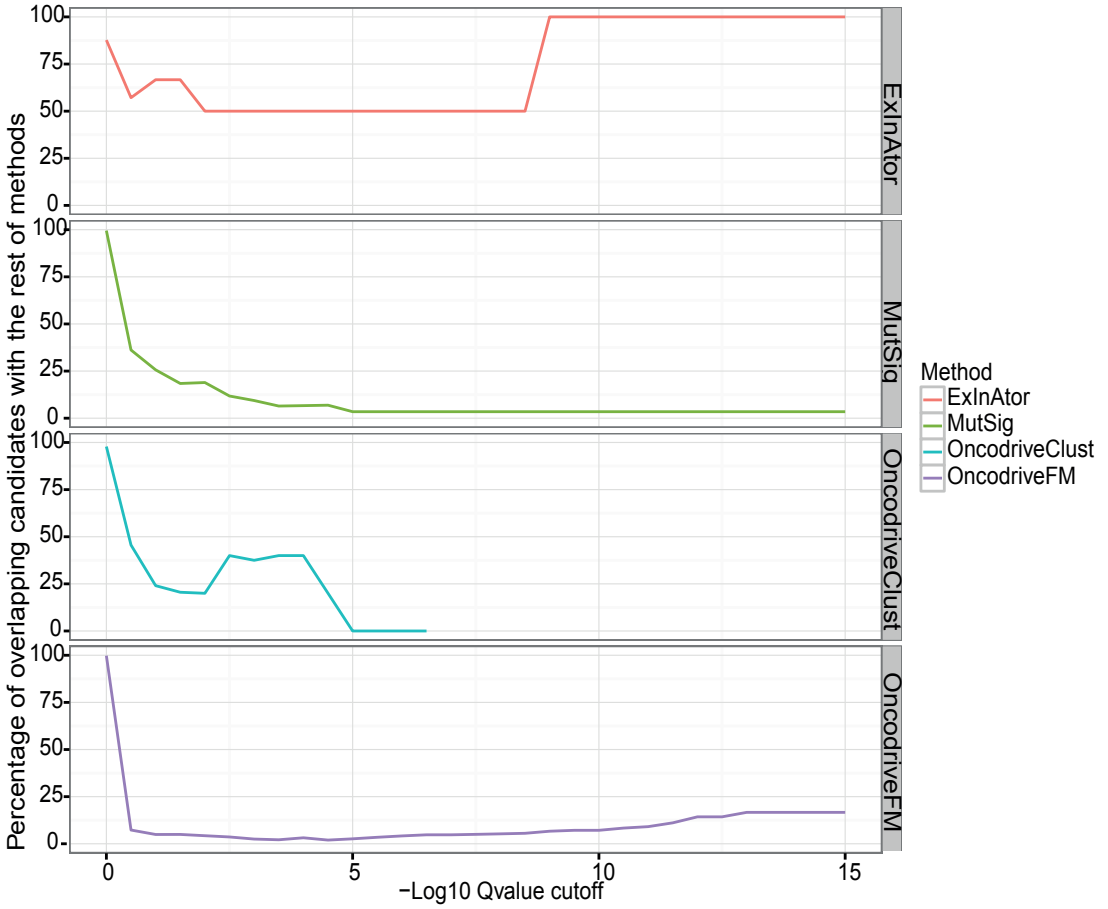


B

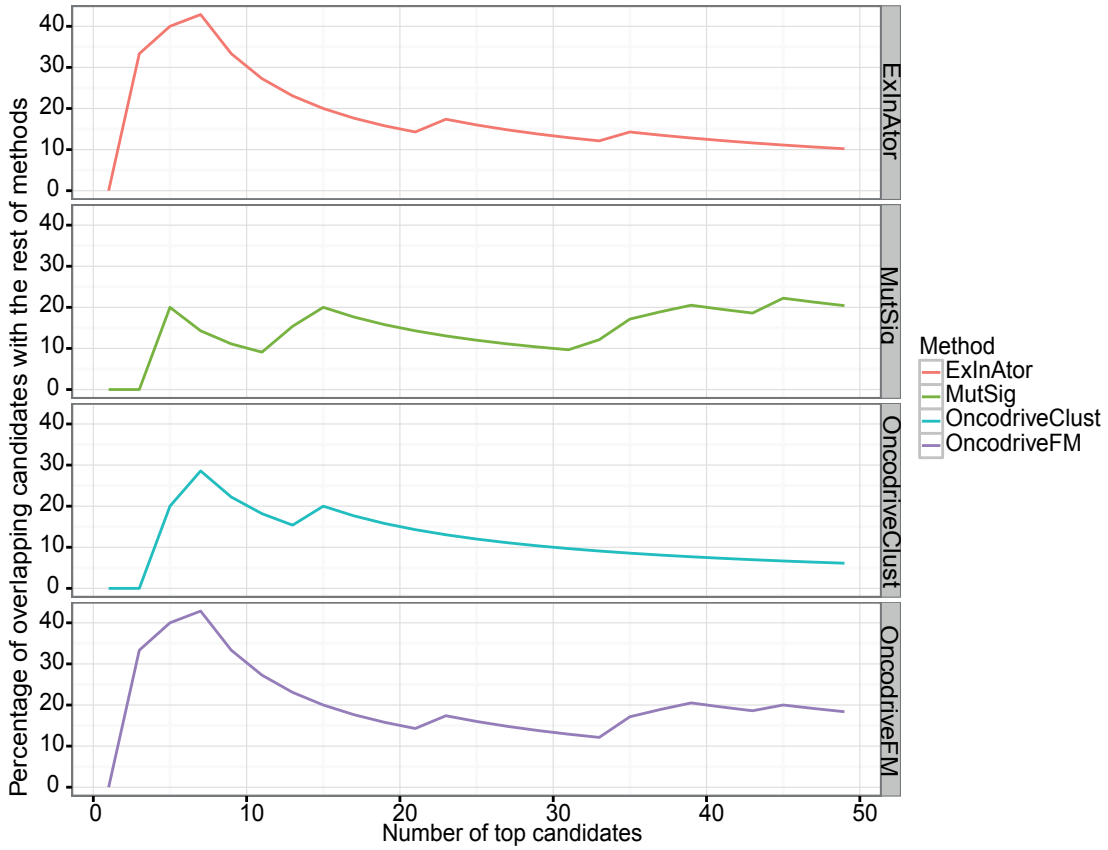


Supplementary Figure S10

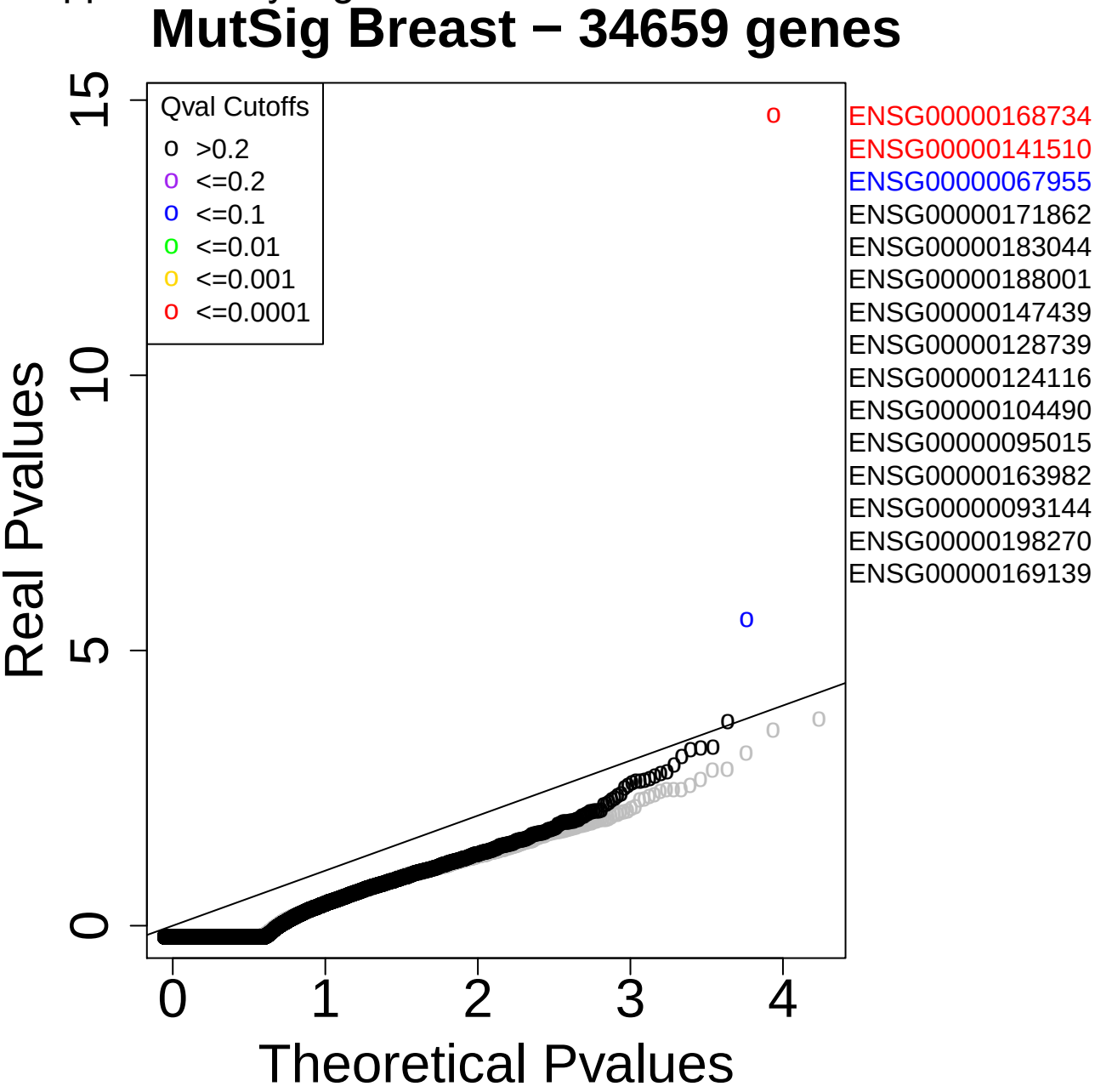
A

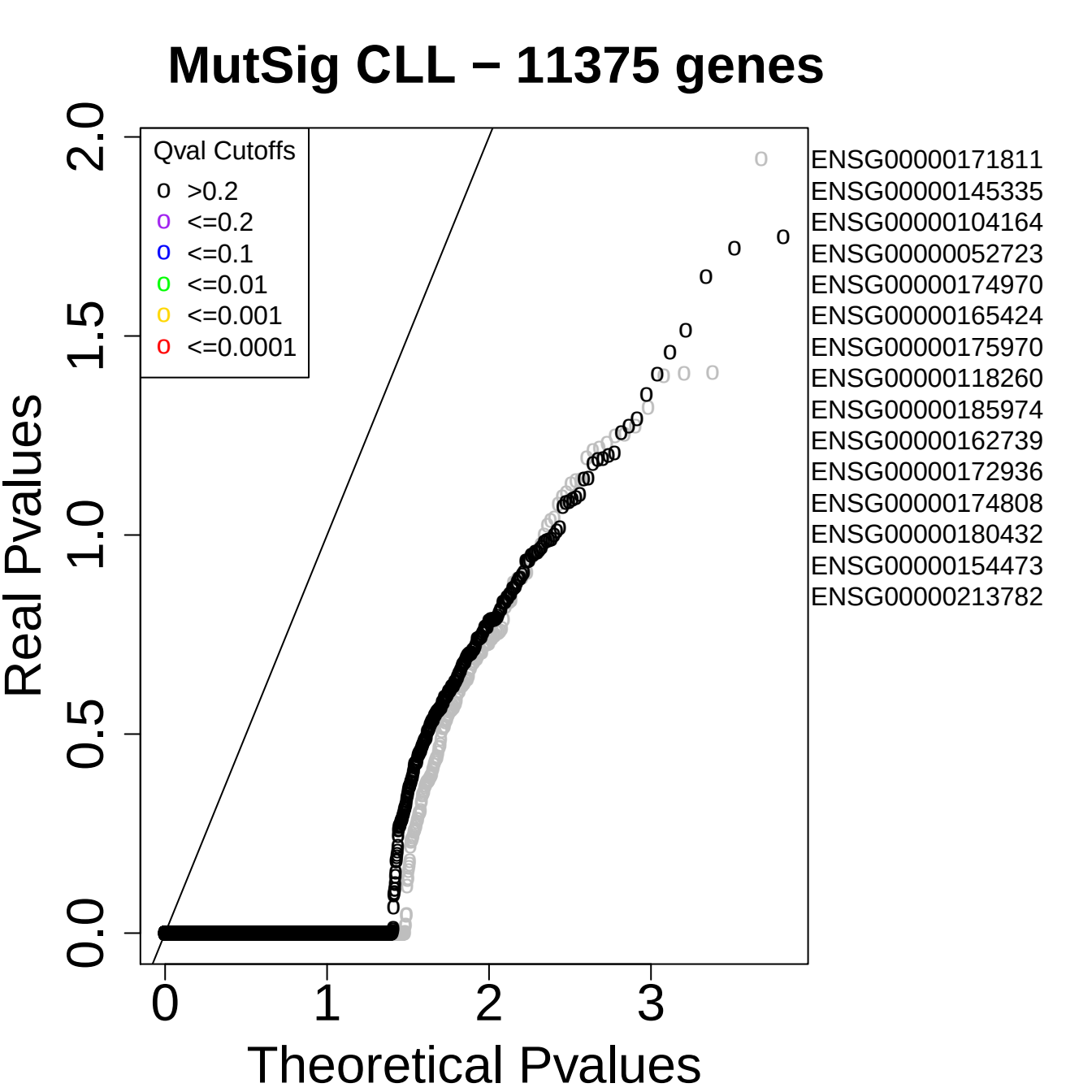


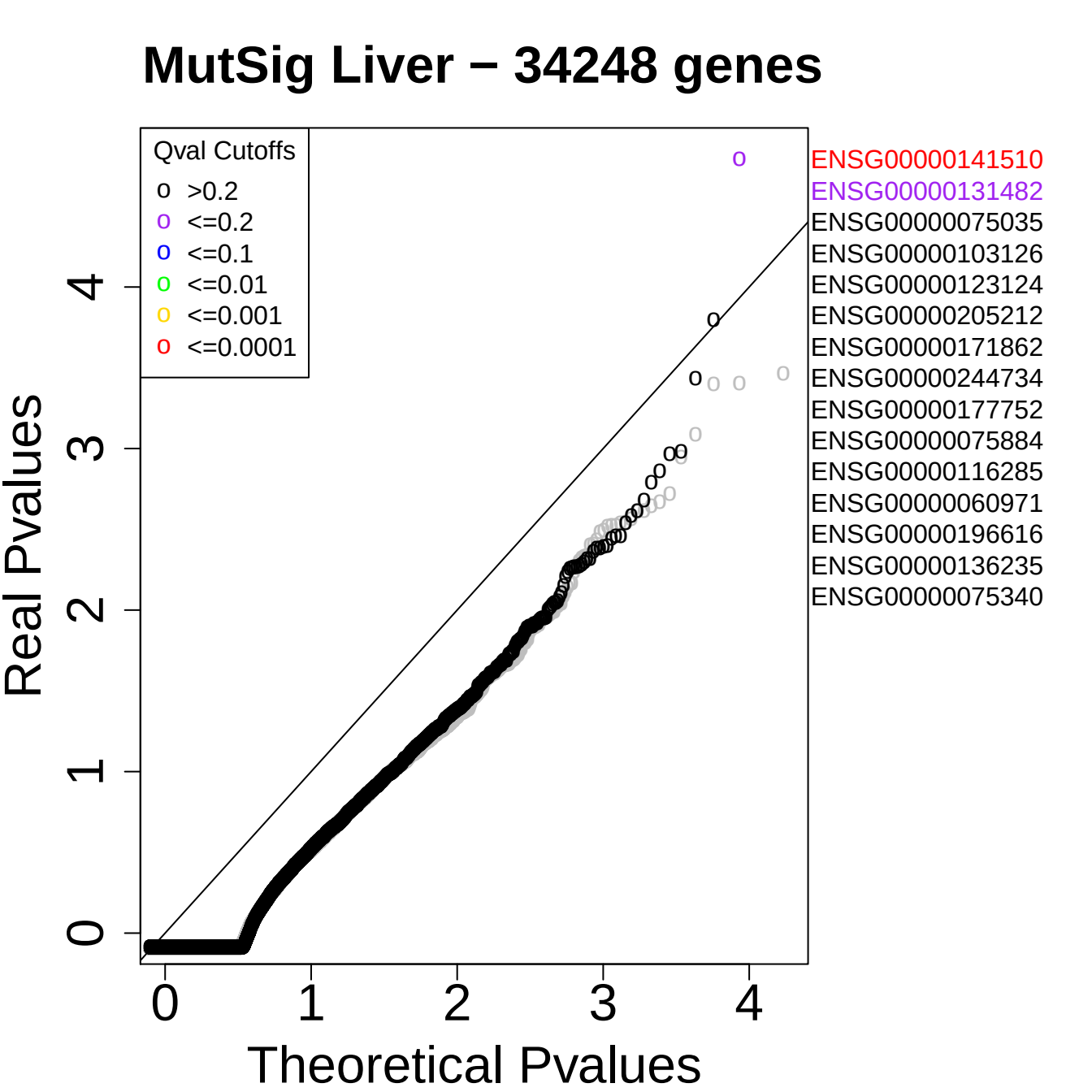
B



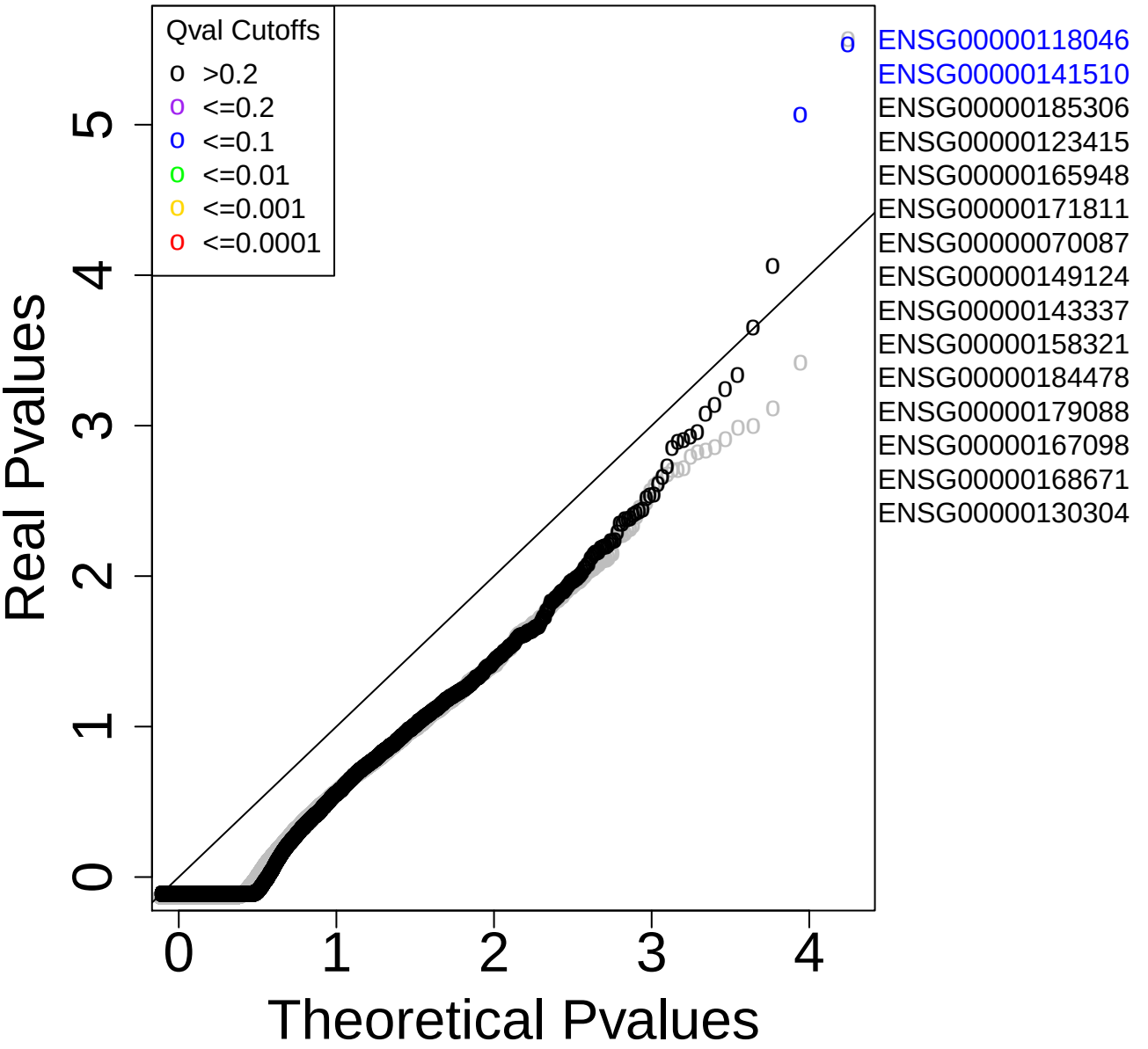
Supplementary Figure S11



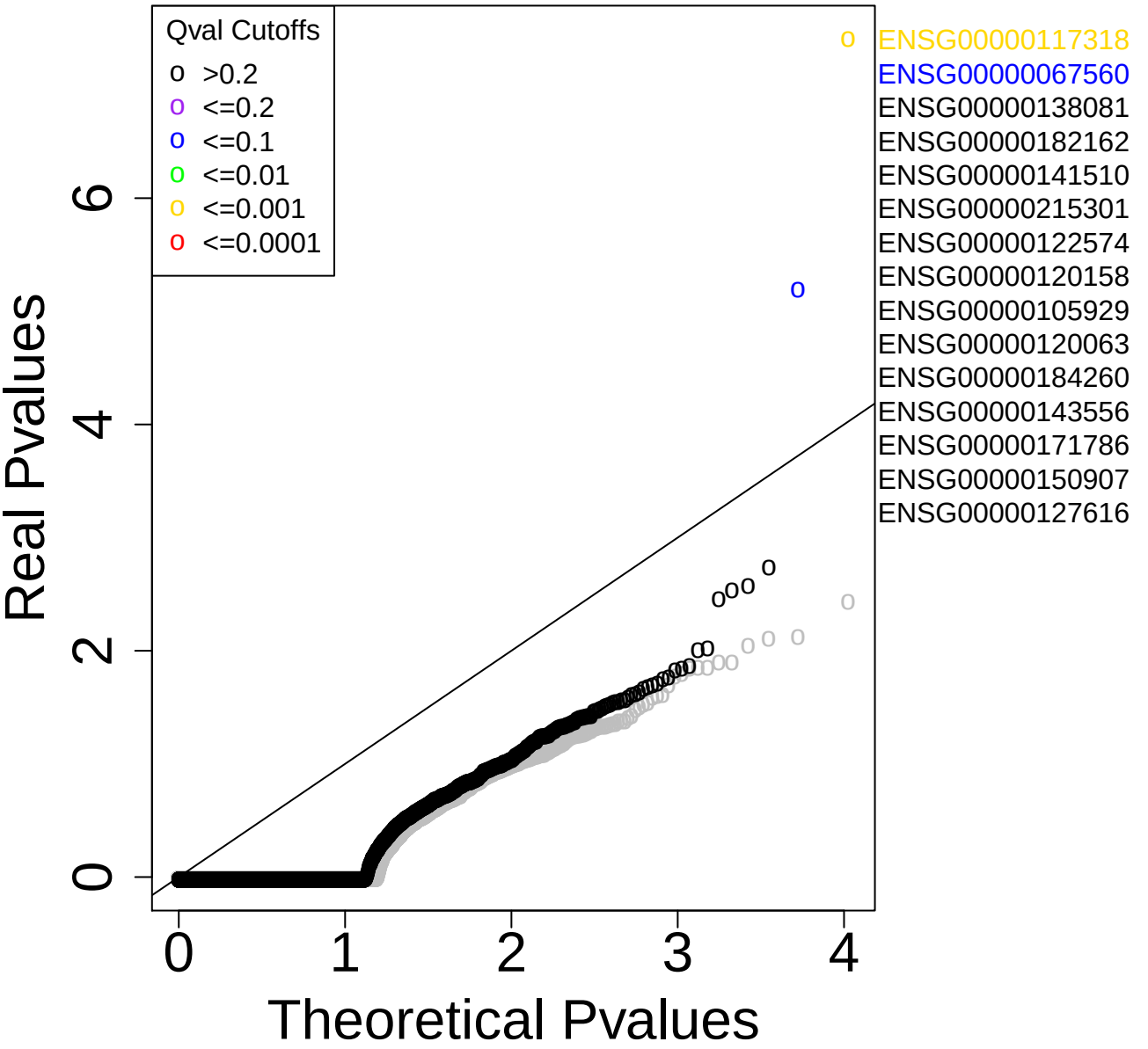

MutSig CLL − 11375 genes
Qval Cutoffs
>0.2
<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
ENSG00000171811
ENSG00000145335
ENSG00000104164
ENSG00000052723
ENSG00000174970
ENSG00000165424
ENSG00000175970
ENSG00000118260
ENSG00000185974
ENSG00000162739
ENSG00000172936
ENSG00000174808
ENSG00000180432
ENSG00000154473
ENSG00000213782
Real Pvalues
0.0
0.5
1.0
1.5
2.0
Theoretical Pvalues
0
1
2
3


MutSig Liver − 34248 genes
Qval Cutoffs
>0.2
<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
ENSG00000141510
ENSG00000131482
ENSG00000075035
ENSG00000103126
ENSG00000123124
ENSG00000205212
ENSG00000171862
ENSG00000244734
ENSG00000177752
ENSG00000075884
ENSG00000116285
ENSG00000060971
ENSG00000196616
ENSG00000136235
ENSG00000075340
Real Pvalues
Theoretical Pvalues
0
1
2
3
4

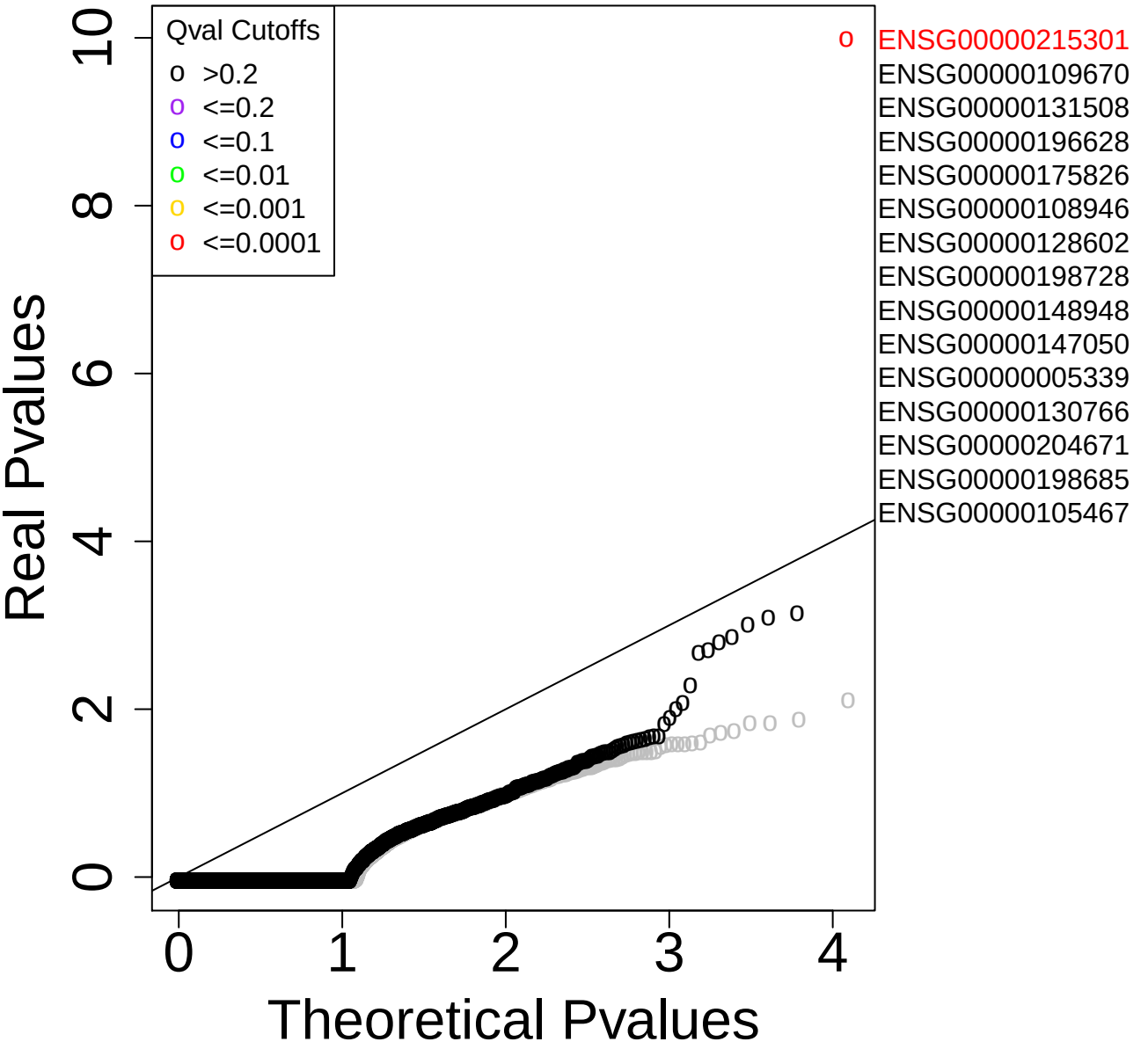
MutSig Lung adeno− 35211 genes



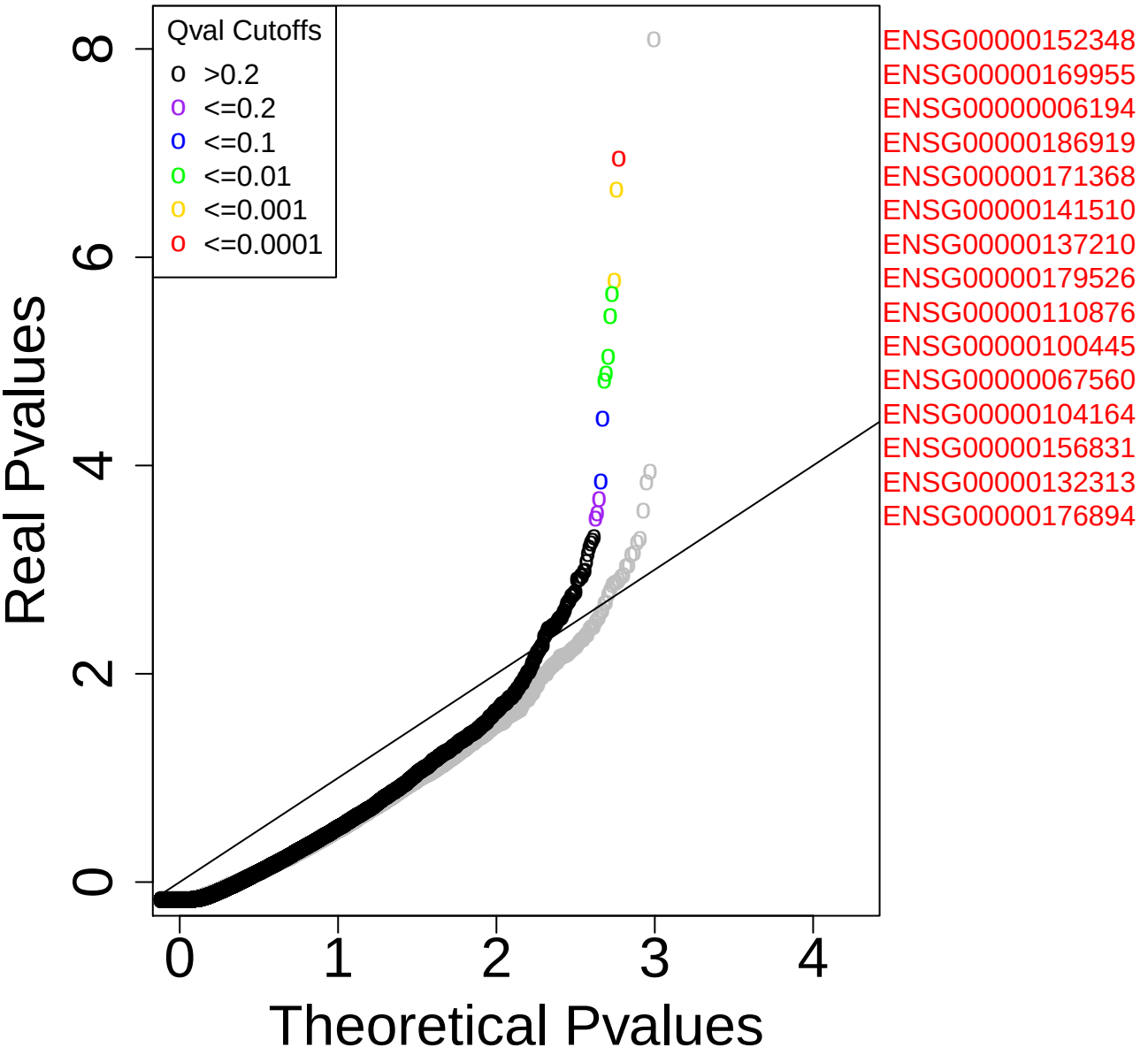
MutSig Lymphoma B-cell – 21158 genes



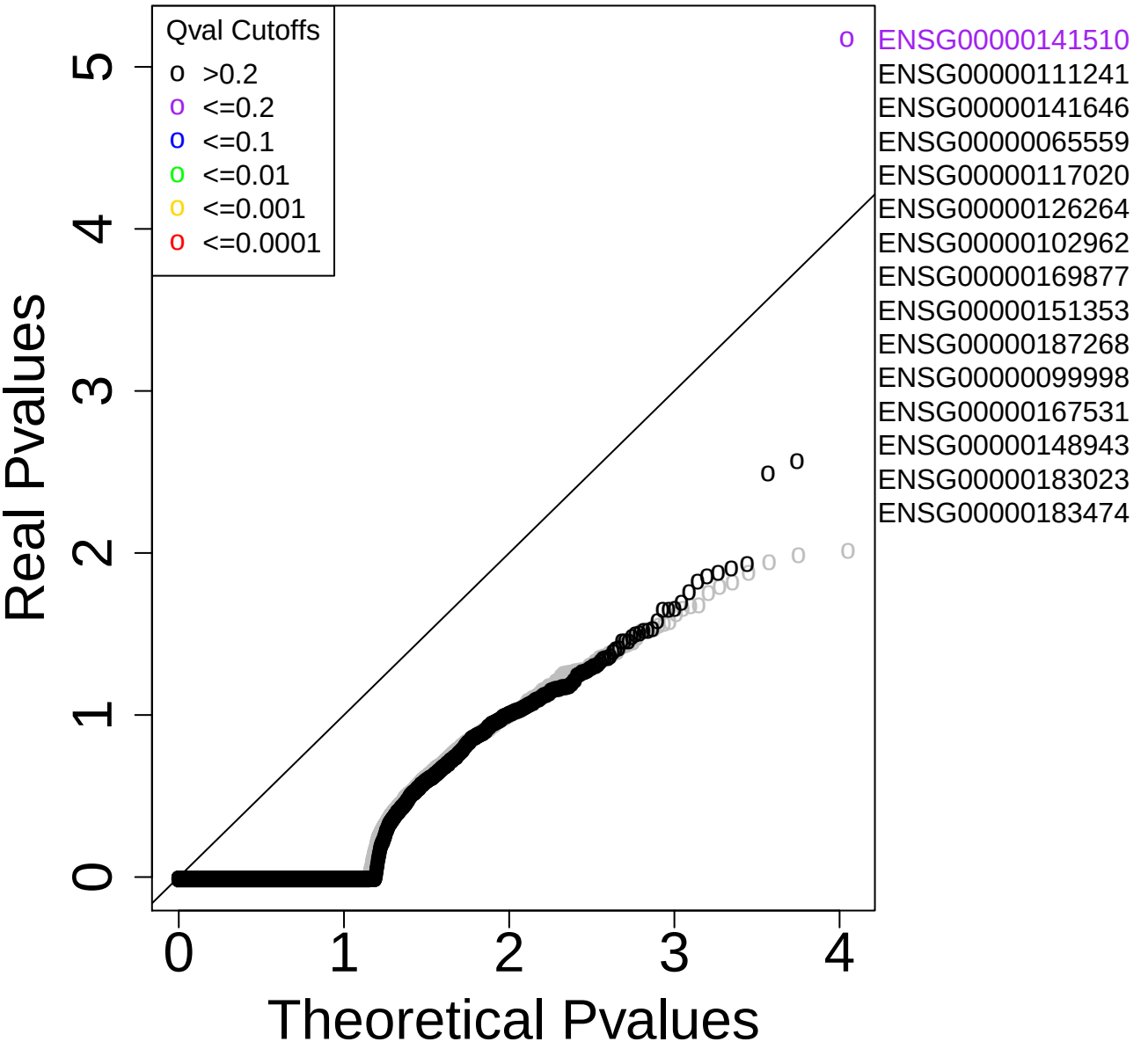
MutSig Medulloblastoma − 24518 genes

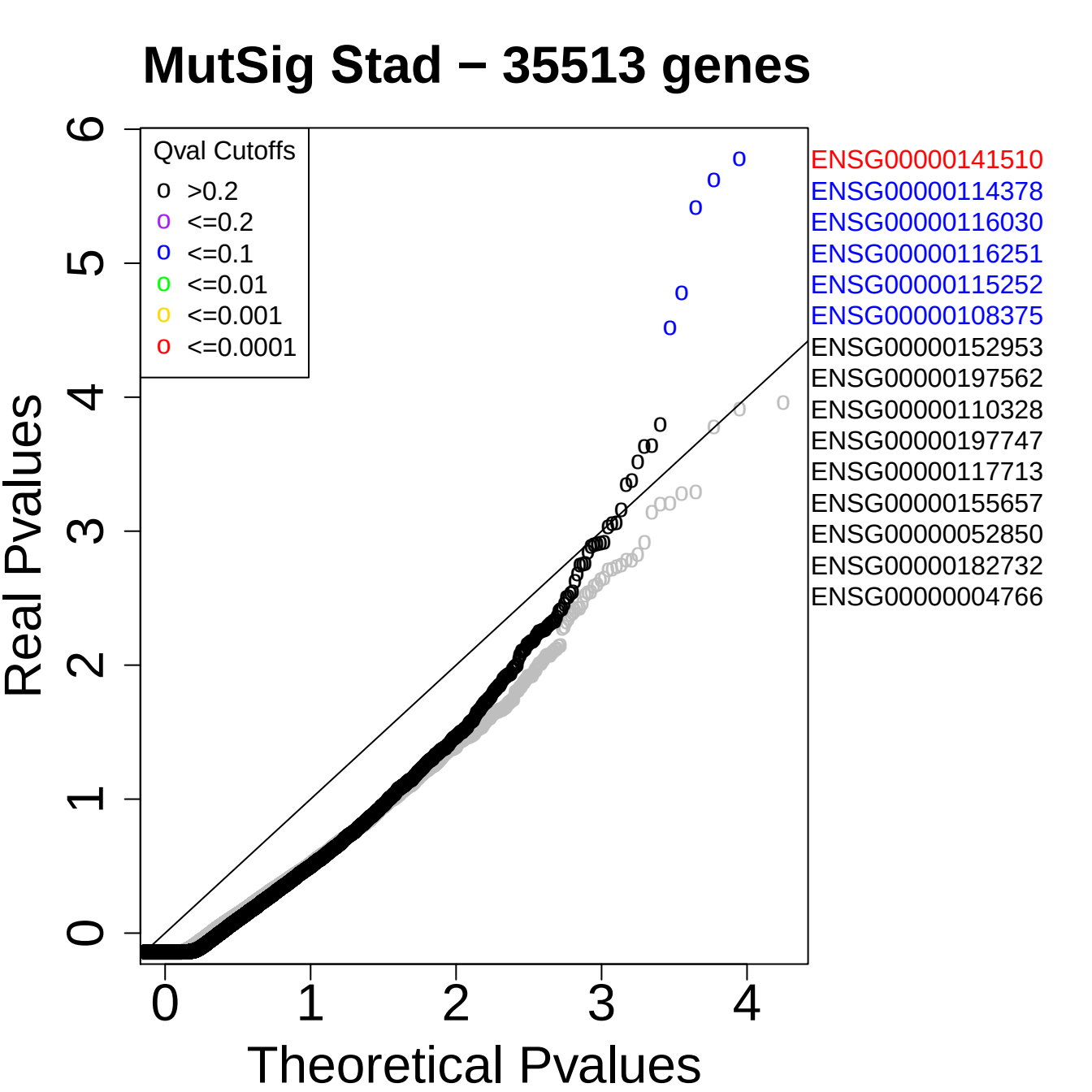


MutSig Pancancer – 35544 genes

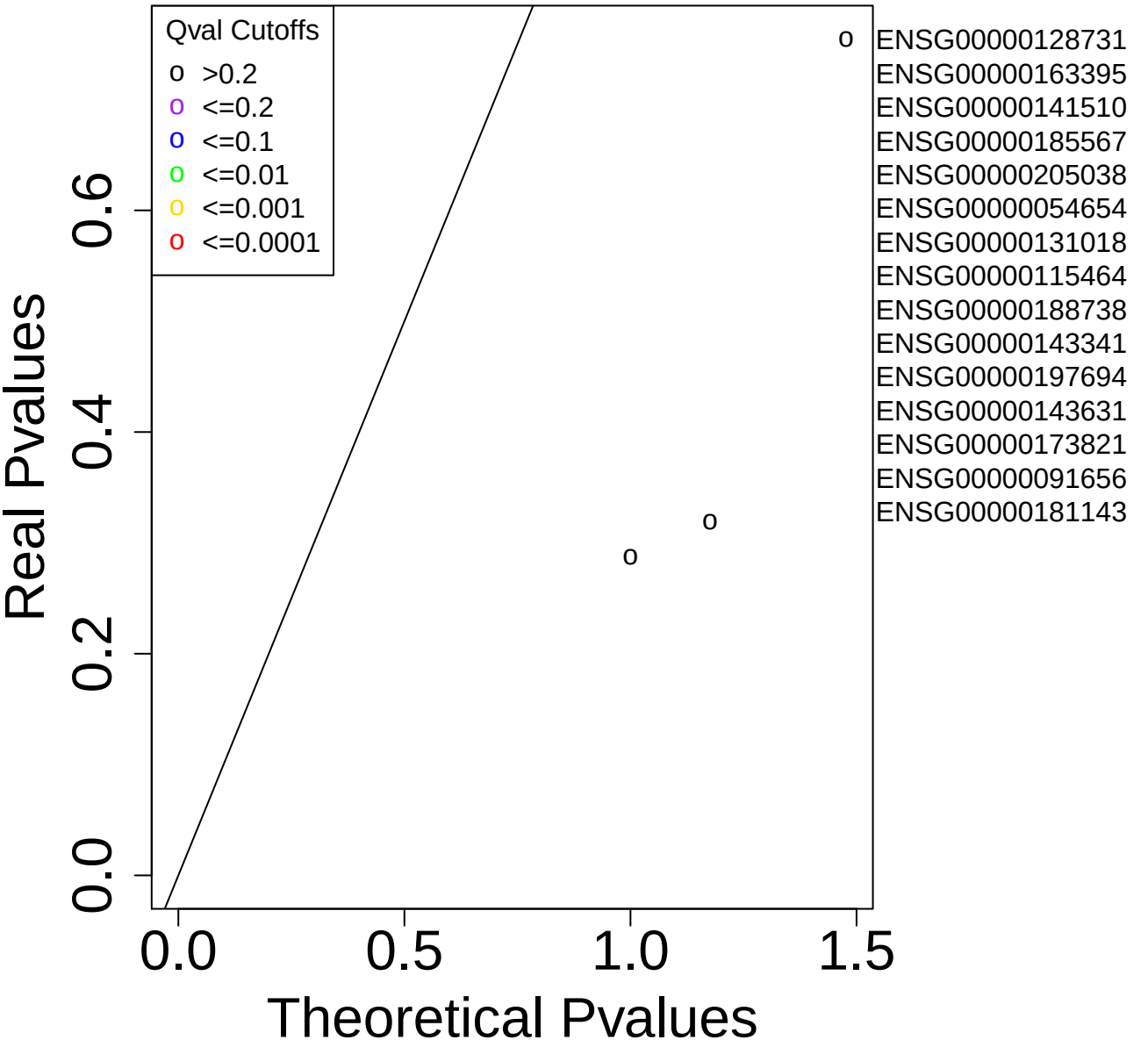


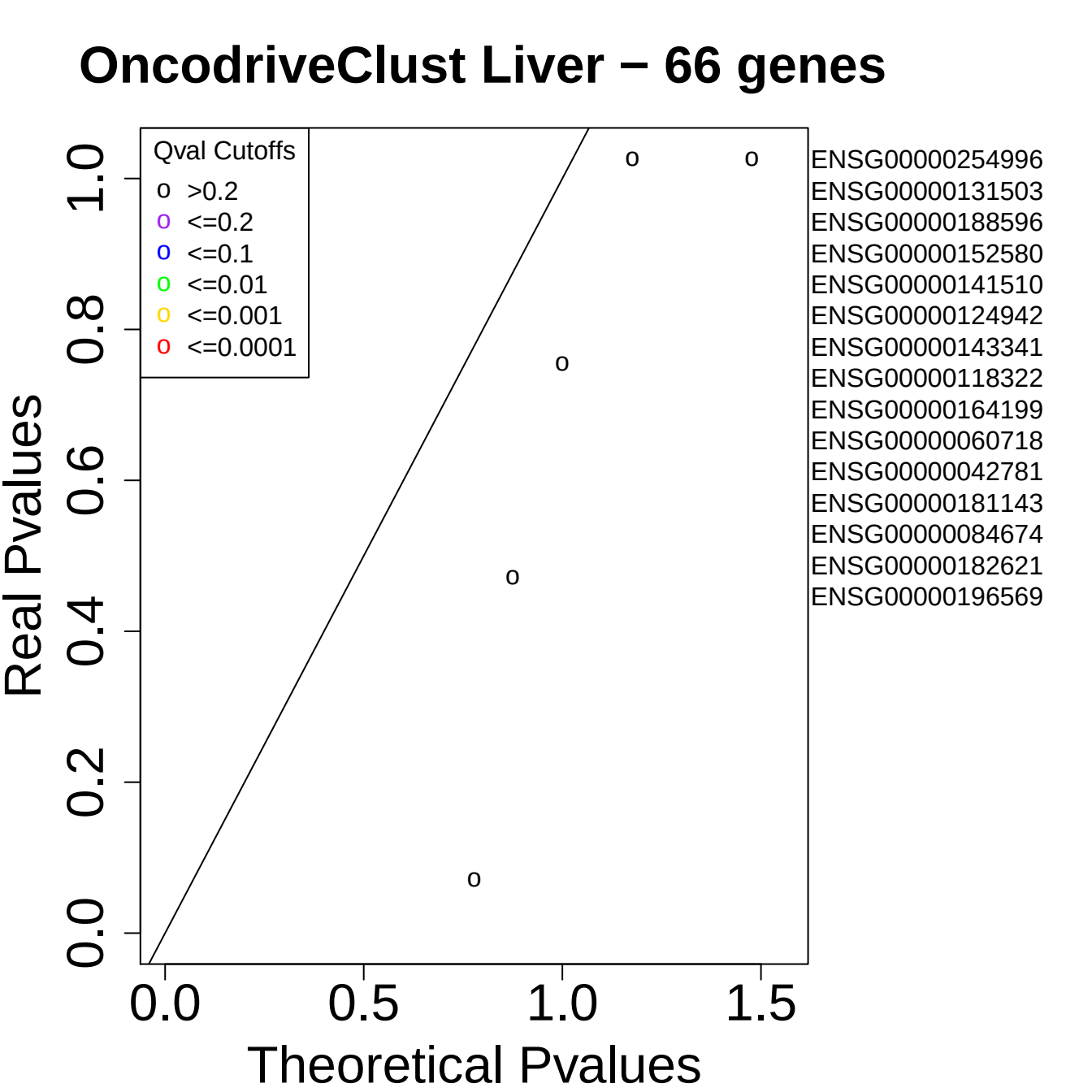
MutSig Pancreas − 22319 genes




MutSig Stad − 35513 genes
Qval Cutoffs
>0.2
<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
ENSG00000141510
ENSG00000114378
ENSG00000116030
ENSG00000116251
ENSG00000115252
ENSG00000108375
ENSG00000152953
ENSG00000197562
ENSG00000110328
ENSG00000197747
ENSG00000117713
ENSG00000155657
ENSG00000052850
ENSG00000182732
ENSG00000004766
Real Pvalues
Theoretical Pvalues
0
1
2
3
4
5
6

OncodriveClust Breast – 47 genes




OncodriveClust Liver − 66 genes
Qval Cutoffs
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<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
ENSG00000254996
ENSG00000131503
ENSG00000188596
ENSG00000152580
ENSG00000141510
ENSG00000124942
ENSG00000143341
ENSG00000118322
ENSG00000164199
ENSG00000060718
ENSG00000042781
ENSG00000181143
ENSG00000084674
ENSG00000182621
ENSG00000196569
Real Pvalues
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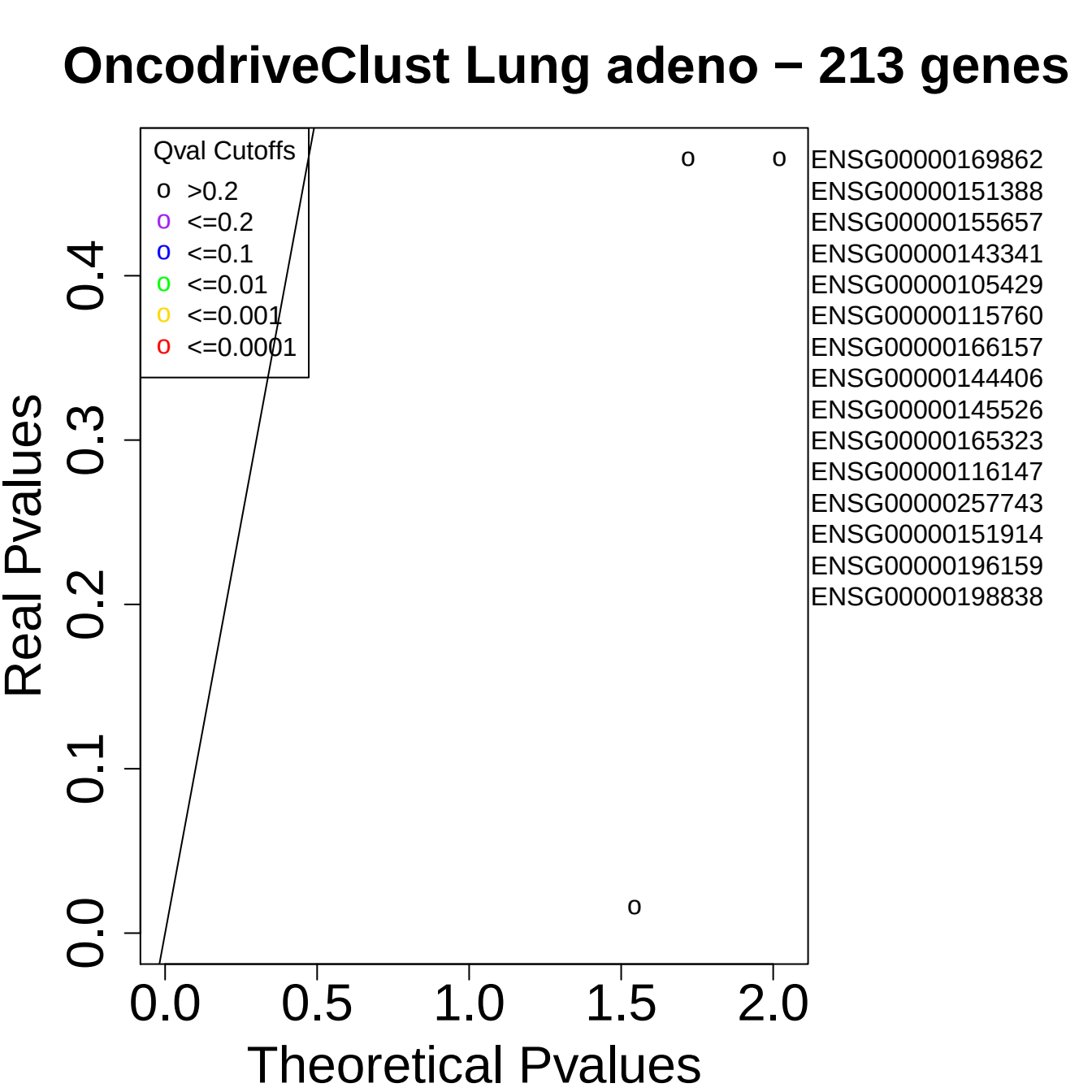
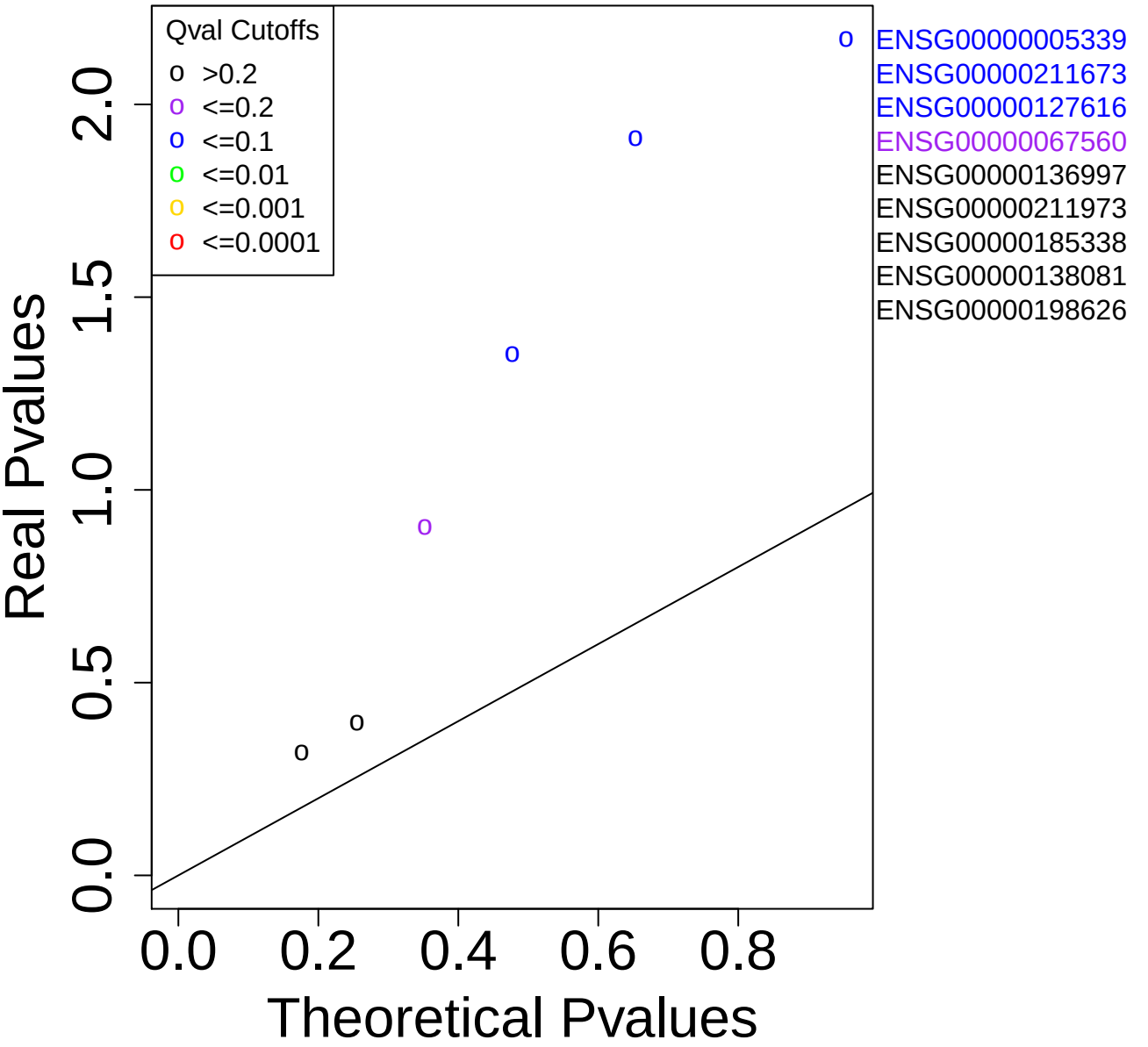
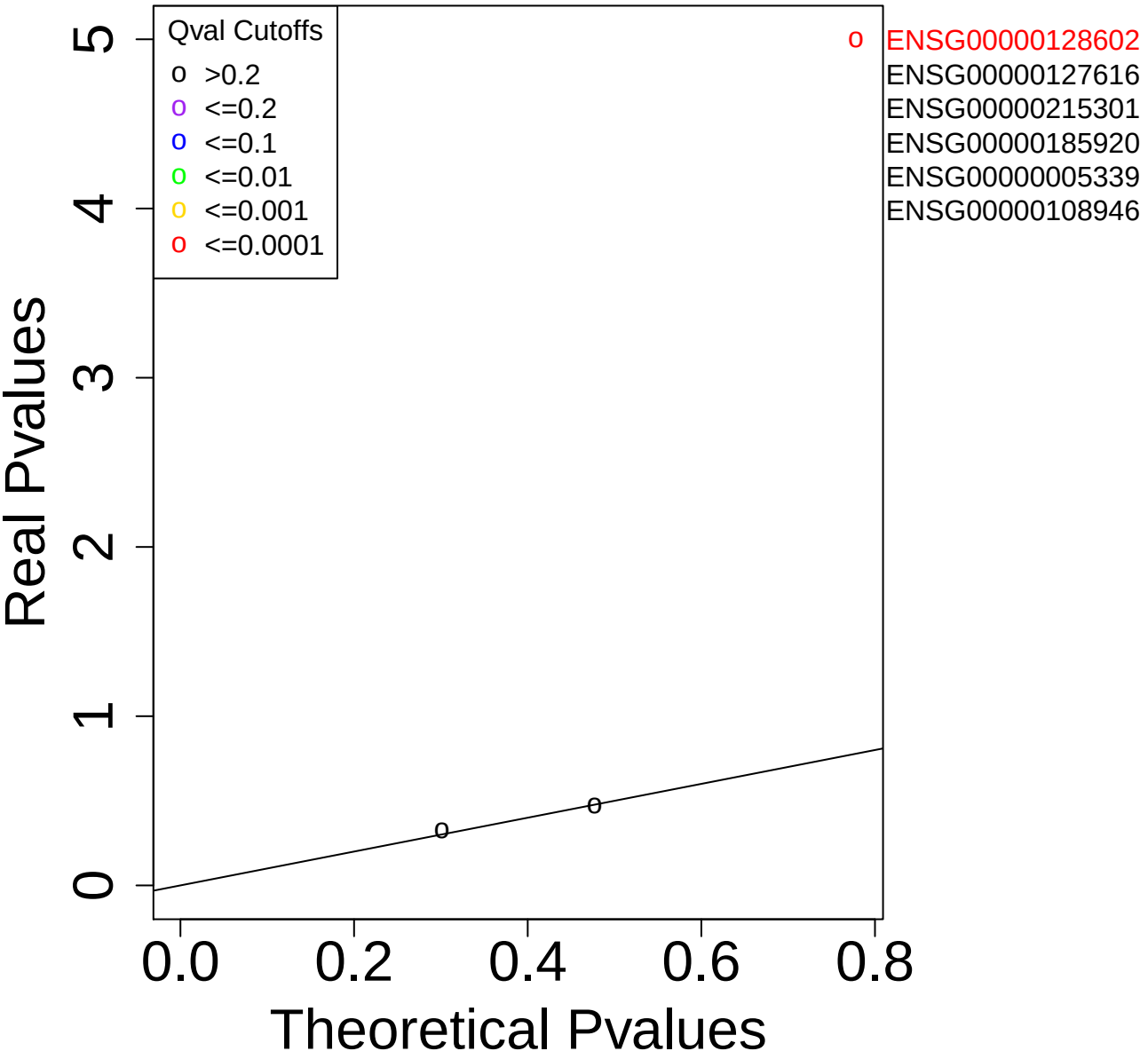
0.2
0.4
0.6
0.8
1.0
Theoretical Pvalues
0.0
0.5
1.0
1.5


OncodriveClust Lung adeno − 213 genes
Qval Cutoffs
>0.2
<=0.2
<=0.1
<=0.01
<=0.001
<=0.0001
ENSG00000169862
ENSG00000151388
ENSG00000155657
ENSG00000143341
ENSG00000105429
ENSG00000115760
ENSG00000166157
ENSG00000144406
ENSG00000145526
ENSG00000165323
ENSG00000116147
ENSG00000257743
ENSG00000151914
ENSG00000196159
ENSG00000198838
Real Pvalues
0.0
0.1
0.2
0.3
0.4
0.0
0.5
1.0
1.5
2.0
Theoretical Pvalues

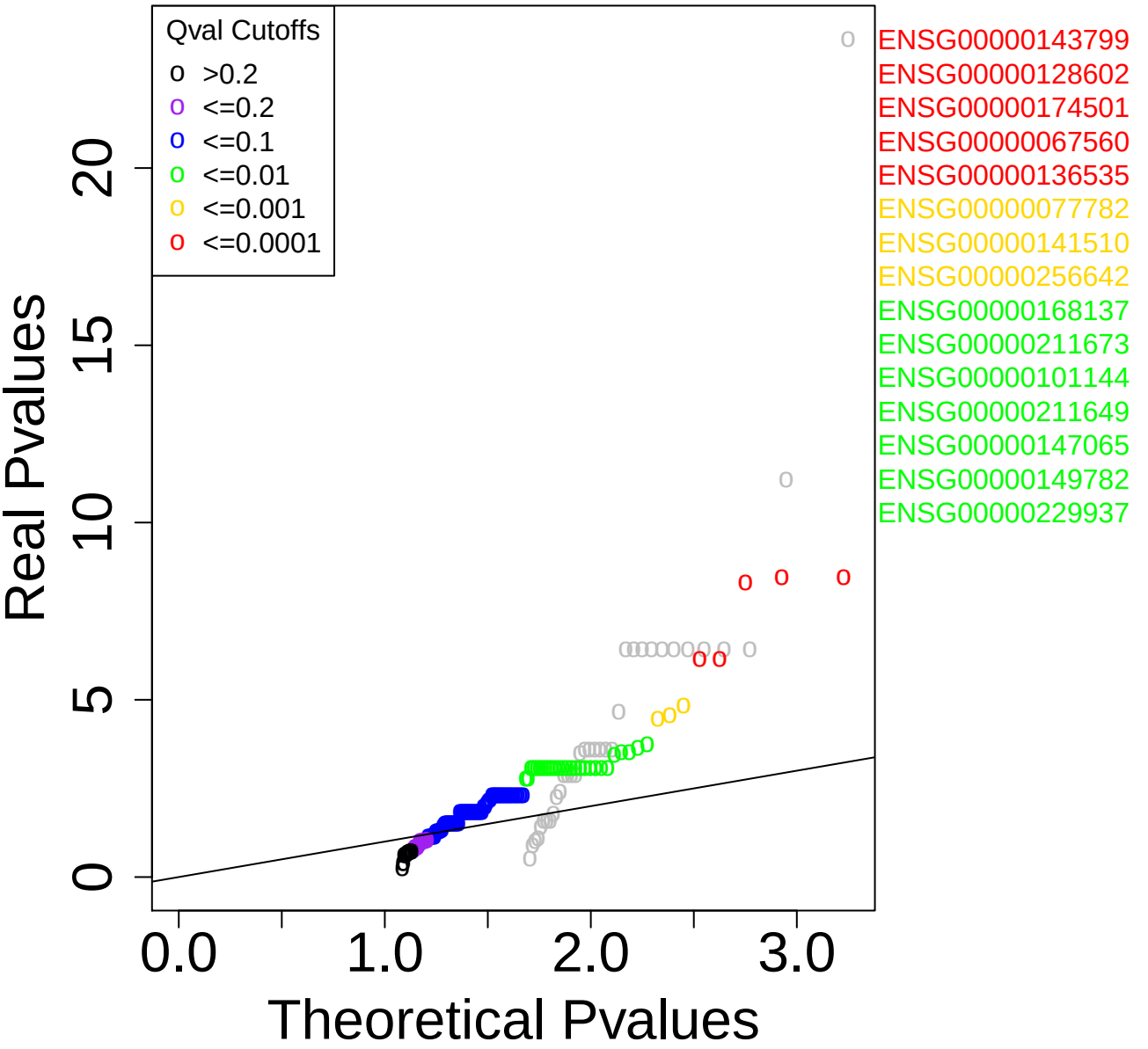
OncodriveClust Lymphoma B-cell – 11 genes



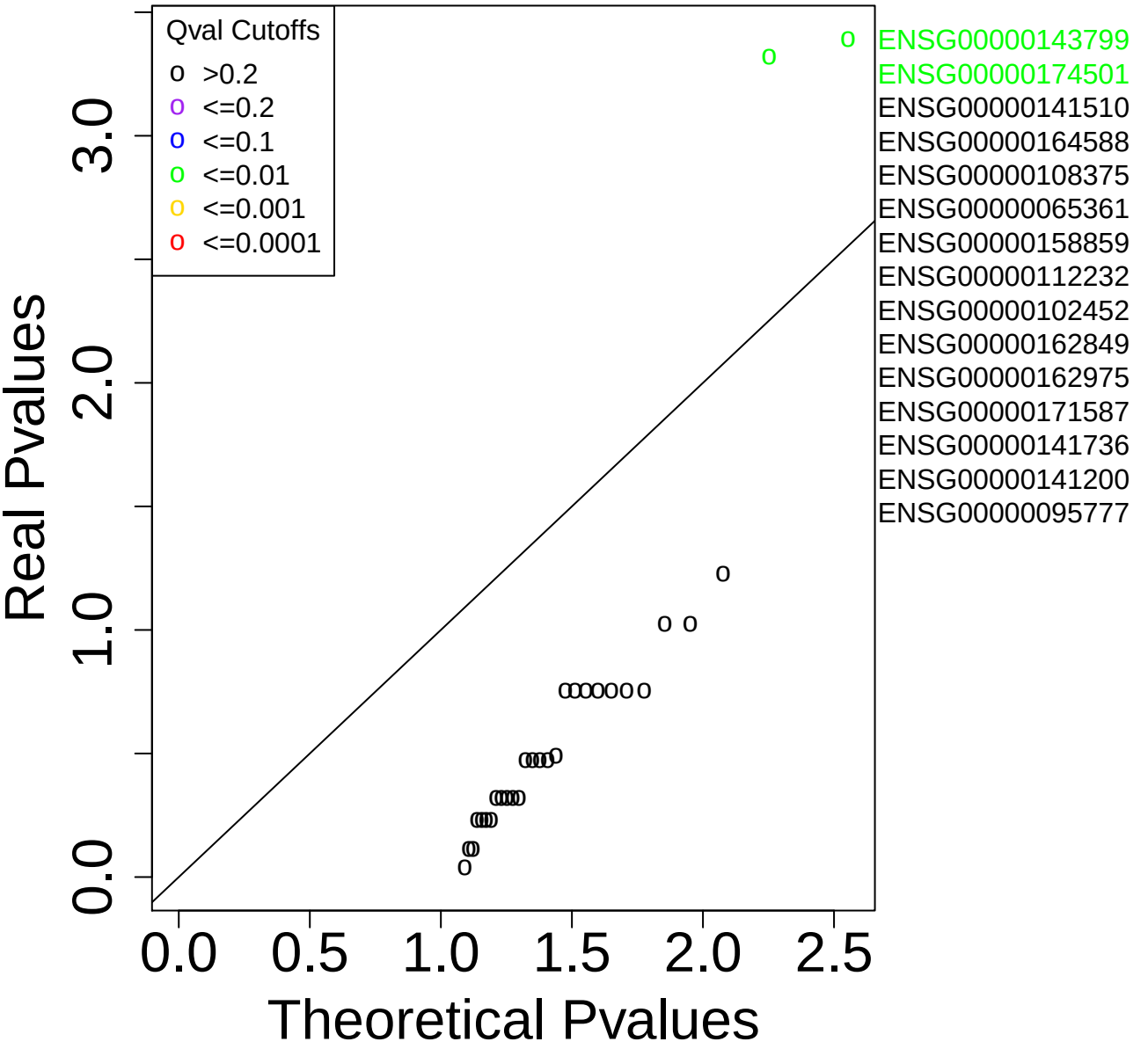
OncodriveClust Medulloblastoma − 7 genes



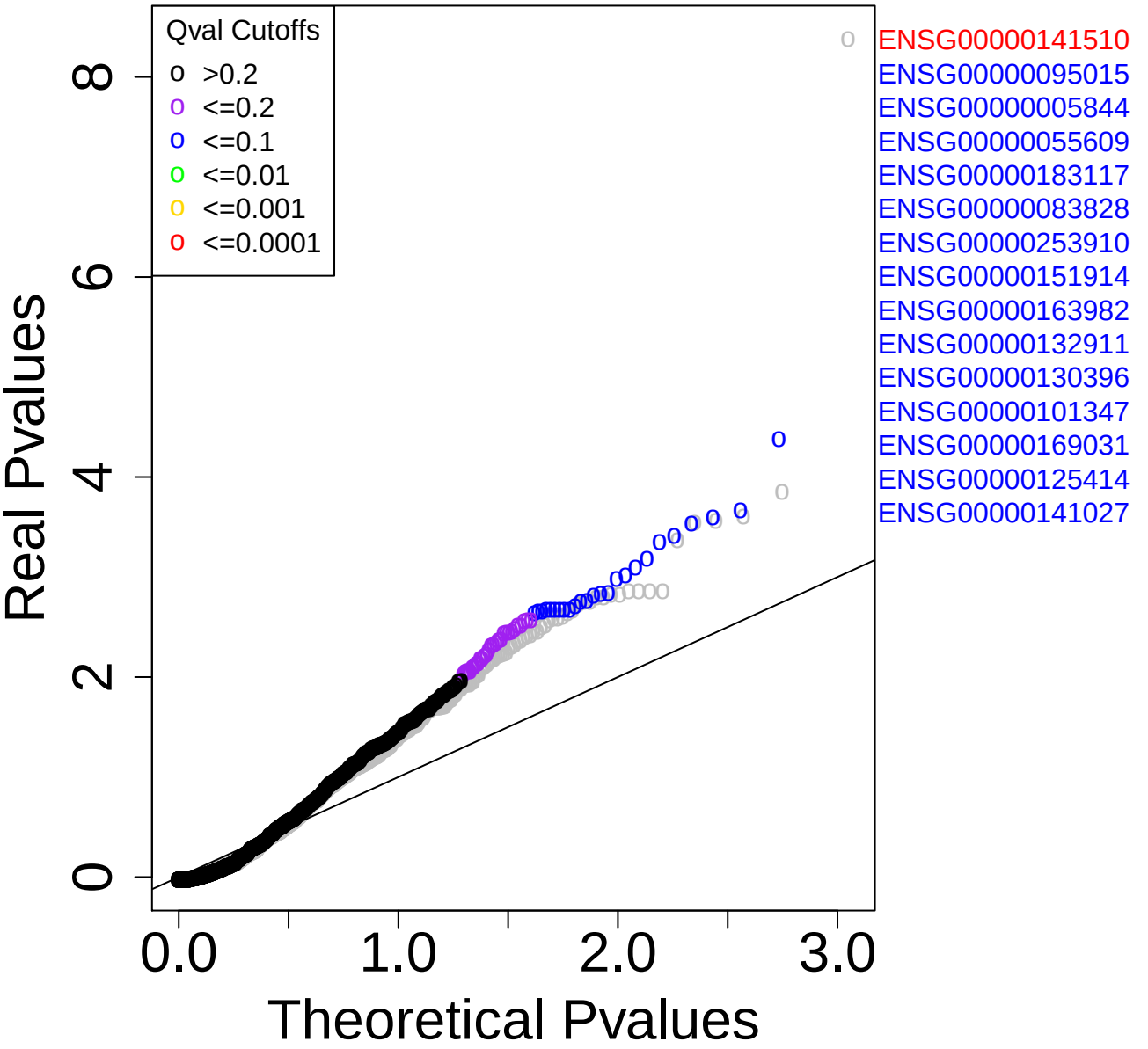
OncodriveClust Pancancer − 3464 genes



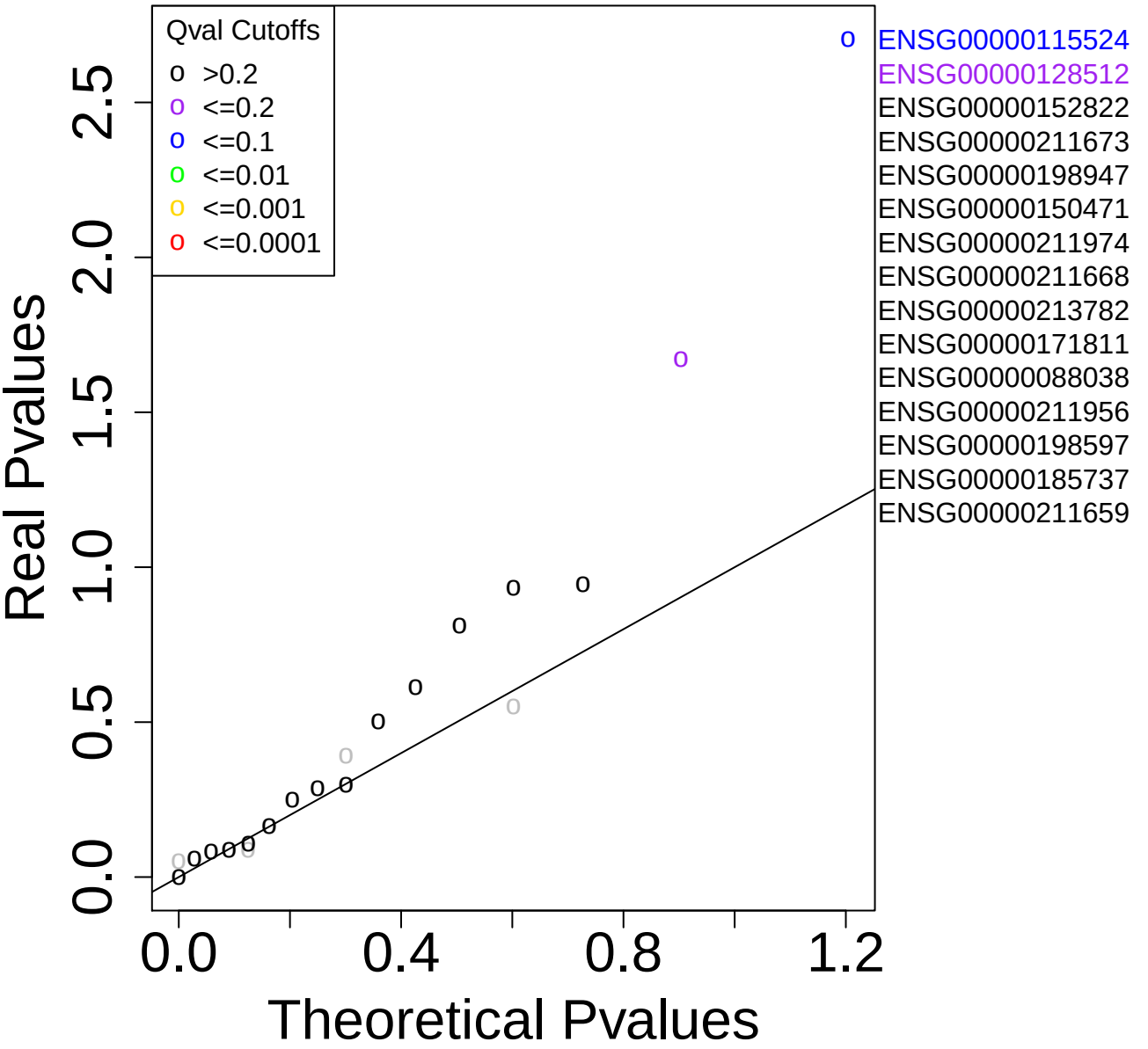
OncodriveClust Stad – 616 genes



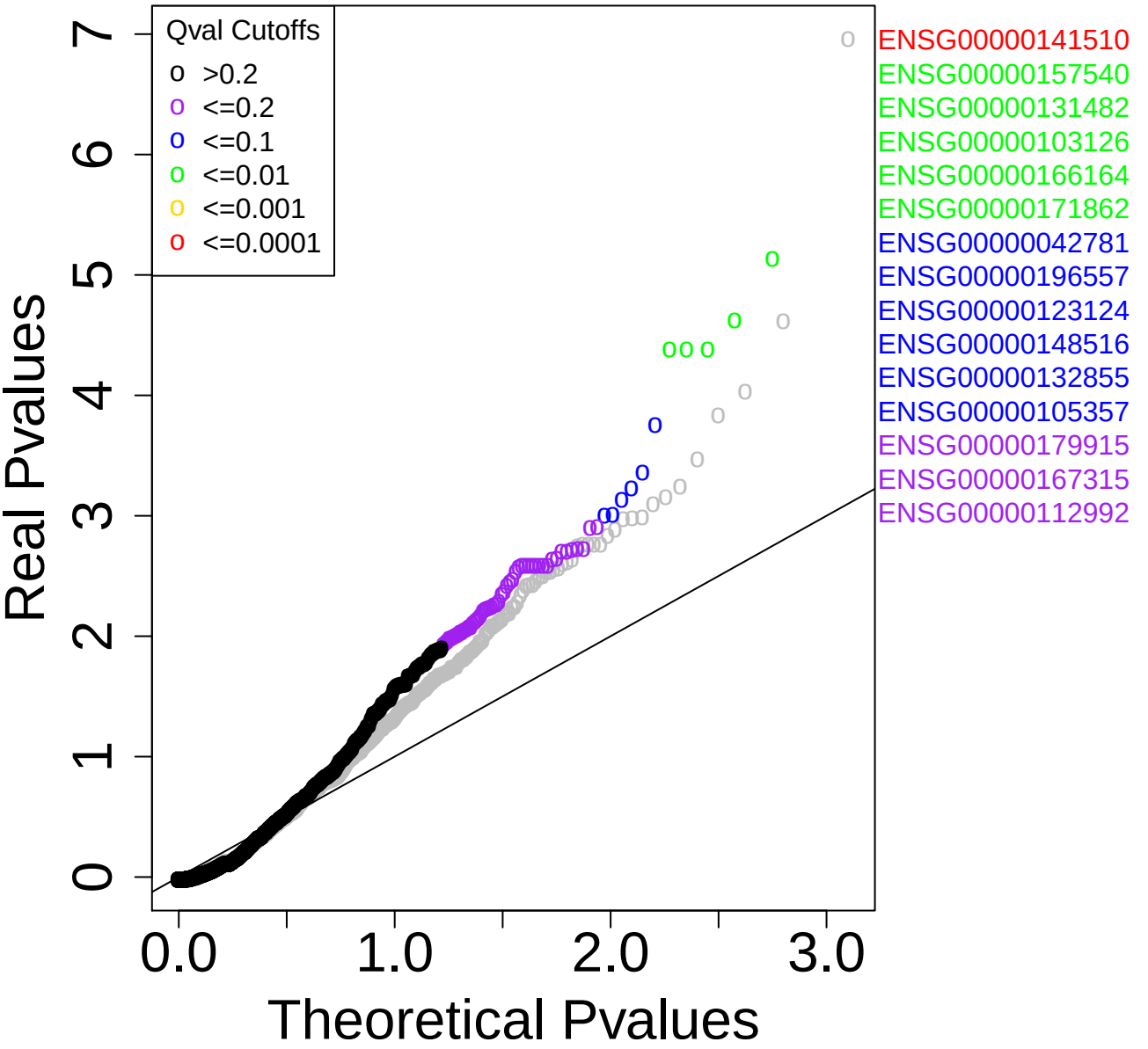
OncodriveFM Breast – 2201 genes



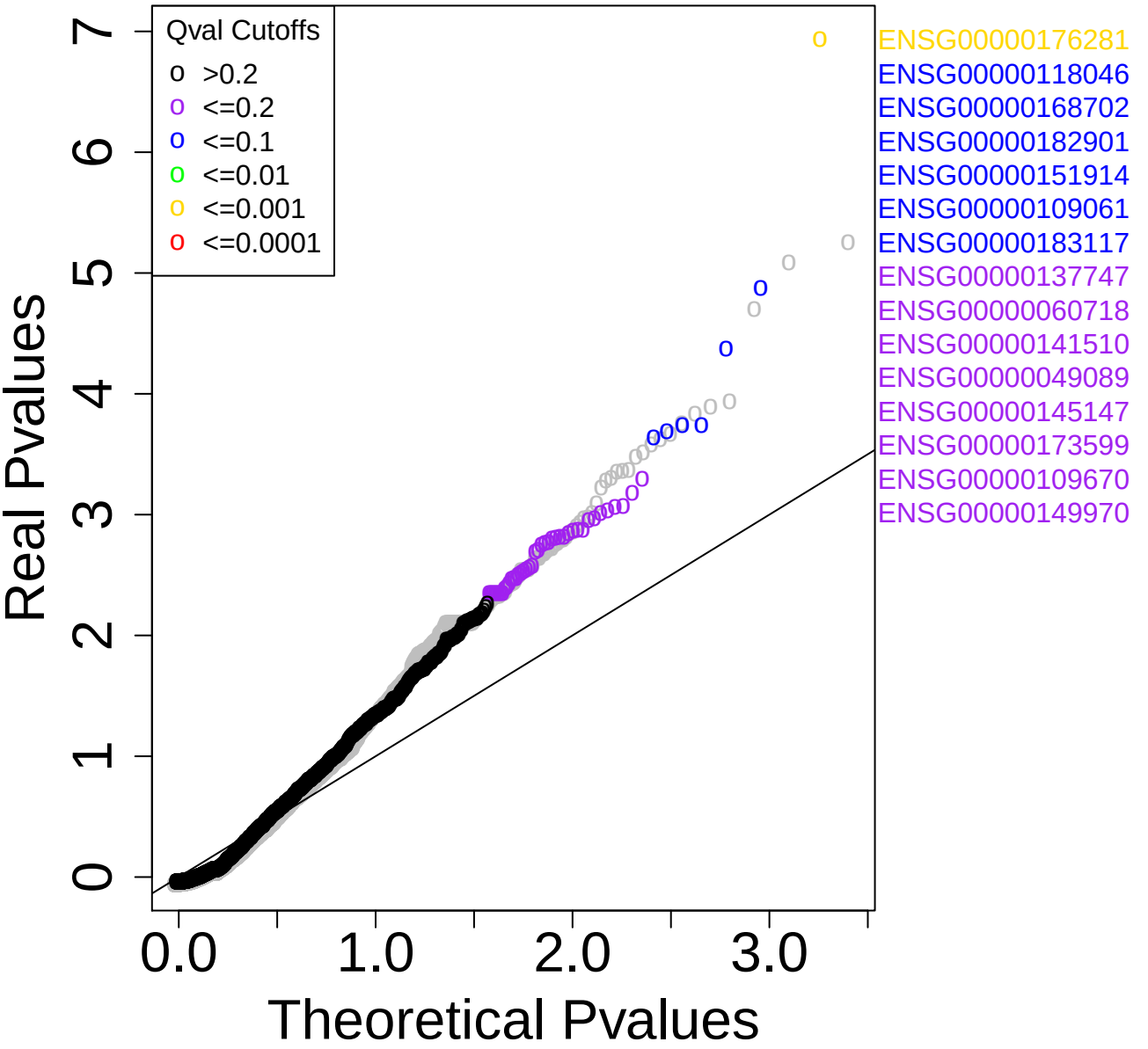
OncodriveFM CLL – 20 genes



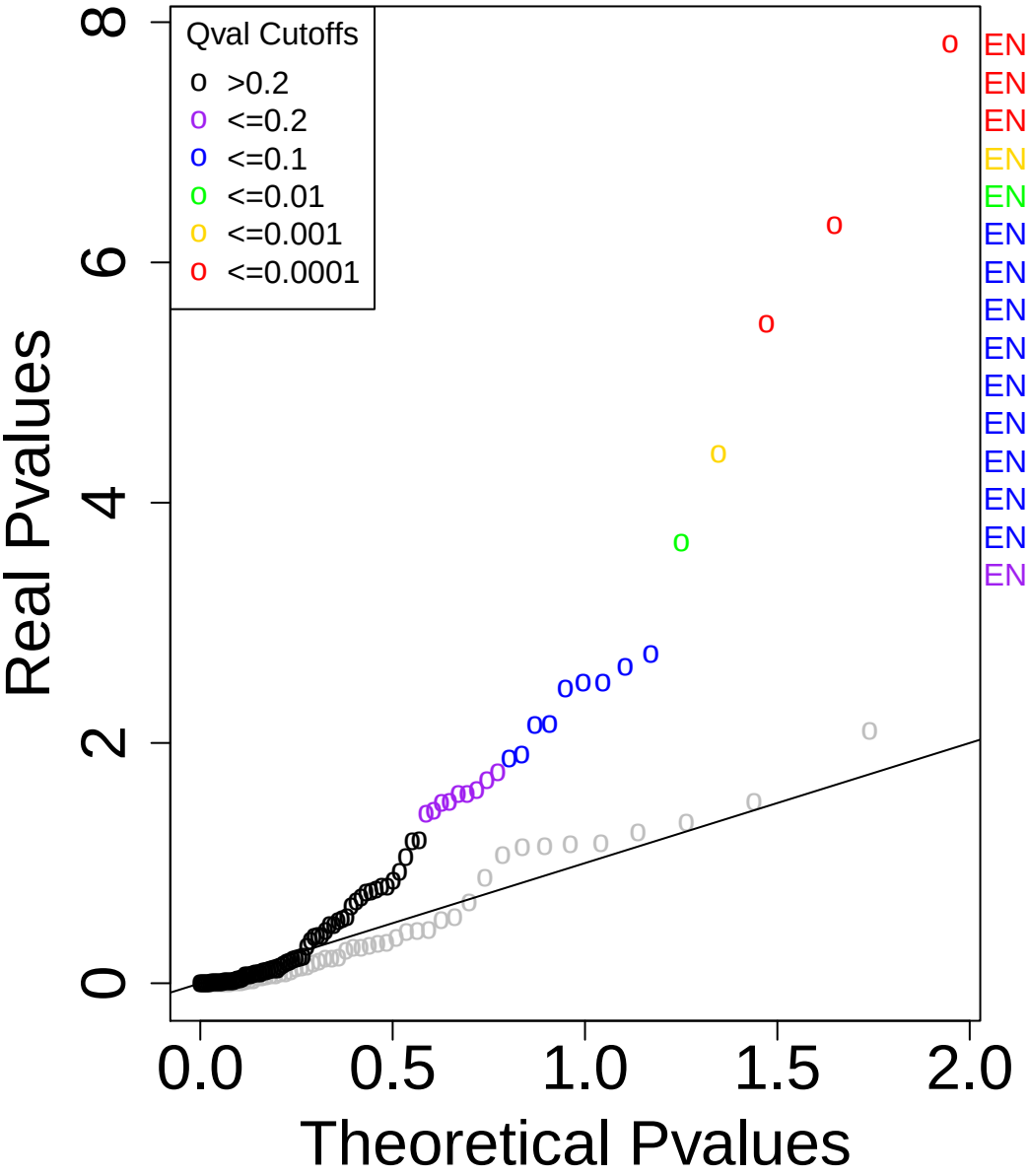
OncodriveFM Liver – 2383 genes



OncodriveFM Lung adeno − 4319 genes

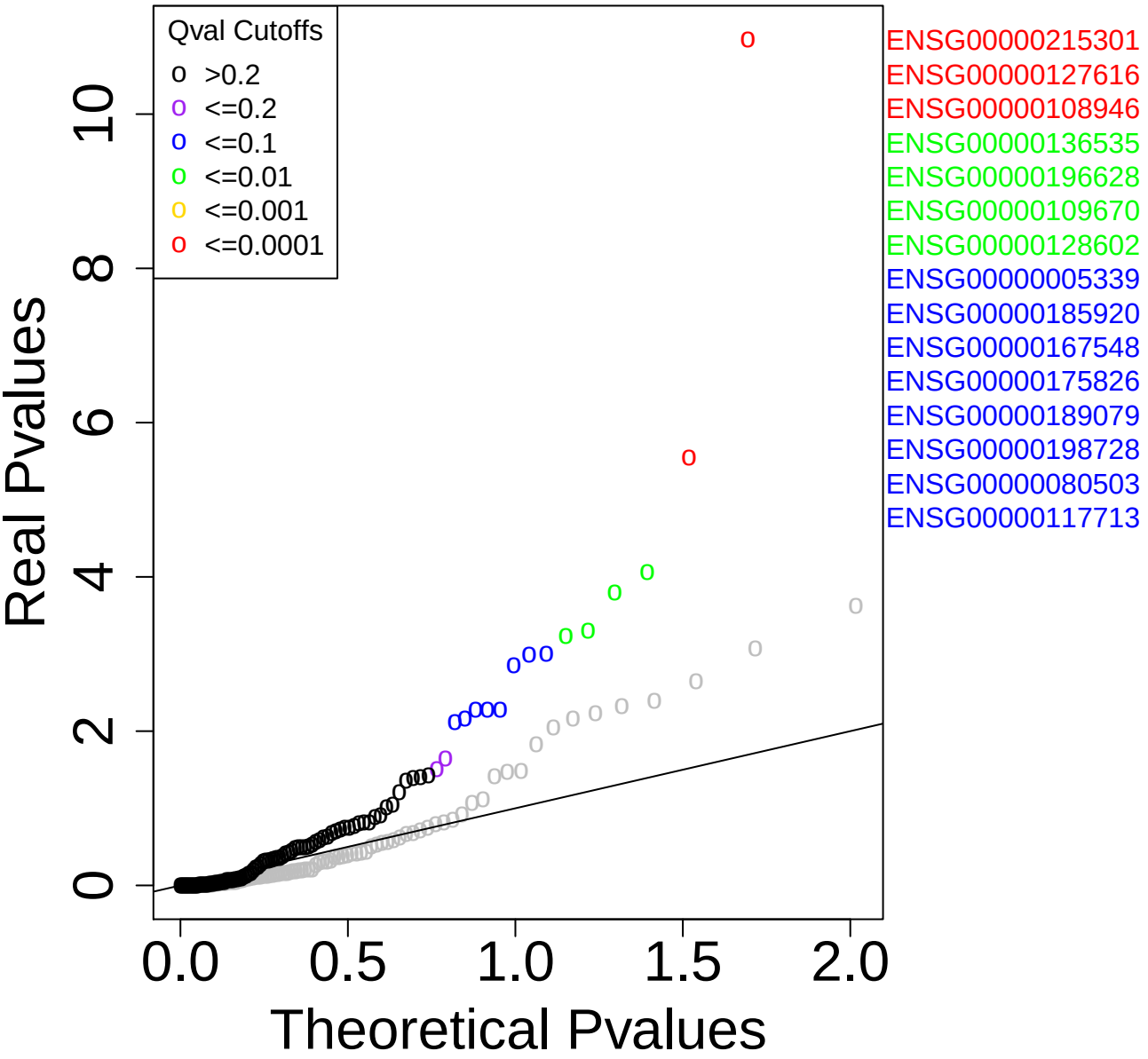


OncodriveFM Lymphoma B-cell – 144 genes

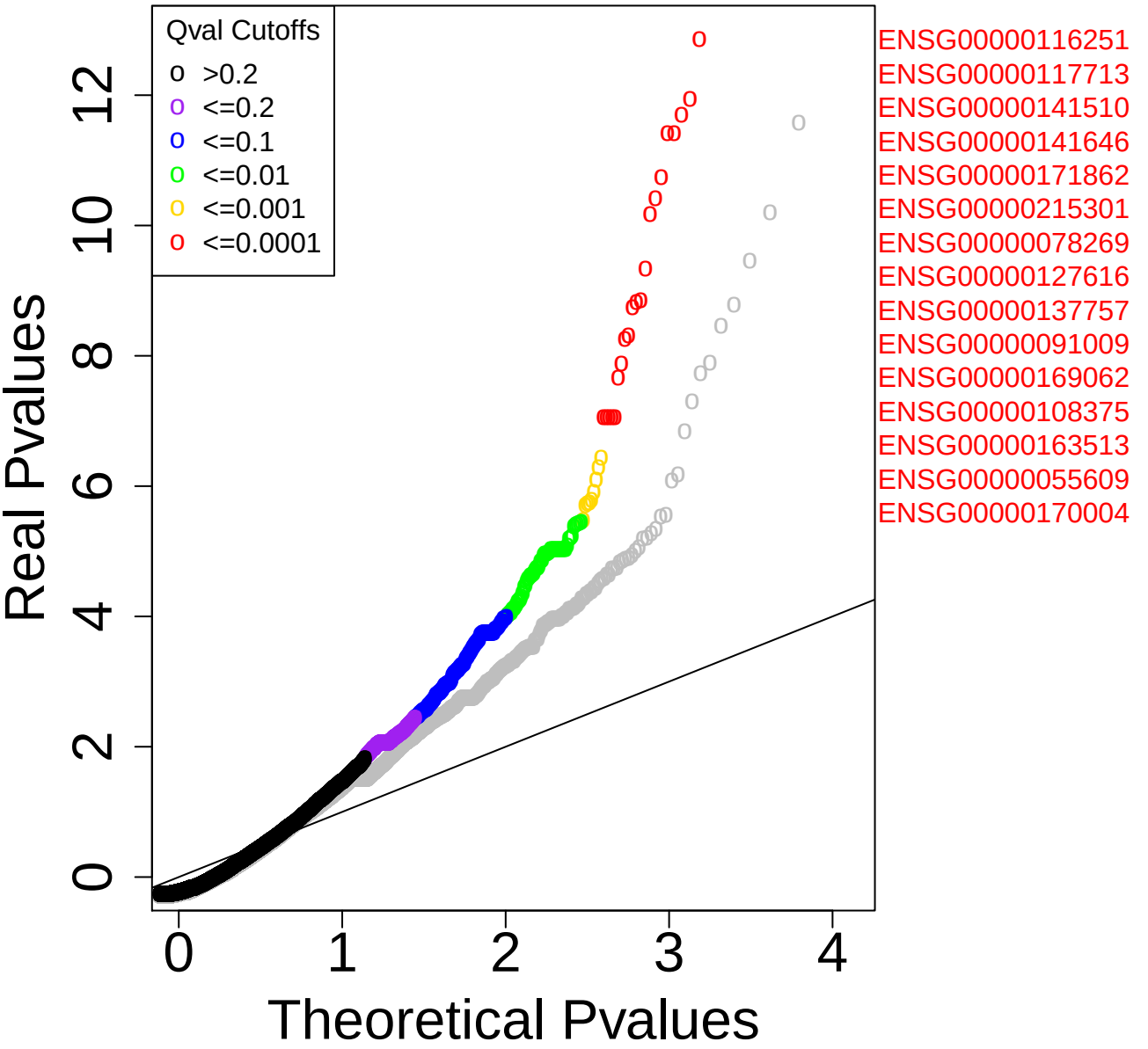


ENSG00000005339
ENSG00000127616
ENSG00000117318
ENSG00000138081
ENSG00000106278
ENSG00000120063
ENSG00000141510
ENSG00000117713
ENSG00000181827
ENSG00000211673
ENSG00000090402
ENSG00000116954
ENSG00000150907
ENSG00000198626
ENSG00000067560

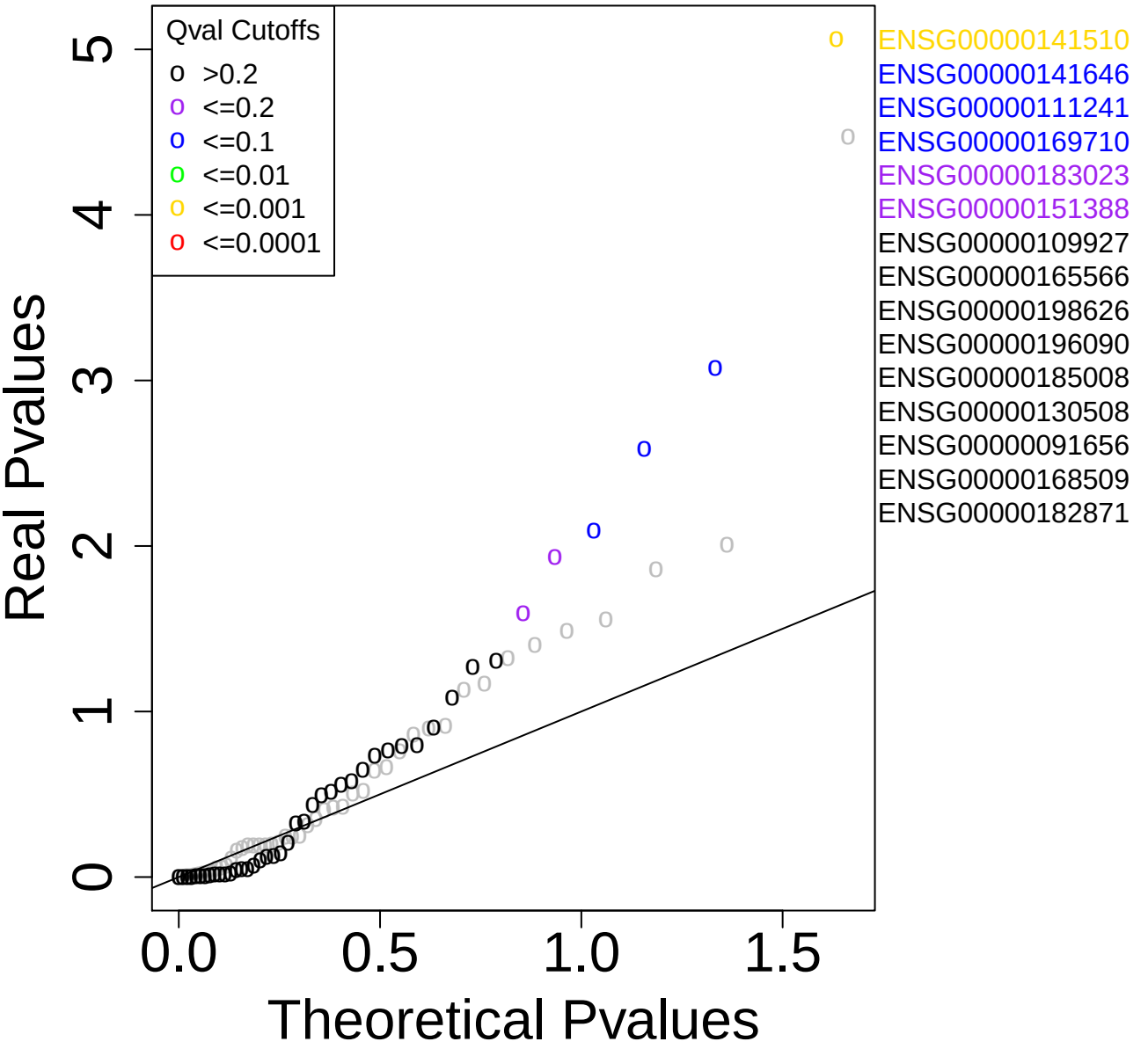
OncodriveFM Medulloblastoma – 203 genes



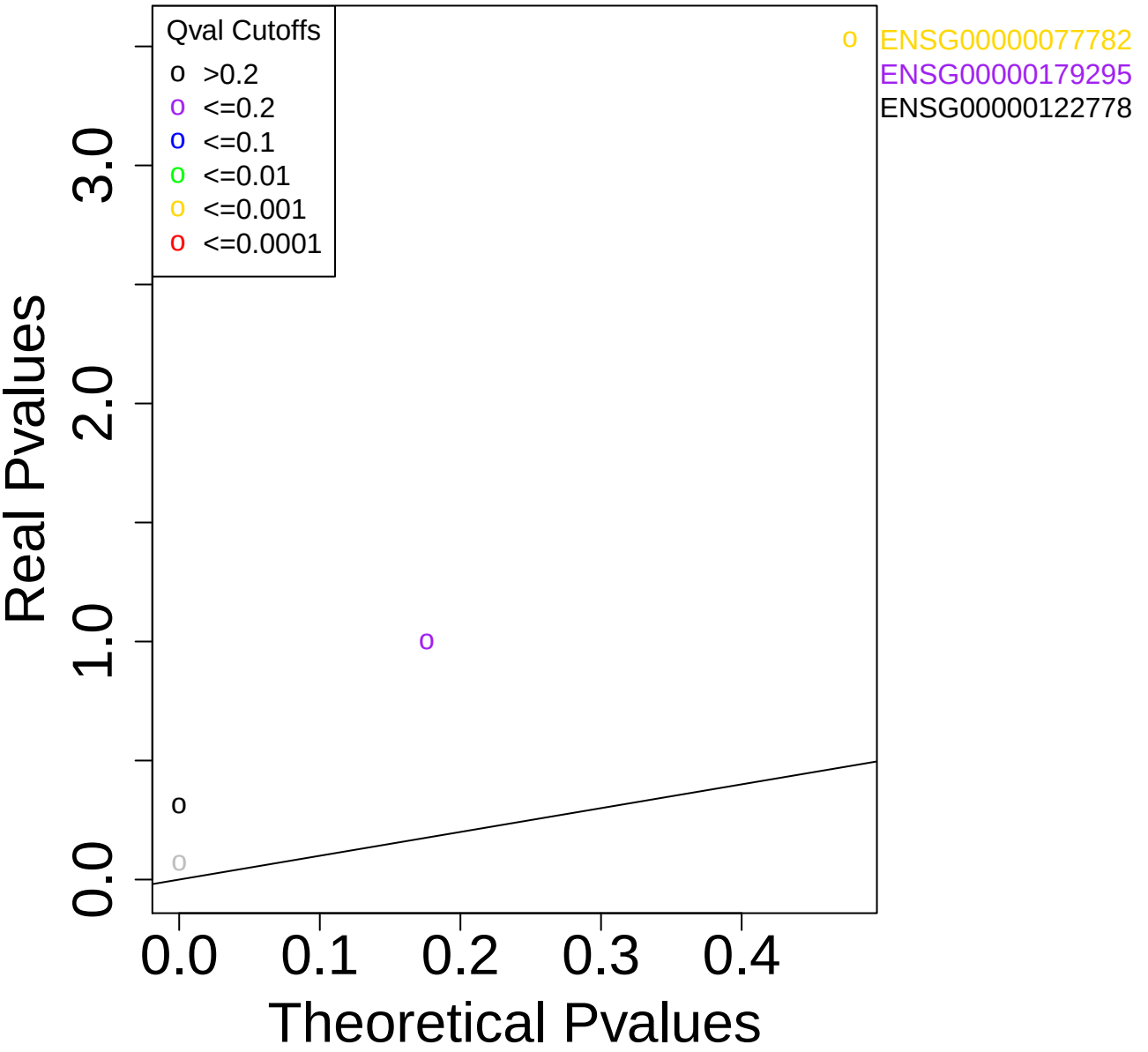
OncodriveFM Pancancer – 23195 genes



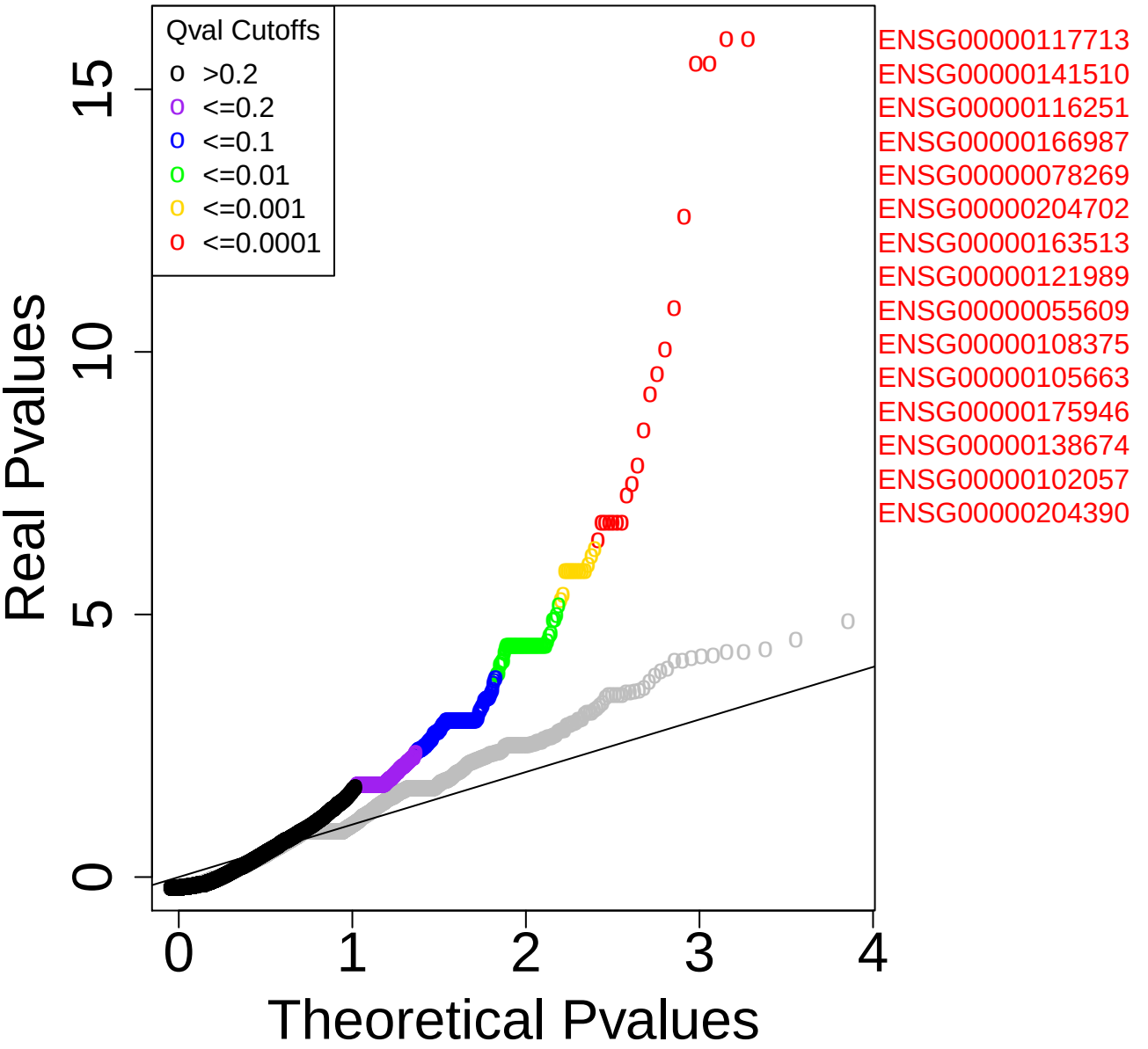
OncodriveFM Pancreas – 89 genes



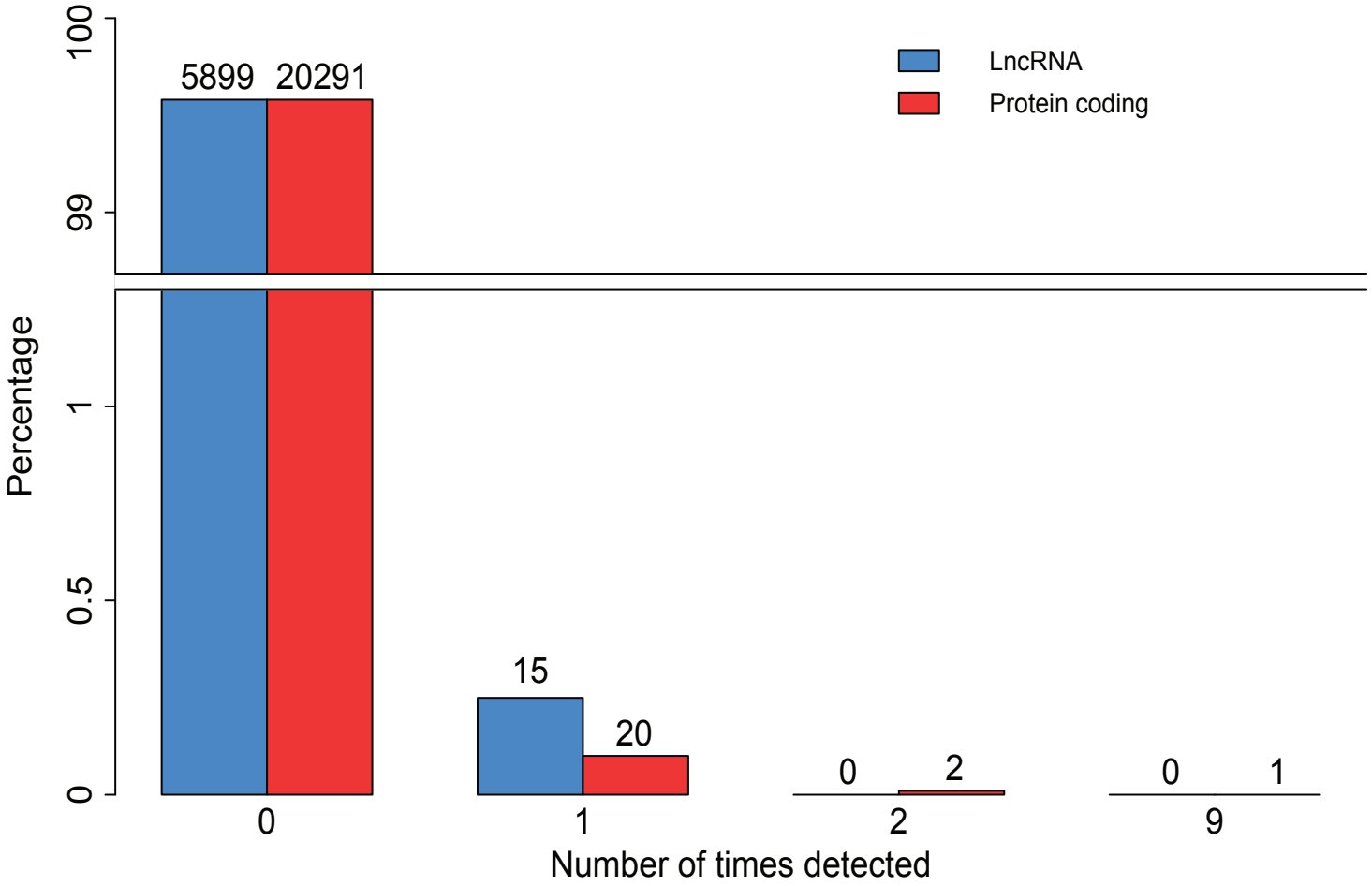
OncodriveFM Pilocytic astrocytoma – 4 genes



OncodriveFM Stad − 12899 genes



Supplementary Figure S12



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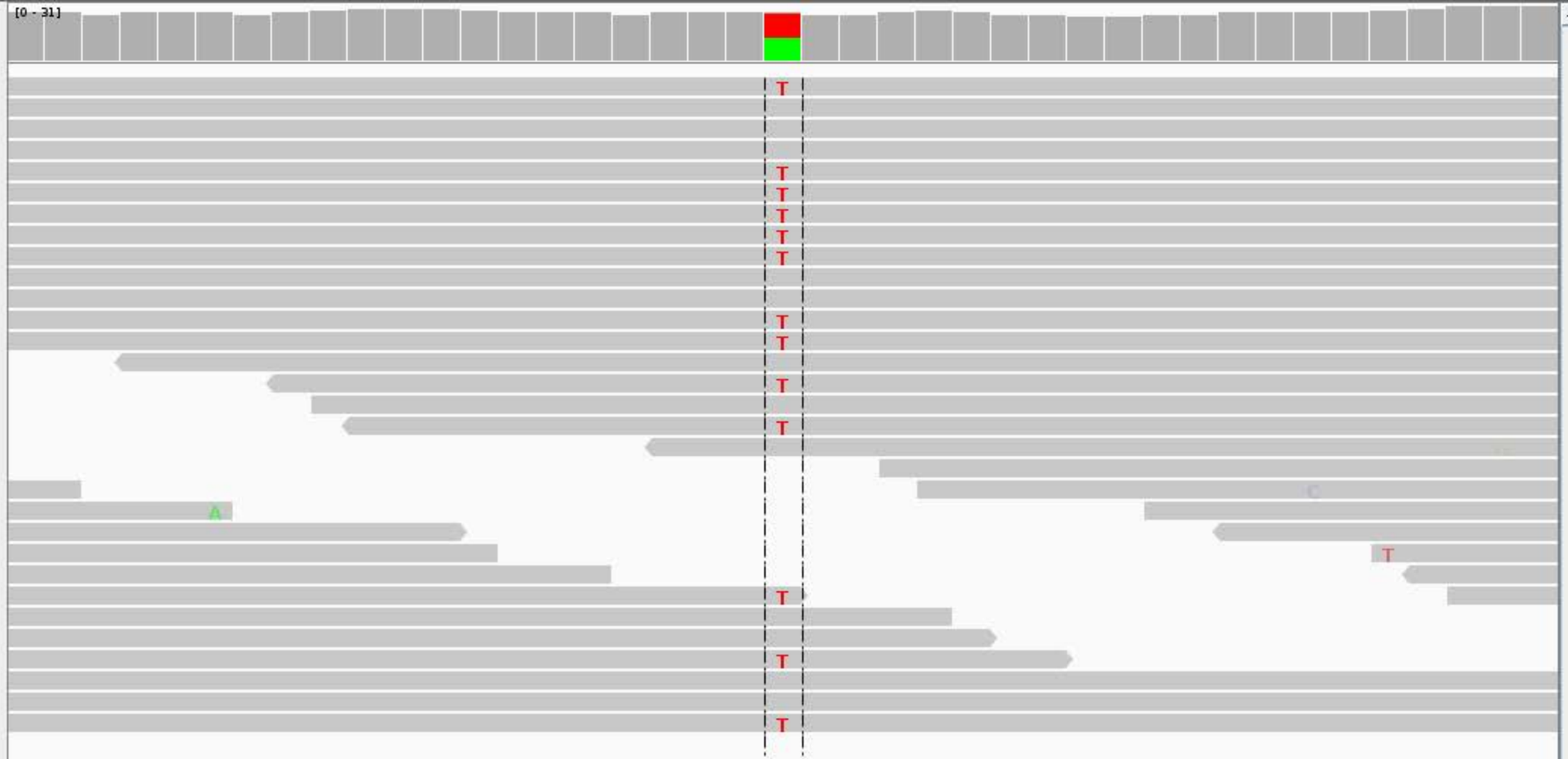

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Supplementary Figure S14