

Working Notes: Prediction of the DNA methylation of the MGMT promoter with EPICv2 in using the model mgmtstp27.

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 - **Abstract:**
-

The document explains how is possible to used the R package mgmtstp27 with CpG-probes from infinium EPICv2 platforms of Illumina.

- **Keywords:** MGMT, DNA methylation, glioma, GBM, LGG
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1 Motivations

This short document explains how is possible to used the R package mgmtstp27 with CpG-probes from infinium EPICv2 platforms of Illumina (<https://www.illumina.com/products/by-type/microarray-kits/infinium-methylation-epic.html>). The version 0.8 (and latter) of the R packages converts automatically the probes names in using the two probes called “cg12434587_BC11” and “cg12981137_TC11” which will be renamed as “cg12434587” and “cg12981137”. The selection of these two probes is based on the concordance of the annotation information and the sequences of the probes (see variable “AlleleA_ProbeSeq” from manifest file).

2 Probe Selections

The selection of the probes “cg12434587_BC11” and “cg12981137_TC11” was established as follow:

```
# import R packages
require(mgmtstp27)
```

```
## Le chargement a nécessité le package : mgmtstp27
## Le chargement a nécessité le package : lumi
## Pas de méthodes trouvées dans le package 'RSQLite' pour la requête : 'dbListFields' lors du chargement
## Le chargement a nécessité le package : methylumi
## Le chargement a nécessité le package : scales
## Le chargement a nécessité le package : reshape2
## Le chargement a nécessité le package : ggplot2
## Le chargement a nécessité le package : FDb.InfiniumMethylation.hg19
## Le chargement a nécessité le package : GenomicFeatures
## Le chargement a nécessité le package : AnnotationDbi
## Le chargement a nécessité le package : TxDb.Hsapiens.UCSC.hg19.knownGene
## Le chargement a nécessité le package : org.Hs.eg.db
##
##
## Attachement du package : 'methylumi'
## Les objets suivants sont masqués depuis 'package:lumi':
##
##     estimateM, getHistory
## Le chargement a nécessité le package : MASS
##
## Attachement du package : 'MASS'
## L'objet suivant est masqué depuis 'package:AnnotationDbi':
##
##     select
##
## Warning: remplacement de l'importation précédente 'lumi::getHistory' par
## 'methylumi::getHistory' lors du chargement de 'mgmtstp27'
##
## Warning: remplacement de l'importation précédente 'lumi::estimateM' par
## 'methylumi::estimateM' lors du chargement de 'mgmtstp27'
```

```
##
## Attachement du package : 'mgmtstp27'
## L'objet suivant est masqué _par_ '.GlobalEnv':
##
##      .sclass
coef(MGMTSTP27)

## (Intercept)  cg12434587  cg12981137
##      4.3215451    0.5271018    0.9264582
probemodels <- names(coef(MGMTSTP27))[-1]

# data source: https://zwdzwd.github.io/InfiniumAnnotation
# manifest for EPIC v2
annotepicv2 <- read.table("EPICv2.hg38.manifest.tsv",header=TRUE,sep="\t")
dim(annotepicv2)

## [1] 937690      28
head(annotepicv2)

##      CpG_chrm  CpG_beg  CpG_end address_A address_B target nextBase channel
## 1    chr16  53434199  53434201  41791408         NA    CG      <NA>    <NA>
## 2    chr3   172198246  172198248  66725308         NA    CG      <NA>    <NA>
## 3    chr7    2550930   2550932  87669537         NA    CG      <NA>    <NA>
## 4    chr9   92248272  92248274  47668938         NA    CG      <NA>    <NA>
## 5    chr1   90729116  90729118  45649248         NA    CG      <NA>    <NA>
## 6   chr17   56456886  56456888  82633489         NA    CG      <NA>    <NA>
##      Probe_ID mapFlag_A mapChrm_A mapPos_A mapQ_A mapCigar_A
## 1 cg00000029_TC21      16    chr16   53434201     60      50M
## 2 cg00000109_TC21      16    chr3   172198248     60      50M
## 3 cg00000155_BC21      16    chr7    2550932     60      50M
## 4 cg00000158_BC21      16    chr9   92248274     60      50M
## 5 cg00000165_TC21       0    chr1   90729068     60      50M
## 6 cg00000221_BC21       0   chr17   56456838     60      50M
##      AlleleA_ProbeSeq mapNM_A mapAS_A mapYD_A
## 1 AACTATACTAACRAAAAAATATCCAAAAAACACTAACRTATAAAAAATTTC      0     50      f
## 2 CAATACTAACAAACACATATACCCCCCACAAATCTTAACCTCTAAATAC      0     50      f
## 3 AATAAAAAAACACTACACCCAACCTAAACATAATAATTAAATATTCAAAC      0     50      f
## 4 AACTAAACATTCCRTATTATTTACTTCAAACCTATTCTCATTTTCCCATCC      0     50      f
## 5 CAAAATCTATTAATAACAATACTTTTAATAAAACAATAAAACACACATC      0     50      r
## 6 ATATTTTTTTAAATACATTCCAAAAAACACAAAATTACAAACCACAAACC      0     50      r
##      mapFlag_B mapChrm_B mapPos_B mapQ_B mapCigar_B AlleleB_ProbeSeq mapNM_B mapAS_B
## 1      NA      <NA>      NA      NA      <NA>      <NA>      NA      NA
## 2      NA      <NA>      NA      NA      <NA>      <NA>      NA      NA
## 3      NA      <NA>      NA      NA      <NA>      <NA>      NA      NA
## 4      NA      <NA>      NA      NA      <NA>      <NA>      NA      NA
## 5      NA      <NA>      NA      NA      <NA>      <NA>      NA      NA
## 6      NA      <NA>      NA      NA      <NA>      <NA>      NA      NA
##      mapYD_B type
## 1      <NA>    II
## 2      <NA>    II
## 3      <NA>    II
## 4      <NA>    II
## 5      <NA>    II
```

```
## 6      <NA>      II
probenamesv2 <- annotepicv2$Probe_ID

# manifest for EPIC
annotepic <- read.table("EPIC.hg38.manifest.tsv",header=TRUE,sep="\t")
dim(annotepic)

## [1] 866553      28
head(annotepic)

##      CpG_chrm  CpG_beg  CpG_end address_A address_B target nextBase channel
## 1      chr16  53434199  53434201  40668283      NA      CG      <NA>      <NA>
## 2      chr4   72604468  72604470  76703527      NA      CG      <NA>      <NA>
## 3      chr3  172198246  172198248  39798525      NA      CG      <NA>      <NA>
## 4      chr7   2550930   2550932  22679178      NA      CG      <NA>      <NA>
## 5      chr9  92248272  92248274  33624521      NA      CG      <NA>      <NA>
## 6      chr1  90729116  90729118  8711382      NA      CG      <NA>      <NA>
##      Probe_ID mapFlag_A mapChrm_A mapPos_A mapQ_A mapCigar_A
## 1 cg00000029      16      chr16  53434201      60      50M
## 2 cg00000103      16      chr4   72604470      60      50M
## 3 cg00000109      16      chr3  172198248      60      50M
## 4 cg00000155      16      chr7   2550932      60      50M
## 5 cg00000158      16      chr9  92248274      60      50M
## 6 cg00000165      0      chr1   90729068      60      50M
##      AlleleA_ProbeSeq mapNM_A mapAS_A mapYD_A
## 1 AACTATACTAACRAAAAAATATCCAAAAAACACTAACRTATAAAAAATTC      0      50      f
## 2 AACTTAACTTACAACCAATTATCCCAACRATTTCAACTAATAATATTAAC      0      50      f
## 3 CAATACTAACAAACACATATACCCCCCACAATCTTAACTTCTAAATAC      0      50      f
## 4 AATAAAAAACCCTACACCCAACCTAAACATAATAATTAAATATTCAAAC      0      50      f
## 5 AACTAAACATTCCRTATTATTACTTCAAACCTATTCTCATTTTCCCATCC      0      50      f
## 6 CAAAATCTATTAATACAATAACTTTAATAAAACAACATAAAACACACATC      0      50      r
##      mapFlag_B mapChrm_B mapPos_B mapQ_B mapCigar_B AlleleB_ProbeSeq mapNM_B mapAS_B
## 1      NA      <NA>      NA      NA      <NA>      <NA>      NA      NA
## 2      NA      <NA>      NA      NA      <NA>      <NA>      NA      NA
## 3      NA      <NA>      NA      NA      <NA>      <NA>      NA      NA
## 4      NA      <NA>      NA      NA      <NA>      <NA>      NA      NA
## 5      NA      <NA>      NA      NA      <NA>      <NA>      NA      NA
## 6      NA      <NA>      NA      NA      <NA>      <NA>      NA      NA
##      mapYD_B type
## 1      <NA>      II
## 2      <NA>      II
## 3      <NA>      II
## 4      <NA>      II
## 5      <NA>      II
## 6      <NA>      II
probenames <- annotepic$Probe_ID

##
# checknames
V2probes1 <- annotepicv2[grepl(probenamesv2),]
V2probes2 <- annotepicv2[grepl(probenamesv2),]
V1probes1 <- annotepic[grepl(probenames),]
V1probes2 <- annotepic[grepl(probenames),]
```

```
## for probe 1: "cg12434587"
```

```
V1probes1
```

```
##      CpG_chrm  CpG_beg  CpG_end address_A address_B target nextBase channel
## 414107    chr10 129466944 129466946 59800220 7671507    CG      C      G
##      Probe_ID mapFlag_A mapChrm_A mapPos_A mapQ_A mapCigar_A
## 414107 cg12434587      0    chr10 129466897    60    50M
##      AlleleA_ProbeSeq mapNM_A mapAS_A mapYD_A
## 414107 ACTTATACCAACCAAAAAACCATCCAAATCAAACACACAAAAACAACA      0    50    r
##      mapFlag_B mapChrm_B mapPos_B mapQ_B mapCigar_B
## 414107      0    chr10 129466897    60    50M
##      AlleleB_ProbeSeq mapNM_B mapAS_B mapYD_B
## 414107 ACTTATACCGACCGAAAAACCATCCGAATCAAACGCACAAAAACAACGACG      0    50    r
##      type
## 414107      I
```

```
V2probes1
```

```
##      CpG_chrm  CpG_beg  CpG_end address_A address_B target nextBase channel
## 432048    chr10 129466944 129466946 1742151 71657910    CG      C      G
## 432049    chr10 129466944 129466946 77782982 16808131    CG      G      G
##      Probe_ID mapFlag_A mapChrm_A mapPos_A mapQ_A mapCigar_A
## 432048 cg12434587_BC11      0    chr10 129466897    60    50M
## 432049 cg12434587_B011      0    chr10 129466896    60    50M
##      AlleleA_ProbeSeq mapNM_A mapAS_A mapYD_A
## 432048 ACTTATACCAACCAAAAAACCATCCAAATCAAACACACAAAAACAACA      0    50    r
## 432049 GGTTTGTATTGGTTGAAGGGTTATTGGGTTAGGTGTATAGGGTAGTGGT      0    50    f
##      mapFlag_B mapChrm_B mapPos_B mapQ_B mapCigar_B
## 432048      0    chr10 129466897    60    50M
## 432049      0    chr10 129466896    60    50M
##      AlleleB_ProbeSeq mapNM_B mapAS_B mapYD_B
## 432048 ACTTATACCGACCGAAAAACCATCCGAATCAAACGCACAAAAACAACGACG      0    50    r
## 432049 GGTTTGTATCGGTCGAAGGGTTATTCGGGTTAGCGGTATAGGGTAGCGGC      0    50    f
##      type
## 432048      I
## 432049      I
```

```
V2probes1[is.element(V2probes1$AlleleA_ProbeSeq,V1probes1$AlleleA_ProbeSeq),]
```

```
##      CpG_chrm  CpG_beg  CpG_end address_A address_B target nextBase channel
## 432048    chr10 129466944 129466946 1742151 71657910    CG      C      G
##      Probe_ID mapFlag_A mapChrm_A mapPos_A mapQ_A mapCigar_A
## 432048 cg12434587_BC11      0    chr10 129466897    60    50M
##      AlleleA_ProbeSeq mapNM_A mapAS_A mapYD_A
## 432048 ACTTATACCAACCAAAAAACCATCCAAATCAAACACACAAAAACAACA      0    50    r
##      mapFlag_B mapChrm_B mapPos_B mapQ_B mapCigar_B
## 432048      0    chr10 129466897    60    50M
##      AlleleB_ProbeSeq mapNM_B mapAS_B mapYD_B
## 432048 ACTTATACCGACCGAAAAACCATCCGAATCAAACGCACAAAAACAACGACG      0    50    r
##      type
## 432048      I
```

```
## for probe 2: "cg12981137"
```

```
V1probes2
```

```
##      CpG_chrm  CpG_beg  CpG_end address_A address_B target nextBase channel
## 431077   chr10 129467310 129467312 82605453 25662269    CG      C      G
##      Probe_ID mapFlag_A mapChrm_A  mapPos_A mapQ_A mapCigar_A
## 431077 cg12981137      0    chr10 129467263    60    50M
##      AlleleA_ProbeSeq mapNM_A mapAS_A mapYD_A
## 431077 ACAAATCCTCACAAATACACACCATTTACAACCTTAATAAATATCTAAATCA    0    50    r
##      mapFlag_B mapChrm_B  mapPos_B mapQ_B mapCigar_B
## 431077      0    chr10 129467263    60    50M
##      AlleleB_ProbeSeq mapNM_B mapAS_B mapYD_B
## 431077 GCAAATCCTCGGATACGCACCGTTTACGACTTAATAAATATCTAAATCG    0    50    r
##      type
## 431077    I
```

V2probes2

```
##      CpG_chrm  CpG_beg  CpG_end address_A address_B target nextBase channel
## 450164   chr10 129467310 129467312 36621144      NA    CG    <NA>    <NA>
## 450165   chr10 129467310 129467312 33728460 28759120    CG      G      G
## 450166   chr10 129467310 129467312 87676589 65682310    CG      C      G
## 450167   chr10 129467310 129467312 77743893      NA    CG    <NA>    <NA>
##      Probe_ID mapFlag_A mapChrm_A  mapPos_A mapQ_A mapCigar_A
## 450164 cg12981137_BC21      16    chr10 129467312    60    50M
## 450165 cg12981137_B011      16    chr10 129467312    60    50M
## 450166 cg12981137_TC11      0    chr10 129467263    60    50M
## 450167 cg12981137_TC21      0    chr10 129467262    60    50M
##      AlleleA_ProbeSeq mapNM_A mapAS_A mapYD_A
## 450164 AAATACCACCRCTCCRAAAAAAACTCCRCACCTCTCCRAAAACRAAAC    0    50    f
## 450165 AGGTTGTTATTGTTTTGAGGGAGAGTTTTGTATTTTTTTGGGAGTGAGGT    0    50    r
## 450166 ACAAATCCTCACAAATACACACCATTTACAACCTTAATAAATATCTAAATCA    0    50    r
## 450167 CRCAAATCCTCRATACRCACCRTTTACRACCTTAATAAATATCTAAATC    0    50    r
##      mapFlag_B mapChrm_B  mapPos_B mapQ_B mapCigar_B
## 450164      NA    <NA>      NA    NA    <NA>
## 450165      16    chr10 129467312    60    50M
## 450166      0    chr10 129467263    60    50M
## 450167      NA    <NA>      NA    NA    <NA>
##      AlleleB_ProbeSeq mapNM_B mapAS_B mapYD_B
## 450164      <NA>      NA    NA    <NA>
## 450165 AGGTTGTTATCGTTTTGAGGGAGAGTTTCGTATTTTTTCGGGAGCGAGGC    0    50    r
## 450166 GCAAATCCTCGGATACGCACCGTTTACGACTTAATAAATATCTAAATCG    0    50    r
## 450167      <NA>      NA    NA    <NA>
##      type
## 450164    II
## 450165    I
## 450166    I
## 450167    II
```

```
V2probes2[is.element(V2probes2$AlleleA_ProbeSeq,V1probes2$AlleleA_ProbeSeq),]
```

```
##      CpG_chrm  CpG_beg  CpG_end address_A address_B target nextBase channel
## 450166   chr10 129467310 129467312 87676589 65682310    CG      C      G
##      Probe_ID mapFlag_A mapChrm_A  mapPos_A mapQ_A mapCigar_A
## 450166 cg12981137_TC11      0    chr10 129467263    60    50M
##      AlleleA_ProbeSeq mapNM_A mapAS_A mapYD_A
## 450166 ACAAATCCTCACAAATACACACCATTTACAACCTTAATAAATATCTAAATCA    0    50    r
##      mapFlag_B mapChrm_B  mapPos_B mapQ_B mapCigar_B
```

```
## 450166      0      chr10 129467263      60      50M
##                                     AlleleB_ProbeSeq mapNM_B mapAS_B mapYD_B
## 450166 GCAAATCCTCGCGATACGCACCGTTTACGACTTAATAAATATCTAAATCG      0      50      r
##      type
## 450166      I
```

the two selected probes are given below:

```
## final selection
V2probes1[is.element(V2probes1$AlleleA_ProbeSeq,V1probes1$AlleleA_ProbeSeq),"Probe_ID"]
```

```
## [1] "cg12434587_BC11"
```

```
V2probes2[is.element(V2probes2$AlleleA_ProbeSeq,V1probes2$AlleleA_ProbeSeq),"Probe_ID"]
```

```
## [1] "cg12981137_TC11"
```

3 Example

The dataset called **NCHgbm450** is used to test the new implementation of the function **MGMTpredict**

```
# table S3 (bady et al 2012)
data(NCHgbm450)
head(NCHgbm450)
```

```
##      Code Age  Sex OS Status PrGBM TMZ_RT NTB PatientID MGMTmsp IDH1status CIMP
## 1076 1076  NA <NA> NA  <NA> <NA> <NA> yes      NB      U      <NA> <NA>
## 1297 1297  36   M  60  dead  yes  yes  no      P-206    M      mut  yes
## 1308 1308  45   F  17  dead  yes  yes  no      P-209    M      wt   no
## 1316 1316  68   M   9  dead  no   no  no      P-210    M      wt   no
## 1317 1317  26   M  17  dead  yes  yes  no      P-216    U      wt   no
## 1357 1357  36   M  28  dead  yes  yes  no      P-221    M      mut  yes
##      ExpressionSubtype Trial  STP27link STP27response STP27class cg00618725
## 1076      <NA> <NA> -1.3541449  0.20519355      U -3.422297
## 1297      Proneural  II  5.2499748  0.99477974      M  1.097324
## 1308      Neural  II -0.5676182  0.36178658      M -1.741160
## 1316      <NA>  II -0.5829781  0.35824762      M -3.178880
## 1317      Mesenchymal II -3.9271788  0.01931861      U -2.768264
## 1357      Proneural  II  3.8658949  0.97948549      M  1.434138
##      cg01341123 cg02022136 cg02330106 cg02802904 cg02941816 cg05068430 cg12434587
## 1076 -1.243313 -2.306583  1.2576520 -6.083308 -1.9802932 -6.260079 -4.7258459
## 1297 -3.292762 -5.275700  0.3837486 -5.462675 -2.1437602 -5.053034  0.8801676
## 1308 -1.553476 -2.258045  2.1592601 -5.547356  0.4515545 -5.056570 -2.8832714
## 1316 -3.009282 -4.061190  1.3143637 -5.298483 -1.9085699 -4.636367 -5.6446923
## 1317 -2.680349 -4.255895  1.3498265 -6.349866 -3.3916097 -4.540740 -5.5134785
## 1357  1.521176  1.741255  2.9821919 -0.773308  2.0145288 -4.627655 -0.5507819
##      cg12575438 cg12981137 cg14194875 cg16215402 cg18026026 cg19706602 cg23998405
## 1076  2.9406394 -3.4374869 -3.5257869 -2.905424 -5.452360 -4.595452 -3.488498
## 1297  0.6723771  0.5013628  0.9674217 -2.604399 -4.131637 -3.554933 -8.371162
## 1308  2.7801878 -3.6368459  0.1503638 -2.826422 -5.407175 -3.895061 -3.734608
## 1316  3.2577110 -2.0823342 -3.5946992 -2.880080 -5.417665 -3.994994 -5.561344
## 1317  2.3736290 -5.7666489 -3.8061406 -2.967308 -6.164778 -3.690479 -5.416903
## 1357  3.7289590 -0.1784560  1.4450450 -2.286086 -4.744554 -4.247654  1.436775
##      cg25946389 cg26201213 cg26950715
## 1076 -1.3153960  0.3780831  2.6723170
## 1297 -3.1859031  0.1438742  0.2285859
```



```
## 1308 0.3778683 1.1799064 2.3179269
## 1316 -2.4138114 1.2650305 3.1000689
## 1317 -2.2298325 -0.7856374 2.7592846
## 1357 1.9882962 2.2996091 2.9904467
```

```
tabmgmt <- NCHgbm450[,c("cg12434587","cg12981137")]
testv1 <- MGMTpredict(tabmgmt)
```

The names of the probes is changed by the EPICv2 names and the function is used to predict DNA methylation of the MGMT promoter again.

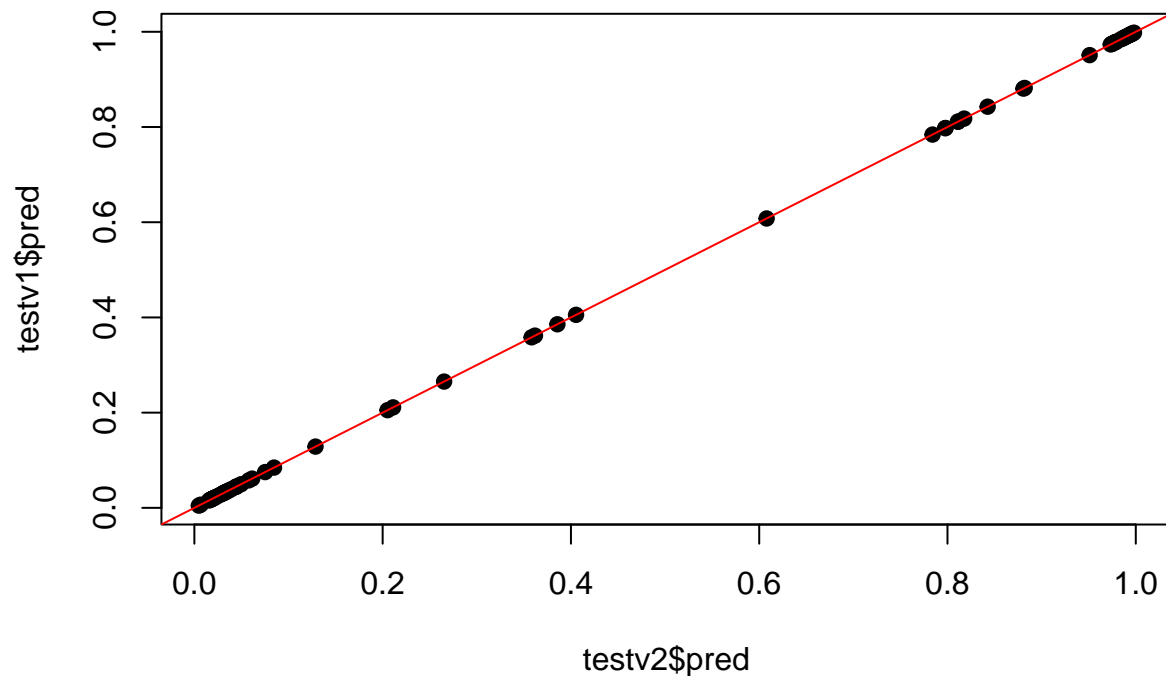
```
tabmgmtv2 <- tabmgmt
colnames(tabmgmtv2) <- ifelse(colnames(tabmgmtv2)=="cg12434587","cg12434587_BC11",colnames(tabmgmtv2))
colnames(tabmgmtv2) <- ifelse(colnames(tabmgmtv2)=="cg12981137","cg12981137_TC11",colnames(tabmgmtv2))
head(tabmgmtv2)
```

```
##      cg12434587_BC11 cg12981137_TC11
## 1076      -4.7258459      -3.4374869
## 1297       0.8801676       0.5013628
## 1308      -2.8832714      -3.6368459
## 1316      -5.6446923      -2.0823342
## 1317      -5.5134785      -5.7666489
## 1357      -0.5507819      -0.1784560
```

```
testv2 <- MGMTpredict(tabmgmtv2)
```

The comparison of the prediction probability are compared below:

```
plot(testv2$pred,testv1$pred,panel.first=c(grid),pch=19)
abline(0,1,col="red")
```



4 References

- Bady, P., D. Sciuscio, A.-C. Diserens, J. Bloch, M. J. van den Bent, C. Marosi, P.-Y. Dietrich, M. Weller, L. Mariani, F. L. Heppner, D. R. McDonald, D. Lacombe, R. Stupp, M. Delorenzi, and M. E. Hegi. (2012). MGMT methylation analysis of glioblastoma on the Infinium methylation BeadChip identifies two distinct CpG regions associated with gene silencing and outcome, yielding a prediction model for comparisons across datasets, tumor grades, and CIMP-status. *Acta Neuropathologica* 124:547-560. PubMed:<http://www.ncbi.nlm.nih.gov/pubmed/22810491>
- Bady P., Delorenzi M., Hegi M. (2016) Sensitivity analysis of the MGMT-STP27 model and impact of genetic/epigenetic context to predict the MGMT methylation status in gliomas and other tumors, *Journal of Molecular Diagnostics*, xx,xxxx-xxxx. PubMed: <http://www.ncbi.nlm.nih.gov/pubmed/26927331>
- R Core Team (2023). *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org/>.

5 Annexes

5.1 Zzzz

5.2 Session information

```
options(prompt="R> ")
print(sessionInfo(), locale=FALSE)

## R version 4.4.0 (2024-04-24)
## Platform: x86_64-pc-linux-gnu
## Running under: Linux Mint 20.3
##
## Matrix products: default
## BLAS: /usr/lib/x86_64-linux-gnu/blas/libblas.so.3.9.0
## LAPACK: /usr/lib/x86_64-linux-gnu/lapack/liblapack.so.3.9.0
##
## attached base packages:
## [1] parallel datasets stats graphics utils stats4 tools grDevices
## [9] methods base
##
## other attached packages:
## [1] mgmtstp27_0.8 MASS_7.3-60.2
## [3] methylumi_2.50.0 FDb.InfiniumMethylation.hg19_2.2.0
## [5] org.Hs.eg.db_3.19.1 TxDb.Hsapiens.UCSC.hg19.knownGene_3.2.2
## [7] GenomicFeatures_1.56.0 AnnotationDbi_1.66.0
## [9] ggplot2_3.5.1 reshape2_1.4.4
## [11] scales_1.3.0 lumi_2.56.0
## [13] circlize_0.4.16 minfi_1.50.0
## [15] bumphunter_1.46.0 locfit_1.5-9.9
## [17] iterators_1.0.14 foreach_1.5.2
## [19] Biostrings_2.72.0 XVector_0.44.0
## [21] SummarizedExperiment_1.34.0 Biobase_2.64.0
## [23] MatrixGenerics_1.16.0 matrixStats_1.3.0
## [25] xtable_1.8-4 tinytex_0.51
## [27] rmarkdown_2.27 knitr_1.46
## [29] pixmap_0.4-13 ade4_1.7-22
## [31] RColorBrewer_1.1-3 rtracklayer_1.64.0
## [33] GenomicRanges_1.56.0 GenomeInfoDb_1.40.0
```

```

## [35] IRanges_2.38.0                      S4Vectors_0.42.0
## [37] BiocGenerics_0.50.0
##
## loaded via a namespace (and not attached):
## [1] shape_1.4.6.1          rstudioapi_0.16.0      jsonlite_1.8.8
## [4] magrittr_2.0.3         GlobalOptions_0.1.2    BiocIO_1.14.0
## [7] zlibbioc_1.50.0        vctrs_0.6.5            multtest_2.60.0
## [10] memoise_2.0.1          Rsamtools_2.20.0       DelayedMatrixStats_1.26.0
## [13] RCurl_1.98-1.14        askpass_1.2.0          htmltools_0.5.8.1
## [16] S4Arrays_1.4.0         curl_5.2.1             rjags_4-15
## [19] Rhdf5lib_1.26.0        SparseArray_1.4.3      rhdf5_2.48.0
## [22] KernSmooth_2.23-24     nor1mix_1.3-3          plyr_1.8.9
## [25] cachem_1.1.0           GenomicAlignments_1.40.0 lifecycle_1.0.4
## [28] pkgconfig_2.0.3        Matrix_1.7-0           R6_2.5.1
## [31] fastmap_1.2.0          GenomeInfoDbData_1.2.12 digest_0.6.35
## [34] colorspace_2.1-0       siggenes_1.78.0        reshape_0.8.9
## [37] RSQLite_2.3.6          base64_2.0.1           fansi_1.0.6
## [40] mgcv_1.9-1            httr_1.4.7             abind_1.4-5
## [43] compiler_4.4.0         beanplot_1.3.1         rngtools_1.5.2
## [46] withr_3.0.0           bit64_4.0.5            BiocParallel_1.38.0
## [49] DBI_1.2.2             highr_0.10             HDF5Array_1.32.0
## [52] openssl_2.2.0         DelayedArray_0.30.1    rjson_0.2.21
## [55] glue_1.7.0            quadprog_1.5-8         restfulr_0.0.15
## [58] nlme_3.1-164          rhdf5filters_1.16.0    grid_4.4.0
## [61] generics_0.1.3        gtable_0.3.5           tzdb_0.4.0
## [64] preprocessCore_1.66.0 tidyr_1.3.1            data.table_1.15.4
## [67] hms_1.1.3            xml2_1.3.6             utf8_1.2.4
## [70] stringr_1.5.1         pillar_1.9.0           limma_3.60.2
## [73] genefilter_1.86.0     splines_4.4.0          dplyr_1.1.4
## [76] lattice_0.22-6        survival_3.6-4         bit_4.0.5
## [79] GEOquery_2.72.0       annotate_1.82.0        tidyselect_1.2.1
## [82] xfun_0.44            scrime_1.3.5           statmod_1.5.0
## [85] stringi_1.8.4         UCSC.utils_1.0.0       yaml_2.3.8
## [88] evaluate_0.23         codetools_0.2-20       tibble_3.2.1
## [91] BiocManager_1.30.23   affyio_1.74.0          cli_3.6.2
## [94] munsell_0.5.1         Rcpp_1.0.12            coda_0.19-4.1
## [97] png_0.1-8            XML_3.99-0.16.1        readr_2.1.5
## [100] blob_1.2.4           mclust_6.1.1          doRNG_1.8.6
## [103] sparseMatrixStats_1.16.0 bitops_1.0-7          affy_1.82.0
## [106] illuminaio_0.46.0     nleqslv_3.3.5         purrr_1.0.2
## [109] crayon_1.5.2          rlang_1.1.3           KEGGREST_1.44.0

```