

# Summary of TMB runs

Lena Morrill

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```
## Warning in .recacheSubclasses(def@class, def, env): undefined subclass
## "numericVector" of class "Mnumeric"; definition not updated

## Warning in checkMatrixPackageVersion(): Package version inconsistency detected.
## TMB was built with Matrix version 1.3.4
## Current Matrix version is 1.4.0
## Please re-install 'TMB' from source using install.packages('TMB', type = 'source') or ask CRAN for a b

## Loading required package: viridisLite
## Loading required package: ggplot2
## Loading required package: tikzDevice
## Loading required package: coda
## Loading required package: MASS

## Warning in .recacheSubclasses(def@class, def, env): undefined subclass
## "numericVector" of class "Mnumeric"; definition not updated

## ##
## ## Markov Chain Monte Carlo Package (MCMCpack)
## ## Copyright (C) 2003-2022 Andrew D. Martin, Kevin M. Quinn, and Jong Hee Park
## ##
## ## Support provided by the U.S. National Science Foundation
## ## (Grants SES-0350646 and SES-0350613)
## ##

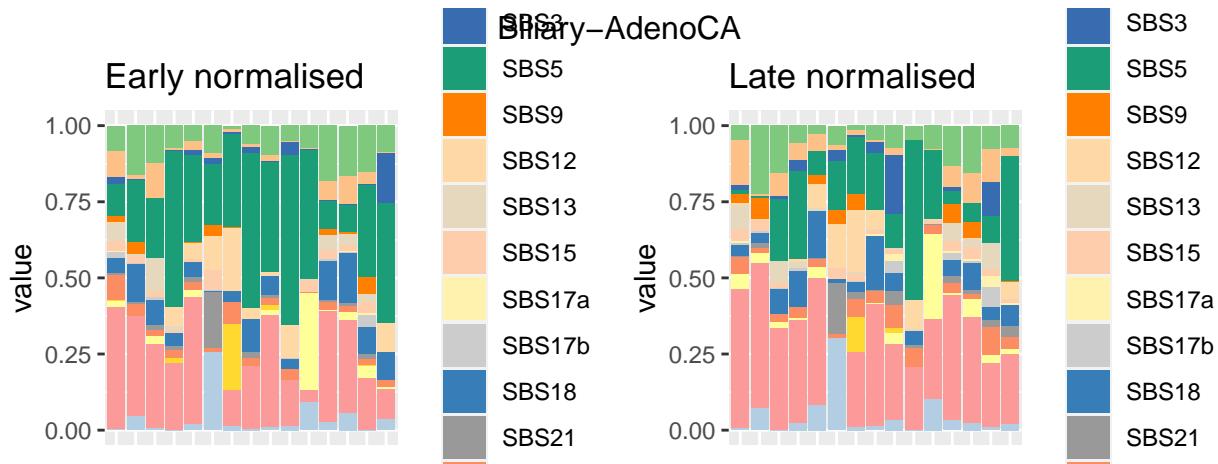
##
## Attaching package: 'ggthemr'

## The following objects are masked from 'package:ggpunbr':
##
##      rotate_x_text, rotate_y_text

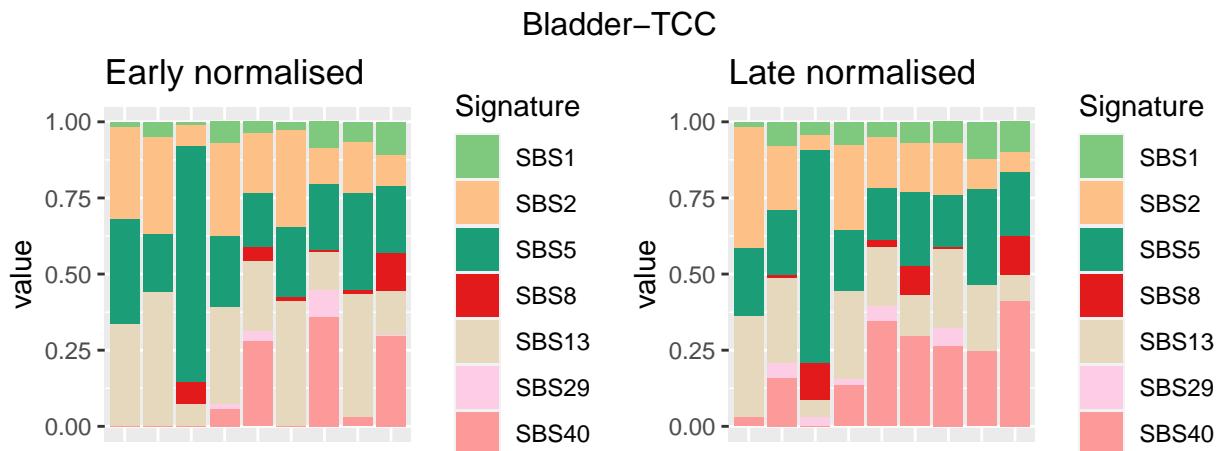
sigs_cosmic0 <- read.table(paste0( ".../data/cosmic/sigProfiler_SBS_signatures_2019_05_22.csv"),
                           stringsAsFactors = FALSE, sep = ',', header = TRUE)
rownames(sigs_cosmic0) <- paste0(substr(sigs_cosmic0$SubType, 1, 1), '[',
                                 sigs_cosmic0$type, ']', substr(sigs_cosmic0$SubType, 3, 3))
sigs_cosmic0 <- sigs_cosmic0[-c(1,2)];
sigs_cosmic <- colnames(sigs_cosmic0)
```

## Using subset of active signatures from the PCAWG paper

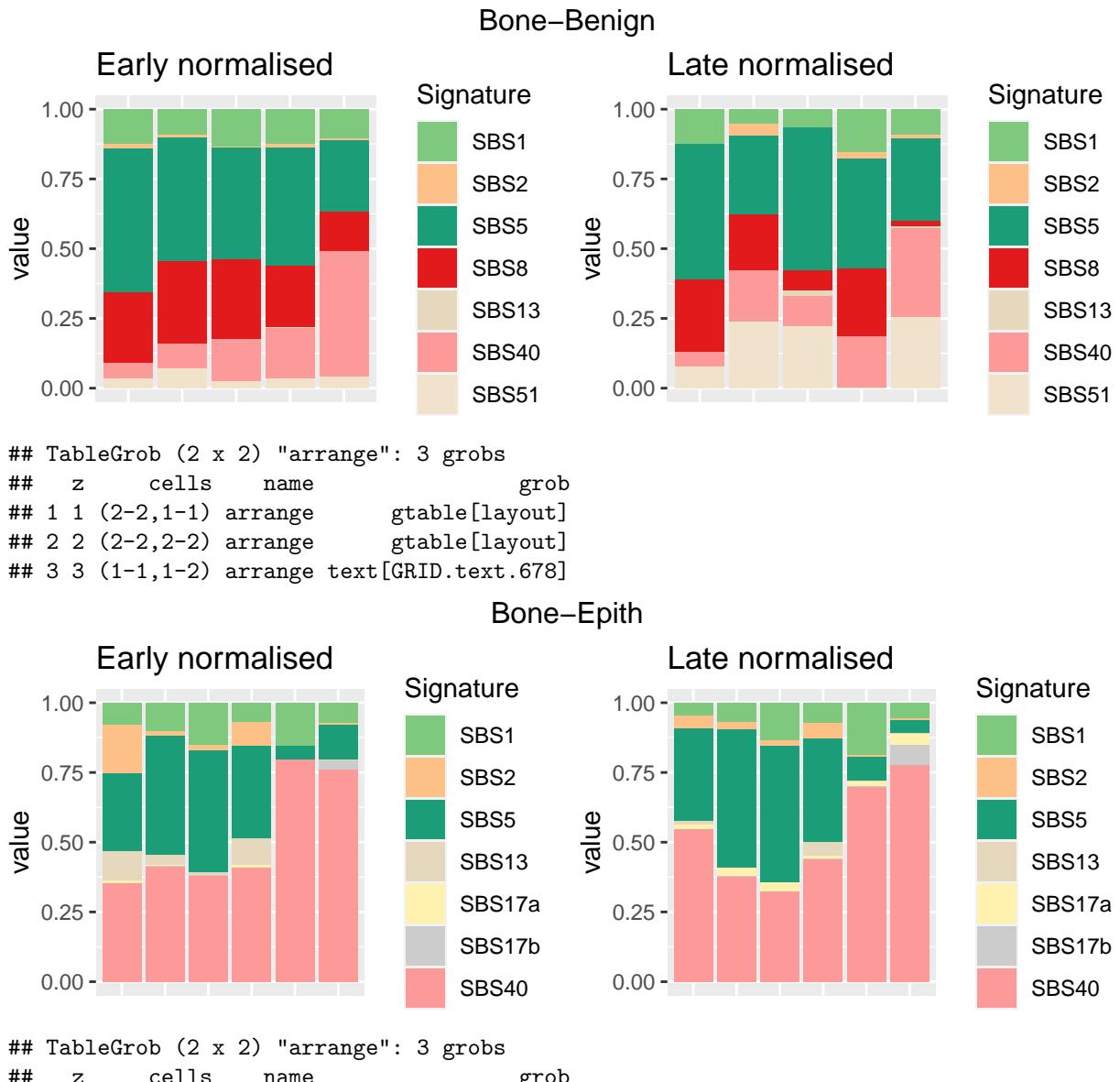
```
pcawg_palette <- pcawg.colour.palette(gsub("\\\\.*", "", enough_samples), scheme = "tumour.subtype")
names(pcawg_palette) <- enough_samples
pcawg_palette[names(pcawg_palette) == 'Lung-SCC'] <- '#ffff29' # #a8a800
```

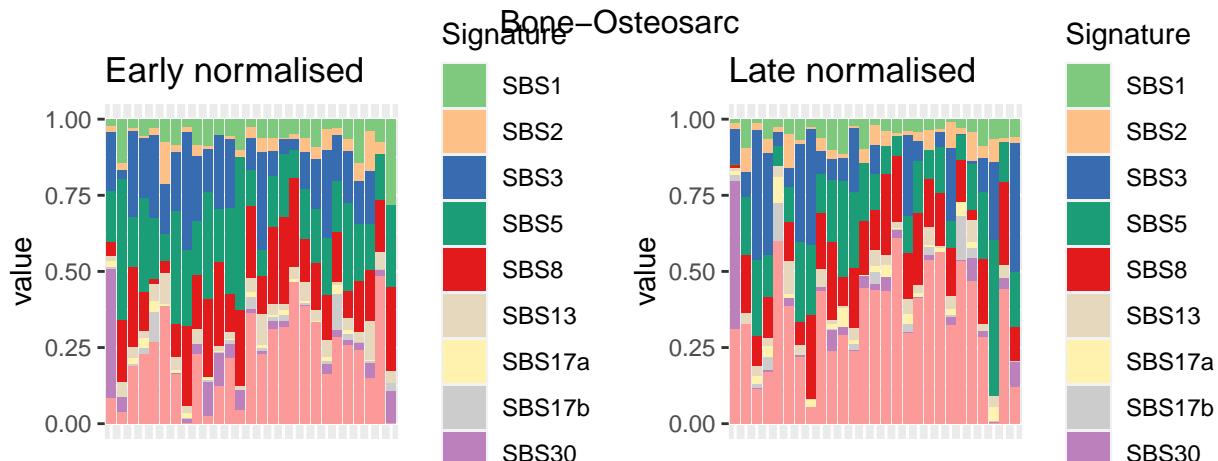


```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.328]
```

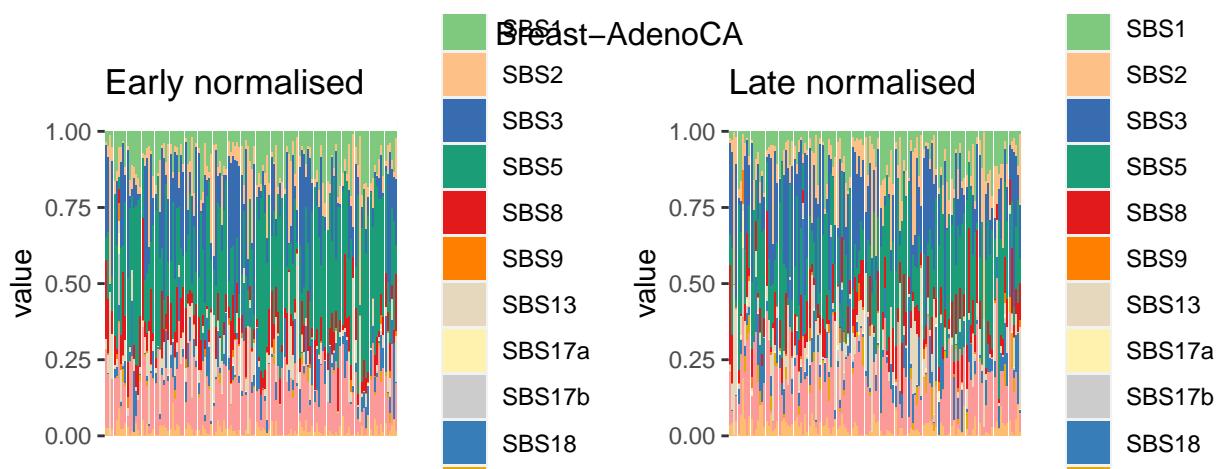


```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.503]
```



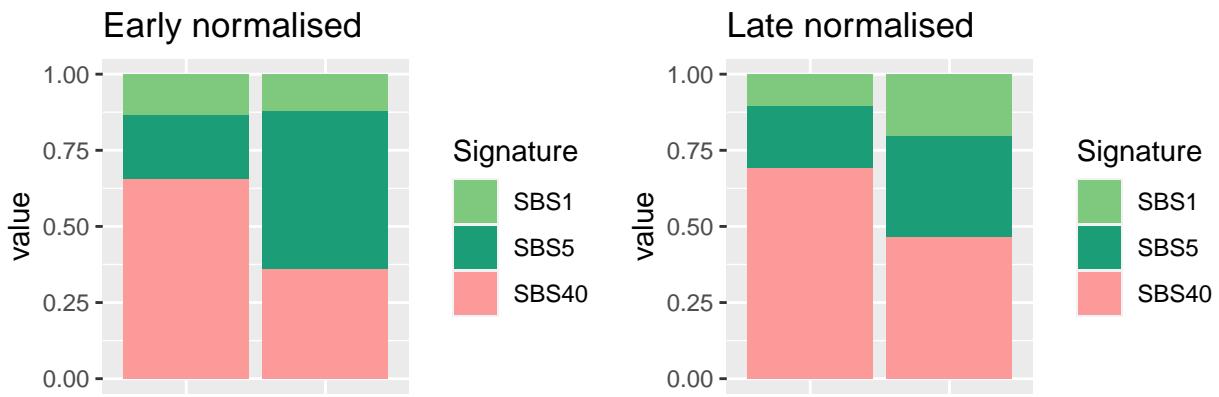


```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1070]
```



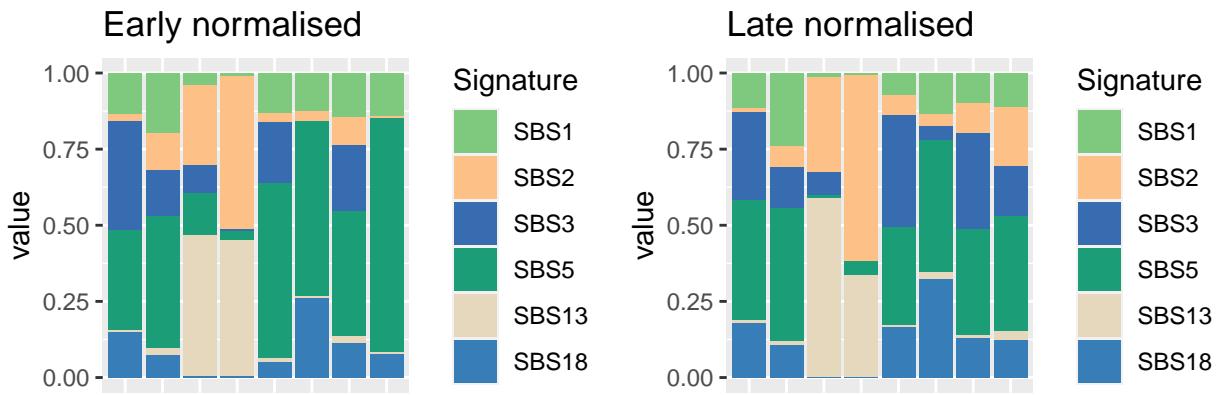
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1329]
```

## Breast-DCIS



```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1448]
```

## Breast-LobularCA



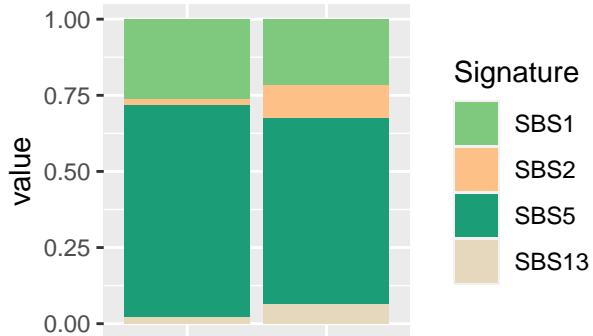
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1609]
```

### Cervix–AdenoCA

Early normalised



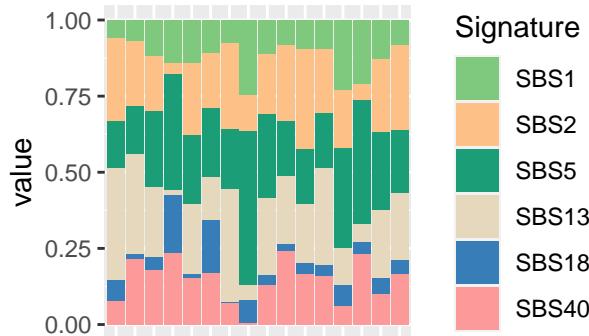
Late normalised



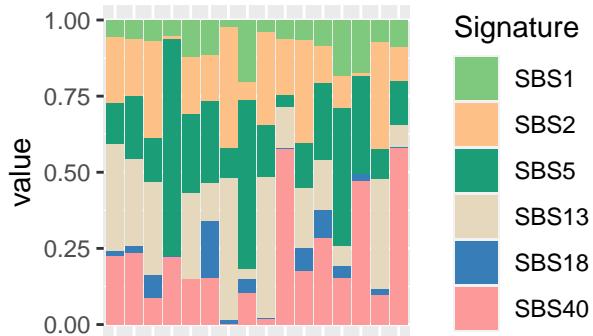
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1742]
```

### Cervix–SCC

Early normalised

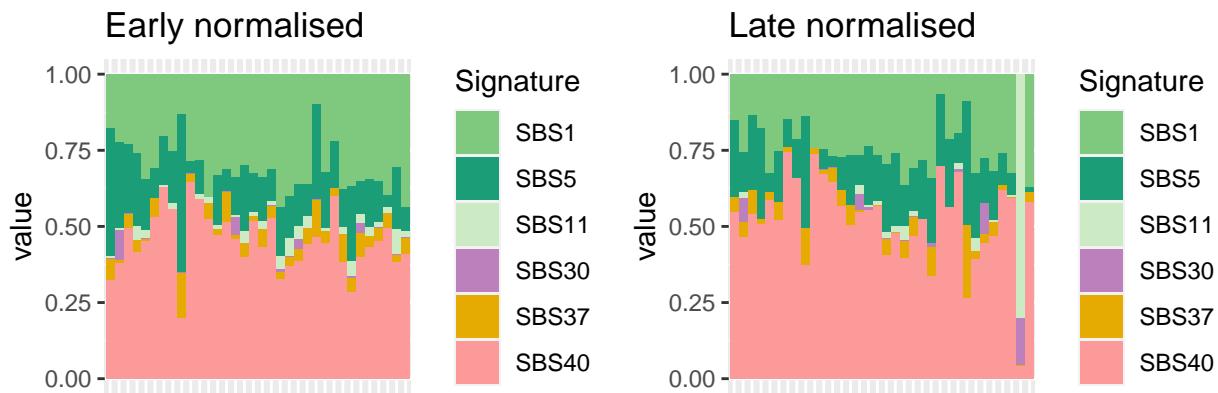


Late normalised



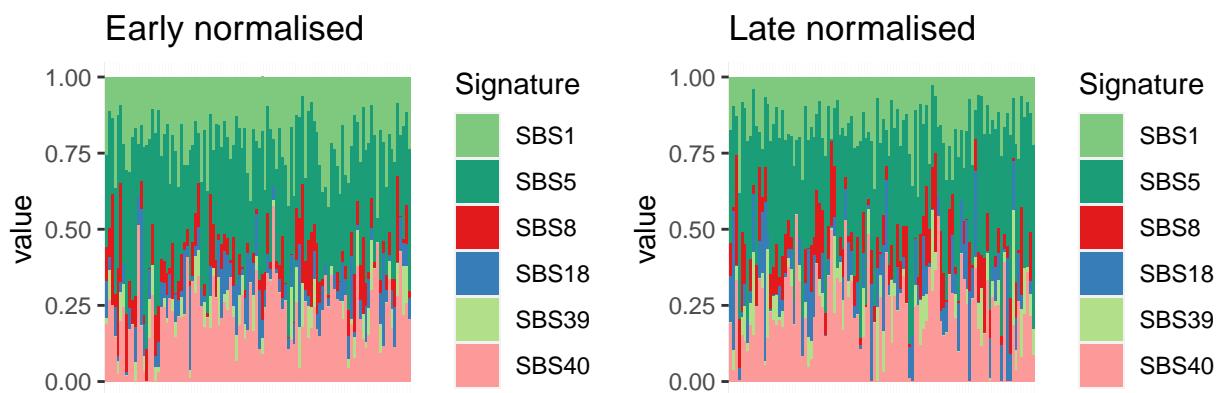
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1903]
```

## CNS–GBM



```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2064]
```

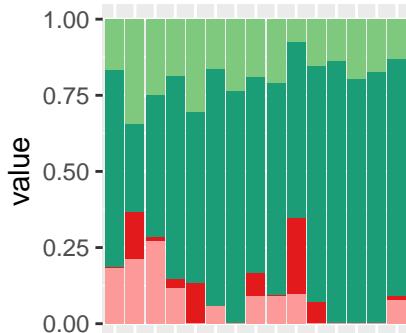
## CNS–Medullo



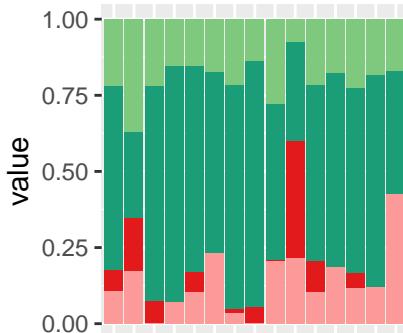
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2225]
```

### CNS–Oligo

Early normalised



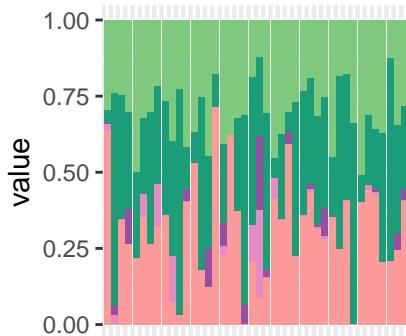
Late normalised



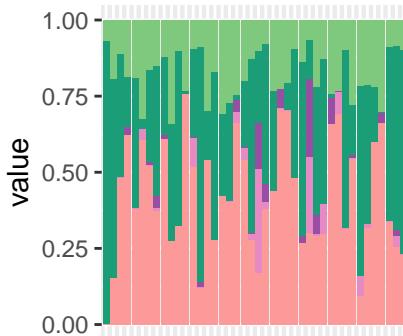
```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2358]
```

### CNS–PiloAstro

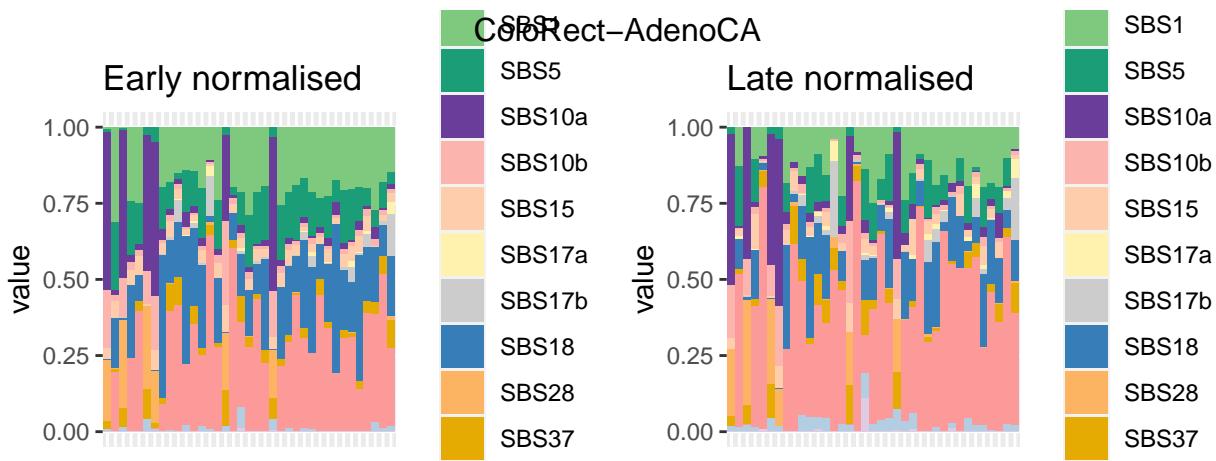
Early normalised



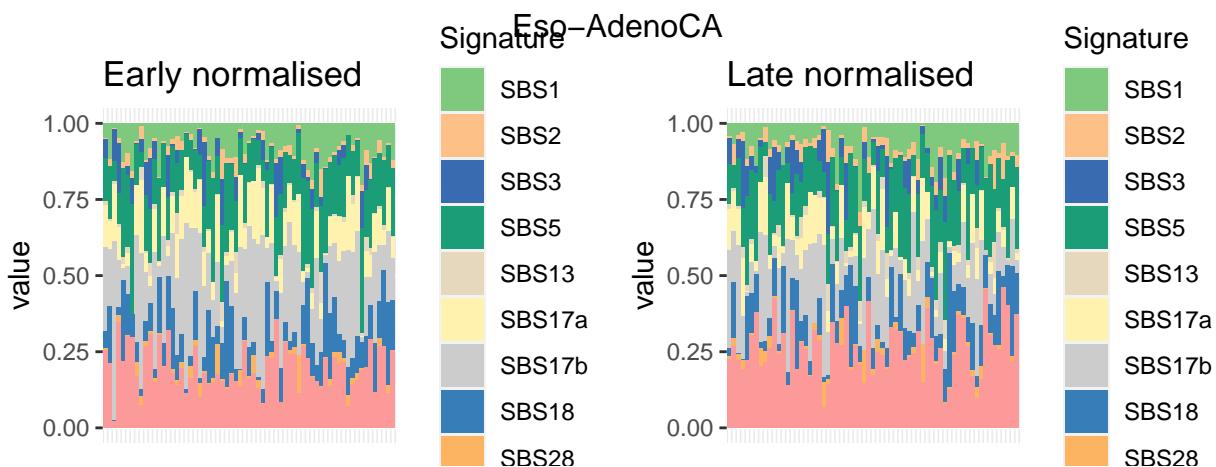
Late normalised



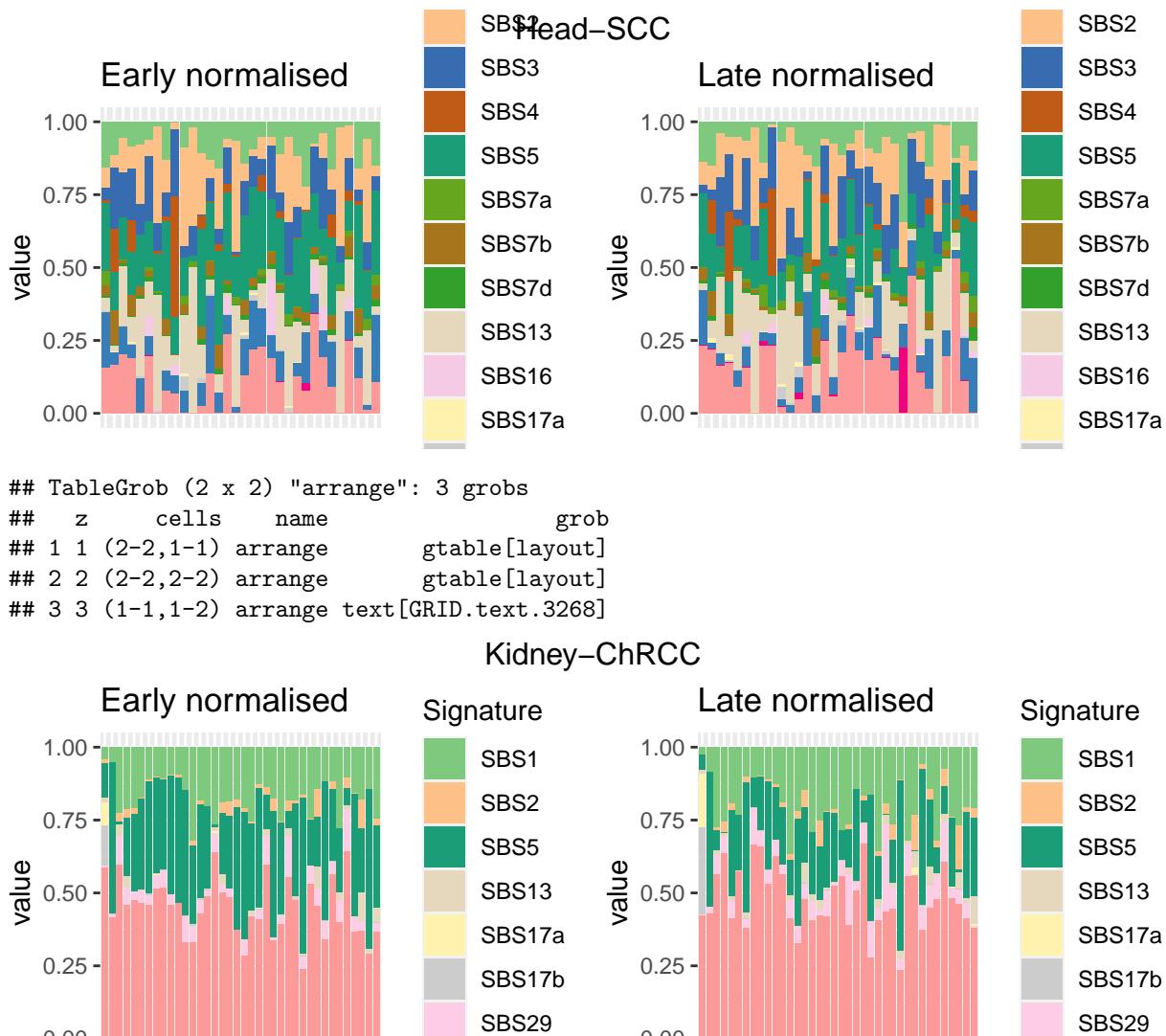
```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2505]
```



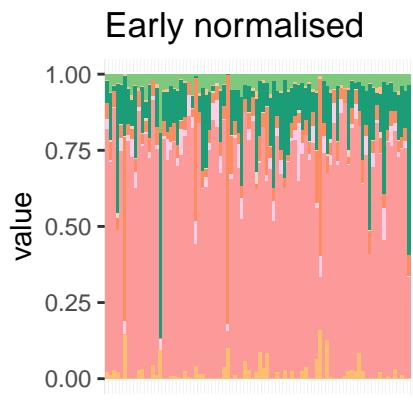
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2764]
```



```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2981]
```



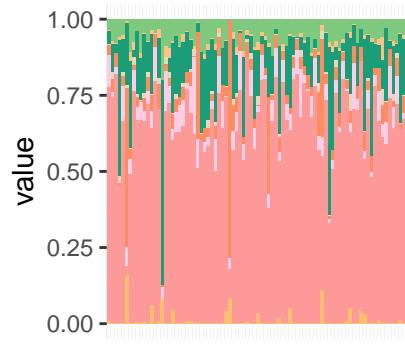
### Kidney–RCC.clearcell



Signature

- SBS1
- SBS2
- SBS5
- SBS13
- SBS22
- SBS29
- SBS40
- SBS41

### Late normalised

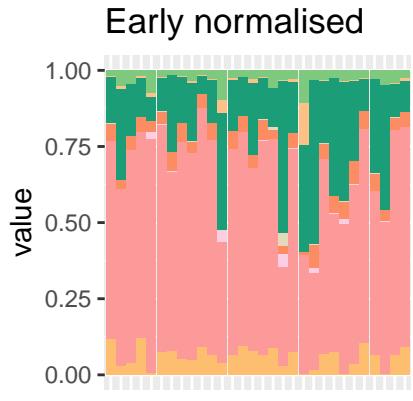


Signature

- SBS1
- SBS2
- SBS5
- SBS13
- SBS22
- SBS29
- SBS40
- SBS41

```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.3646]
```

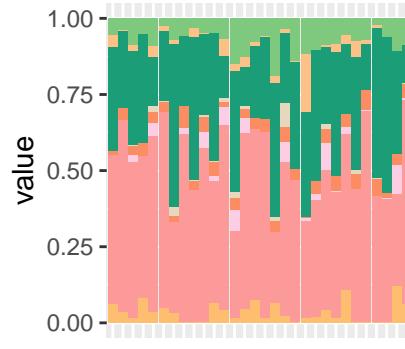
### Kidney–RCC.papillary



Signature

- SBS1
- SBS2
- SBS5
- SBS13
- SBS22
- SBS29
- SBS40
- SBS41

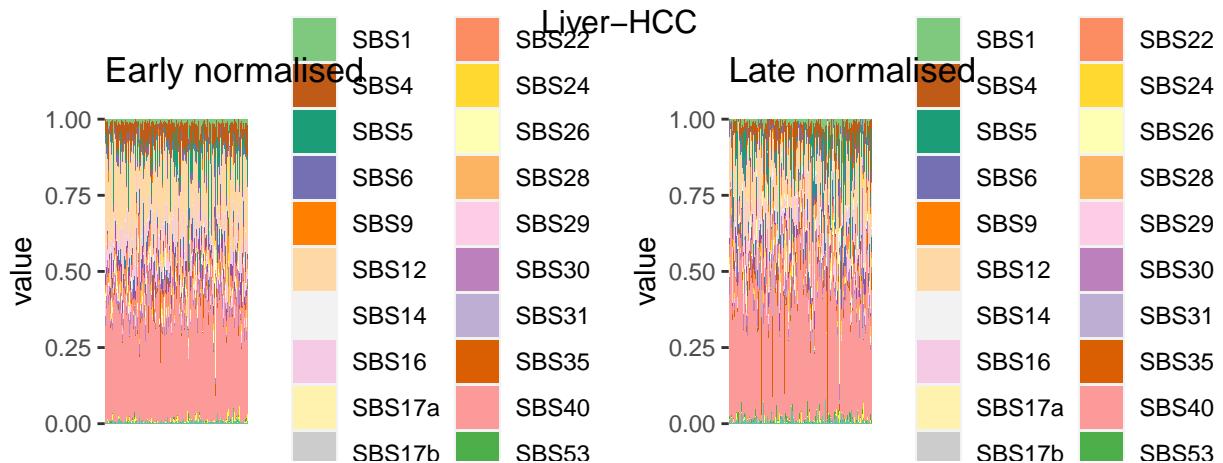
### Late normalised



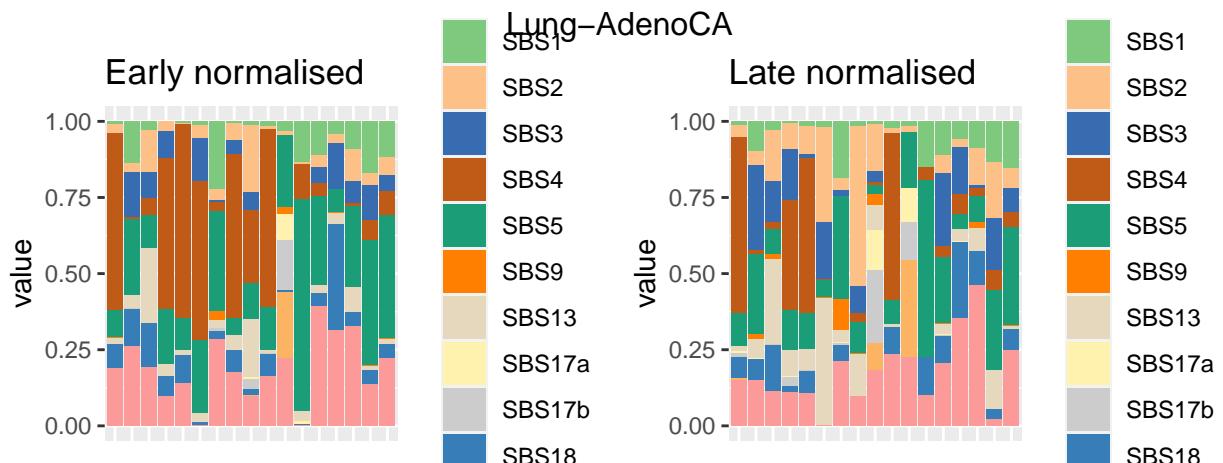
Signature

- SBS1
- SBS2
- SBS5
- SBS13
- SBS22
- SBS29
- SBS40
- SBS41

```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.3835]
```



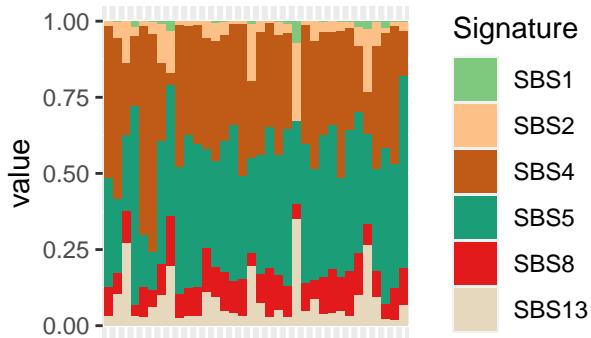
```
## TableGrob (2 x 2) "arrange": 3 grobs
## z cells name grob
## 1 1 (2-2,1-1) arrange gtable[layout]
## 2 2 (2-2,2-2) arrange gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4248]
```



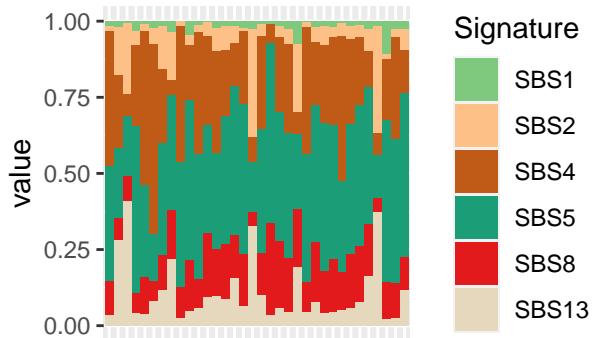
```
## TableGrob (2 x 2) "arrange": 3 grobs
## z cells name grob
## 1 1 (2-2,1-1) arrange gtable[layout]
## 2 2 (2-2,2-2) arrange gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4493]
```

## Lung-SCC

Early normalised



Late normalised



```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4654]
```

Early normalised



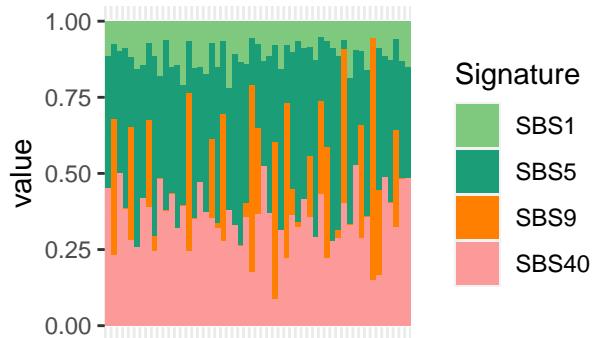
Late normalised



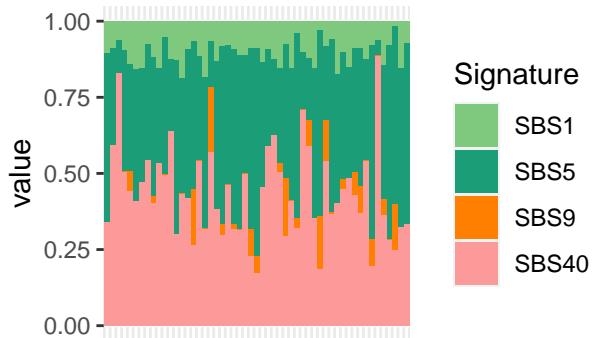
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4927]
```

### Lymph-CLL

Early normalised



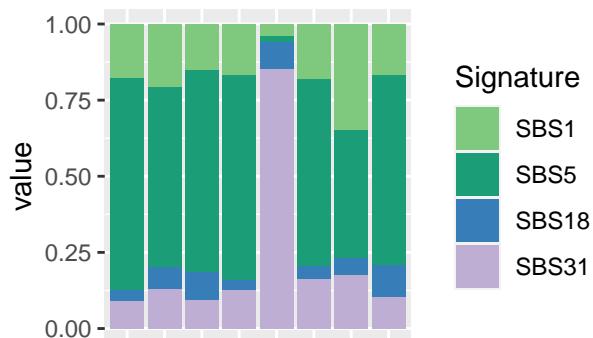
Late normalised



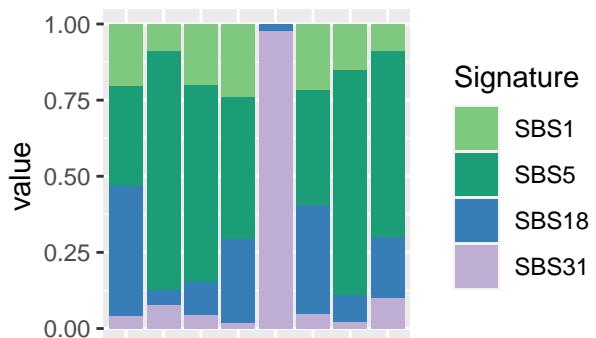
```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5060]
```

### Myeloid-AML

Early normalised

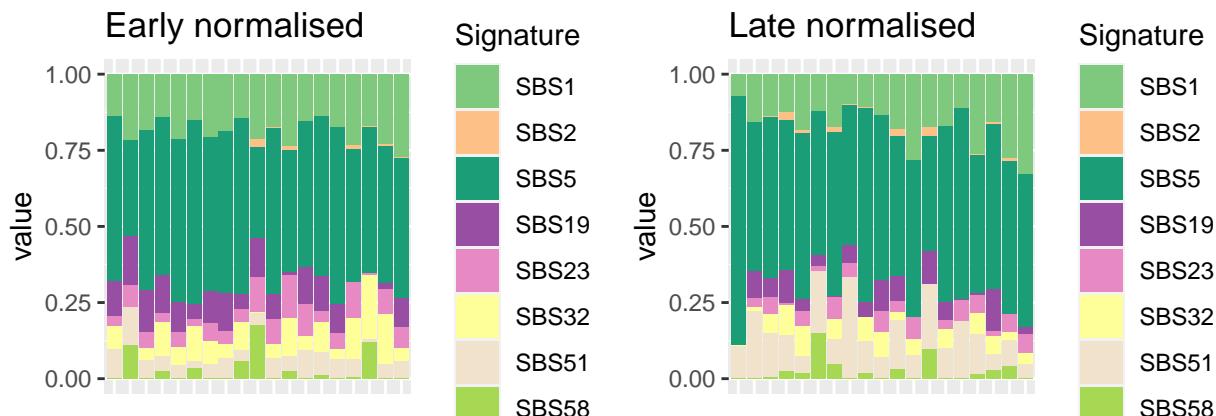


Late normalised

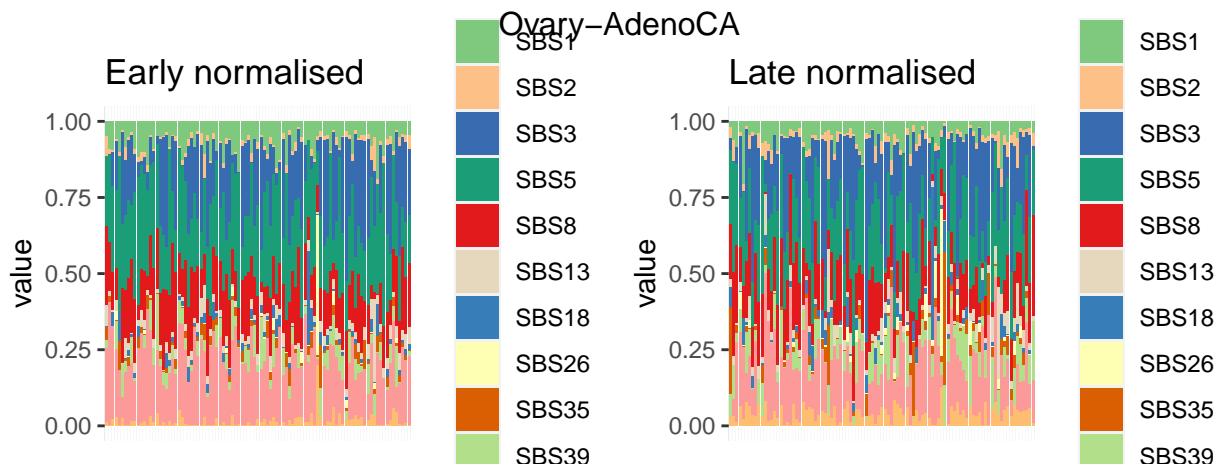


```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5193]
```

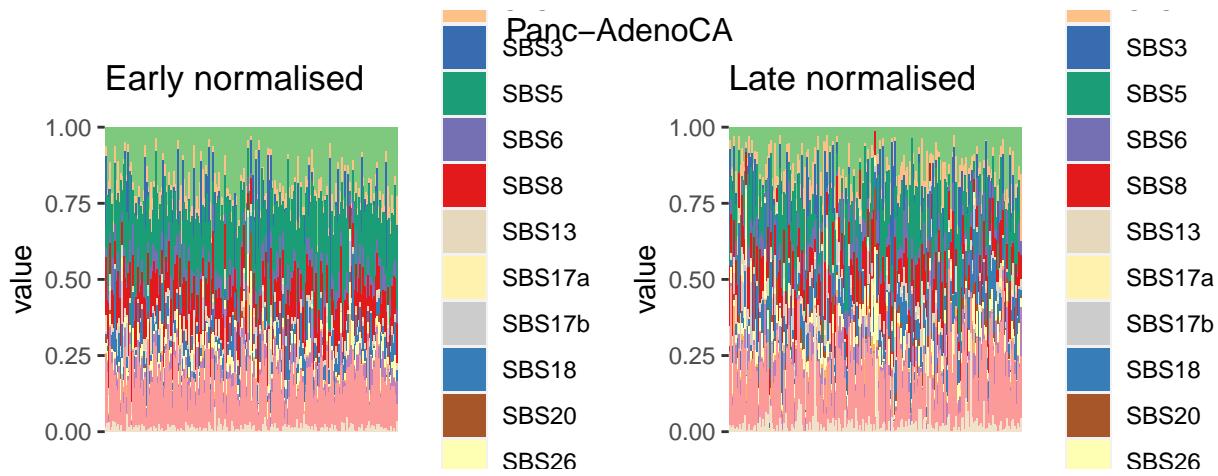
### Myeloid–MPN



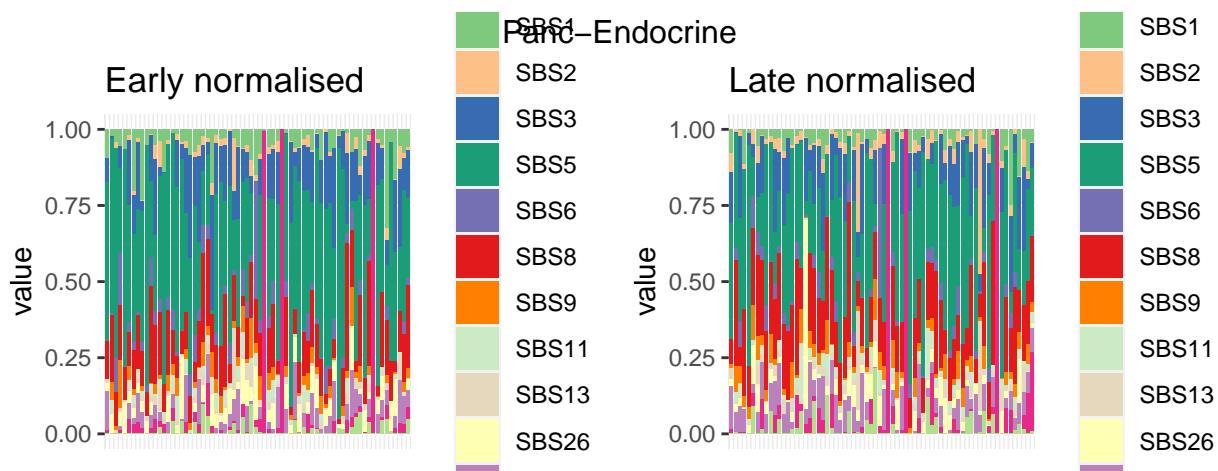
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5382]
```



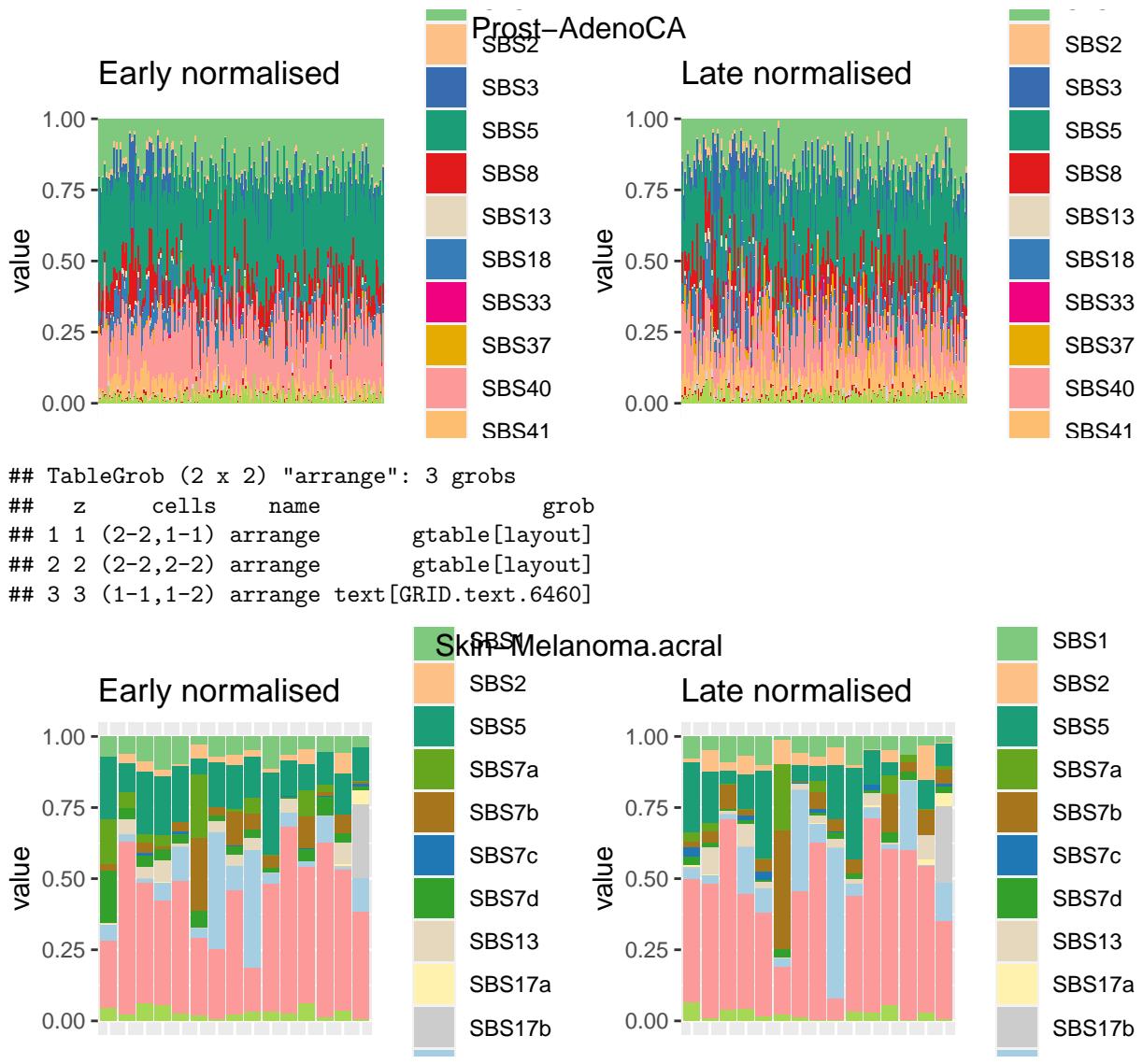
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5627]
```



```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5928]
```

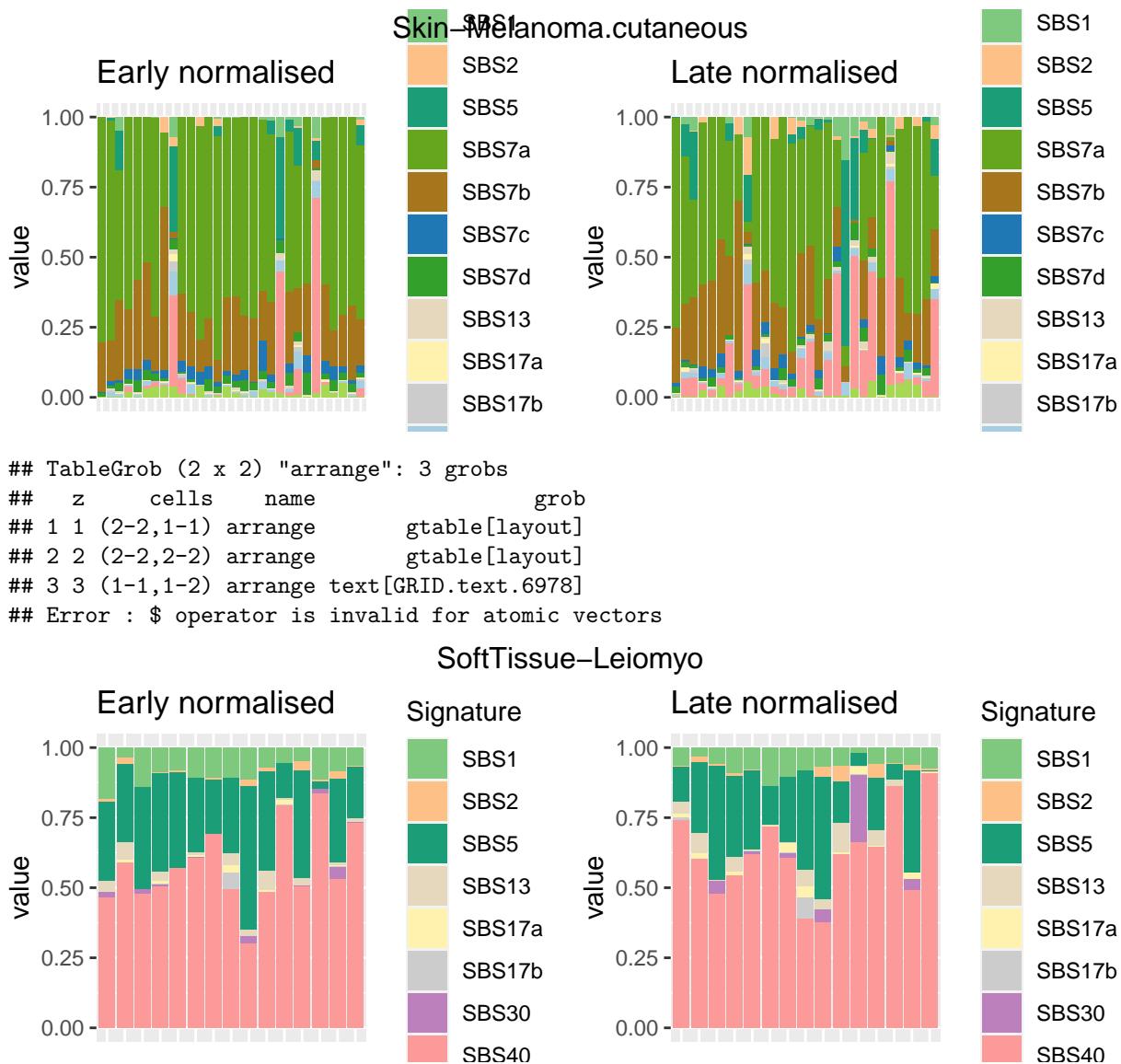


```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.6187]
```

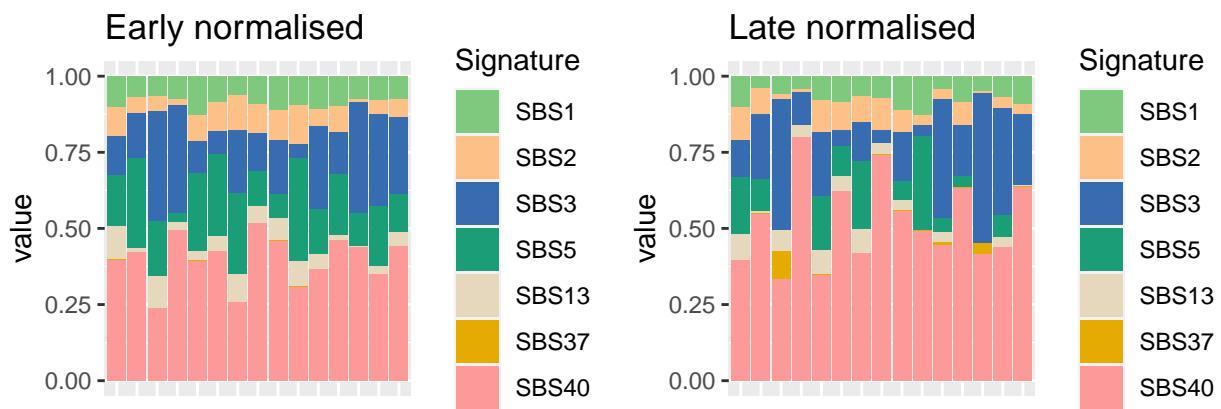


```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.6460]
```

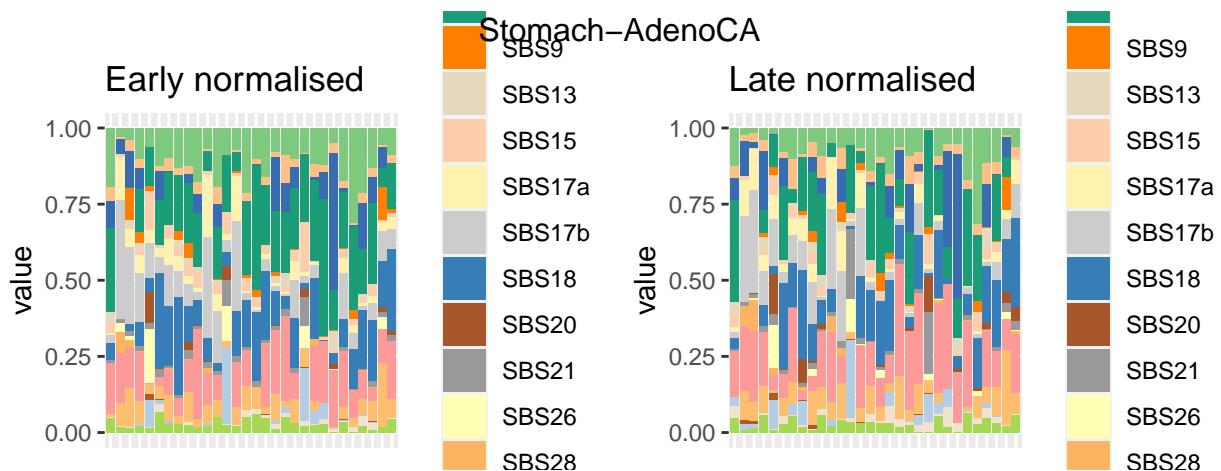
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.6719]
```



### SoftTissue–Liposarc

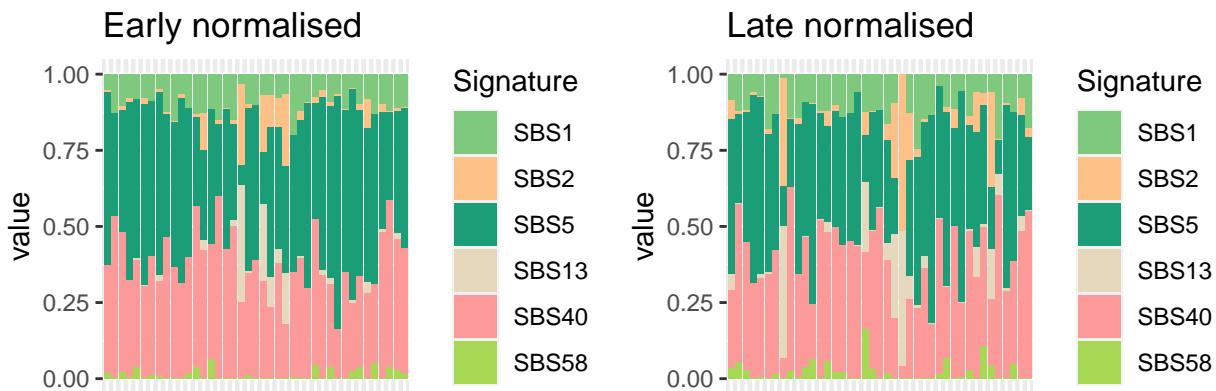


```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.7342]
```

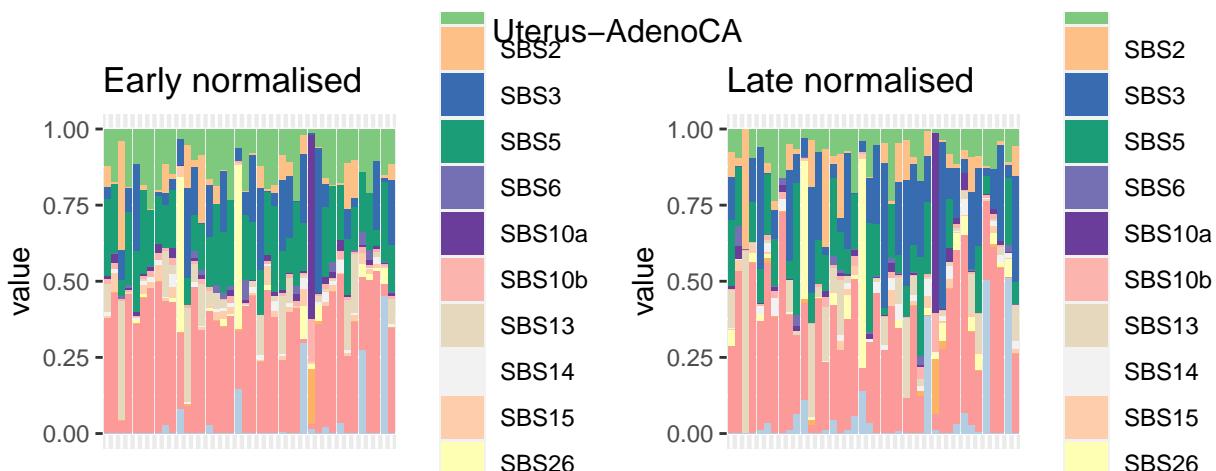


```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.7699]
```

### Thy–AdenoCA



```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.7860]
```



```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.8133]

## $`Biliary-AdenoCA`
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.328]
##
## $`Bladder-TCC`
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.503]
```

```

## 
## $`Bone-Benign` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.678]
##
## $`Bone-Epith` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.853]
##
## $`Bone-Osteosarc` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1070]
##
## $`Breast-AdenoCA` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1329]
##
## $`Breast-DCIS` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1448]
##
## $`Breast-LobularCA` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1609]
##
## $`Cervix-AdenoCA` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1742]
##
## $`Cervix-SCC` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1903]
##
## $`CNS-GBM` 
##   z   cells   name           grob

```

```

## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2064]
##
## $`CNS-Medullo`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2225]
##
## $`CNS-Oligo`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2358]
##
## $`CNS-PiloAstro`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2505]
##
## $`ColoRect-AdenoCA`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2764]
##
## $`Eso-AdenoCA`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2981]
##
## $`Head-SCC`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.3268]
##
## $`Kidney-ChRCC`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.3457]
##
## $`Kidney-RCC.clearcell`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.3646]

```

```

## 
## $`Kidney-RCC.papillary` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.3835]
##
## $`Liver-HCC` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4248]
##
## $`Lung-AdenoCA` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4493]
##
## $`Lung-SCC` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4654]
##
## $`Lymph-BNHL` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4927]
##
## $`Lymph-CLL` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5060]
##
## $`Myeloid-AML` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5193]
##
## $`Myeloid-MPN` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5382]
##
## $`Ovary-AdenoCA` 
##   z   cells   name           grob

```

```

## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5627]
##
## $`Panc-AdenoCA`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5928]
##
## $`Panc-Endocrine`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.6187]
##
## $`Prost-AdenoCA`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.6460]
##
## $`Skin-Melanoma.acral`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.6719]
##
## $`Skin-Melanoma.cutaneous`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.6978]
##
## $`Skin-Melanoma.mucosal`
## [1] "Error : $ operator is invalid for atomic vectors\n"
## attr(,"class")
## [1] "try-error"
## attr(,"condition")
## <simpleError: $ operator is invalid for atomic vectors>
##
## $`SoftTissue-Leiomyo`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.7167]
##
## $`SoftTissue-Liposarc`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]

```



```

pvals_fullRE_M_nonexo_SP <- sapply(fullRE_M_nonexo_SP, function(i) try(wald_TMB_wrapper(i)))

## Check data - slope appears to be of length one (binomial)
pvals_fullRE_DMSL_nonexo_SP <- sapply(fullRE_DMSL_nonexo_SP, function(i) try(wald_TMB_wrapper(i)))

## Check data - slope appears to be of length one (binomial)
pvals_fullREDMnoscaling_SP_nonexo_subsets_and_amalgamations <- sapply(fullREDMnoscaling_SP_nonexo_subsets_and_amalgamations, function(i) try(wald_TMB_wrapper(i)))

## Check data - slope appears to be of length one (binomial)
pvals_fullREDMonefixedlambdanonexo_SP <- sapply(fullREDMonefixedlambdanonexo_SP, function(i) try(wald_TMB_wrapper(i)))

## Check data - slope appears to be of length one (binomial)
pvals_fullREDMonefixedlambdanonexo_SPSaA <- sapply(fullREDMonefixedlambdanonexo_SPSaA, function(i) try(wald_TMB_wrapper(i)))

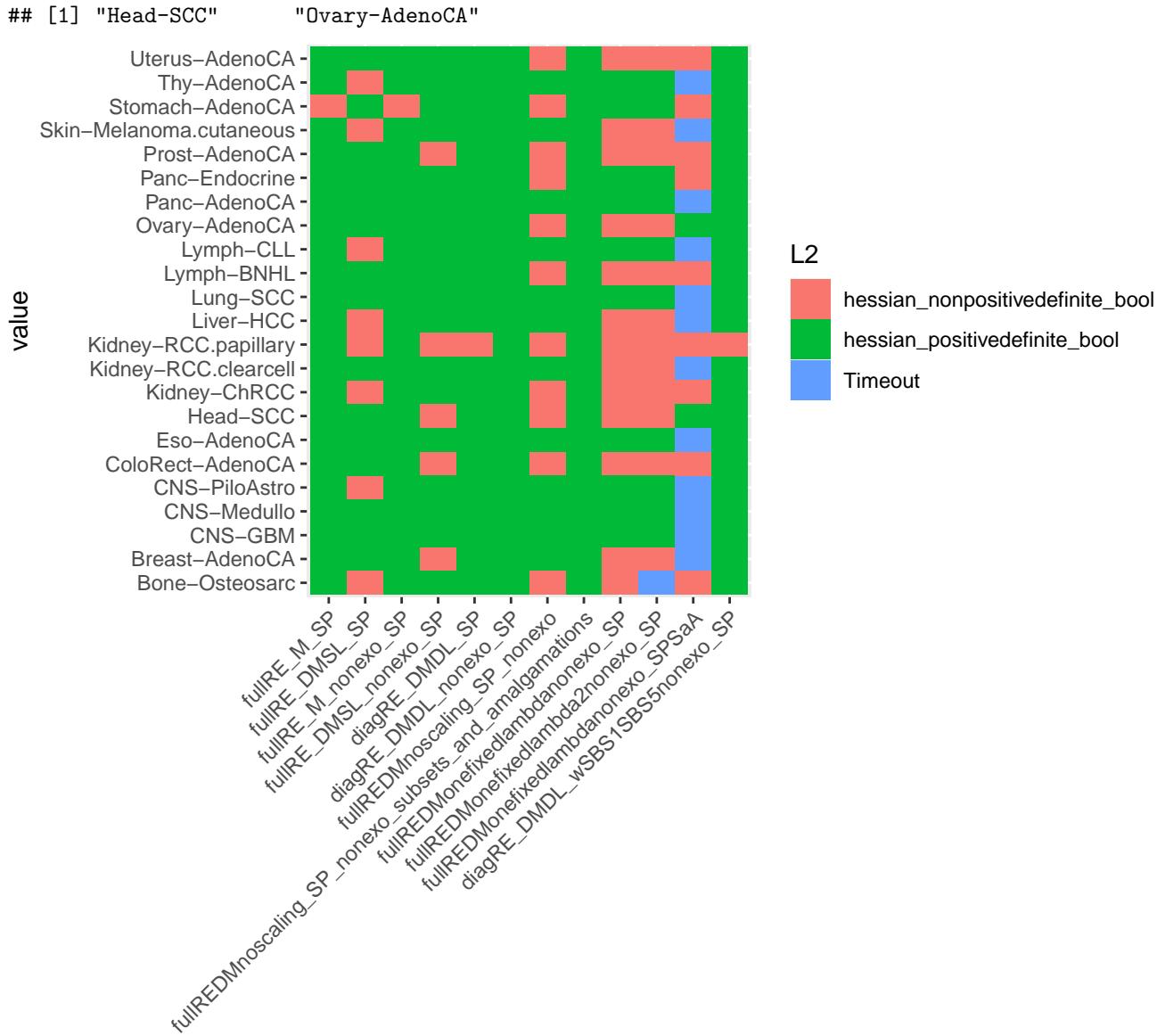
names(fullREDMonefixedlambdanonexo_SPSaA) <- names(pvals_fullREDMonefixedlambdanonexo_SP) <- names(pvals_fullRE_DMSL_nonexo_SP)
names(pvals_fullRE_DMSL_nonexo_SP) <- enough_samples

pvals_diagRE_DMDL_SP

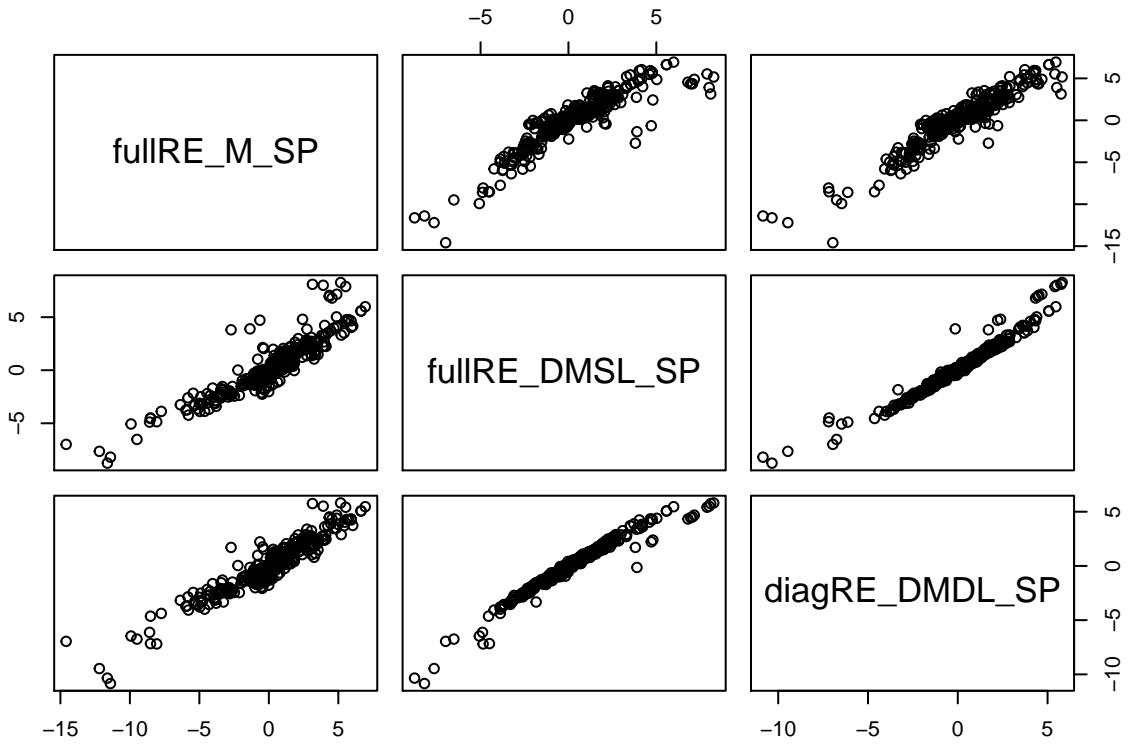
##          Bone-Osteosarc      Breast-AdenoCA          CNS-GBM
## 1.080828e-04 2.239756e-28 3.390137e-03
##          CNS-Medullo      CNS-PiloAstro      ColoRect-AdenoCA
## 8.431463e-03 5.615238e-04 6.356131e-26
##          Eso-AdenoCA        Head-SCC          Kidney-ChRCC
## 5.329093e-21 4.975610e-05 1.562125e-09
## Kidney-RCC.clearcell Kidney-RCC.papillary      Liver-HCC
## 4.027485e-18                NA 4.747822e-107
##          Lung-SCC          Lymph-BNHL          Lymph-CLL
## 7.747310e-22 3.908637e-19 6.611927e-20
##          Ovary-AdenoCA      Panc-AdenoCA      Panc-Endocrine
## 8.965185e-38 4.096402e-119 3.987099e-10
##          Prost-AdenoCA Skin-Melanoma.cutaneous      Stomach-AdenoCA
## 6.474116e-99 9.272113e-25 1.715150e-06
##          Thy-AdenoCA        Uterus-AdenoCA
## 8.821583e-06 4.819867e-10

## $Timeout
## [1] "Breast-AdenoCA"      "CNS-GBM"
## [3] "CNS-Medullo"         "CNS-PiloAstro"
## [5] "Eso-AdenoCA"         "Kidney-RCC.clearcell"
## [7] "Liver-HCC"            "Lung-SCC"
## [9] "Lymph-CLL"             "Panc-AdenoCA"
## [11] "Skin-Melanoma.cutaneous" "Thy-AdenoCA"
##
## $hessian_nonpositivedefinite_bool
## [1] "Bone-Osteosarc"      "ColoRect-AdenoCA"      "Kidney-ChRCC"
## [4] "Kidney-RCC.papillary" "Lymph-BNHL"           "Panc-Endocrine"
## [7] "Prost-AdenoCA"       "Stomach-AdenoCA"       "Uterus-AdenoCA"
##
## $hessian_positivedefinite_bool

```



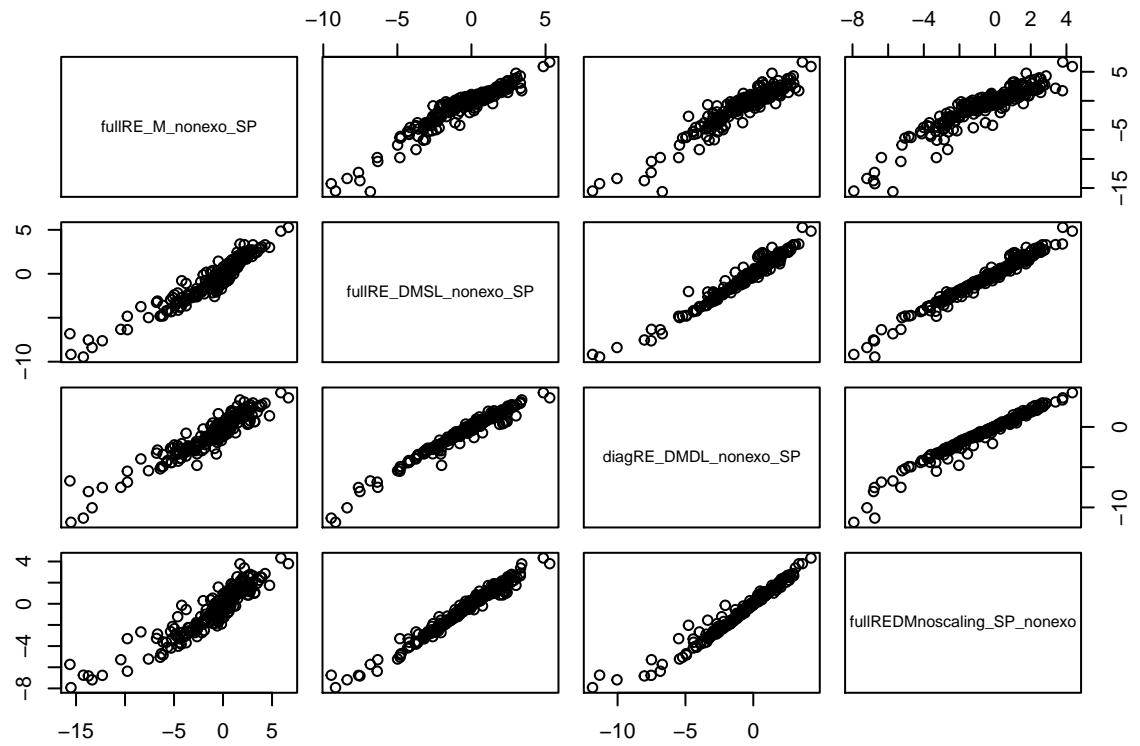
```
## comparison of betas
# give_betas(get(list_models_SP)[[1]][[1]])
all_betas_SP <- do.call('cbind', lapply(c( 'fullRE_M_SP', 'fullRE_DMSL_SP',
                                             'diagRE_DMDL_SP'), function(j) do.call('c', sapply(get(j), function(i) as.vector(give_b
colnames(all_betas_SP) <- c( 'fullRE_M_SP', 'fullRE_DMSL_SP',
                             'diagRE_DMDL_SP')
pairs(all_betas_SP)
```



```

all_betas_SP_nonexo <- do.call('cbind', lapply(c('fullRE_M_nonexo_SP','fullRE_DMSL_nonexo_SP',
                                                 'diagRE_DMDL_nonexo_SP', 'fullREDMnoscaling_SP_nonexo'), function(j) do.call('c', sapply
colnames(all_betas_SP_nonexo) <- c('fullRE_M_nonexo_SP','fullRE_DMSL_nonexo_SP',
                                         'diagRE_DMDL_nonexo_SP', 'fullREDMnoscaling_SP_nonexo')
pairs(all_betas_SP_nonexo)

```

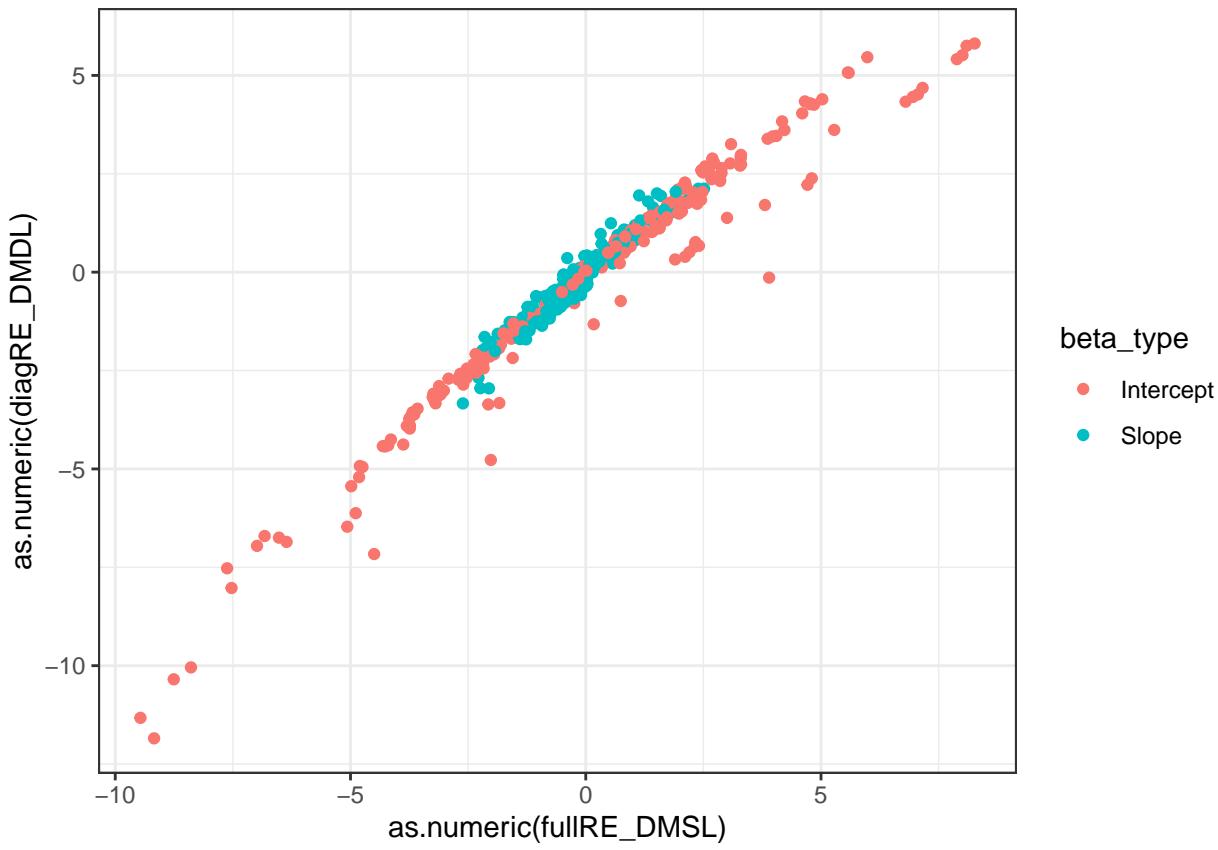


```

##   fullRE_DMSL diagRE_DMDL   fullRE_M beta_type      ct  ct2    sigs
## 1 -0.31531015 -0.1086854 -0.2237241 Slope Bone-Osteosarc B0 nonexo
## 2 -0.71770886 -0.6897242 -0.6712599 Slope Bone-Osteosarc B0 nonexo
## 3 -0.86019179 -0.7960993 -0.6637865 Slope Bone-Osteosarc B0 nonexo
## 4 -0.69897610 -0.4851852 -0.4948419 Slope Bone-Osteosarc B0 nonexo
## 5 -0.09619079  0.1160637  0.1756435 Slope Bone-Osteosarc B0 nonexo
## 6 -0.64276669 -0.4495100 -0.1553669 Slope Bone-Osteosarc B0 nonexo

## Warning: Removed 218 rows containing missing values (geom_point).

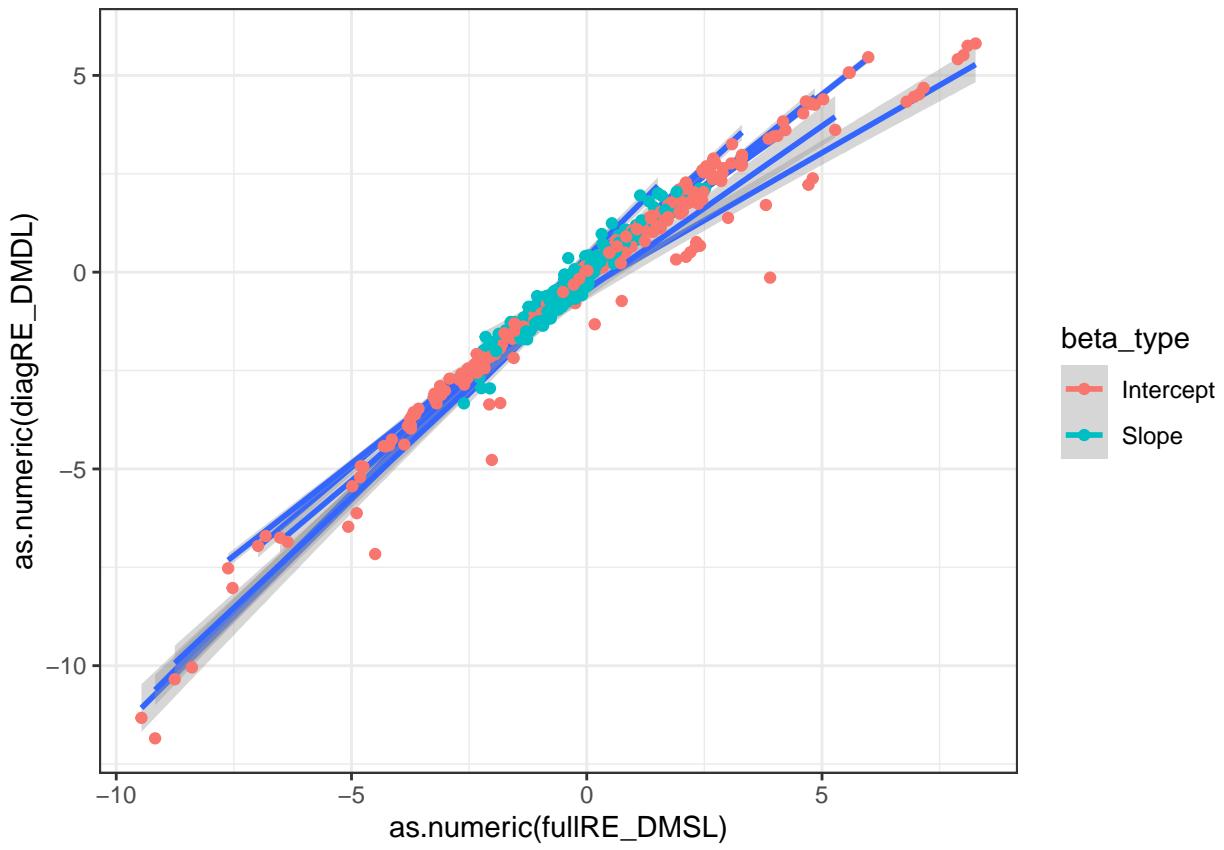
```



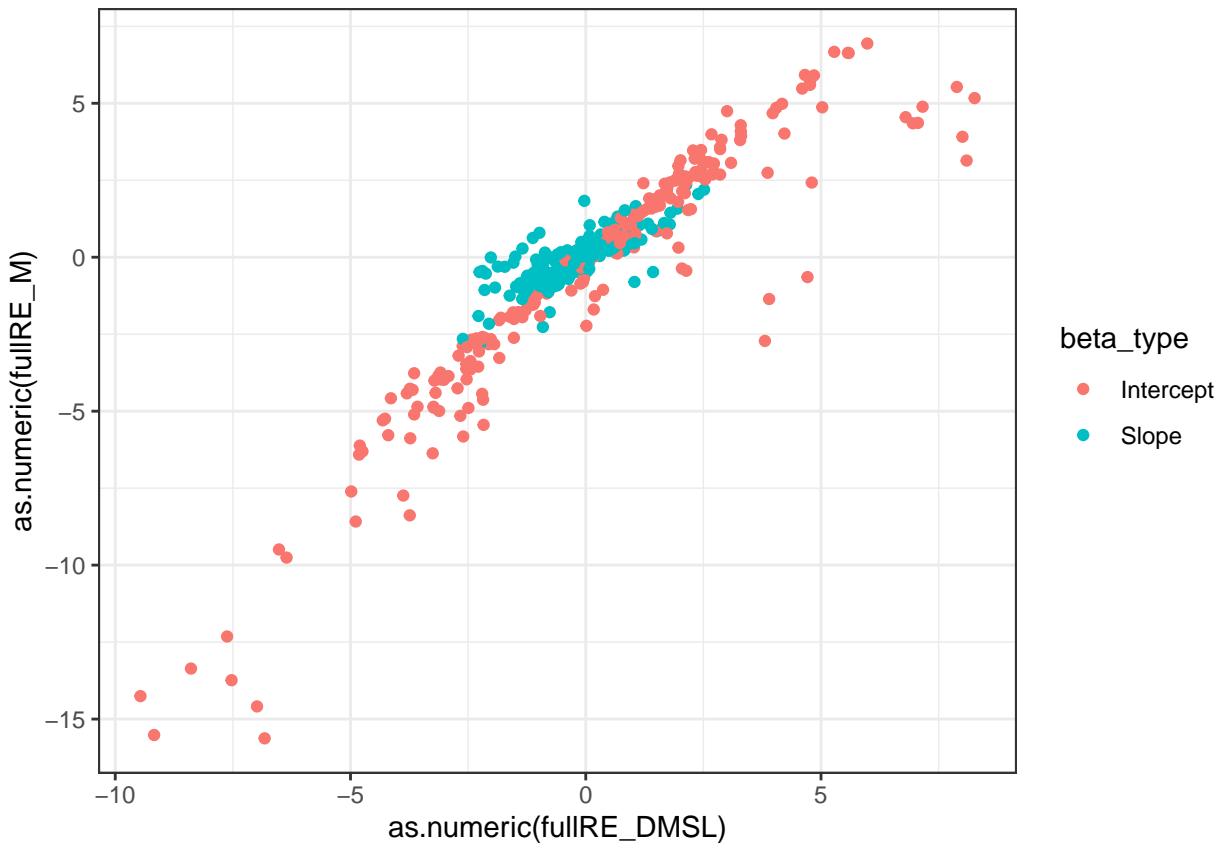
```

## `geom_smooth()` using formula 'y ~ x'
## Warning: Removed 218 rows containing non-finite values (stat_smooth).
## Warning in qt((1 - level)/2, df): NaNs produced
## Warning in max(ids, na.rm = TRUE): no non-missing arguments to max; returning
## -Inf
## Warning: Removed 218 rows containing missing values (geom_point).

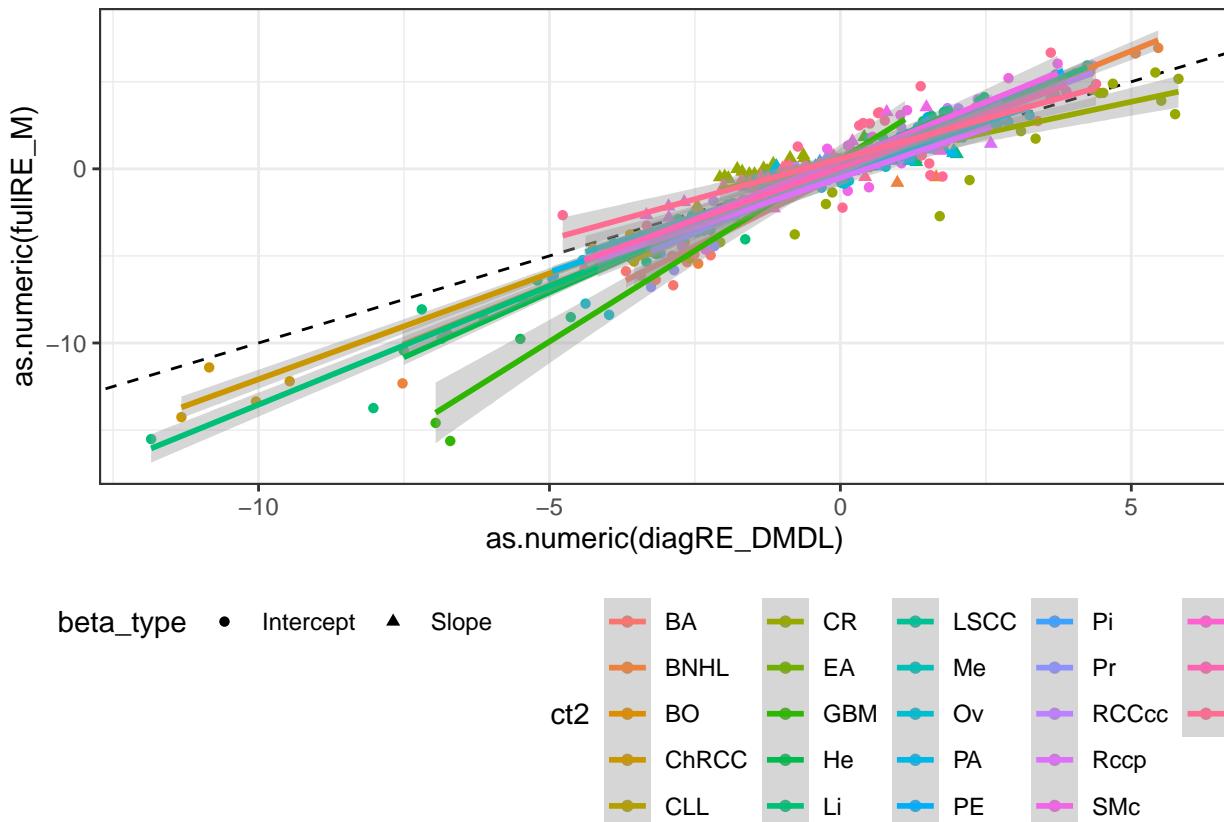
```



```
## Warning: Removed 284 rows containing missing values (geom_point).
```



```
## `geom_smooth()` using formula 'y ~ x'  
## Warning: Removed 80 rows containing non-finite values (stat_smooth).  
## Warning: Removed 80 rows containing missing values (geom_point).
```



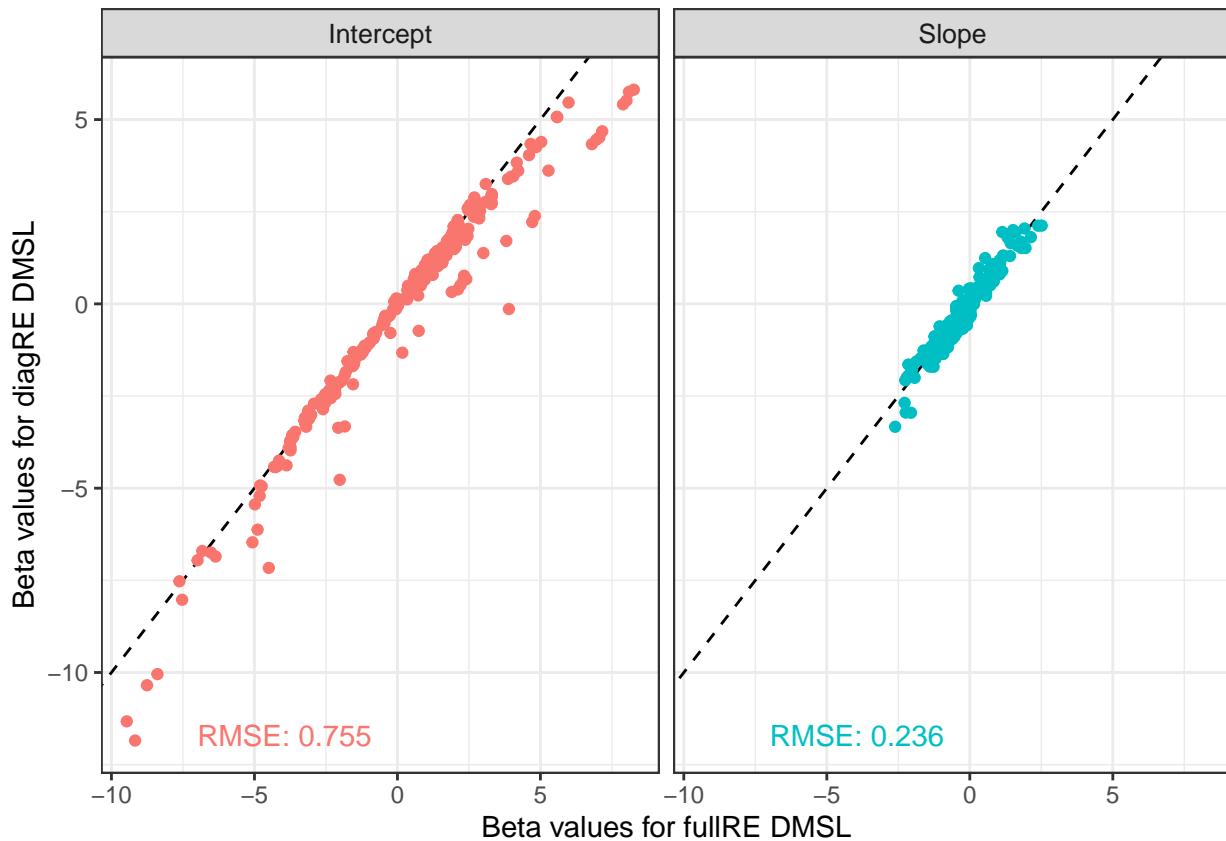
```

##   rmse_diag_full_DMSL rmse_fullDMSL_fullM beta_type
## 1      0.2362400      0.5467457     Slope
## 2      0.7551778      1.7127751 Intercept

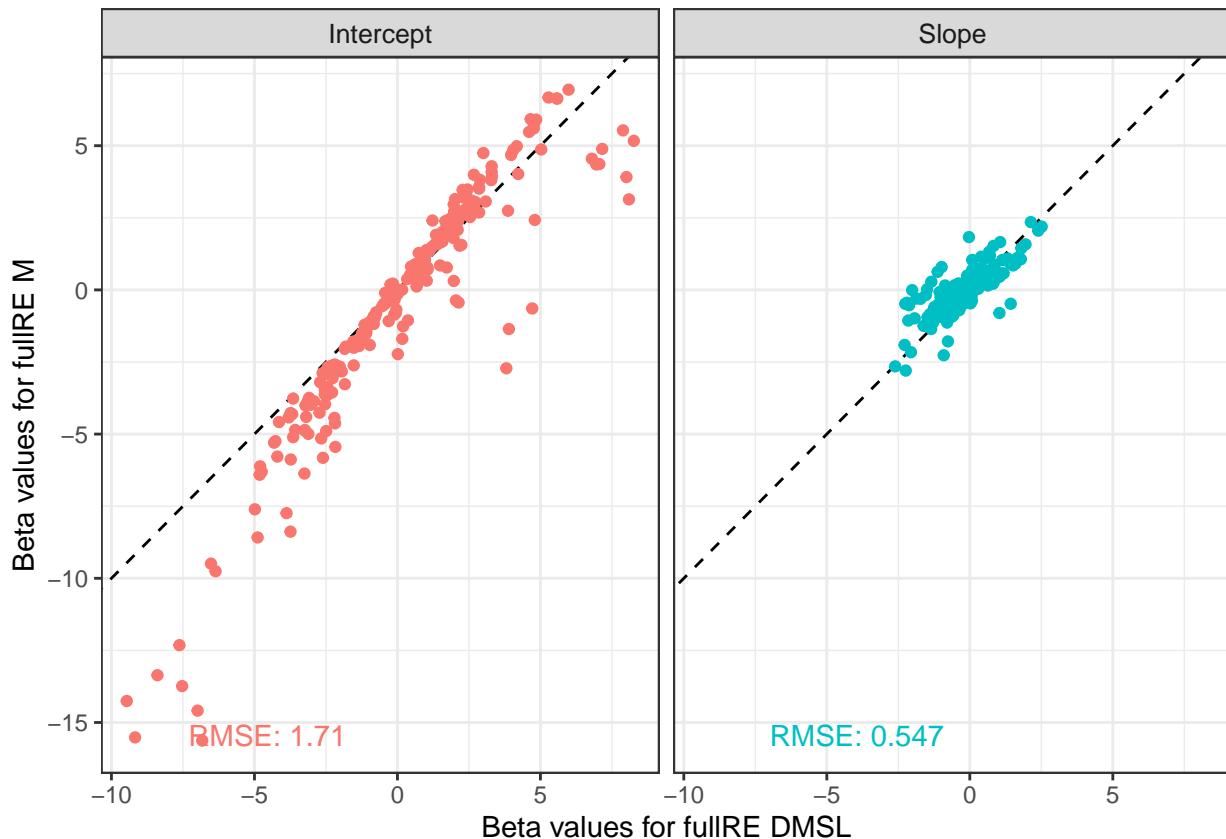
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 218 rows containing missing values (geom_point).

```



```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
## Warning: Removed 284 rows containing missing values (geom_point).
```



```

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 218 rows containing missing values (geom_point).

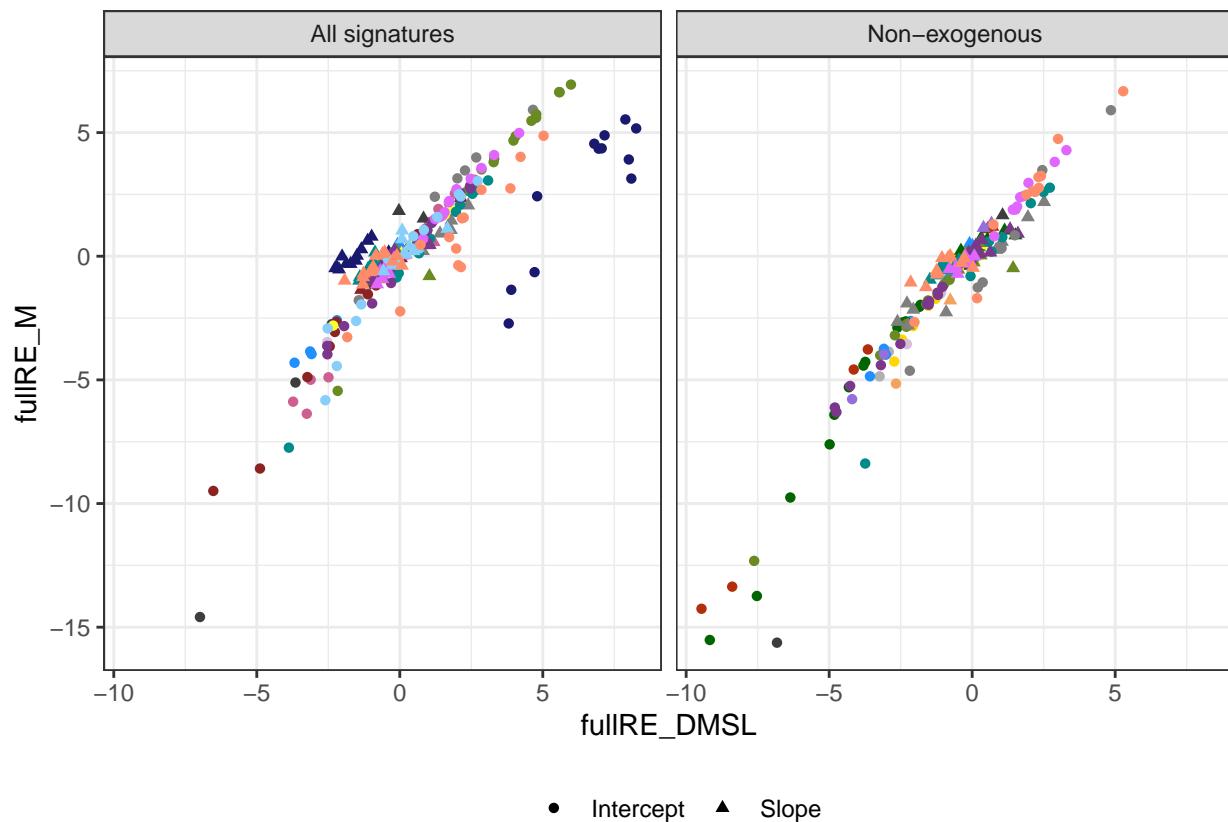
## Warning: Removed 284 rows containing missing values (geom_point).

## pdf
## 2

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

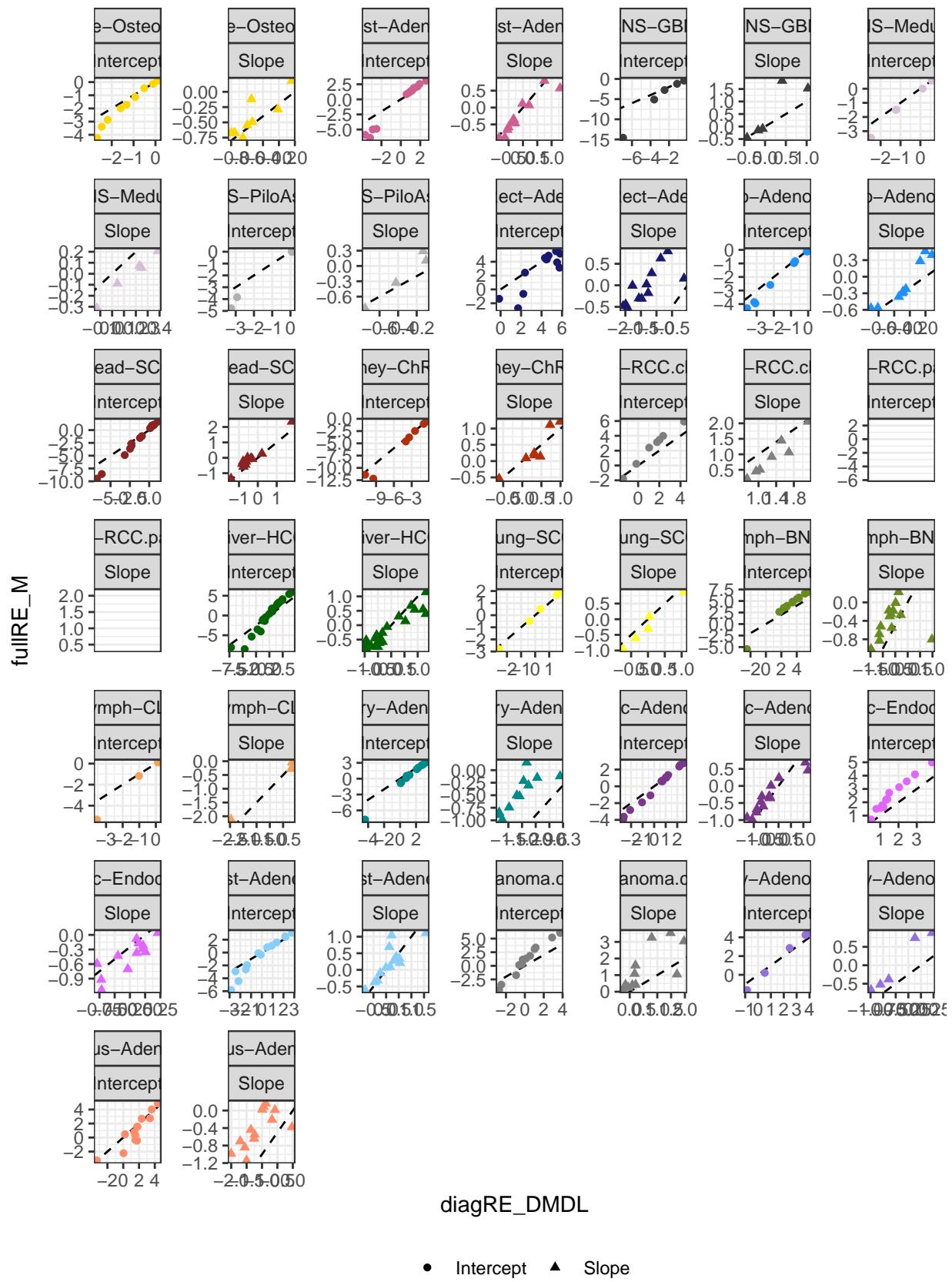
## Warning: Removed 218 rows containing missing values (geom_point).

```



Comparison of beta coefficients for fullRE M and DM

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
## Warning: Removed 14 rows containing missing values (geom_point).
```



● Intercept ▲ Slope

```

head(comparison_betas_models_rbind)

##   fullRE_DMSL diagRE_DMDL   fullRE_M beta_type          ct  ct2      sigs
## 1 -0.31531015 -0.1086854 -0.2237241 Slope Bone-Osteosarc BO Non-exogenous
## 2 -0.71770886 -0.6897242 -0.6712599 Slope Bone-Osteosarc BO Non-exogenous
## 3 -0.86019179 -0.7960993 -0.6637865 Slope Bone-Osteosarc BO Non-exogenous
## 4 -0.69897610 -0.4851852 -0.4948419 Slope Bone-Osteosarc BO Non-exogenous
## 5 -0.09619079  0.1160637  0.1756435 Slope Bone-Osteosarc BO Non-exogenous
## 6 -0.64276669 -0.4495100 -0.1553669 Slope Bone-Osteosarc BO Non-exogenous

comparison_betas_models_rbind_stats_per_ct <- rbind.data.frame(
  cbind.data.frame(comparison_betas_models_rbind %>% filter(beta_type == 'Slope') %>%
    group_by(ct) %>%
    summarise(rmse_diag_full_DMDL=sqrt(mean( (diagRE_DMDL-fullRE_DMSL)^2, na.rm = T )), 
              slope_diag_full_DMDL=as.numeric(try(coefficients(lm(y~x, data = cbind.data
                rmse_fullDMSL_fullM=sqrt(mean( (fullRE_M-fullRE_DMSL)^2, na.rm = T )), 
                slope_fullDMSL_fullM=as.numeric(try(coefficients(lm(y~x, data = cbind.data
      beta_type='Slope'),
  cbind.data.frame(comparison_betas_models_rbind %>% filter(beta_type == 'Intercept') %>%
    group_by(ct) %>%
    summarise(rmse_diag_full_DMDL=sqrt(mean( (diagRE_DMDL-fullRE_DMSL)^2, na.rm = T )), 
              slope_diag_full_DMDL=as.numeric(try(coefficients(lm(y~x, data = cbind.data
                rmse_fullDMSL_fullM=sqrt(mean( (fullRE_M-fullRE_DMSL)^2, na.rm = T )), 
                slope_fullDMSL_fullM=as.numeric(try(coefficients(lm(y~x, data = cbind.data
      beta_type='Intercept'))))

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...):
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...):
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...):
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...):
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...):
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...):
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...):
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...):
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

comparison_betas_models_rbind_stats_per_ct$ct2=renaming_pcawg[,2][match(comparison_betas_models_rbind_st

```

```

comparison_betas_models_rbind_stats_per_ct_pool_beta <- cbind.data.frame(comparison_betas_models_rbind%>%
    group_by(ct) %>%
    summarise(rmse_diag_full_DMDL=sqrt(mean( (diagRE_DMDL-fullRE_DMSL)^2, na.rm = T )), 
              slope_diag_full_DMDL=as.numeric(try(coefficients(lm(y~x, data = cbind.data,
    rmse_fullDMSL_fullM=sqrt(mean( (fullRE_M-fullRE_DMSL)^2, na.rm = T )), 
    slope_fullDMSL_fullM=as.numeric(try(coefficients(lm(y~x, data = cbind.data

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...) :
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...) :
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...) :
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...) :
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

comparison_betas_models_rbind_stats_per_ct_pool_beta$ct2=renaming_pcawg[,2] [match(comparison_betas_models

pcawg_palette <- pcawg.colour.palette(gsub("\\\\..*", "", comparison_betas_models_rbind_stats_per_ct$ct),
                                         scheme = "tumour_subtype")
pcawg_palette[names(pcawg_palette) == 'Lung-SCC'] <- '#ffff29'
names(pcawg_palette) <- comparison_betas_models_rbind_stats_per_ct$ct

ggplot(comparison_betas_models_rbind, aes(x=as.numeric(fullRE_DMSL), y=as.numeric(fullRE_M), col=ct))+
  geom_abline(slope = 1, intercept = 0, lty='dashed')+theme_bw()+
  geom_point() + theme_bw() +
  facet_wrap(~beta_type) +
  labs(x='Beta values for fullRE DMSL', y='Beta values for fullRE M')+
  geom_smooth(aes(group=ct2), method = "lm")+
  theme(legend.title=element_blank(),
        strip.text.x = element_text(size = 10),
        legend.text=element_text(size=10), legend.position = "bottom") + guides(col=FALSE) +
  scale_color_manual(values = pcawg_palette)

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## `geom_smooth()` using formula 'y ~ x'

## Warning: Removed 284 rows containing non-finite values (stat_smooth).

## Warning in qt((1 - level)/2, df): NaNs produced

## Warning in qt((1 - level)/2, df): NaNs produced

## Warning in qt((1 - level)/2, df): NaNs produced

## Warning in qt((1 - level)/2, df): NaNs produced

## Warning in qt((1 - level)/2, df): NaNs produced

```

```

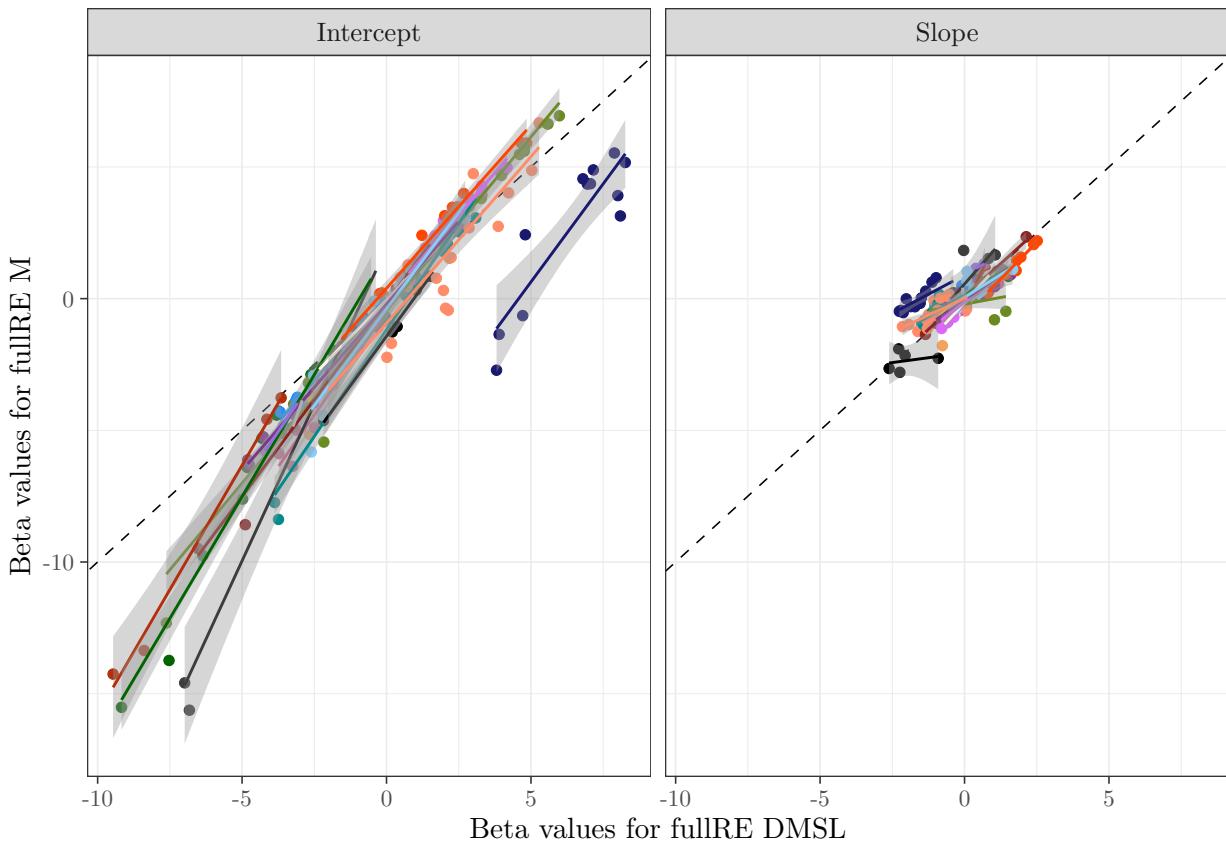
## Warning: Removed 284 rows containing missing values (geom_point).
## Warning in max(ids, na.rm = TRUE): no non-missing arguments to max; returning
## -Inf

## Warning in max(ids, na.rm = TRUE): no non-missing arguments to max; returning
## -Inf

## Warning in max(ids, na.rm = TRUE): no non-missing arguments to max; returning
## -Inf

## Warning in max(ids, na.rm = TRUE): no non-missing arguments to max; returning
## -Inf

```



```

# ggplot(comparison_betas_models_rbind_stats_per_ct_pool_beta, aes(x=rmse_fullDMSL_fullM,
# #                                     y=slope_fullDMSL_fullM, col=ct, label=ct2))+ 
#   geom_point()+geom_label_repel()+theme_bw()+labs(x='RMSE of betas between\nfullDMSL and fullM',
# #                                     y = 'Slope of linear model of betas\n(fullDMSL ~ fullM)')

# ggplot(comparison_betas_models_rbind_stats_per_ct, aes(x=rmse_fullDMSL_fullM,
# #                                     y=slope_fullDMSL_fullM, col=ct, label=ct))+ 
#   geom_point()+geom_label_repel()+theme_bw()+labs(x='RMSE of betas between\nfullRE DMSL and fullRE M',
# #                                     y = 'Slope of linear model of betas\n(fullRE DMSL ~ fullRE M)')
#   facet_wrap(~beta_type)+theme(strip.text.x = element_text(size = 10))

```

```

# head(comparison_betas_models_rbind_stats_per_ct)

ggplot(comparison_betas_models_rbind_stats_per_ct, aes(x=rmse_fullDMSL_fullM,
                                                       y=slope_fullDMSL_fullM, col=ct, label=ct))+
  geom_point() + geom_label_repel() + theme_bw() + labs(x='RMSE of betas between\nfullRE DMSL and fullRE M',
                                                       y = 'Slope of linear model of betas\n(fullRE DMSL ~ fullRE M)') +
  facet_wrap(~beta_type) + theme(strip.text.x = element_text(size = 10)) +
  scale_color_manual(values = pcawg_palette)

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

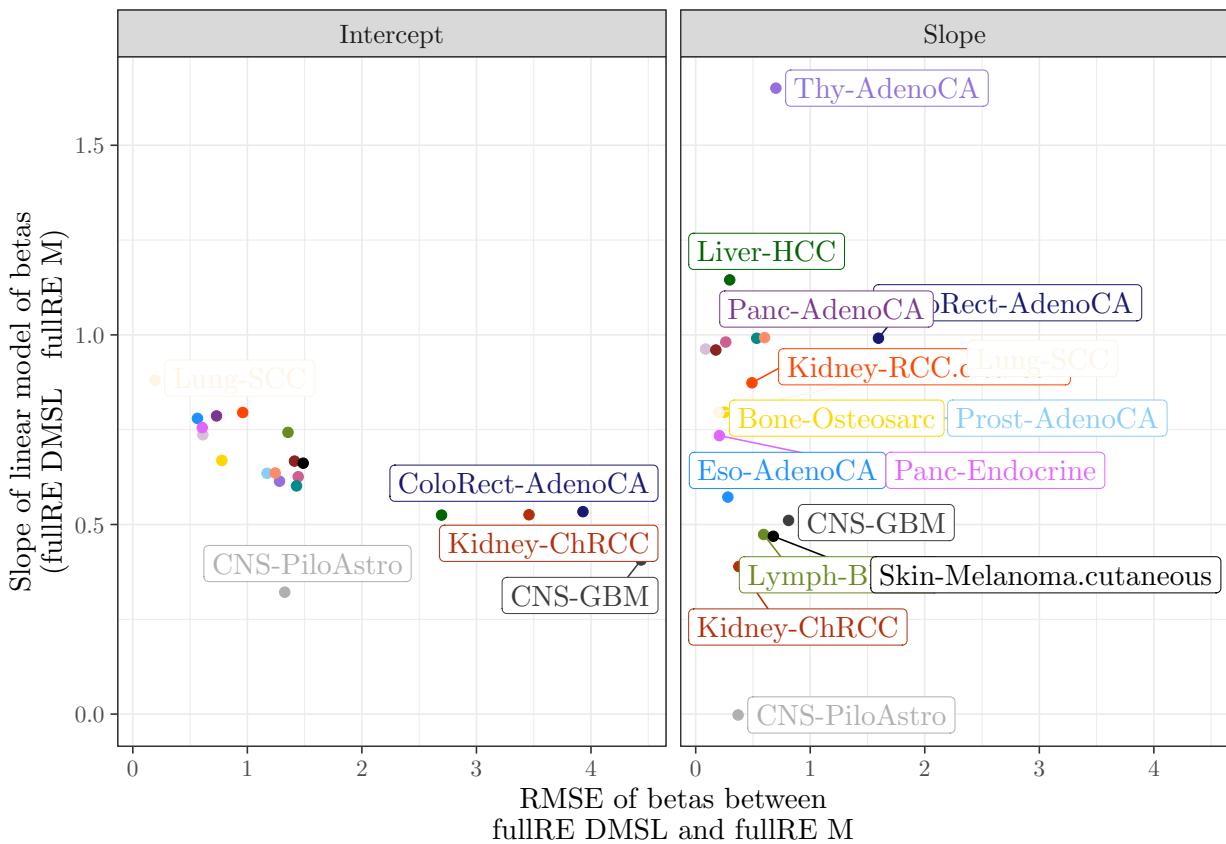
## Warning: Removed 6 rows containing missing values (geom_point).

## Warning: Removed 6 rows containing missing values (geom_label_repel).

## Warning: ggrepel: 15 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

## Warning: ggrepel: 5 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

```



```

tikz( 'summary_TMB_PCAWG_SP_files/figure-latex/beta_coef_differences_in_models_plots_tikz2.tex',
      height = 2.5, width=5.5)
cowplot::plot_grid(ggplot(comparison_betas_models_rbind_cut, aes(x=fullRE_DMSL, y=fullRE_M, col=ct, shape=ct),
                           geom_abline(slope = 1, intercept = 0, lty='dashed'))+

```

```

geom_point() + theme_bw() + facet_wrap(~sigs) +
scale_color_manual(values = pcawg_palette) + guides(col=F, shape=F) +
labs(shape='', x='fullRE DMSL', y='fullRE M'), #+theme(legend.position = "bottom"),
ggplot(comparison_betas_models_rbind_cut, aes(x=fullRE_DMSL, y=diagRE_DMDL, col=ct, shape=beta_type)) +
  geom_abline(slope = 1, intercept = 0, lty='dashed') +
geom_point() + theme_bw() + facet_wrap(~sigs) +
scale_color_manual(values = pcawg_palette) + guides(col=F, shape=F) +
labs(shape='', x='fullRE DMSL', y='diagRE DMDL'), rel_widths = c(1, 1), ncol = 2)

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 218 rows containing missing values (geom_point).

## Warning: Removed 218 rows containing missing values (geom_point).

dev.off()

## tikz output
##          2

tikz('summary_TMB_PCAWG_SP_files/figure-latex/beta_coef_differences_in_models_plots_tikz3.tex',
      height = 2.5, width=5.5)
ggplot(comparison_betas_models_rbind_stats_per_ct, aes(x=rmse_fullDMSL_fullM,
                                                       y=slope_fullDMSL_fullM, col=ct, label=ct)) +
  geom_point() + geom_label_repel() + theme_bw() + labs(x='RMSE of betas between\nfullRE DMSL and fullRE M',
                                                       y = 'Slope of linear model of betas\n(fullRE DMSL ~ ful
  facet_wrap(~beta_type) + theme(strip.text.x = element_text(size = 10)) +
  scale_color_manual(values = pcawg_palette) #+theme(legend.position = "bottom")

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 6 rows containing missing values (geom_point).

## Warning: Removed 6 rows containing missing values (geom_label_repel).

## Warning: ggrepel: 18 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

## Warning: ggrepel: 17 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

dev.off()

## tikz output
##          2

head(comparison_betas_models_rbind_stats_per_ct)

##           ct rmse_diag_full_DMDL slope_diag_full_DMDL rmse_fullDMSL_fullM
## 1 Bone-Osteosarc      0.18479169      0.85364222      0.25351523
## 2 Breast-AdenoCA     0.10332852      0.91205139      0.26250850
## 3 CNS-GBM             0.28542654      1.01099718      0.81084551

```

```

## 4      CNS-Medullo      0.09067728      0.94821655      0.08629327
## 5      CNS-PiloAstro    0.32907695     -0.00807609      0.37025033
## 6 ColoRect-AdenoCA    0.24657998      0.95097590      1.59564225
## slope_fullDMSL_fullM beta_type ct2
## 1      0.796157804    Slope  B0
## 2      0.981125224    Slope  BA
## 3      0.510734188    Slope  GBM
## 4      0.962647186    Slope  Me
## 5      -0.002269125   Slope  Pi
## 6      0.991218105   Slope  CR

tikz( 'summary_TMB_PCAWG_SP_files/figure-latex/beta_coef_differences_in_models_plots_tikz3b.tex',
       height = 2.5, width=5.5)
ggplot(comparison_betas_models_rbind_stats_per_ct, aes(x=rmse_fullDMSL_fullM,
                                                       y=rmse_diag_full_DMDL, col=ct, label=ct))+
  geom_point() + geom_label_repel(size=3) + theme_bw() +
  # labs(x='RMSE of betas between\nfullRE DMSL and fullRE M',
  #       y = 'Slope of linear model of betas\n(fullRE DMSL ~ j'
  guides(col=F) +
  labs(x='rmse fullDMSL fullM', y='rmse diag full DMDL') +
  facet_wrap(~beta_type, scales="free") + theme(strip.text.x = element_text(size = 10)) +
  scale_color_manual(values = pcawg_palette) #+theme(legend.position = "bottom")

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 4 rows containing missing values (geom_point).

## Warning: Removed 4 rows containing missing values (geom_label_repel).

## Warning: ggrepel: 16 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

## Warning: ggrepel: 13 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

dev.off()

## tikz output
##      2

## `summarise()` has grouped output by 'ct'. You can override using the `groups` argument.
## `summarise()` has grouped output by 'ct'. You can override using the `groups` argument.

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## pdf
##      2

```

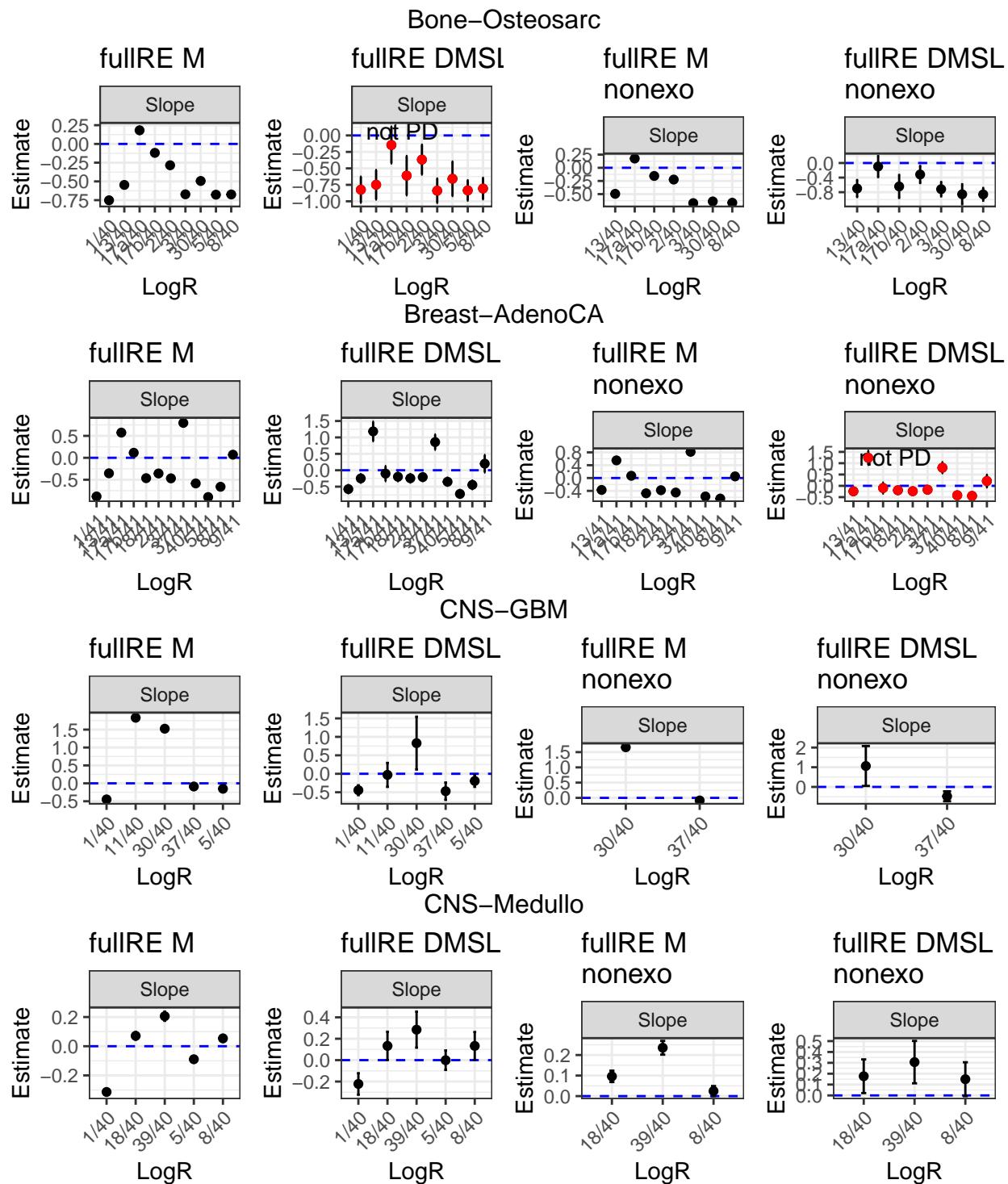
differences between signatures from sigprofiler from the paper, and the ones I get

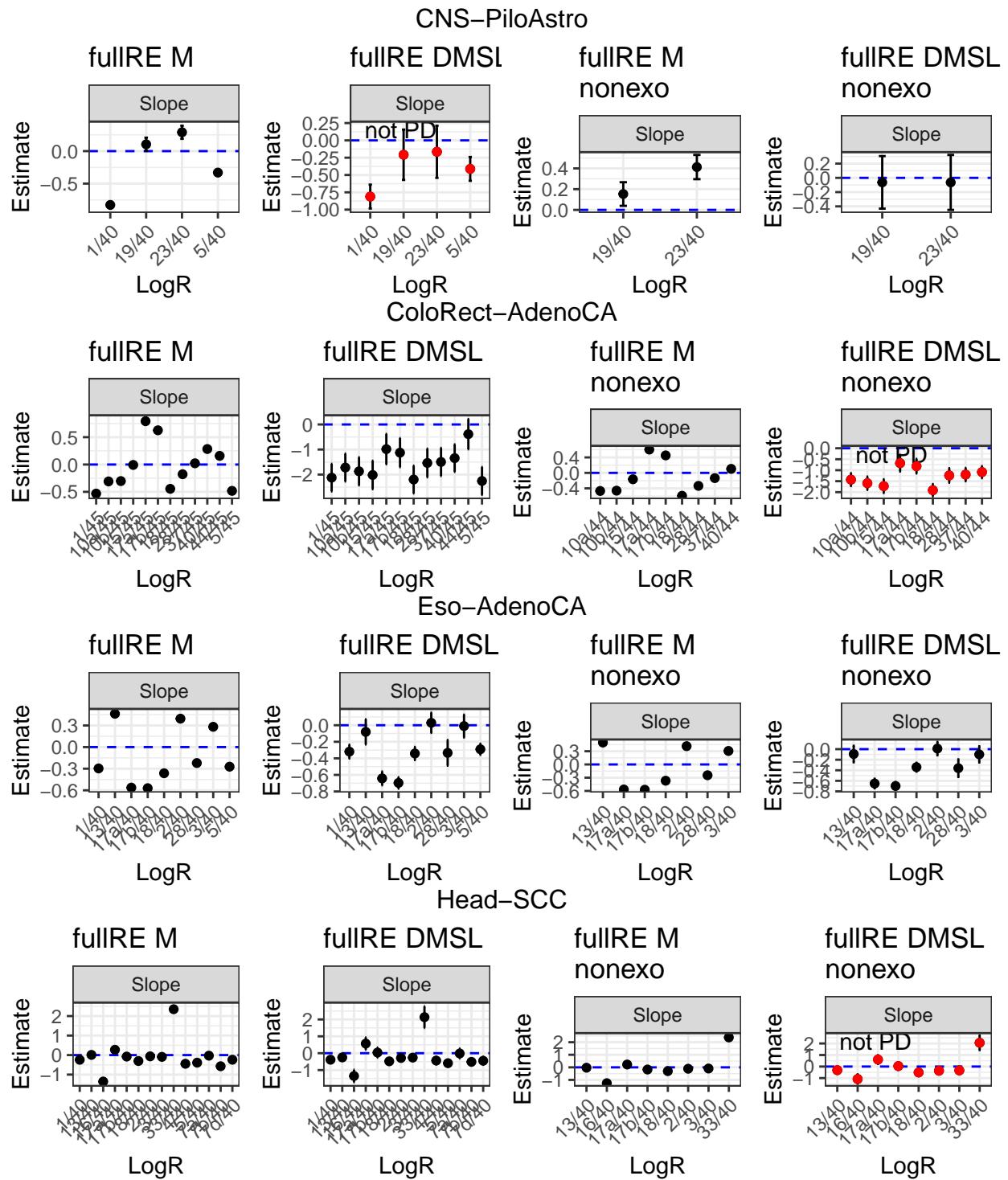
See Rmd signatures\_from\_PCAWG\_paper.Rmd for the figures

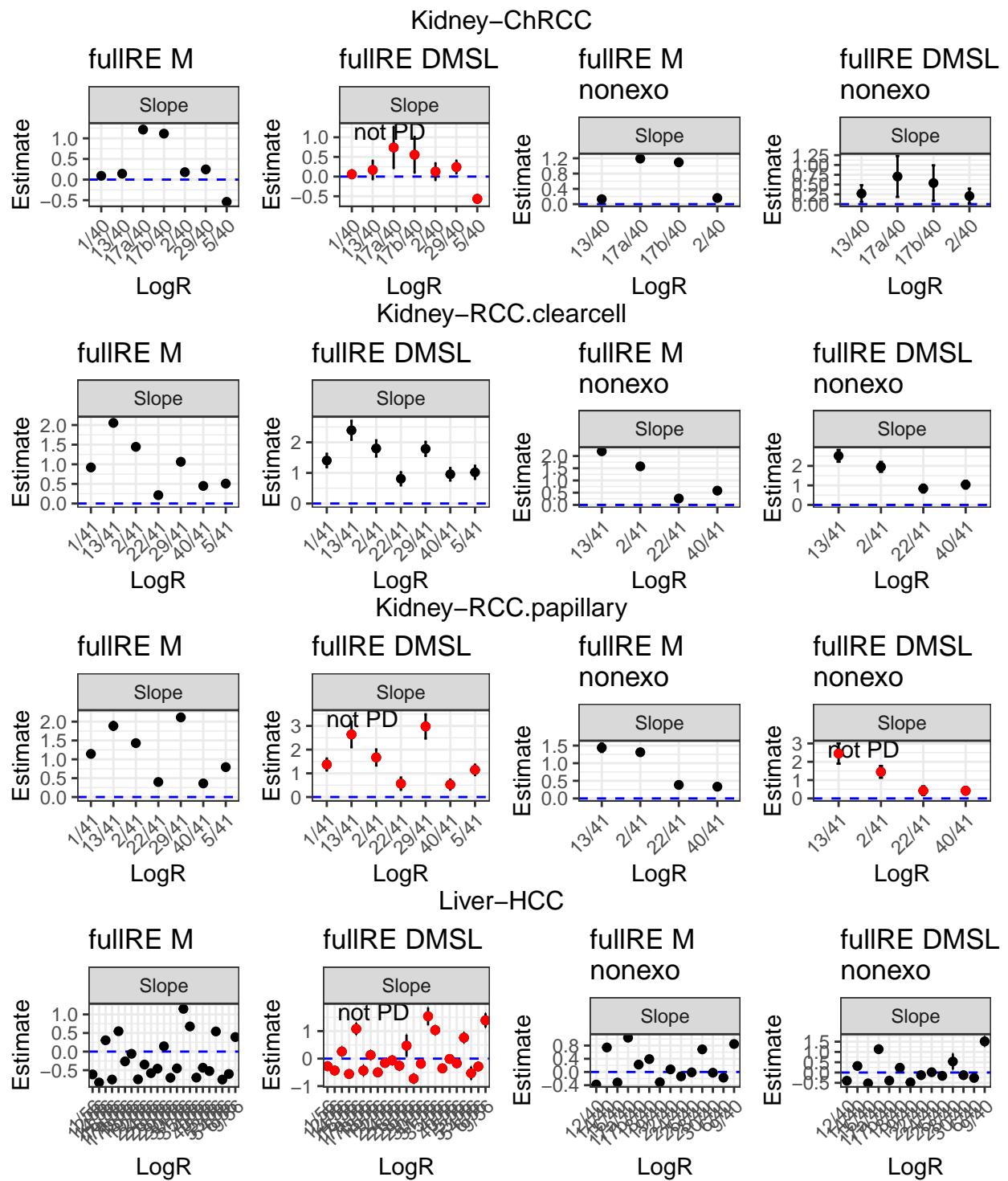
- biliary adenoca similar, though not exact
- bladder tcc: very similar
- bone benign: similar

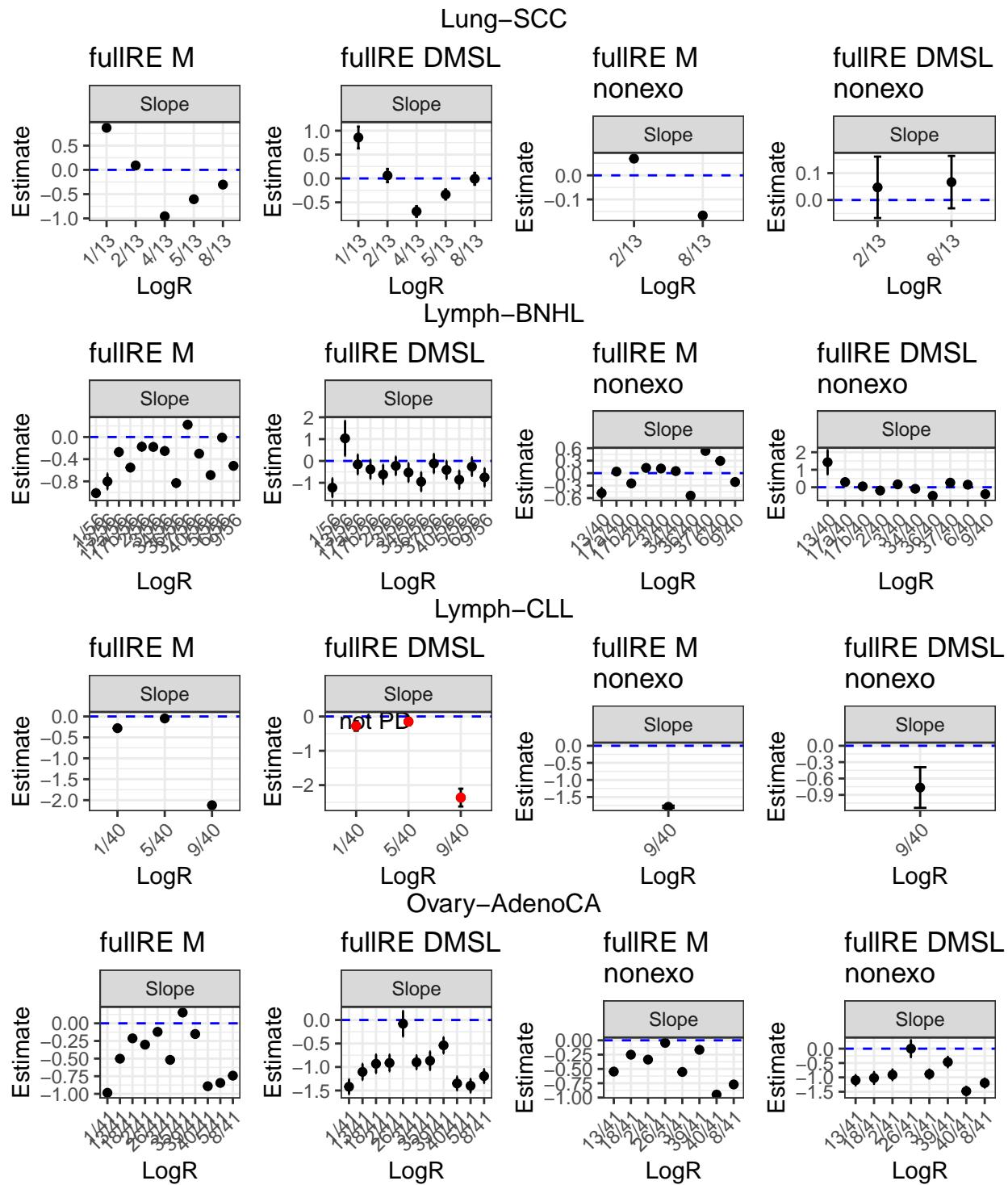
- bone epith: extremely similar
- bone osteosarc: I have a lot of SBS8, which they don't. Other than that, similar
- breast adenicaL I have a lot of SBS9, which they don't. Other than that, similar
- breast DCIS: I have more SBS40 than they do
- breast lobularca: very similar
- cervix adenoca: very similar
- cervix SCC: very similar, although I have more SBS40
- CNS GBM: very similar, mine seem to be more homogeneous
- CNS medullo: very similar, mine seem to be more homogeneous
- CNS oligo: very similar, mine seem to be more homogeneous
- CNS piloastro: very similar, mine seem to be more homogeneous
- Colorect adenoca: quite similar
- eso adenoca: very similar
- head scc: very similar, mine seem to be more homogeneous
- kidney chrc: very similar
- kidney rcc.clearcell: very similar, although I have more SBS29
- kidney papillary: only I have it
- liver hcc: different. I have a lot of SBS40 and SBS12, they have mostly SBS5 \*\*\*
- lung adenoca: very similar
- lung SCC: very similar, though I have more SBS8
- lymph BNHL: very similar
- Lymph CLL: very similar, althpugh theirs are much more sparse
- myeloid AML: very similar, although I don't have any SBS60 and they seem to have
- myeloid MDS: I don't have it
- myeloid MPN: similar, although mine is much more sparse
- ovary adenoca: different. I have a lot of SBS40, which in their case is rare, and they have much more of SBS3 than I do \*\*\*
- panc-adenoca: different. I have a lot of SBS8 that they don't have. \*\*\*
- panc-endocrine: sort of similar. I have more SBS8 than they and they have more SBS5
- Prost-adenoca: sort of similar, I have more SBS8
- skin-melanoma.acral: they don't have this category. They have "skin-melanoma", which might be both together? (!!!) Similar exposures...
- softtissue-leiomyo: very similar exposures
- softtissue-liposarc: very similar exposures
- stomach adenoca: very similar, mine seem to be more homogeneous
- thy-adenoca: very similar
- uterus-adenoca: very similar

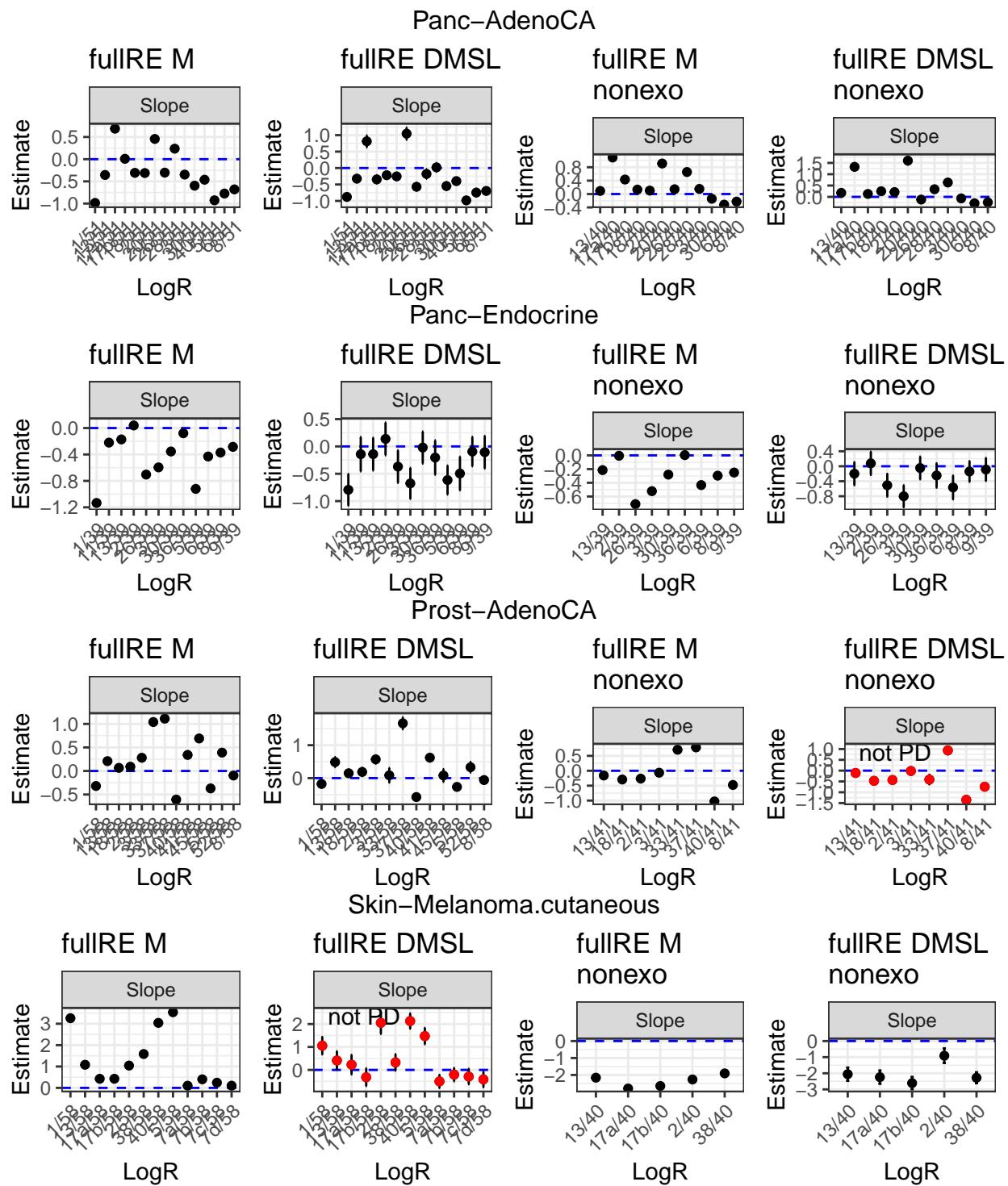
## Betas from PCAWG subset of signatures

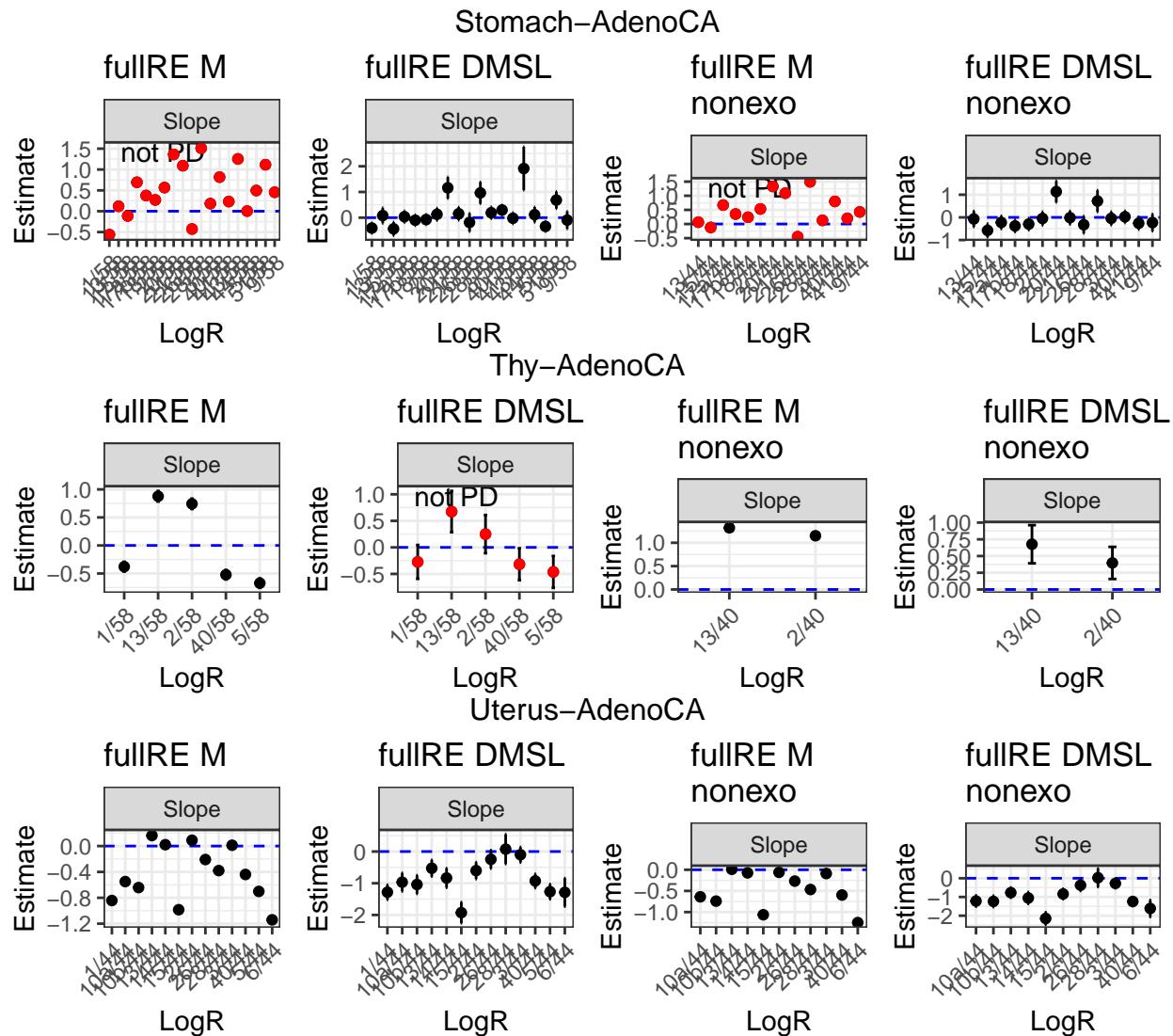












## Overdispersion parameters in double-lambda DM

```

ovrdisp <- do.call('rbind.data.frame', lapply(1:length(diagRE_DMDL_nonexo_SP), try(function(idx){
  if(diagRE_DMDL_nonexo_SP[[idx]]$pdHess){
    cbind.data.frame( plot_lambdas(diagRE_DMDL_nonexo_SP[[idx]], return_df=T, plot=F), ct=names(diagRE_DM
} else{
  c(NA, NA)
}
})))
ovrdisp[ovrdisp$name == 'Lambda 1','name'] = 'Early'
ovrdisp[ovrdisp$name == 'Lambda 2','name'] = 'Late'

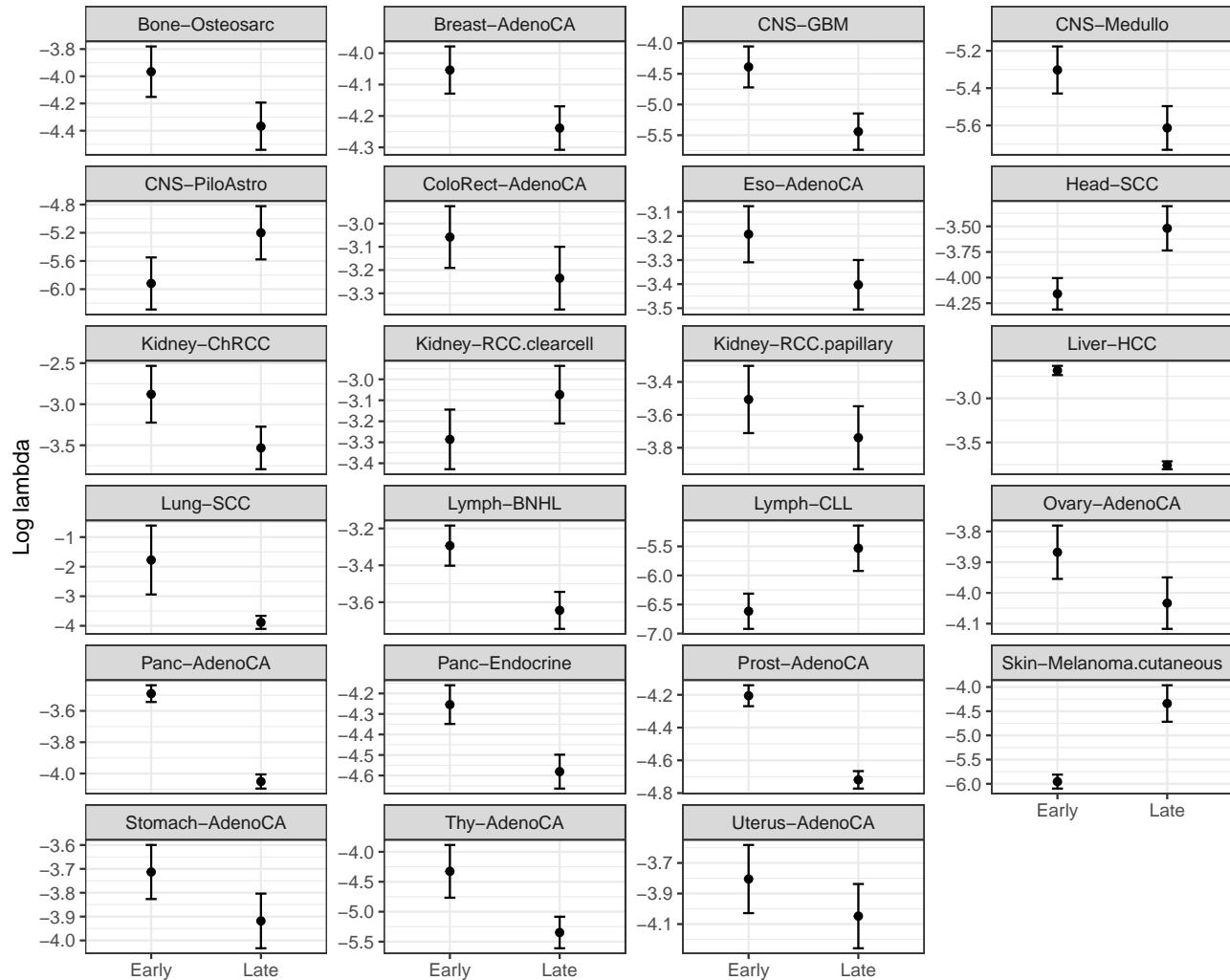
ggplot(ovrdisp, aes(x=name, y=Estimate))+
  geom_point()+
  geom_errorbar(aes(ymin=Estimate-Std..Error,

```

```

  ymax=`Estimate`+`Std..Error`), width=.1)+
theme_bw()+
facet_wrap(~ct, scales = "free_y", nrow=6)+
labs(x=' ', y='Log lambda')

```



Test for differential precision (1/overdispersion) parameter

```

differential_precision <- p.adjust(sapply(diagRE_DMDL_nonexo_SP, wald_TMB_wrapper_overdisp), method = 'fdr')
names(differential_precision) <- names(diagRE_DMDL_nonexo_SP)
sort(differential_precision)

```

|    |                |              |                         |
|----|----------------|--------------|-------------------------|
| ## | Liver-HCC      | Panc-AdenoCA | Skin-Melanoma.cutaneous |
| ## | 5.160159e-58   | 7.096293e-18 | 9.923539e-09            |
| ## | Prost-AdenoCA  | Lung-SCC     | Head-SCC                |
| ## | 1.219769e-07   | 1.139987e-05 | 8.968677e-02            |
| ## | Panc-Endocrine | CNS-GBM      | Lymph-CLL               |
| ## | 8.968677e-02   | 1.094428e-01 | 1.257732e-01            |
| ## | Thy-AdenoCA    | Lymph-BNHL   | CNS-Medullo             |
| ## | 1.332616e-01   | 1.707526e-01 | 2.670091e-01            |

```

##          Breast-AdenoCA      Kidney-ChRCC      CNS-PiloAstro
##          3.645074e-01      3.883654e-01      4.524310e-01
##          Stomach-AdenoCA     Uterus-AdenoCA     Bone-Osteosarc
##          4.524310e-01      4.524310e-01      4.745719e-01
##          Eso-AdenoCA        Ovary-AdenoCA      Kidney-RCC.clearcell
##          4.815932e-01      4.979627e-01      5.431631e-01
##          ColoRect-AdenoCA   Kidney-RCC.papillary
##          6.589716e-01      6.806308e-01



|    | Liver-HCC     | Lung-SCC                | Panc-AdenoCA |
|----|---------------|-------------------------|--------------|
| ## | 5.160159e-58  | 1.139987e-05            | 7.096293e-18 |
| ## | Prost-AdenoCA | Skin-Melanoma.cutaneous |              |
| ## | 1.219769e-07  | 9.923539e-09            |              |



```

ovrdisp$differentially_abundant = ifelse(ovrdisp$ct %in% names(differential_precision[(differential_precision <= 0.05)]), 1, 0)
ovrdisp$differentially_abundant
```

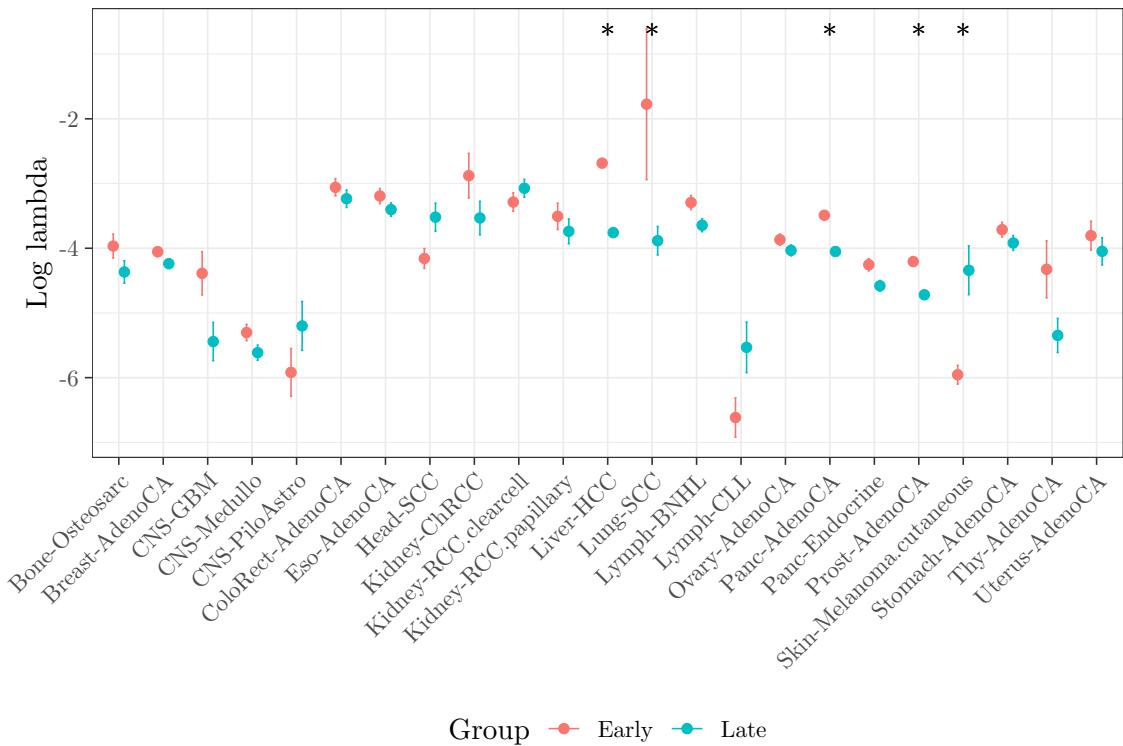


```

## [1] ""  ""  ""  ""  ""  ""  ""  ""  ""  ""  ""  ""  ""  ""  ""  ""  ""
## [20] ""  ""  "*"  "*"  "*"  "*"  ""  ""  ""  ""  ""  "*"  "*"  ""  ""  "*"
## [39] "*"  "*"  ""  ""  ""  ""  ""  ""

ggplot(ovrdisp, aes(x=ct, y=Estimate, group=name, col=name))+
  geom_point(position=position_dodge(width=0.5))+
  geom_errorbar(aes(ymin=Estimate-Std..Error,
                     ymax=Estimate+Std..Error), width=.1, position=position_dodge(width=0.5))+
  theme_bw()+
  geom_text(aes(y=Inf, label=differentially_abundant, vjust=1.8), col='black')+
  theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+
  labs(x=' ', y='Log lambda', col='Group')+theme(legend.position = "bottom")+
  theme(
    legend.margin=margin(0,0,0,0),
    legend.box.margin=margin(-10,-10,-10,-10),
    plot.margin = unit(c(1,1,1,1), "cm"))
```


```



Test for differential precision (1/overdispersion) parameter

```
differential_precision_2 <- p.adjust(sapply(diagRE_DMDL_nonexo_SP, ttest_TMB_wrapper_overdisp), method = "BH")
names(differential_precision_2) <- names(diagRE_DMDL_nonexo_SP)
sort(differential_precision_2)
```

|    |                         |                      |                  |
|----|-------------------------|----------------------|------------------|
| ## | Liver-HCC               | Panc-AdenoCA         | Prost-AdenoCA    |
| ## | 8.145123e-24            | 2.860615e-07         | 1.126237e-04     |
| ## | Skin-Melanoma.cutaneous | CNS-GBM              | Head-SCC         |
| ## | 1.723631e-02            | 2.834265e-01         | 2.834265e-01     |
| ## | Lymph-BNHL              | Panc-Endocrine       | Lung-SCC         |
| ## | 2.834265e-01            | 2.834265e-01         | 3.053481e-01     |
| ## | Lymph-CLL               | Thy-AdenoCA          | Breast-AdenoCA   |
| ## | 3.053481e-01            | 3.147768e-01         | 3.578140e-01     |
| ## | CNS-Medullo             | Bone-Osteosarc       | Kidney-ChRCC     |
| ## | 3.578140e-01            | 4.331744e-01         | 4.331744e-01     |
| ## | CNS-PiloAstro           | Eso-AdenoCA          | Ovary-AdenoCA    |
| ## | 4.352908e-01            | 4.352908e-01         | 4.352908e-01     |
| ## | Stomach-AdenoCA         | Kidney-RCC.clearcell | ColoRect-AdenoCA |
| ## | 4.502790e-01            | 5.128995e-01         | 5.601231e-01     |
| ## | Kidney-RCC.papillary    | Uterus-AdenoCA       |                  |
| ## | 5.770837e-01            | 5.770837e-01         |                  |

```
table(differential_precision_2 <= 0.05)
```

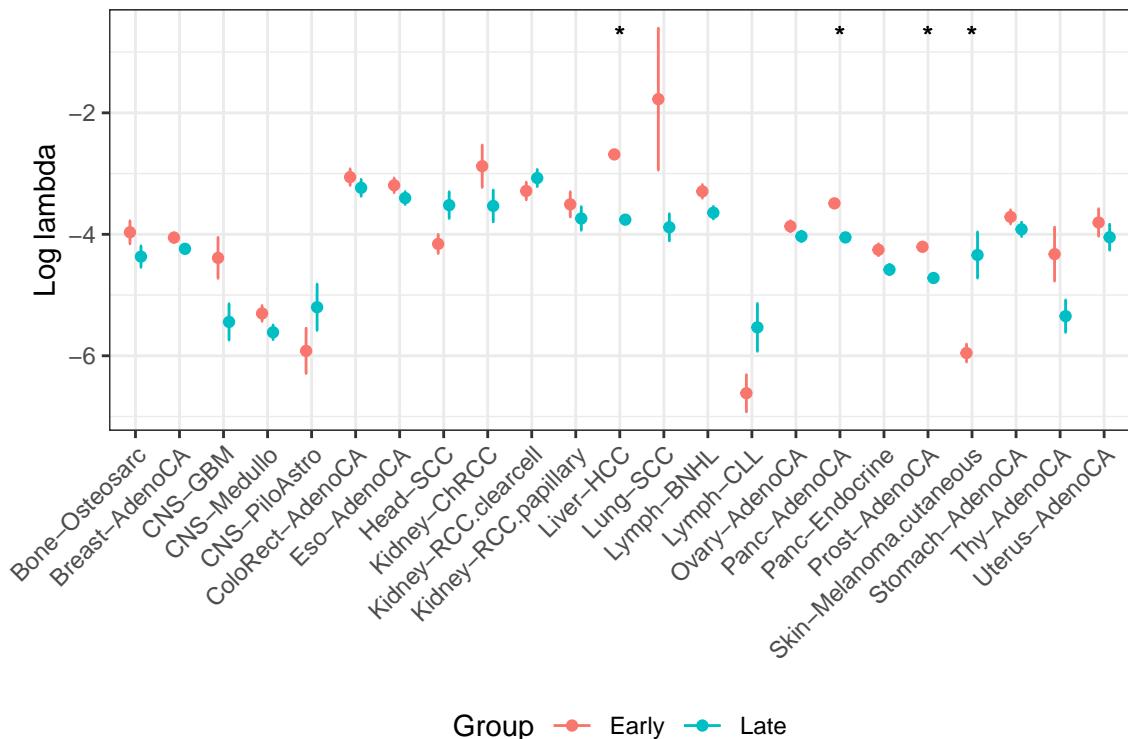
```
##
## FALSE TRUE
## 19 4
```

```
differential_precision_2[(differential_precision_2 <= 0.05)]
```

```
##          Liver-HCC      Panc-AdenoCA      Prost-AdenoCA
## 8.145123e-24 2.860615e-07 1.126237e-04
## Skin-Melanoma.cutaneous
## 1.723631e-02

ovrdisp$differential_precision_2 = ifelse(ovrdisp$ct %in% names(differential_precision_2)[(differential_precision_2 <= 0.05)], 1, 0)

ggplot(ovrdisp, aes(x=ct, y=Estimate, group=name, col=name))+
  geom_point(position=position_dodge(width=0.5))+
  geom_errorbar(aes(ymin=Estimate-Std..Error,
                     ymax=Estimate+Std..Error), width=.1, position=position_dodge(width=0.5))+
  theme_bw()+
  geom_text(aes(y=Inf, label=differential_precision_2, vjust=1.8), col='black')+
  theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+
  labs(x='', y='Log lambda', col='Group')+theme(legend.position = "bottom")+
  theme(
    legend.margin=margin(0,0,0,0),
    legend.box.margin=margin(-10,-10,-10,-10),
    plot.margin = unit(c(1,1,1,1), "cm"))
```



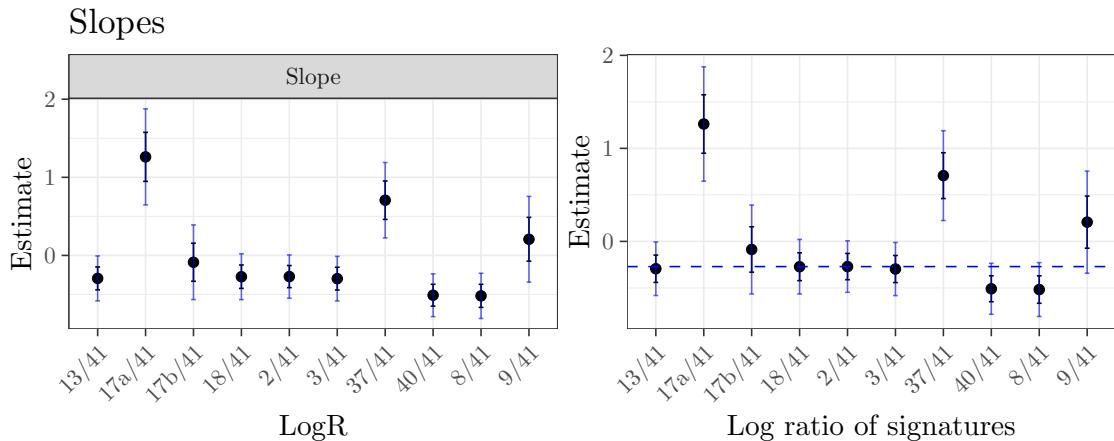
## Minimal perturbation

Note: this is using the original, non SP, signatures (hence not the best version).

```
minimalpert_L2 <- function(i){
  sum(i)/sum(i^2)
}
```

```

#
# betas_breast <- data.frame(plot_betas(diagRE_DMSL_nonexo[["Breast-AdenoCA"]], names_cats= logR_nonexo_r
#                               return_df=T, plot=F))
#
# .slopes_minpert <- betas_breast %>% dplyr::filter(type_beta == "Slope") %>% dplyr::select(Estimate) %>%
# #
# # minimalpert_L2(softmax(c(.slopes_minpert, 0)))
# median(c(.slopes_minpert, 0))
#
# aa <- plot_betas(diagRE_DMSL_nonexo[["Breast-AdenoCA"]], names_cats= logR_nonexo_notsorted[["Breast-AdenoCA"]]
#                   return_df=F, plot=F, only_slope = T, line_zero=F)
# # aa <- geom_hline(yintercept = 0)+geom_vline(xintercept = 1)+geom_hline(yintercept = median(c(.slopes_minpert, 0)))
# aa + geom_hline(yintercept = median(c(.slopes_minpert, 0)), lty='dashed', col='blue')+geom_hline(yintercept = mean(c(.slopes_minpert, 0)), lty='dashed', col='red')
# 
```



For the thesis:

```

pdf("../results/results_TMB/pcawg/minimalperturbation_SP_all.pdf", width = 4, height = 3)
for(ct in names(diagRE_DMDL_nonexo_SP)){
  .betas_ct_it <- data.frame(plot_betas(TMB_obj = diagRE_DMDL_nonexo_SP[[ct]],
                                         names_cats= logR_nonexo_notsorted_SP[[ct]],
                                         return_df=T, plot=F))
  .slopes_minpert <- .betas_ct_it %>% dplyr::filter(type_beta == "Slope") %>% dplyr::select(Estimate) %>%
  print(aaa <- plot_betas(TMB_obj = diagRE_DMDL_nonexo_SP[[ct]], names_cats= logR_nonexo_notsorted_SP[[ct]],
                           return_df=F, plot=F, only_slope = T, line_zero=F, add_confint = T, return_ggplot=TRUE)
  +
  geom_hline(yintercept = median(c(.slopes_minpert, 0)), lty='dashed', col='blue')+ggtitle(ct))
}
dev.off()

## pdf
## 2

\subsection{Minimal perturbation in diagRE_DMDL_nonexo_S}

perturbed_betas_diagRE_DMDL_nonexo_SP <- lapply(names(diagRE_DMDL_nonexo_SP), try(function(idx_sp){
  .betas_SP <- data.frame(plot_betas(diagRE_DMDL_nonexo_SP[[idx_sp]], names_cats= logR_nonexo_notsorted_SP[[idx_sp]]),
                            return_df=T, plot=F))

  .slopes_minpert_SP <- .betas_SP %>% dplyr::filter(type_beta == "Slope") %>% dplyr::select(Estimate) %>%
  
```

```

# print(.slopes_minpert_SP)
## check if the CI of the betas touches this median value
.summary_betas_slope_SP <- python_like_select_rownames(summary(diagRE_DMDL_nonexo_SP[[idx_sp]]), 'beta'
nrow(.summary_betas_slope_SP)

minimal_change_baseline <- median(c(.slopes_minpert_SP, 0))
# print(.summary_betas_slope_SP)
# print(logR_nonexo_notsorted_SP[[idx_sp]])
# print(dim(.summary_betas_slope_SP))
if(!is.null(dim(.summary_betas_slope_SP))){
  .params_in_ci <- give_params_in_CI(vec_est=.summary_betas_slope_SP[,1],
                                       vec_stderr=.summary_betas_slope_SP[,2],
                                       vec_true=rep(minimal_change_baseline, nrow(.summary_betas_slope_SP)))
} else{
  .params_in_ci <- give_params_in_CI(vec_est=.summary_betas_slope_SP[1],
                                       vec_stderr=.summary_betas_slope_SP[2],
                                       vec_true=minimal_change_baseline)
}
.params_in_ci <- sapply(1:length(.params_in_ci), function(i){
  ## for the ones in which there is a change, say whether it's up- or down-regulated
  if(!.params_in_ci[i]){
    ## if there is a change: not in confidence interval
    if(is.null(dim(.summary_betas_slope_SP))){ 
      ## one-dim
      if(.summary_betas_slope_SP[1] > minimal_change_baseline){
        'increase'
      } else{
        'decrease'
      }
    } else{
      ## multi-dim
      if(.summary_betas_slope_SP[i,1] > minimal_change_baseline){
        'increase'
      } else{
        'decrease'
      }
    }
  } else{
    'FALSE'
  }
})
names(.params_in_ci) <- sapply(logR_nonexo_notsorted_SP[[idx_sp]], function(i) strsplit(i, '/')[[1]][1]
.baseline <- strsplit(logR_nonexo_notsorted_SP[[idx_sp]][[1]], '/')[[1]][2]
return(list(betas_perturbed=.params_in_ci, baseline=.baseline))
})
perturbed_betas_diagRE_DMDL_nonexo_SP <- lapply(names(diagRE_DMDL_nonexo_SP), try(give_min_pert))

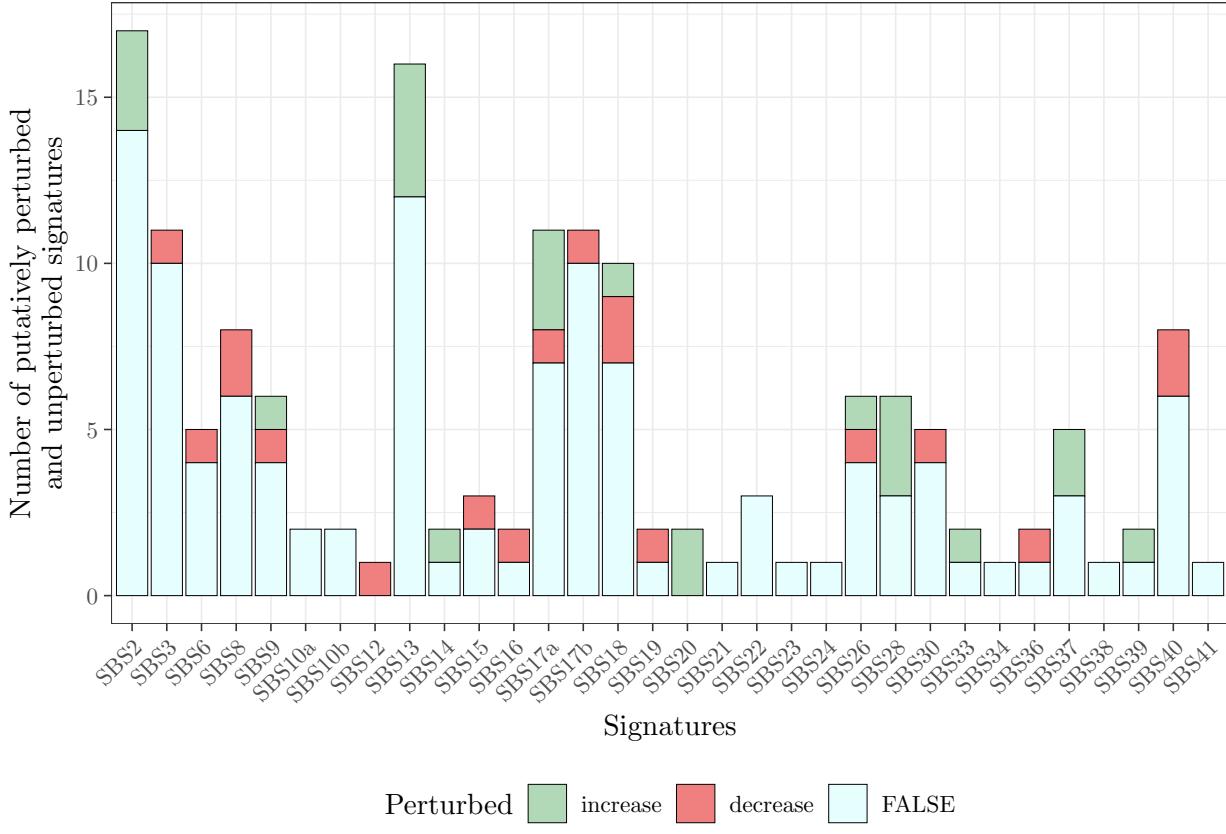
perturbed_betas_diagRE_DMDL_nonexo_SP_vec <- do.call('c', sapply(perturbed_betas_diagRE_DMDL_nonexo_SP, f
perturbed_betas_diagRE_DMDL_nonexo_SP_df <- cbind.data.frame(sig=gsub("betas_perturbed.", "", 
names(perturbed_betas_diagRE_DMDL_r

```

```

perturbed=perturbed_betas_diagRE_DMDL_nonexo_SP_df
ggplot(perturbed_betas_diagRE_DMDL_nonexo_SP_df, aes(x=factor(sig, levels=gtools::mixedsort(unique(sig))), fill=factor(perturbed, levels=c('increase', 'decrease'))))
  geom_bar(col='black', size=0.001)+theme_bw()+
  scale_fill_manual(values=c( '#b1d8b7', '#f08080', '#e7feff'))+
  theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1), legend.position = "bottom")+
  labs(x='Signatures', y='Number of putatively perturbed\nand unperturbed signatures', fill='Perturbed')

```

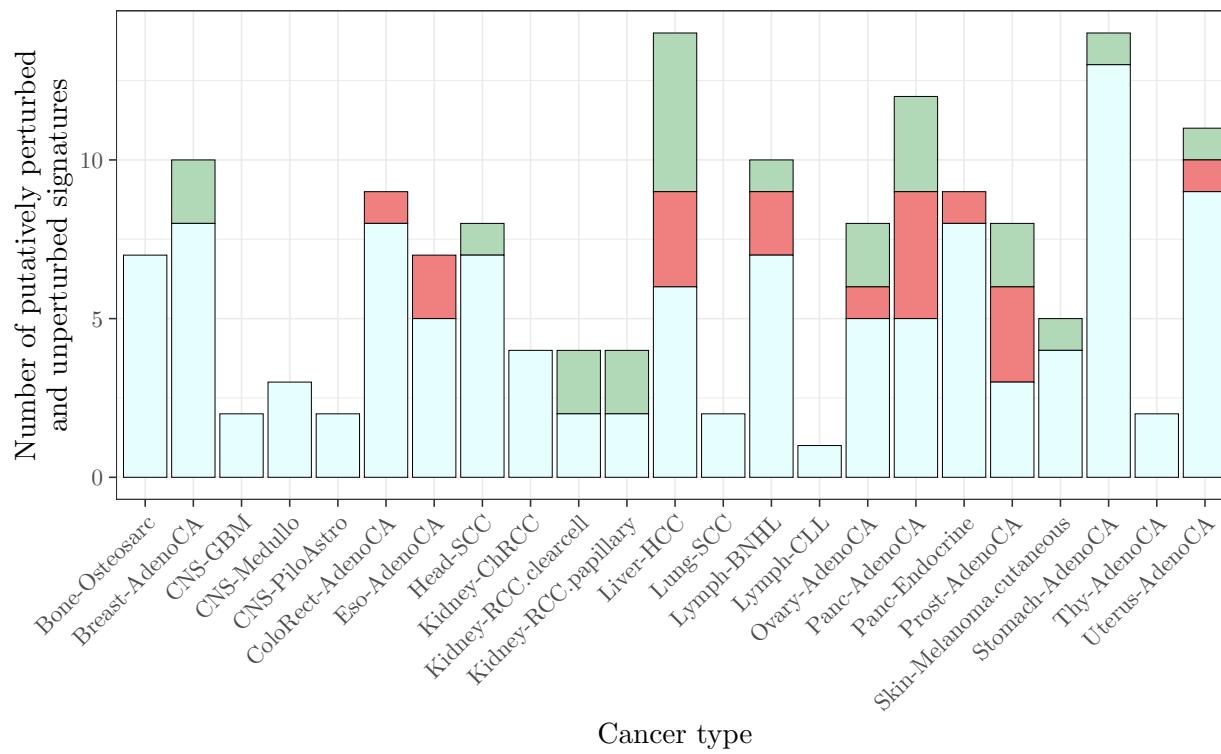


Minimal perturbation per signature

```

names(perturbed_betas_diagRE_DMDL_nonexo_SP) <- names(diagRE_DMDL_nonexo_SP)
ggplot(reshape2::melt(lapply(perturbed_betas_diagRE_DMDL_nonexo_SP, `[, 'betas_perturbed'])),
  aes(x=L1, fill=factor(value, levels=c('increase', 'decrease', 'FALSE')))+geom_bar(col='black', size=0.001)+scale_fill_manual(values=c('#b1d8b7', '#f08080', '#e7feff'))+theme(legend.position = "bottom")+
  theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+labs(x='Cancer type',
  y='Number of putatively perturbed and unperturbed signatures', fill='Perturbed')

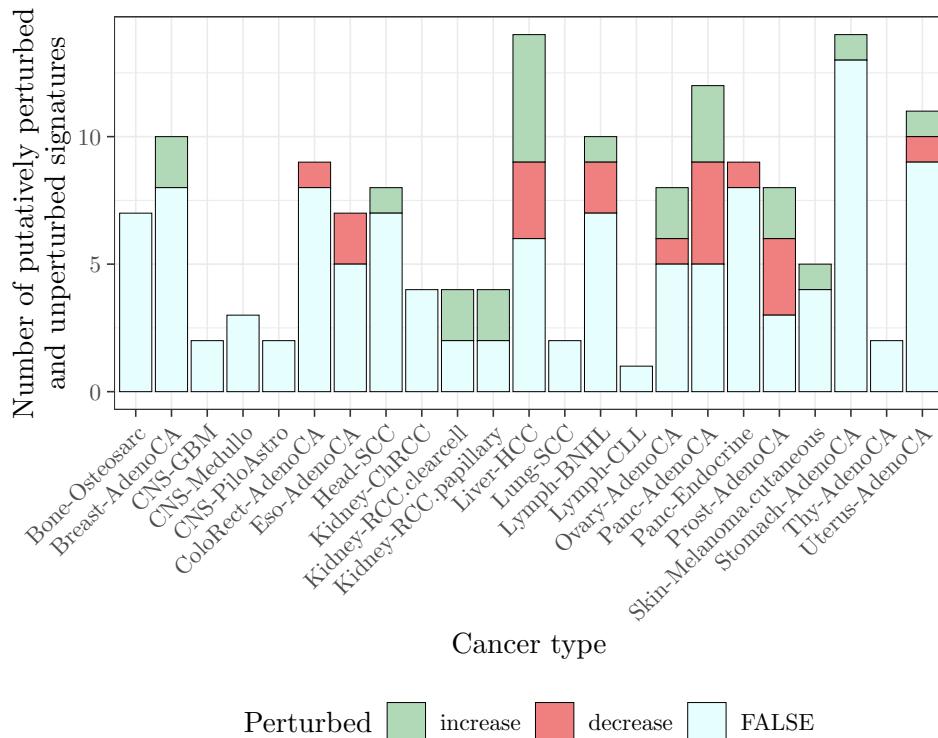
```



```

names(perturbed_betas_diagRE_DMDL_nonexo_SP) <- names(diagRE_DMDL_nonexo_SP)
ggplot(reshape2::melt(lapply(perturbed_betas_diagRE_DMDL_nonexo_SP, `[, 'betas_perturbed']),
  aes(x=L1, fill=factor(value, levels=c('increase', 'decrease', 'FALSE')))+geom_bar(col='black', size=1),
  scale_fill_manual(values=c('#b1d8b7', '#f08080', '#e7feff'))+theme(legend.position = "bottom")+
  theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+labs(x='Cancer type',
  y='Number of putatively perturbed and unperturbed signatures'))

```



```
ggplot(perturbed_betas_diagRE_DMDL_nonexo_SP_df, aes(x=factor(sig, levels=gtools::mixedsort(unique(sig))))+
  fill=factor(perturbed, levels=c('increase', 'decrease'))+
  geom_bar(col='black', size=0.001)+theme_bw()+
  scale_fill_manual(values=c( '#b1d8b7', '#f08080', '#e7feff'))+
  theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1), legend.position = "bottom")+
  labs(x='Signatures', y='Number of putatively perturbed\n and unperturbed signatures', fill='Perturbed')
```

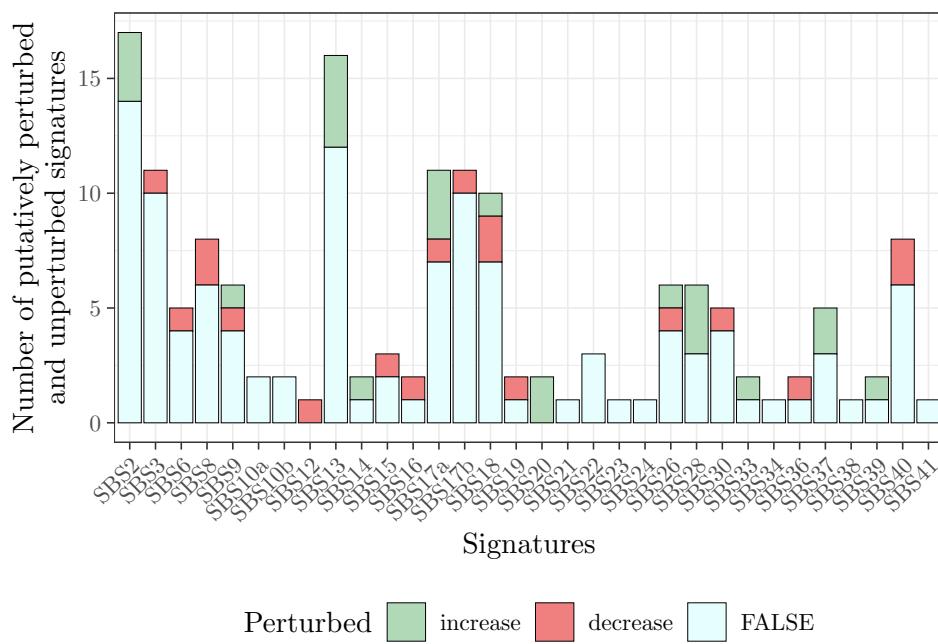


Table of perturbed signatures

```

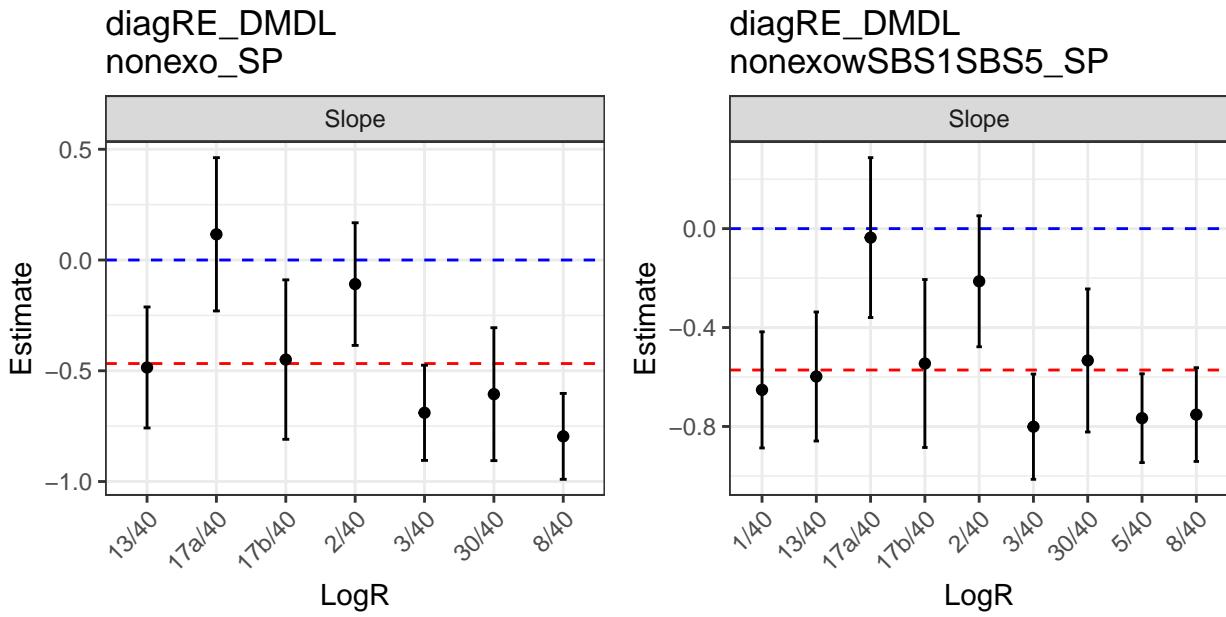
relevel_perturbation <- cbind(c('increase', 'decrease'), c('+', '-'))

write("", ".../results/results_TMB/pcawg/minimal_perturbation_sigs.txt", append = F)
# for(i in names(perturbed_betas_diagRE_DMDL_nonexo_SP)){
#   write(paste0(i, '&', paste0(names(perturbed_betas_diagRE_DMDL_nonexo_SP[[i]]$betas_perturbed)[perturbed_betas_diagRE_DMDL_nonexo_SP[[i]]$beta_index], '+', 'relevel_perturbation')), collapse=', ', sep=''), file=".../results/results_TMB/pcawg/minimal_perturbation_sigs.txt")
# }

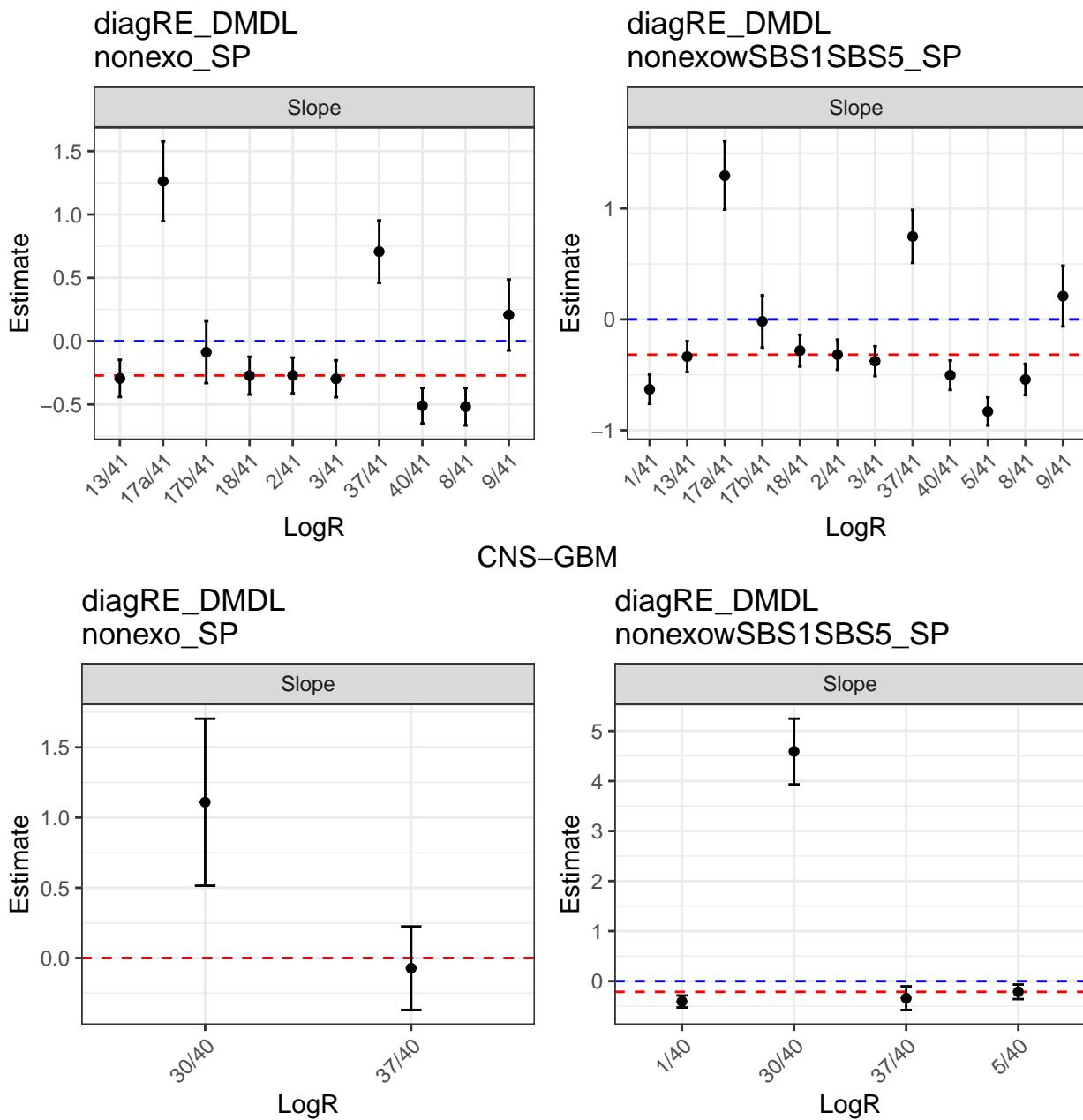
for(i in names(perturbed_betas_diagRE_DMDL_nonexo_SP)){
  # write(x = paste0(i, '&', paste0(sapply(which(perturbed_betas_diagRE_DMDL_nonexo_SP[[i]]$betas_perturbed), collapse=', ', sep=''), '\\\\'), file=".../results/results_TMB/pcawg/minimal_perturbation_sigs.txt"))
  write(x = paste0(paste0(i, '&', paste0(sapply(which(perturbed_betas_diagRE_DMDL_nonexo_SP[[i]]$betas_perturbed), collapse=', ', sep=''), '\\\\'), file=".../results/results_TMB/pcawg/minimal_perturbation_sigs.txt"))
}

```

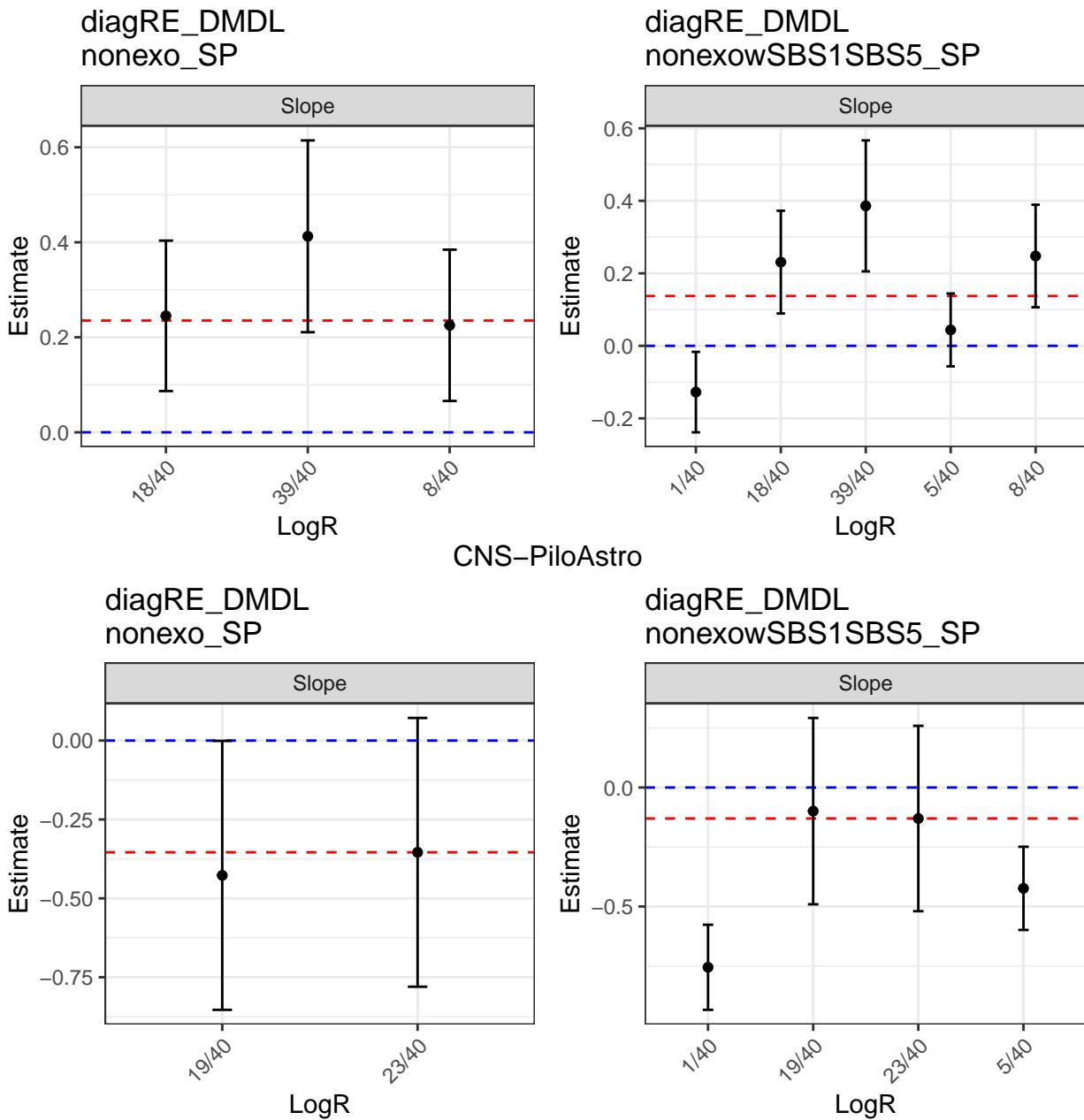
### Bone–Osteosarc



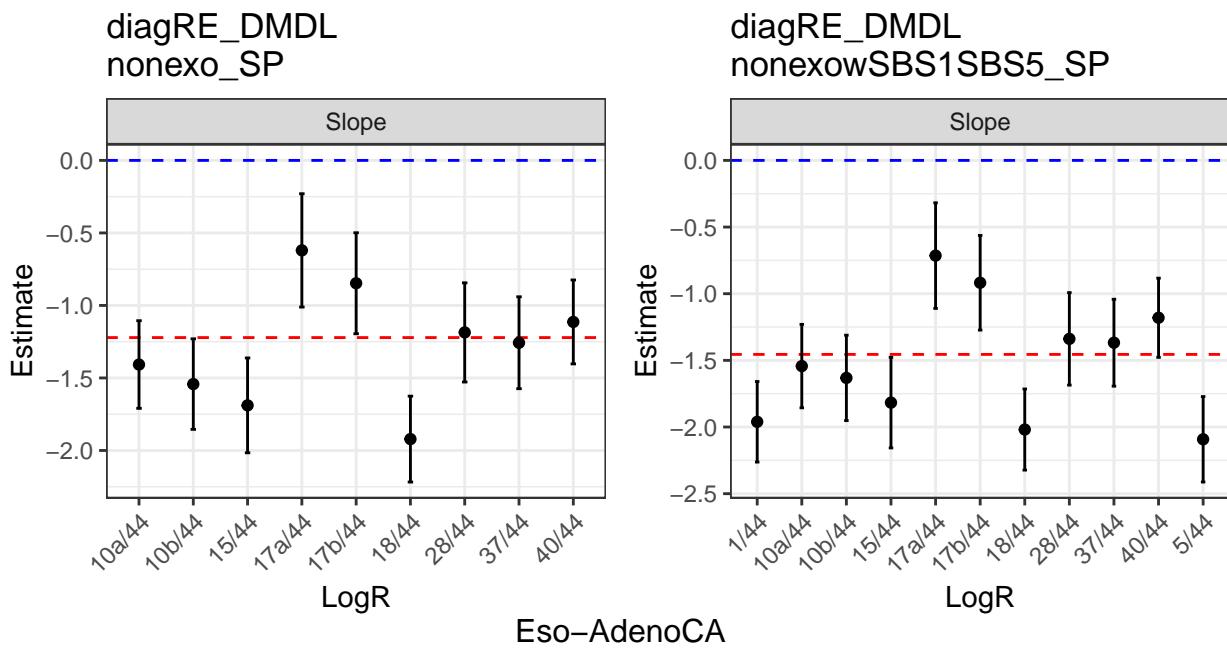
### Breast–AdenoCA



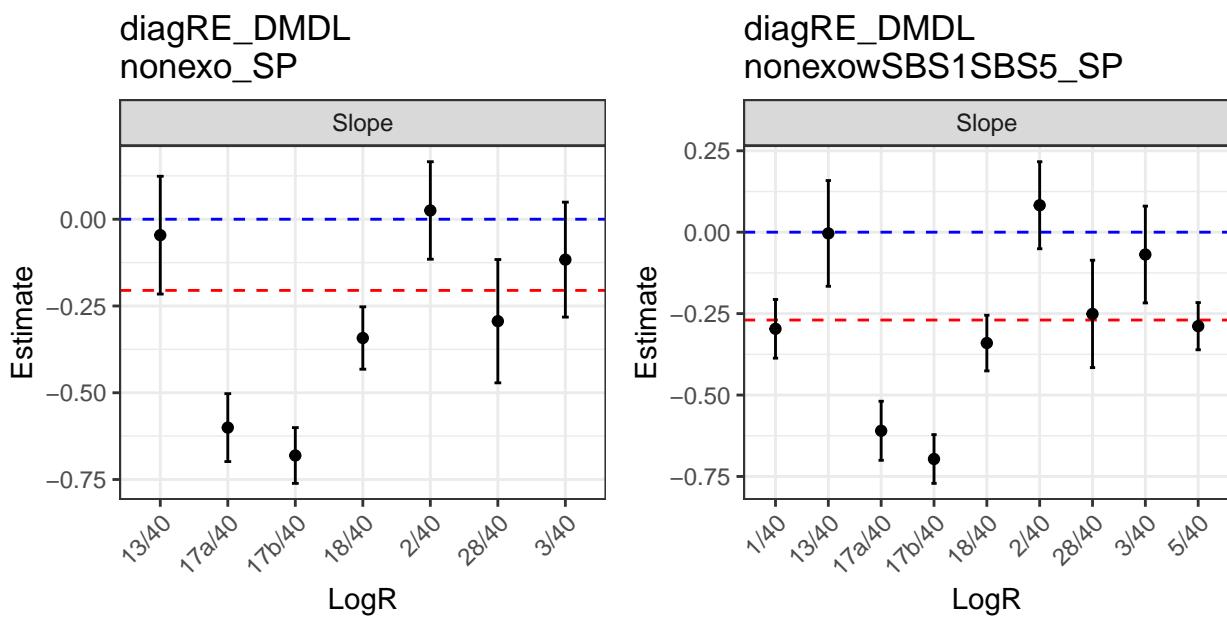
### CNS-Medullo



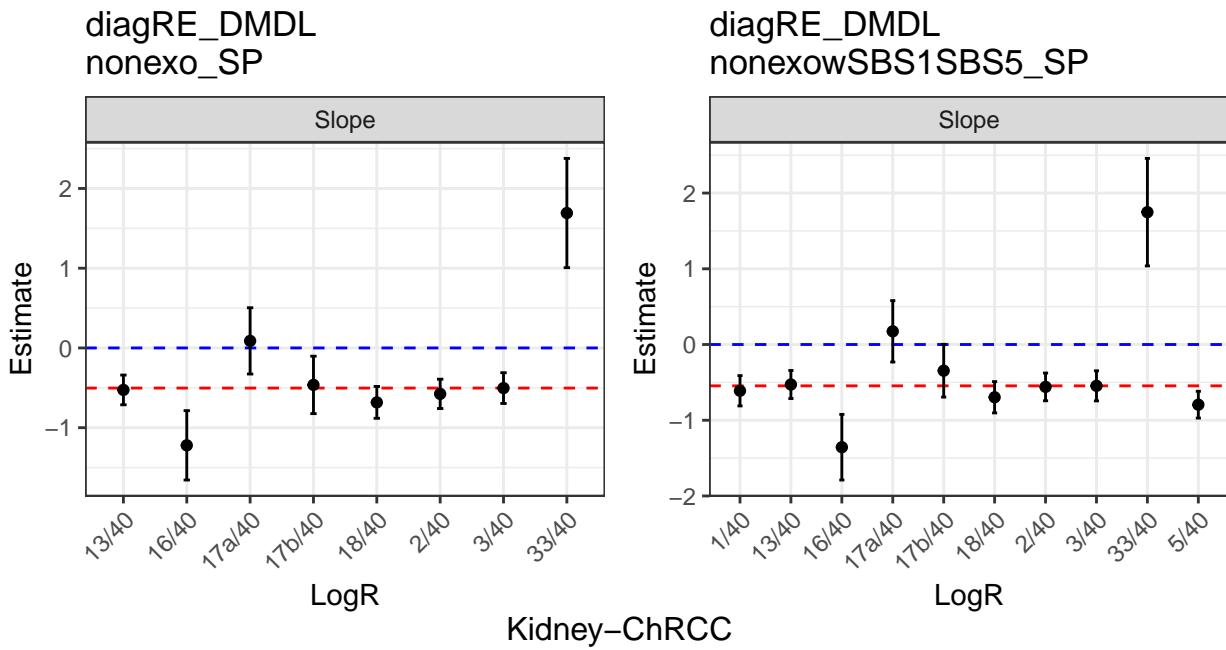
### ColoRect–AdenoCA



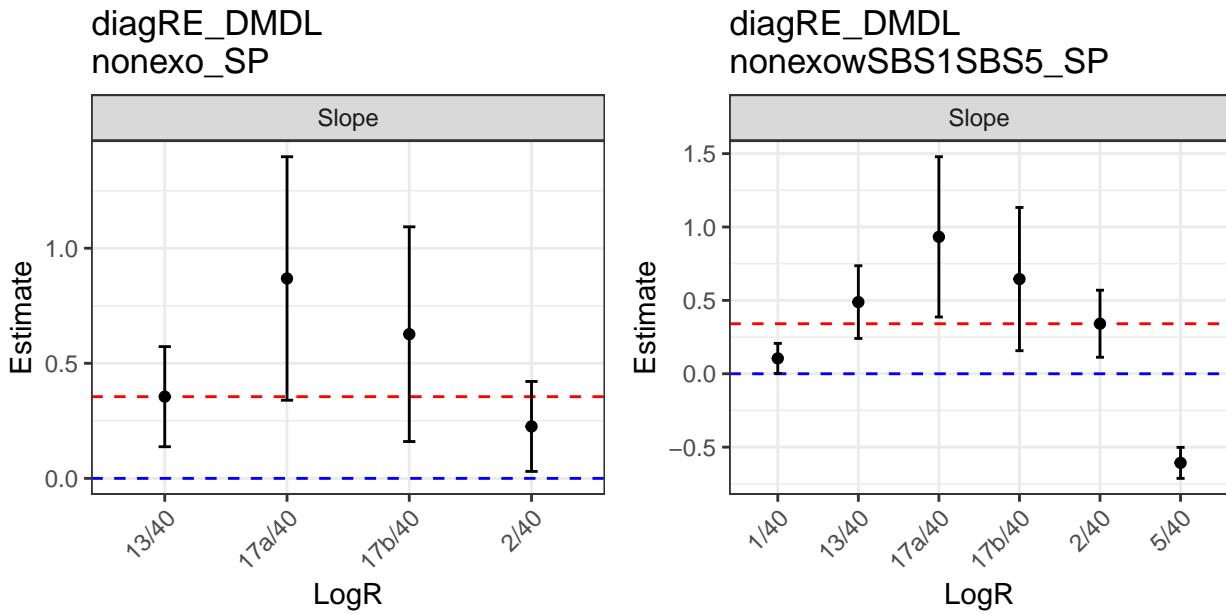
### Eso–AdenoCA



### Head-SCC

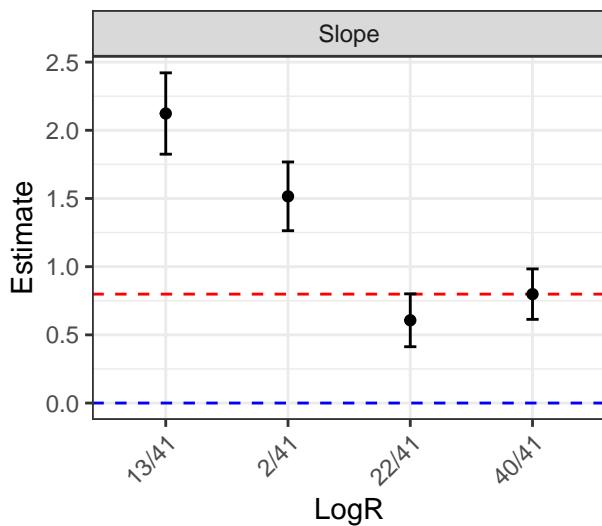


### Kidney-ChRCC

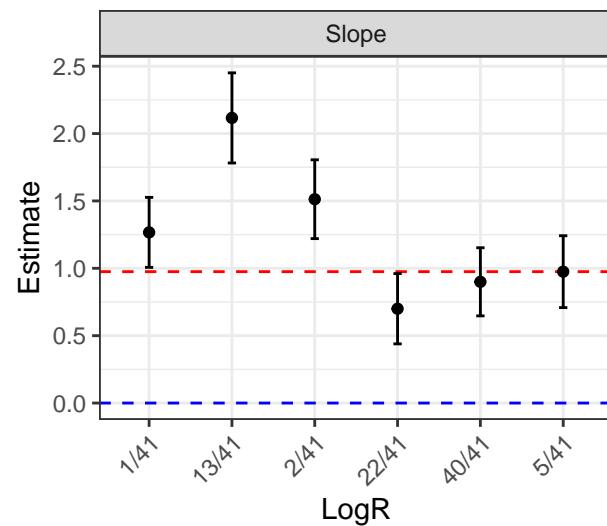


Kidney–RCC.clearcell

diagRE\_DMDL  
nonexo\_SP

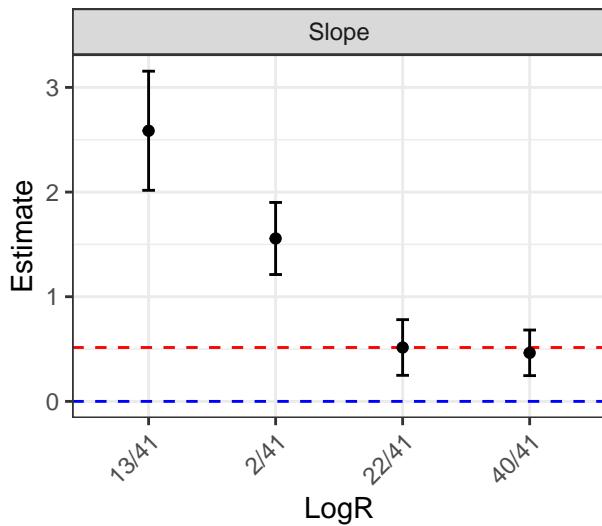


diagRE\_DMDL  
nonexowSBS1SBS5\_SP

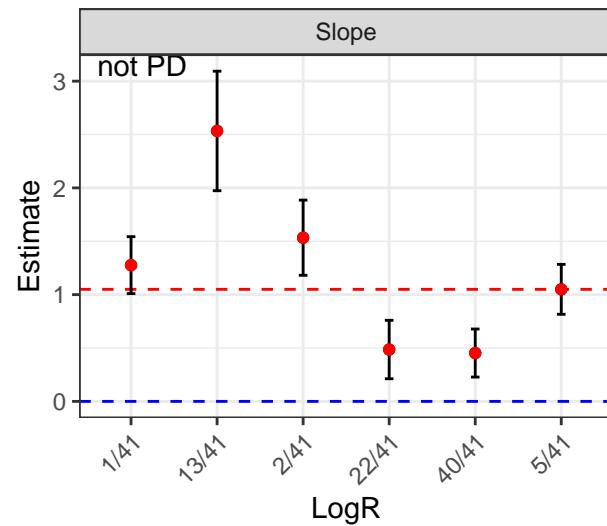


Kidney–RCC.papillary

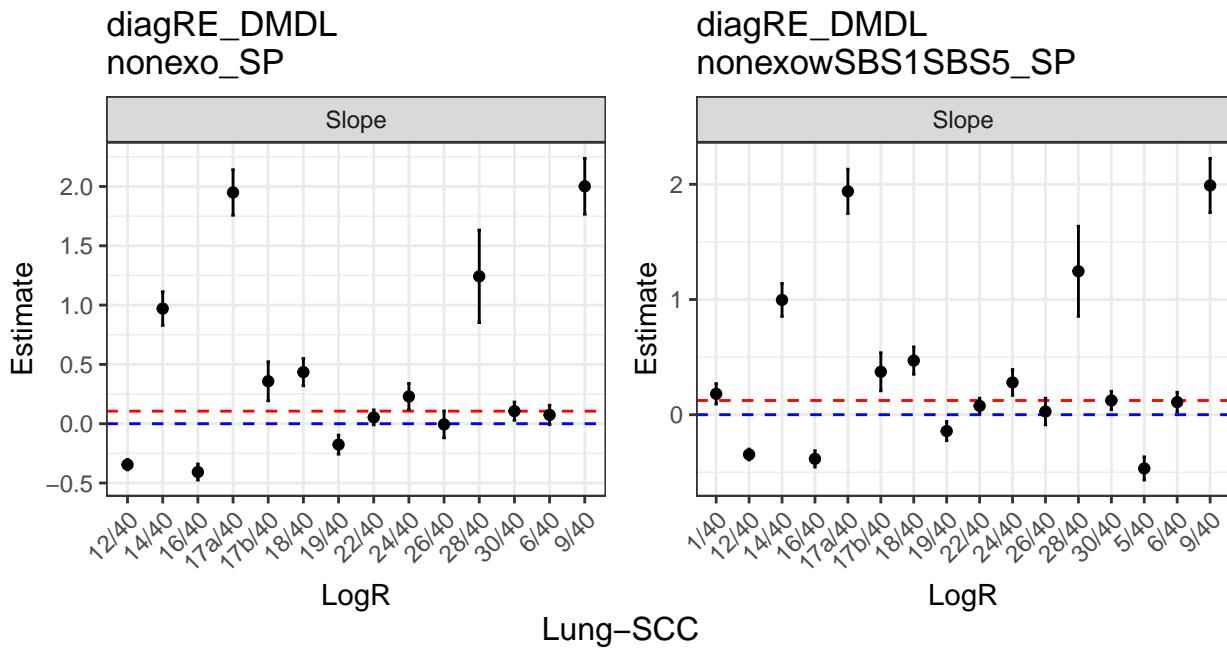
diagRE\_DMDL  
nonexo\_SP



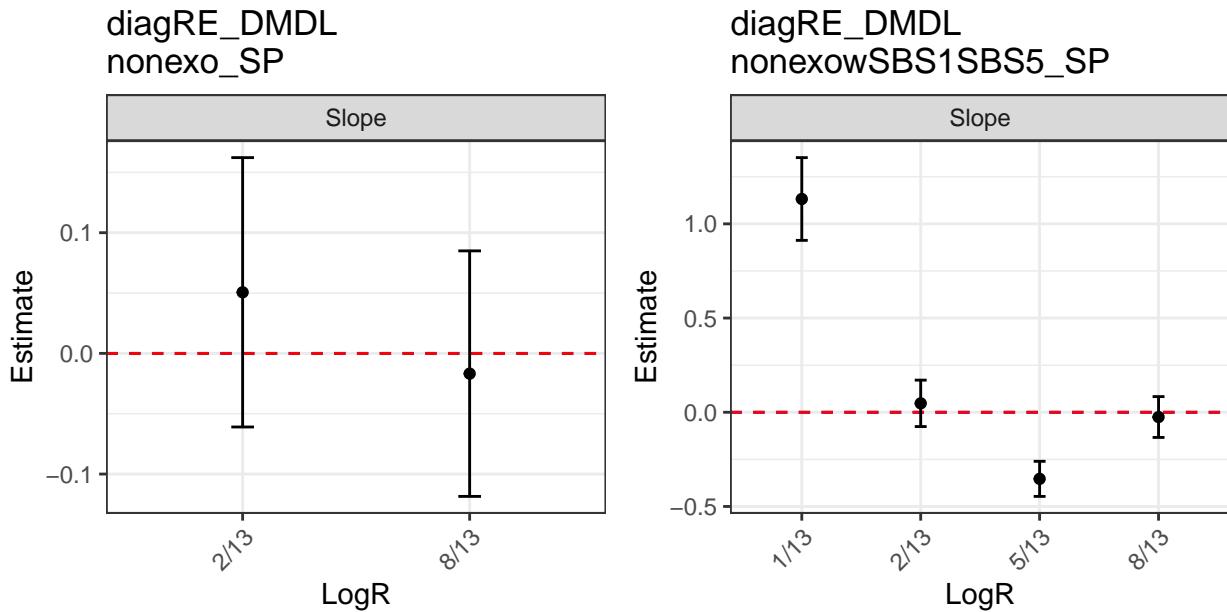
diagRE\_DMDL  
nonexowSBS1SBS5\_SP



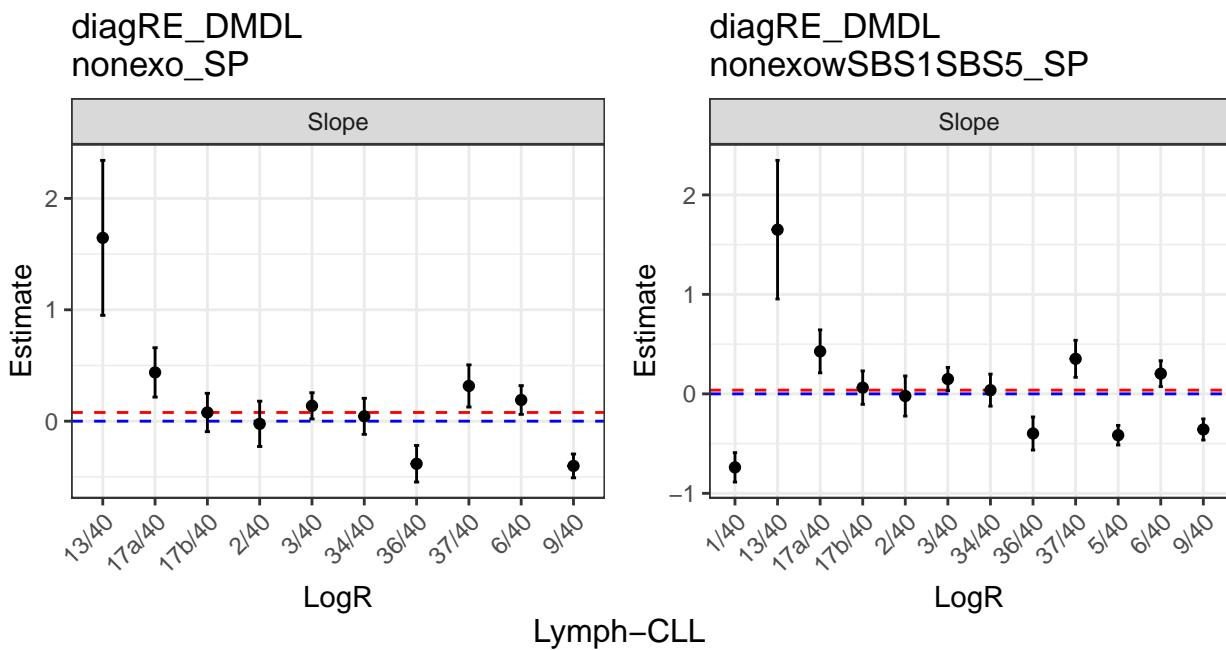
### Liver-HCC



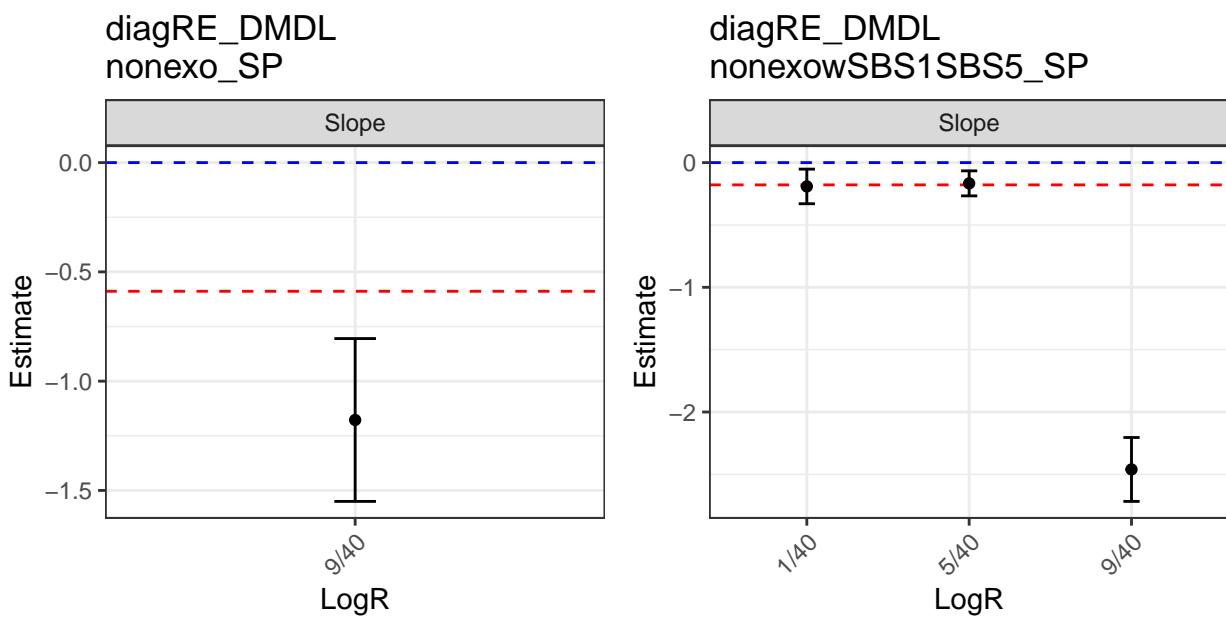
### Lung-SCC



### Lymph-BNHL

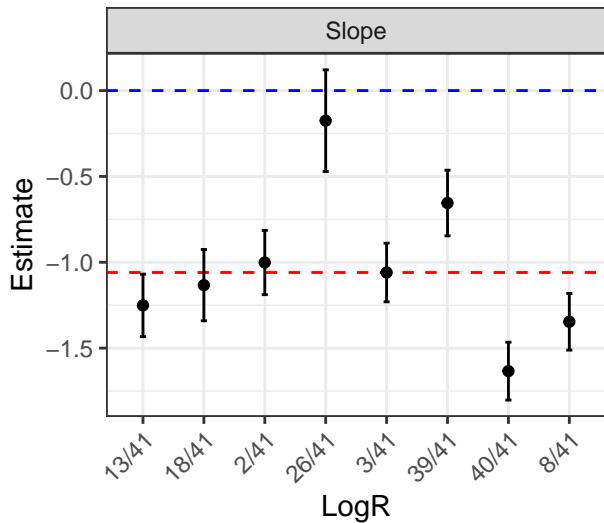


### Lymph-CLL

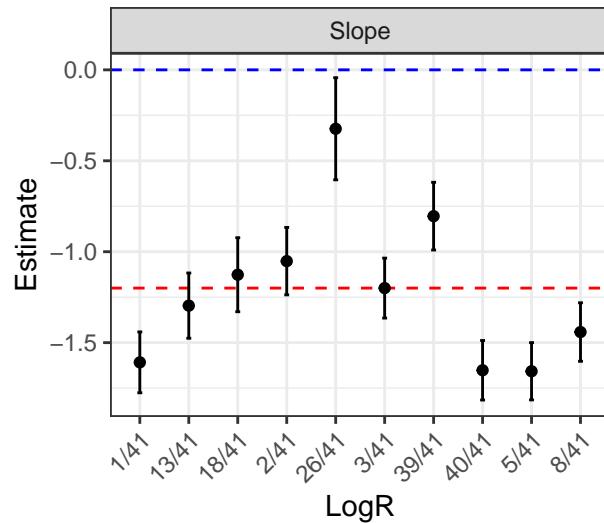


### Ovary–AdenoCA

diagRE\_DMDL  
nonexo\_SP

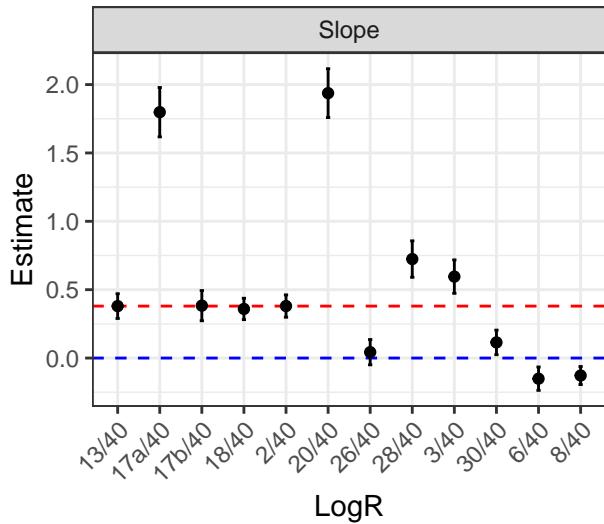


diagRE\_DMDL  
nonexowSBS1SBS5\_SP

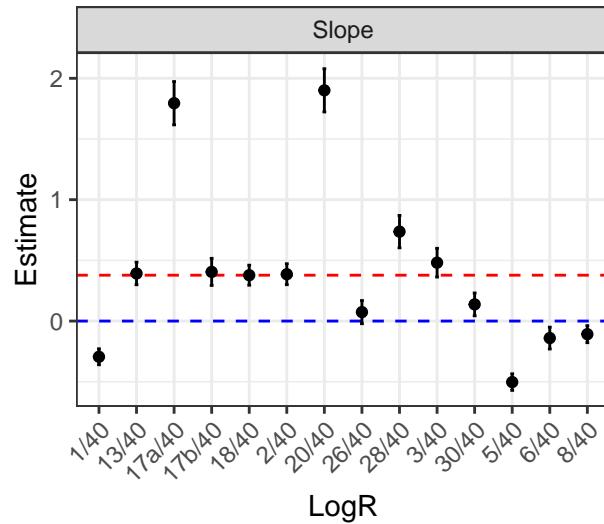


### Panc–AdenoCA

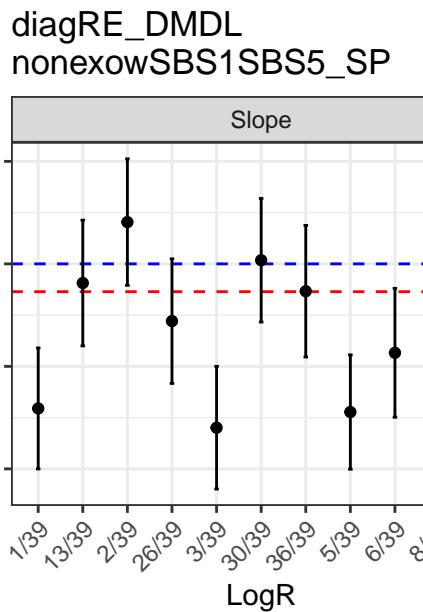
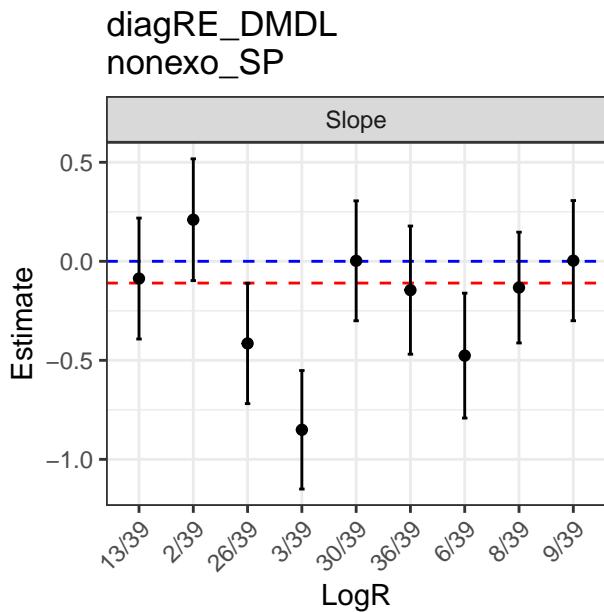
diagRE\_DMDL  
nonexo\_SP



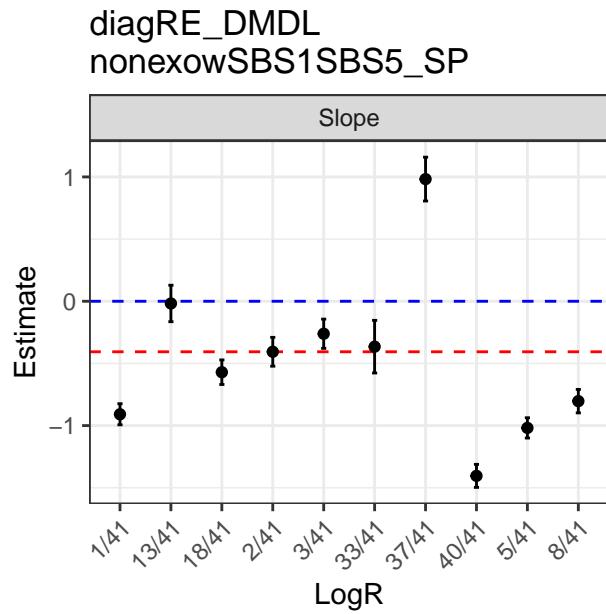
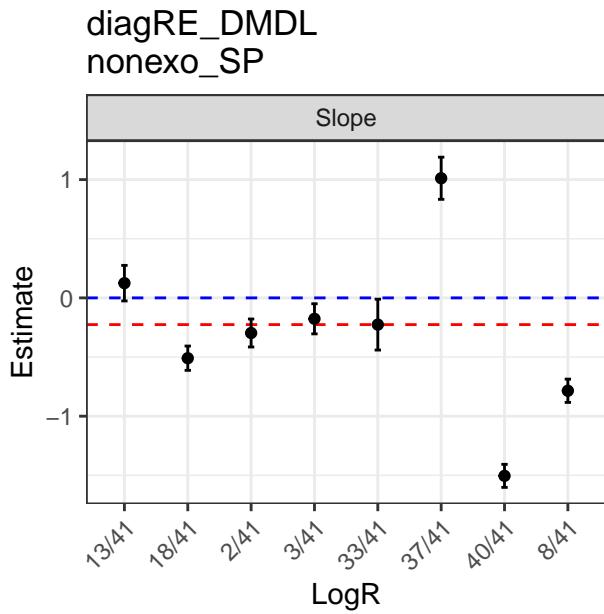
diagRE\_DMDL  
nonexowSBS1SBS5\_SP



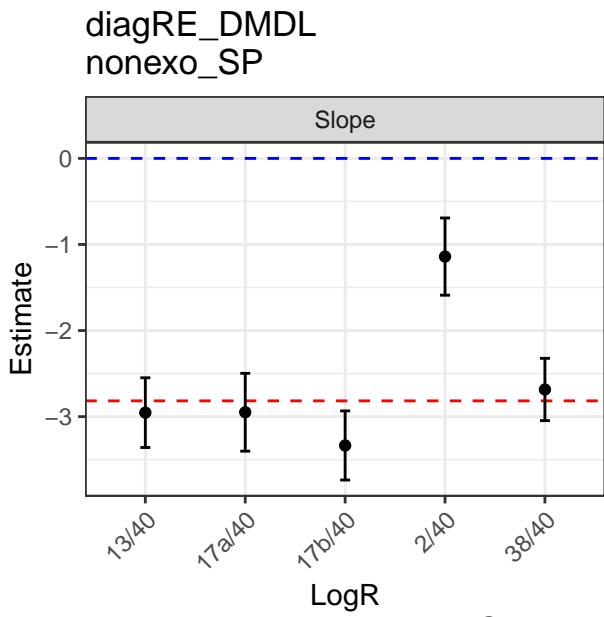
### Panc–Endocrine



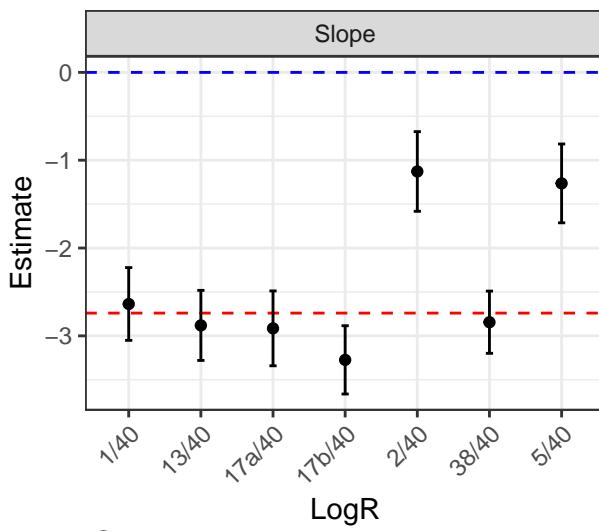
### Prost–AdenoCA



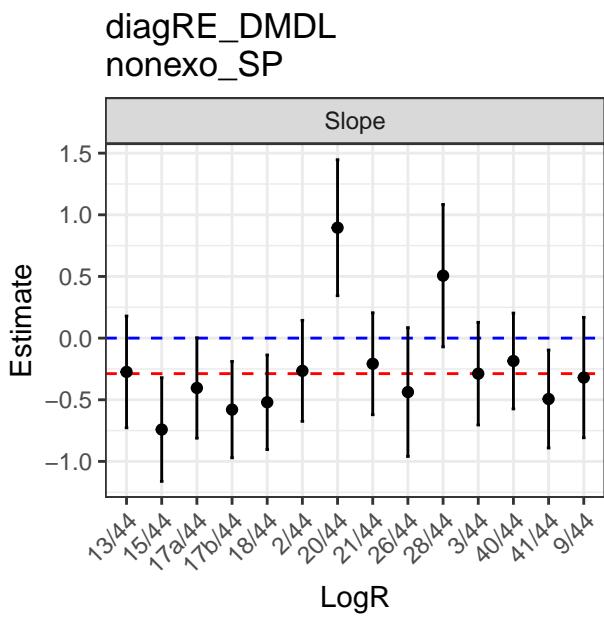
### Skin–Melanoma.cutaneous



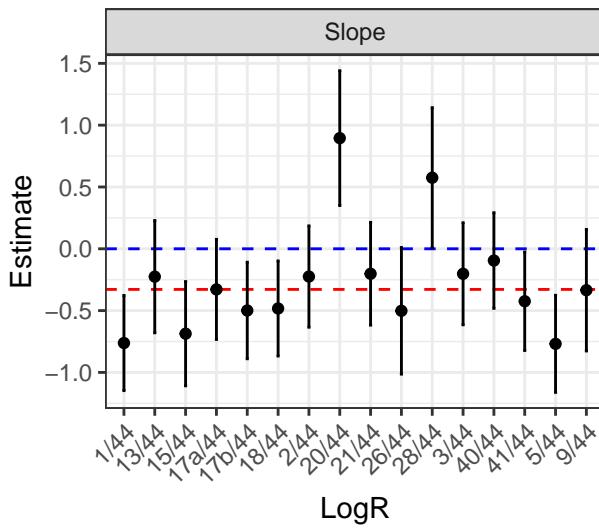
**diagRE\_DMDL**  
**nonexowSBS1SBS5\_SP**



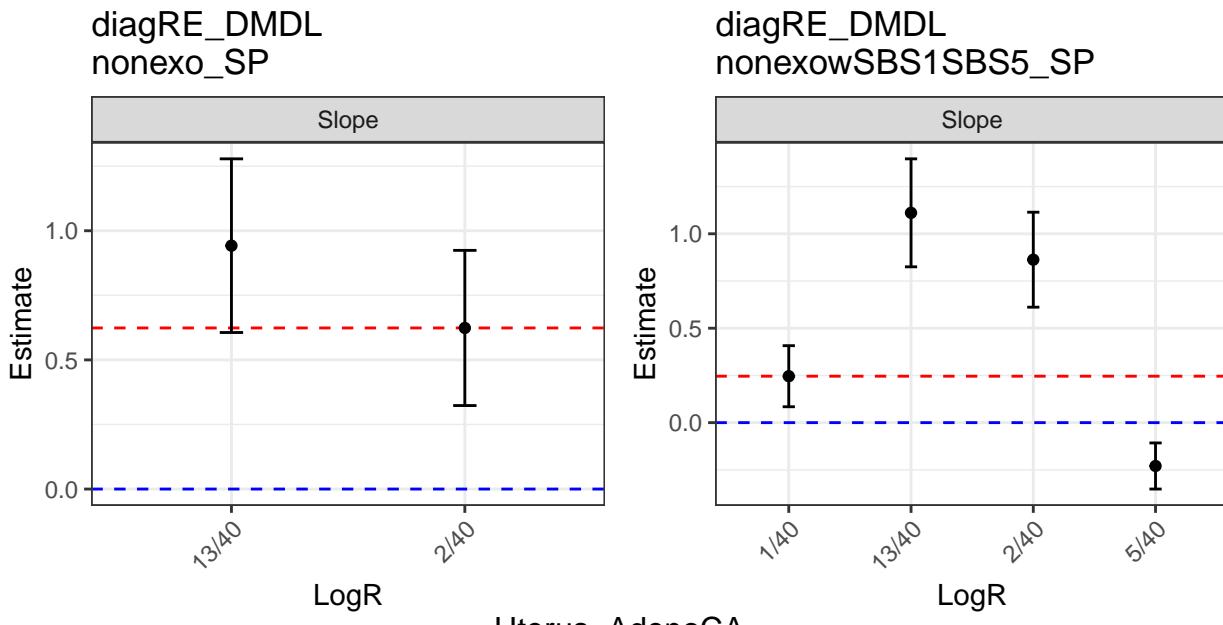
### Stomach–AdenoCA



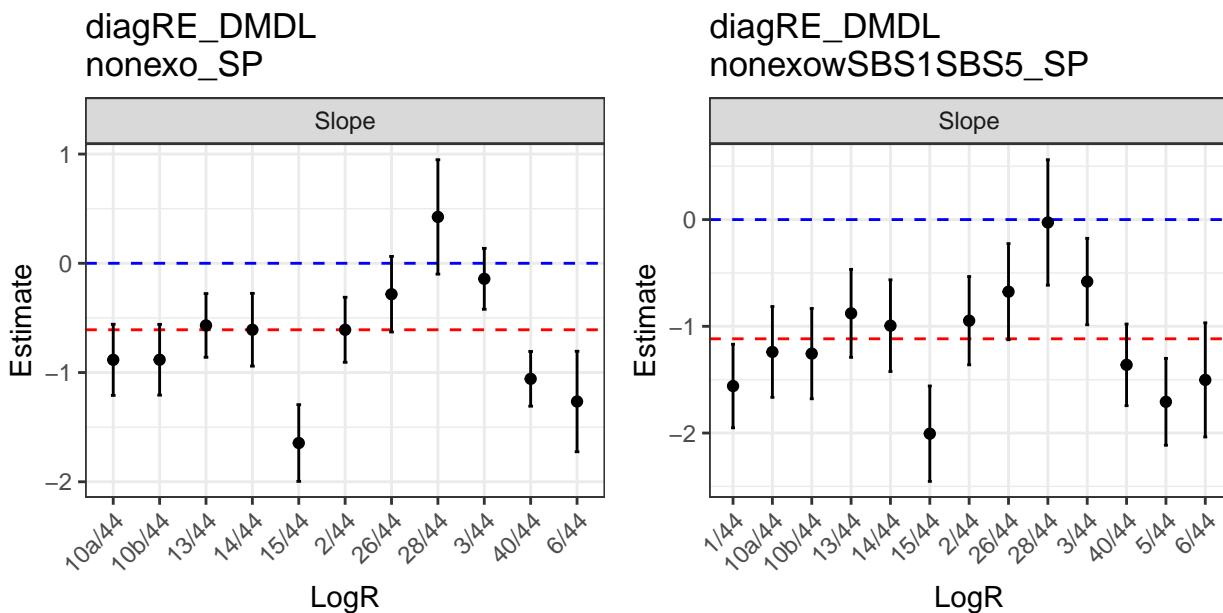
**diagRE\_DMDL**  
**nonexowSBS1SBS5\_SP**



### Thy–AdenoCA



### Uterus–AdenoCA



### Comparing the s1/s5 baseline to the minimal perturbation results

```
##      [,1]     [,2]     [,3]     [,4]     [,5]     [,6]     [,7]
## SBS1 "FALSE" "decrease" "FALSE" "decrease" "decrease" "FALSE" "FALSE"
## SBS5 "FALSE" "decrease" "FALSE" "FALSE"   "FALSE"   "decrease" "FALSE"
##      [,8]     [,9]     [,10]    [,11]    [,12]    [,13]    [,14]
## SBS1 "FALSE" "decrease" "FALSE" "FALSE"   "FALSE"   "increase" "decrease"
## SBS5 "FALSE" "decrease" "FALSE" "FALSE"   "decrease" "decrease" "decrease"
##      [,15]    [,16]    [,17]    [,18]    [,19]    [,20]    [,21]
## SBS1 "FALSE" "decrease" "decrease" "FALSE"   "decrease" "FALSE"   "FALSE"
```

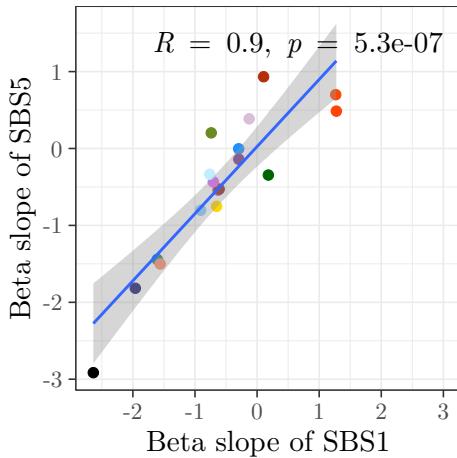
```

## SBS5 "FALSE" "decrease" "decrease" "decrease" "decrease" "increase" "FALSE"
## [,22]      [,23]
## SBS1 "FALSE"      "FALSE"
## SBS5 "decrease" "FALSE"
## [1] 2 23
## [1] "Ct for which SBS1 and SBS5 are not DA"
## [1] 9
## [1] "Ct for which SBS1 and SBS5 both decrease"
## [1] 6

```

Plotting the betas of SBS1 and SBS5, and their correlation

```
## `geom_smooth()` using formula 'y ~ x'
```



Correlation between the two APOBEC signatures, SBS2 and SBS13:

```
diagRE_DMDL_wSBS1SBS5nonexo_SP_betas_SBS1SBS5_0
```

```

##      LogR Bone-Osteosarc Breast-AdenoCA    CNS-GBM CNS-Medullo CNS-PiloAstro
## 1      1   -0.65205448   -0.63056226 -0.4068313 -0.12757480   -0.75547436
## 2      2   -0.21291191   -0.31810871 -0.2135513  0.04392387   -0.42374188
## 3      3   -0.80086778   -0.37655392  4.5904007  0.24778355   -0.09911198
## 4      4   -0.76647219   -0.83005858 -0.3402184  0.23102511   -0.13019202
## 5      5   -0.75193369   -0.54174300      NA  0.38604360      NA
## 6      6   -0.59793592   0.21011709      NA      NA      NA
## 7      7   -0.03626699   -0.33566311      NA      NA      NA
## 8      8   -0.54542495   1.29663200      NA      NA      NA
## 9      9   -0.53311606   -0.01798581      NA      NA      NA
## 10     10      NA   -0.28202010      NA      NA      NA
## 11     11      NA   0.74818117      NA      NA      NA
## 12     12      NA   -0.50339545      NA      NA      NA
## 13     13      NA      NA      NA      NA      NA
## 14     14      NA      NA      NA      NA      NA
## 15     15      NA      NA      NA      NA      NA
## 16     16      NA      NA      NA      NA      NA
##      ColoRect-AdenoCA  Eso-AdenoCA Head-SCC Kidney-ChRCC Kidney-RCC.clearcell

```

```

## 1 -1.9608217 -0.296603923 -0.6109625 0.1048328 1.2666589
## 2 -2.0921571 0.082743769 -0.5598662 0.3410101 1.5127991
## 3 -1.5429485 -0.068557764 -0.5458705 -0.6070669 0.9750606
## 4 -1.6315098 -0.288525263 -0.7945682 0.4884064 2.1161471
## 5 -1.8169416 -0.003715624 -0.5281156 0.9328886 0.6999134
## 6 -0.7141478 -0.609730394 -1.3562882 0.6452427 0.8996817
## 7 -0.9178427 -0.696390350 0.1740217 NA NA
## 8 -2.0189069 -0.340353080 -0.3459108 NA NA
## 9 -1.3386046 -0.250926253 -0.6965822 NA NA
## 10 -1.3676077 NA 1.7476965 NA NA
## 11 -1.1803477 NA NA NA NA
## 12 NA NA NA NA NA
## 13 NA NA NA NA NA
## 14 NA NA NA NA NA
## 15 NA NA NA NA NA
## 16 NA NA NA NA NA
## Kidney-RCC.papillary Liver-HCC Lung-SCC Lymph-BNHL Lymph-CLL
## 1 1.2764421 0.18121701 1.13205500 -0.73853075 -0.1909831
## 2 1.5335115 -0.46670474 0.04730124 -0.02155235 -0.1664975
## 3 1.0497238 0.10929054 -0.35347146 0.14873148 -2.4606035
## 4 2.5335435 1.98952435 -0.02528508 -0.41539701 NA
## 5 0.4856923 -0.34536130 NA 0.20340232 NA
## 6 0.4528936 0.99614133 NA -0.35782076 NA
## 7 NA -0.38332262 NA 1.65033823 NA
## 8 NA 1.93883092 NA 0.42738903 NA
## 9 NA 0.37266116 NA 0.06248822 NA
## 10 NA 0.46956392 NA 0.03747916 NA
## 11 NA -0.14208627 NA -0.39838546 NA
## 12 NA 0.07649181 NA 0.35234432 NA
## 13 NA 0.28004806 NA NA NA
## 14 NA 0.02771816 NA NA NA
## 15 NA 1.24493307 NA NA NA
## 16 NA 0.12339364 NA NA NA
## Ovary-AdenoCA Panc-AdenoCA Panc-Endocrine Prost-AdenoCA
## 1 -1.6082797 -0.29422601 -0.70515367 -0.90886623
## 2 -1.0518667 0.38598957 0.20384815 -0.40619540
## 3 -1.1999800 0.48104136 -0.79909092 -0.26111647
## 4 -1.6572683 -0.50265940 -0.72276391 -1.01842704
## 5 -1.4416134 -0.14008512 -0.43372724 -0.80323807
## 6 -1.2964332 -0.10780668 -0.13794423 -0.01776658
## 7 -1.1264324 0.39219508 -0.02073439 -0.57061143
## 8 -0.3239953 1.79488708 -0.09355158 -0.36523367
## 9 -0.8045413 0.40504435 -0.27920660 0.98264553
## 10 -1.6518010 0.37786323 0.01775660 -1.40425704
## 11 NA 1.90077896 -0.13335340 NA
## 12 NA 0.07381949 NA NA
## 13 NA 0.73689208 NA NA
## 14 NA 0.13742745 NA NA
## 15 NA NA NA NA
## 16 NA NA NA NA
## Skin-Melanoma.cutaneous Stomach-AdenoCA Thy-AdenoCA Uterus-AdenoCA

```

```

## 1      -2.637102   -0.76210875   0.2458919  -1.55971527
## 2      -1.128145   -0.22457673   0.8629161  -0.94737555
## 3      -1.263913   -0.20226748  -0.2294617  -0.58104103
## 4      -2.881089   -0.76879634   1.1110284  -1.70751291
## 5      -2.914800   -0.33486170        NA  -1.50212706
## 6      -3.273806   -0.22552842        NA  -1.24033653
## 7      -2.844686   -0.68667840        NA  -1.25607734
## 8          NA  -0.32863748        NA  -0.87878860
## 9          NA  -0.49898640        NA  -0.99418452
## 10     NA  -0.48274065        NA  -2.00610779
## 11     NA  0.89496038        NA  -0.67554877
## 12     NA  -0.20196073        NA  -0.02725474
## 13     NA  -0.50159888        NA  -1.36125477
## 14     NA  0.57491183        NA        NA
## 15     NA  -0.09507625        NA        NA
## 16     NA  -0.42431574        NA        NA

## [1] 27  8
## [1] 27  8
## [1] 136 11
## [1] 136 11
## [1] 34  3
## [1] 34  3
## [1] 106  4
## [1] 106  4
## [1] 41  3
## [1] 41  3
## [1] 37 10
## [1] 37 10
## [1] 65  8
## [1] 65  8
## [1] 32  9
## [1] 32  9
## [1] 38  5
## [1] 38  5
## [1] 86  5
## [1] 86  5
## [1] 30  5
## [1] 30  5
## [1] 207 15
## [1] 207 15
## [1] 34  3
## [1] 34  3
## [1] 51 11
## [1] 51 11
## [1] 53  2
## [1] 53  2
## [1] 97  9
## [1] 97  9
## [1] 193 13
## [1] 193 13
## [1] 70 10

```

```

## [1] 70 10
## [1] 208 9
## [1] 208 9
## [1] 29 6
## [1] 29 6
## [1] 30 15
## [1] 30 15
## [1] 41 3
## [1] 41 3
## [1] 40 12
## [1] 40 12

##      Bone-Osteosarc      Breast-AdenoCA      CNS-GBM
##                 8                  11                  3
##      CNS-Medullo      CNS-PiloAstro      ColoRect-AdenoCA
##                 4                  3                  10
##      Eso-AdenoCA      Head-SCC      Kidney-ChRCC
##                 8                  9                  5
##      Kidney-RCC.clearcell      Kidney-RCC.papillary      Liver-HCC
##                           5                  5                  15
##      Lung-SCC      Lymph-BNHL      Lymph-CLL
##                           3                  11                  2
##      Ovary-AdenoCA      Panc-AdenoCA      Panc-Endocrine
##                           9                  13                  10
##      Prost-AdenoCA Skin-Melanoma.cutaneous      Stomach-AdenoCA
##                           9                  6                  15
##      Thy-AdenoCA      Uterus-AdenoCA
##                           3                  12

## Error in apply(pert, 1, function(i) sqrt(sum((i - 1/(ncol(exposures_cancertype_obj$Y)))^2))) :
##   dim(X) must have a positive length
## Error in apply(pert, 1, function(i) sqrt(sum((i - 1/(ncol(exposures_cancertype_obj$Y)))^2))) :
##   dim(X) must have a positive length
## Warning: NAs introduced by coercion

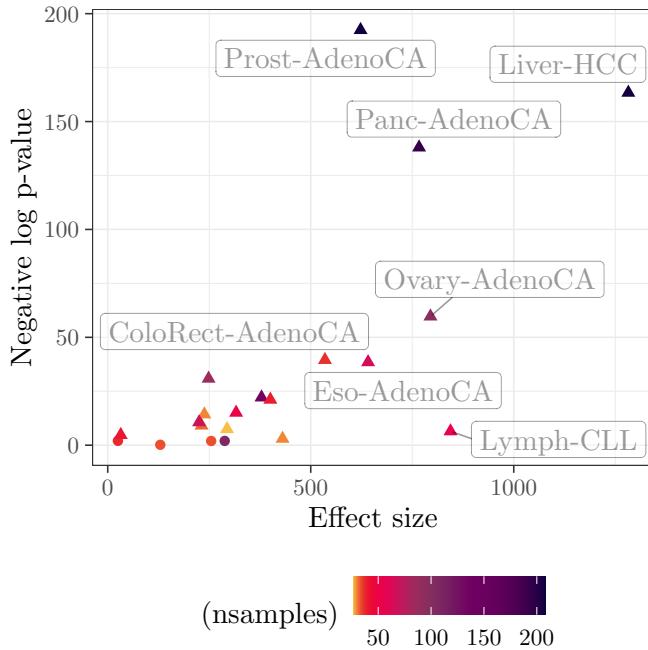
Effect sizes:

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 2 rows containing missing values (geom_point).
## Warning: Removed 2 rows containing missing values (geom_label_repel).
## Warning: ggrepel: 14 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

```

## Total perturbation non-exogenous signatures



|    |                      |                         |                  |
|----|----------------------|-------------------------|------------------|
| ## | Bone-Osteosarc       | Breast-AdenoCA          | CNS-GBM          |
| ## | 320.02704            | 469.29125               | 524.08517        |
| ## | CNS-Medullo          | CNS-PiloAstro           | ColoRect-AdenoCA |
| ## | 217.31161            | 27.02067                | 1031.46320       |
| ## | Eso-AdenoCA          | Head-SCC                | Kidney-ChRCC     |
| ## | 522.66804            | 221.26052               | 103.16727        |
| ## | Kidney-RCC.clearcell | Kidney-RCC.papillary    | Liver-HCC        |
| ## | 247.53963            | 156.30958               | 1332.22216       |
| ## | Lung-SCC             | Lymph-BNHL              | Lymph-CLL        |
| ## | 86.07143             | 345.88535               | 442.78303        |
| ## | Ovary-AdenoCA        | Panc-AdenoCA            | Panc-Endocrine   |
| ## | 755.21919            | 829.19711               | 220.55650        |
| ## | Prost-AdenoCA        | Skin-Melanoma.cutaneous | Stomach-AdenoCA  |
| ## | 459.55271            | 1017.96421              | 540.50633        |
| ## | Thy-AdenoCA          | Uterus-AdenoCA          |                  |
| ## | 82.57481             | 458.24059               |                  |
| ## | Bone-Osteosarc       | Breast-AdenoCA          | CNS-GBM          |
| ## | 1.080828e-04         | 2.239756e-28            | 3.390137e-03     |
| ## | CNS-Medullo          | CNS-PiloAstro           | ColoRect-AdenoCA |
| ## | 8.431463e-03         | 5.615238e-04            | 6.356131e-26     |
| ## | Eso-AdenoCA          | Head-SCC                | Kidney-ChRCC     |
| ## | 5.329093e-21         | 4.975610e-05            | 1.562125e-09     |
| ## | Kidney-RCC.clearcell | Kidney-RCC.papillary    | Liver-HCC        |
| ## | 4.027485e-18         | NA                      | 4.747822e-107    |
| ## | Lung-SCC             | Lymph-BNHL              | Lymph-CLL        |
| ## | 7.747310e-22         | 3.908637e-19            | 6.611927e-20     |
| ## | Ovary-AdenoCA        | Panc-AdenoCA            | Panc-Endocrine   |
| ## | 8.965185e-38         | 4.096402e-119           | 3.987099e-10     |

```

##          Prost-AdenoCA Skin-Melanoma.cutaneous      Stomach-AdenoCA
## 6.474116e-99           9.272113e-25           1.715150e-06
## Thy-AdenoCA            Uterus-AdenoCA
## 8.821583e-06           4.819867e-10

## Scale for 'colour' is already present. Adding another scale for 'colour',
## which will replace the existing scale.

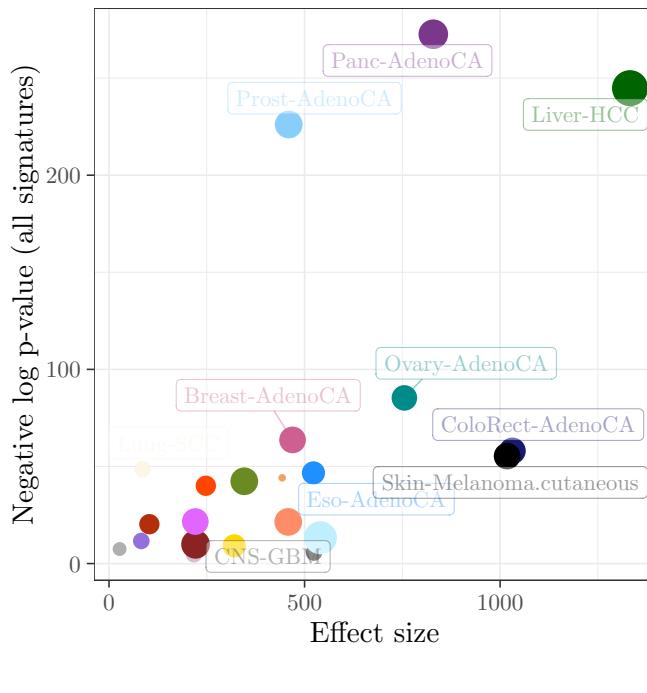
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 1 rows containing missing values (geom_point).

## Warning: Removed 1 rows containing missing values (geom_label_repel).

## Warning: ggrepel: 12 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

```



```

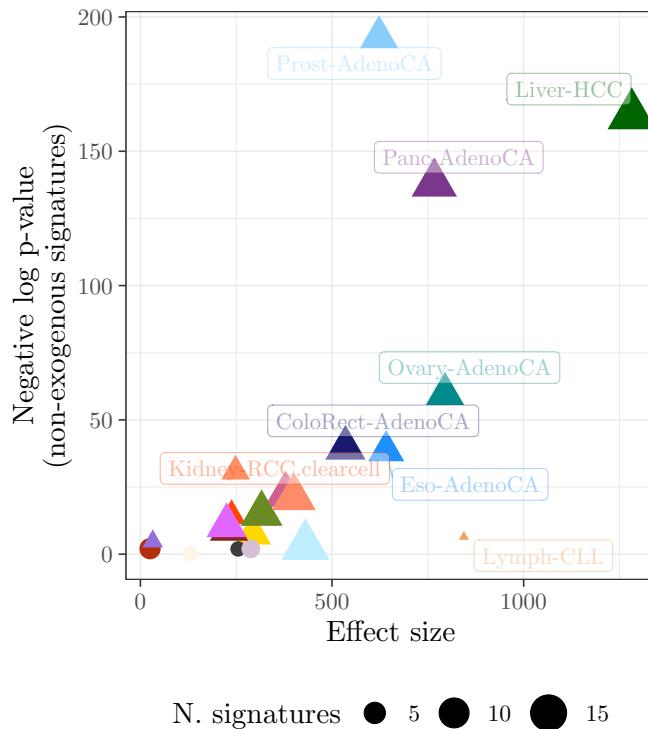
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 2 rows containing missing values (geom_point).

## Warning: Removed 2 rows containing missing values (geom_label_repel).

## Warning: ggrepel: 13 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

```



## HMP

Simple HMP tests to see what is differentially abundant

```
## Loading required package: HMP
## Loading required package: dirmult
##
## Attaching package: 'dirmult'
## The following object is masked from 'package:MCMCpack':
## 
##      rdirichlet
##
## Attaching package: 'HMP'
## The following object is masked from 'package:dirmult':
## 
##      weirMoM
## Error in signatures_PCAWG_it["x"][[1]][, 2] :
##   incorrect number of dimensions
## Error in signature_roo_it[[2]] : subscript out of bounds
## Warning in loglikDM(data, gamma.MoM): full precision may not have been achieved
## in 'lgamma'
## Error in rowSums(sig_obj$Y) :
##   'x' must be an array of at least two dimensions
```

```

## Error in rowSums(sig_obj$Y) :
##   'x' must be an array of at least two dimensions
## Error : $ operator is invalid for atomic vectors

## [1] "Biliary-AdenoCA.p value"          "Bladder-TCC.p value"
## [3] "Bone-Benign.p value"              "Bone-Epith.p value"
## [5] "Bone-Osteosarc.p value"          "Breast-AdenoCA.p value"
## [7] "Breast-DCIS.p value"             "Breast-LobularCA.p value"
## [9] "Cervix-AdenoCA.p value"          "Cervix-SCC.p value"
## [11] "CNS-GBM.p value"                 "CNS-Medullo.p value"
## [13] "CNS-Oligo.p value"               "CNS-PiloAstro.p value"
## [15] "ColoRect-AdenoCA.p value"        "Eso-AdenoCA.p value"
## [17] "Head-SCC.p value"                "Kidney-ChRCC.p value"
## [19] "Kidney-RCC.clearcell.p value"    "Kidney-RCC.papillary.p value"
## [21] "Liver-HCC.p value"                "Lung-AdenoCA.p value"
## [23] "Lung-SCC.p value"                "Lymph-BNHL.p value"
## [25] "Lymph-CLL.p value"                "Myeloid-AML.p value"
## [27] "Myeloid-MPN.p value"              "Ovary-AdenoCA.p value"
## [29] "Panc-AdenoCA.p value"            "Panc-Endocrine.p value"
## [31] "Prost-AdenoCA.p value"           "Skin-Melanoma.acral.p value"
## [33] "Skin-Melanoma.cutaneous.p value" "Skin-Melanoma.mucosal"
## [35] "SoftTissue-Leiomyo.p value"       "SoftTissue-Liposarc.p value"
## [37] "Stomach-AdenoCA.p value"         "Thy-AdenoCA.p value"
## [39] "Uterus-AdenoCA.p value"

## [1] "Bone-Osteosarc"                  "Breast-AdenoCA"
## [3] "CNS-GBM"                         "CNS-Medullo"
## [5] "CNS-PiloAstro"                   "ColoRect-AdenoCA"
## [7] "Eso-AdenoCA"                     "Head-SCC"
## [9] "Kidney-ChRCC"                    "Kidney-RCC.clearcell"
## [11] "Kidney-RCC.papillary"            "Liver-HCC"
## [13] "Lung-SCC"                        "Lymph-BNHL"
## [15] "Lymph-CLL"                       "Ovary-AdenoCA"
## [17] "Panc-AdenoCA"                   "Panc-Endocrine"
## [19] "Prost-AdenoCA"                  "Skin-Melanoma.cutaneous"
## [21] "Stomach-AdenoCA"                 "Thy-AdenoCA"
## [23] "Uterus-AdenoCA"

##      Bone-Osteosarc.p value          Breast-AdenoCA.p value
##      6.918553e-01                  1.000000e+00
##      CNS-GBM.p value                CNS-Medullo.p value
##      1.000000e+00                  3.245284e-01
##      CNS-PiloAstro.p value          ColoRect-AdenoCA.p value
##      1.000000e+00                  1.000000e+00
##      Eso-AdenoCA.p value           Head-SCC.p value
##      1.000000e+00                  1.000000e+00
##      Kidney-ChRCC.p value          Kidney-RCC.clearcell.p value
##      1.000000e+00                  1.000000e+00
##      Kidney-RCC.papillary.p value Liver-HCC.p value
##      1.000000e+00                  1.000000e+00
##      Lung-SCC.p value              Lymph-BNHL.p value
##      1.000000e+00                  1.000000e+00
##      Lymph-CLL.p value             Ovary-AdenoCA.p value

```

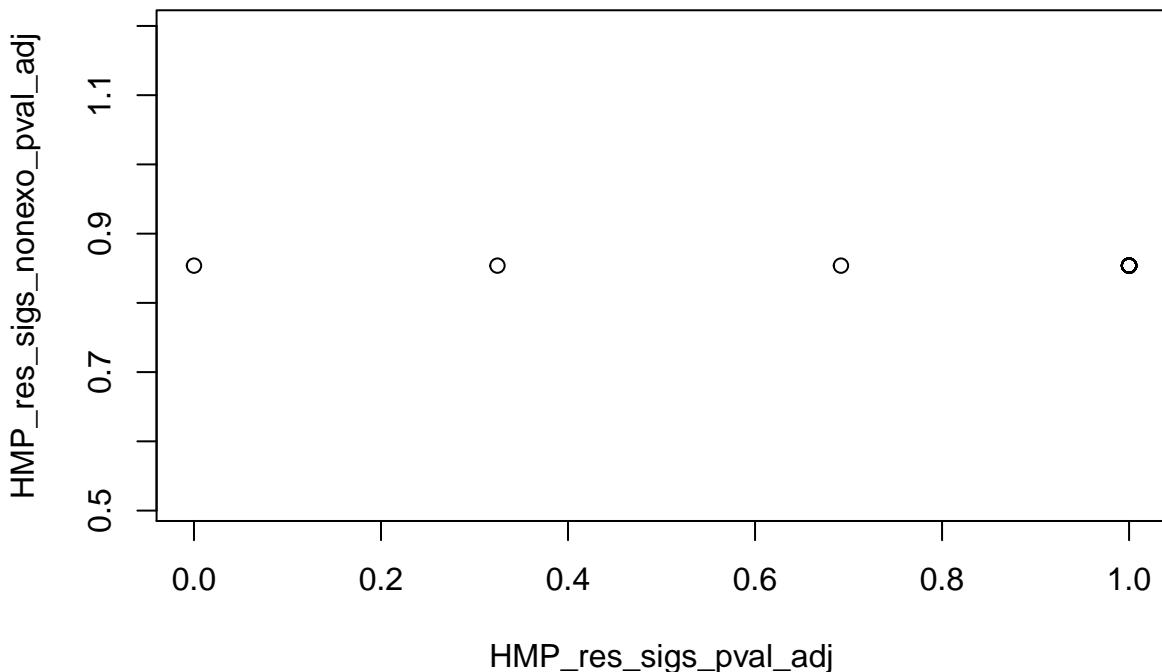
```

##          1.000000e+00          1.000000e+00
## Panc-AdenoCA.p value      Panc-Endocrine.p value
##          1.000000e+00          1.000000e+00
## Prost-AdenoCA.p value Skin-Melanoma.cutaneous.p value
##          1.000000e+00          1.000000e+00
## Stomach-AdenoCA.p value   Thy-AdenoCA.p value
##          1.000000e+00          1.000000e+00
## Uterus-AdenoCA.p value
##          7.559522e-10

## Bone-Osteosarc.p value      Breast-AdenoCA.p value
##          0.8538039           0.8538039
## CNS-GBM.p value            CNS-Medullo.p value
##          0.8538039           0.8538039
## CNS-PiloAstro.p value      ColoRect-AdenoCA.p value
##          0.8538039           0.8538039
## Eso-AdenoCA.p value        Head-SCC.p value
##          0.8538039           0.8538039
## Kidney-ChRCC.p value       Kidney-RCC.clearcell.p value
##          0.8538039           0.8538039
## Kidney-RCC.papillary.p value Liver-HCC.p value
##          0.8538039           0.8538039
## Lung-SCC.p value           Lymph-BNHL.p value
##          0.8538039           0.8538039
## Lymph-CLL.p value          Ovary-AdenoCA.p value
##          0.8538039           0.8538039
## Panc-AdenoCA.p value      Panc-Endocrine.p value
##          0.8538039           0.8538039
## Prost-AdenoCA.p value     Skin-Melanoma.cutaneous.p value
##          0.8538039           0.8538039
## Stomach-AdenoCA.p value   Thy-AdenoCA.p value
##          0.8538039           0.8538039
## Uterus-AdenoCA.p value
##          0.8538039

## Uterus-AdenoCA.p value
##          7.559522e-10

```



```

pvals_diagRE_DMDL_SP_adj <- p.adjust(pvals_diagRE_DMDL_SP, 'fdr')
pvals_diagRE_DMDL_nonexo_SP_adj <- p.adjust(pvals_diagRE_DMDL_nonexo_SP, 'fdr')
pvals_fullREDMnoscaling_SP_nonexo_subsets_and_amalgamations_adj <- p.adjust(pvals_fullREDMnoscaling_SP_no
pvals_fullRE_M_nonexo_SP_adj <- p.adjust(pvals_fullRE_M_nonexo_SP, 'fdr')
pvals_fullRE_DMSL_nonexo_SP_adj <- p.adjust(pvals_fullRE_DMSL_nonexo_SP, 'fdr')
names(pvals_diagRE_DMDL_SP_adj) <- names(pvals_diagRE_DMDL_nonexo_SP_adj) <- names(pvals_fullRE_M_nonexo_)

table(diagRE_DMDL_DA=pvals_diagRE_DMDL_nonexo_SP_adj <= 0.05,
      fullRE_DMSL_DA=pvals_fullRE_DMSL_nonexo_SP_adj <= 0.05)

##               fullRE_DMSL_DA
## diagRE_DMDL_DA FALSE  TRUE
##          FALSE     5     1
##          TRUE      1    11

names(pvals_diagRE_DMDL_nonexo_SP_adj)[which((pvals_diagRE_DMDL_nonexo_SP_adj <= 0.05) & (fullRE_DMSL_DA=0)]
## [1] "Lymph-CLL"
names(pvals_diagRE_DMDL_nonexo_SP_adj)[which((pvals_diagRE_DMDL_nonexo_SP_adj > 0.05) & (fullRE_DMSL_DA=1))
## [1] "Stomach-AdenoCA"
table(diagRE_DMDL_DA=pvals_diagRE_DMDL_nonexo_SP_adj <= 0.05,
      fullRE_M_DA=pvals_fullRE_M_nonexo_SP_adj <= 0.05)

##               fullRE_M_DA
## diagRE_DMDL_DA TRUE
##          FALSE     5
##          TRUE    17
# table(diagRE_DMDL_DA=pvals_diagRE_DMDL_nonexo_SP_adj <= 0.05,
#       HMP_DA=HMP_res_sigs_pval_adj <= 0.05)

```

```

# table(diagRE_DMDL_DA=pvals_diagRE_DMDL_nonexo_SP_adj < 0.05, HMP_res_sigs_DA=HMP_res_sigs < 0.05)

p.adjust(pvals_diagRE_DMDL_SP, method = "BH")

##          Bone-Osteosarc      Breast-AdenoCA           CNS-GBM
## 1.251484e-04    9.854928e-28  3.551572e-03
##          CNS-Medullo      CNS-PiloAstro       ColoRect-AdenoCA
## 8.431463e-03    6.176762e-04  2.330581e-25
##          Eso-AdenoCA        Head-SCC            Kidney-ChRCC
## 1.302667e-20    6.081301e-05  2.291117e-09
## Kidney-RCC.clearcell Kidney-RCC.papillary          Liver-HCC
## 7.383723e-18                NA  5.222605e-106
##          Lung-SCC          Lymph-BNHL          Lymph-CLL
## 2.130510e-21    7.817274e-19  1.454624e-19
##          Ovary-AdenoCA      Panc-AdenoCA       Panc-Endocrine
## 4.930852e-37    9.012085e-118  6.747398e-10
##          Prost-AdenoCA Skin-Melanoma.cutaneous      Stomach-AdenoCA
## 4.747685e-98    2.914093e-24  2.358331e-06
##          Thy-AdenoCA        Uterus-AdenoCA
## 1.141617e-05    7.574077e-10

p.adjust(pvals_diagRE_DMDL_nonexo_SP, method = "BH")

##          Bone-Osteosarc      Breast-AdenoCA           CNS-GBM
## 8.712593e-04    6.123721e-10  1.557247e-01
##          CNS-Medullo      CNS-PiloAstro       ColoRect-AdenoCA
## 1.557247e-01    5.270878e-01  3.141298e-17
##          Eso-AdenoCA        Head-SCC            Kidney-ChRCC
## 7.328650e-17    1.788732e-04  1.557247e-01
## Kidney-RCC.clearcell Kidney-RCC.papillary          Liver-HCC
## 1.137607e-13    1.190455e-06  1.263498e-70
##          Lung-SCC          Lymph-BNHL          Lymph-CLL
## 8.301558e-01    5.881884e-07  2.256505e-03
##          Ovary-AdenoCA      Panc-AdenoCA       Panc-Endocrine
## 6.973340e-26    8.893577e-60  4.169125e-05
##          Prost-AdenoCA Skin-Melanoma.cutaneous      Stomach-AdenoCA
## 6.044387e-83    9.919659e-17  6.320633e-02
##          Thy-AdenoCA        Uterus-AdenoCA
## 1.170750e-02    1.568961e-09

df_pvals_DMDL_SP <- cbind.data.frame(pvals_DM=pvals_diagRE_DMDL_SP_adj,
                                         pvals_DMnonexo=pvals_diagRE_DMDL_nonexo_SP_adj,
                                         num_samples=as.numeric(num_samples_all_SP),
                                         num_sigs_nonexo=as.numeric(num_sigs_nonexo_SP),
                                         ct=enough_samples,
                                         pvals_DM_censored=sapply(-log(pvals_diagRE_DMDL_SP_adj),
                                                                   function(i) min(i, 25)),
                                         pvals_DMnonexo_censored=sapply(-log(pvals_diagRE_DMDL_nonexo_SP_adj),
                                                                   function(i) min(i, 25)),
                                         bool_censored=(( -log(pvals_diagRE_DMDL_nonexo_SP_adj) > 25 ) | ( -log(pvals_diagRE_
```

ggplot(df\_pvals\_DMDL\_SP,

```

aes(x=pvals_DM_censored, y=pvals_DMnonexo_censored,
    # size=num_samples,
    label=ct, size=bool_censored))+geom_point(aes (col=ct))+  

geom_hline(yintercept = -log(0.05), lty='dashed')+geom_vline(xintercept = -log(0.05), lty='dashed')+  

geom_label_repel(size=3.2, alpha=0.6, max.overlaps = 30)+ theme_bw()+
theme(legend.position = "bottom", legend.text=element_text(size=8))+  

labs(x='- Log p-value all signatures', y='- Log p-value nonexogenous signatures')+  

guides(size=FALSE, col=FALSE)+ #, col=guide_legend(ncol=4),
scale_color_manual(values = pcawg_palette)+theme(legend.position = "bottom")+
lims(x=c(0, 30), y=c(0,30))

```

```

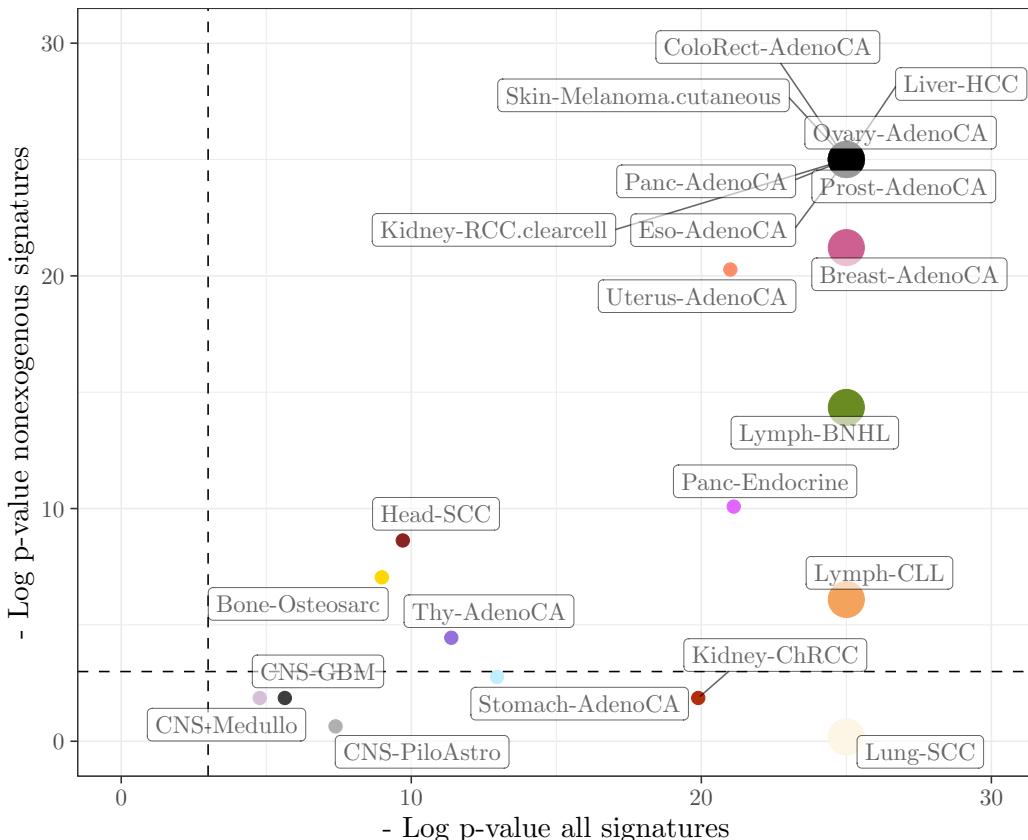
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Using size for a discrete variable is not advised.

## Warning: Removed 1 rows containing missing values (geom_point).

## Warning: Removed 1 rows containing missing values (geom_label_repel).

```



```

t.test(df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo <= 0.05,'num_samples'],
       df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo > 0.05,'num_samples'])

```

```

##  

## Welch Two Sample t-test  

##

```

```

## data: df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo <= 0.05, "num_samples"] and df_pvals_DMDL_SP[[
## t = 1.8016, df = 19.213, p-value = 0.08733
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
## -5.663104 76.055261
## sample estimates:
## mean of x mean of y
## 82.52941 47.33333

t.test(df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo <= 0.05, 'num_sigs_nonexo'],
       df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo > 0.05, 'num_sigs_nonexo'])

##
## Welch Two Sample t-test
##
## data: df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo <= 0.05, "num_sigs_nonexo"] and df_pvals_DMDL_[
## t = 1.466, df = 7.0453, p-value = 0.1858
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
## -1.886557 8.063027
## sample estimates:
## mean of x mean of y
## 8.588235 5.500000

mean(df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo <= 0.05, 'num_sigs_nonexo'])

## [1] 8.588235

mean(df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo > 0.05, 'num_sigs_nonexo'])

## [1] 5.5

```

Does DA or not scale with the avergae number of mutations in the observed exposures (i.e. per patient and group) of the relevant ct?

```

average_num_muts_SP <- sapply(enough_samples, function(ct){
  .xx <- all_objects_SP[[ct]]
  try(mean(rowSums(.xx$Y)))
})

average_num_muts_SP

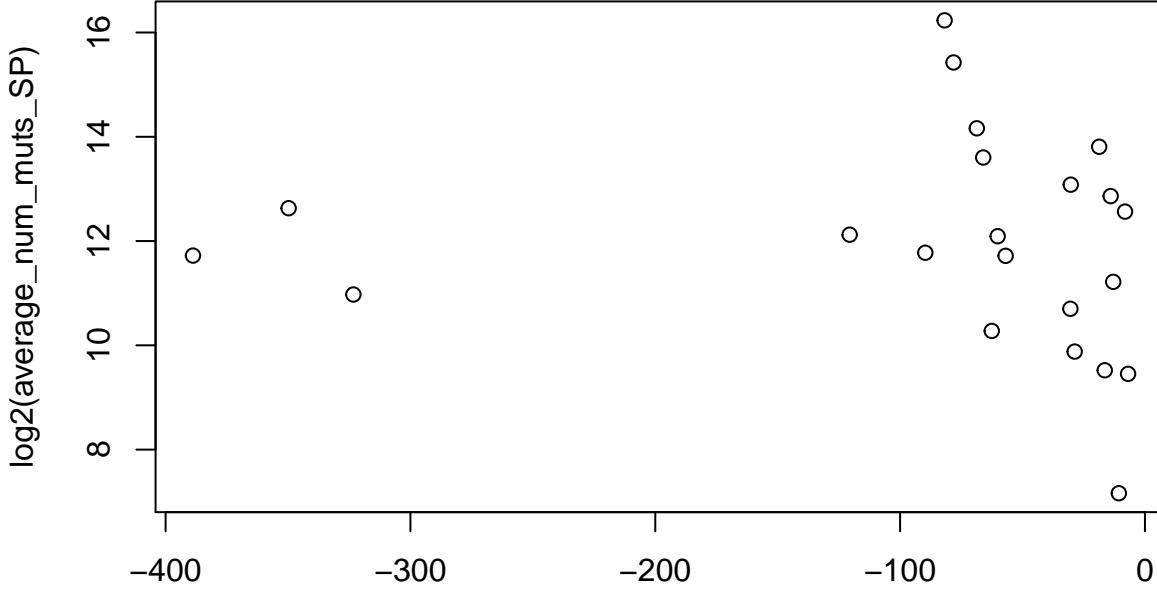
##          Bone-Osteosarc          Breast-AdenoCA          CNS-GBM
##                2382.1852            3507.5588            6057.6618
##          CNS-Medullo          CNS-PiloAstro      ColoRect-AdenoCA
##                700.8915            143.3452            77035.7838
##          Eso-AdenoCA           Head-SCC          Kidney-ChRCC
##                12439.3692            7445.4219            942.5263
## Kidney-RCC.clearcell      Kidney-RCC.papillary          Liver-HCC
##                3365.9477            2740.9833            6340.5121
##          Lung-SCC              Lymph-BNHL          Lymph-CLL
##                18340.1471            4367.0392            1239.9057
##          Ovary-AdenoCA          Panc-AdenoCA          Panc-Endocrine
##                4458.4691            3376.0415            1664.5857
## Prost-AdenoCA Skin-Melanoma.cutaneous      Stomach-AdenoCA

```

```

##          2011.8966      43998.4833      14345.9667
## Thy-AdenoCA      Uterus-AdenoCA
##          734.8902      8670.1125

plot(log2(df_pvals_DMDL_SP$pvals_DM), log2(average_num_muts_SP))



```

log2(average\_num\_muts\_SP)

log2(df\_pvals\_DMDL\_SP\$pvals\_DM)

```

t.test(log2(average_num_muts_SP)[df_pvals_DMDL_SP$pvals_DMnonexo <= 0.05],
       log2(average_num_muts_SP)[df_pvals_DMDL_SP$pvals_DMnonexo > 0.05])

## 
## Welch Two Sample t-test
##
## data: log2(average_num_muts_SP)[df_pvals_DMDL_SP$pvals_DMnonexo <= 0.05] and log2(average_num_muts_SP)[df_pvals_DMDL_SP$pvals_DMnonexo > 0.05]
## t = 0.85052, df = 6.3966, p-value = 0.4257
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
## -1.88287 3.93586
## sample estimates:
## mean of x mean of y
## 12.19856 11.17207

pcawg_palette <- pcawg.colour.palette(gsub("\\.*", "", enough_samples), scheme = "tumour.subtype")
names(pcawg_palette) <- enough_samples

pvals_diagRE_DMDL_nonexo_SP_adj

##          Bone-Osteosarc      Breast-AdenoCA      CNS-GBM
##          8.712593e-04      6.123721e-10      1.557247e-01
##          CNS-Medullo      CNS-PiloAstro      ColoRect-AdenoCA
##          1.557247e-01      5.270878e-01      3.141298e-17
##          Eso-AdenoCA      Head-SCC      Kidney-ChRCC
##          7.328650e-17      1.788732e-04      1.557247e-01

```

```

##      Kidney-RCC.clearcell      Kidney-RCC.papillary      Liver-HCC
##      1.137607e-13      1.190455e-06      1.263498e-70
##      Lung-SCC          Lymph-BNHL          Lymph-CLL
##      8.301558e-01      5.881884e-07      2.256505e-03
##      Ovary-AdenoCA      Panc-AdenoCA      Panc-Endocrine
##      6.973340e-26      8.893577e-60      4.169125e-05
##      Prost-AdenoCA Skin-Melanoma.cutaneous      Stomach-AdenoCA
##      6.044387e-83      9.919659e-17      6.320633e-02
##      Thy-AdenoCA       Uterus-AdenoCA
##      1.170750e-02      1.568961e-09

pvals_fullREDMnoscaling_SP_nonexo_subsets_and_amalgamations_adj

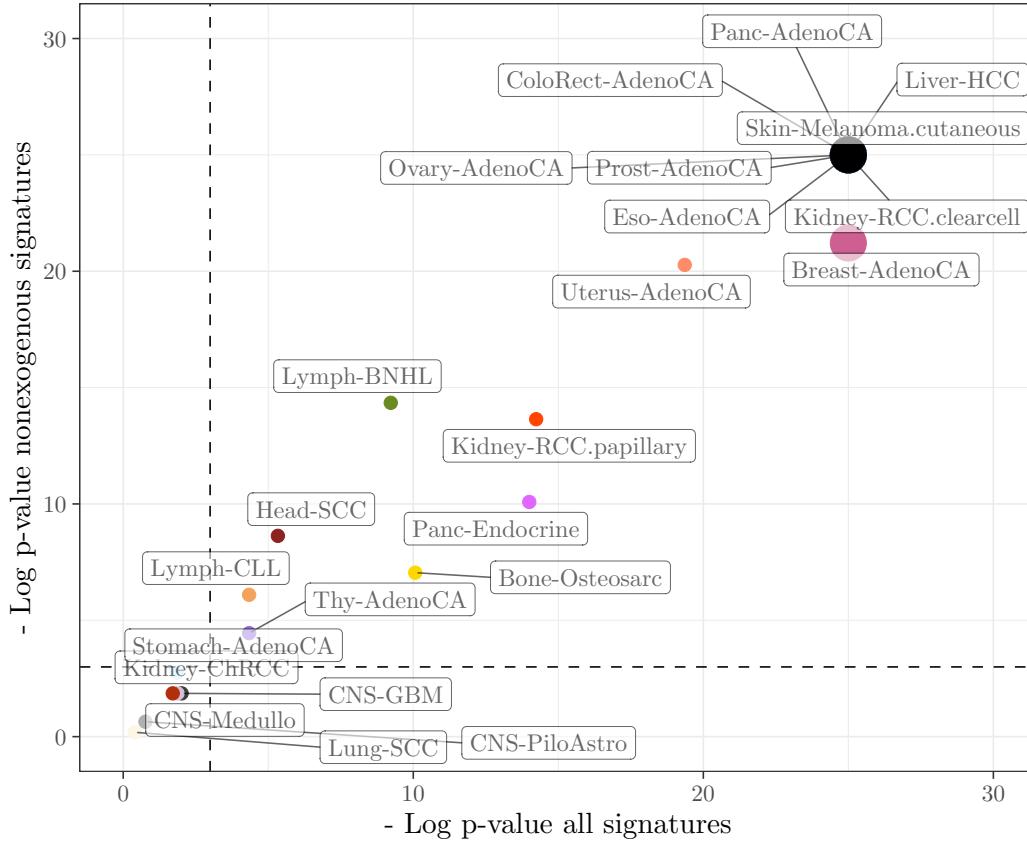
##      Bone-Osteosarc      Breast-AdenoCA      CNS-GBM
##      4.248457e-05      7.759783e-12      1.336685e-01
##      CNS-Medullo      CNS-PiloAstro      ColoRect-AdenoCA
##      1.538381e-01      4.648237e-01      1.023484e-15
##      Eso-AdenoCA       Head-SCC      Kidney-ChRCC
##      3.759670e-18      4.834276e-03      1.814391e-01
##      Kidney-RCC.clearcell      Kidney-RCC.papillary      Liver-HCC
##      3.652385e-14      6.557344e-07      3.704923e-63
##      Lung-SCC          Lymph-BNHL          Lymph-CLL
##      6.693019e-01      9.868396e-05      1.303426e-02
##      Ovary-AdenoCA      Panc-AdenoCA      Panc-Endocrine
##      1.231778e-22      7.710539e-59      8.327076e-07
##      Prost-AdenoCA Skin-Melanoma.cutaneous      Stomach-AdenoCA
##      6.572758e-67      3.732926e-14      1.576047e-01
##      Thy-AdenoCA       Uterus-AdenoCA
##      1.303426e-02      3.911013e-09

df_pvals_fullREDMnoscaling_SP_nonexo_subsets_and_amalgamations <- cbind.data.frame(pvals_DMnonexo_nonscal-
                                         pvals_DMnonexo=pvals_diagRE_DMDL_nonexo_SP_adj,
                                         num_samples=as.numeric(num_samples_all_SP),
                                         num_sigs_nonexo=as.numeric(num_sigs_nonexo_SP),
                                         ct=enough_samples,
                                         pvals_DM_nonscaling_censored=sapply(-log(pvals_fullREDMnoscaling_SP_nonexo_subset
                                              function(i) min(i, 25)),
                                         pvals_DMnonexo_censored=sapply(-log(pvals_diagRE_DMDL_nonexo_SP_adj),
                                              function(i) min(i, 25)),
                                         bool_censored=(( -log(pvals_diagRE_DMDL_nonexo_SP_adj) > 25 ) | ( -log(pvals_fullREDMnoscaling_SP_nonexo_subsets_and_amalgamations,
                                         aes(x=pvals_DM_nonscaling_censored, y=pvals_DMnonexo_censored,
                                         # size=num_samples,
                                         label=ct, size=bool_censored))+geom_point(aes (col=ct))+geom_hline(yintercept = -log(0.05), lty='dashed')+geom_vline(xintercept = -log(0.05), lty='dashed')+geom_label_repel(size=3.2, alpha=0.6, max.overlaps = 30)+ theme_bw()+
                                         theme(legend.position = "bottom", legend.text=element_text(size=8))+labs(x=' - Log p-value all signatures', y=' - Log p-value nonexogenous signatures')+guides(size=FALSE, col=FALSE)+ #, col=guide_legend(ncol=4),
                                         scale_color_manual(values = pcawg_palette)+theme(legend.position = "bottom")+
                                         lims(x=c(0, 30), y=c(0,30))

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =

```

```
## "none")` instead.  
## Warning: Using size for a discrete variable is not advised.
```



See script PCAWG\_HMP\_and\_alternative\_methods.R for the analyses of PCAWG data using alternative models.

## Tracksig

```
tracksig = read.csv("../data/restricted/tracksig/changepoints_stats_tracksig.csv", stringsAsFactors =  
tracksig = tracksig %>% group_by(type) %>%  
  dplyr::summarize(count = n(), bool_changepoints=sum(n_changepoints > 0)) %>%  
  mutate(tracksig_frac= bool_changepoints/count)  
tracksig = cbind.data.frame(pvals_diagRE_DMDL_SP_adj,  
                           tracksig[match(names(pvals_diagRE_DMDL_SP_adj), tracksig$type),],  
                           effect_size3_SP=effect_size3_SP[match(names(pvals_diagRE_DMDL_SP_adj), names(effect_size3_SP)),]  
tracksig$ct = rownames(tracksig)  
tracksig$minpvals = -log2(tracksig$pvals_diagRE_DM)  
  
pcawg_palette <- pcawg.colour.palette(gsub("\\\\..*", "", tracksig$ct), scheme = "tumour.subtype")  
names(pcawg_palette) <- tracksig$ct  
  
ggplot(tracksig, aes(x=-log2(pvals_diagRE_DMDL_SP_adj), y=tracksig_frac, label=ct, size=count))+geom_point()  
  labs(x=' -log2 p-value of diagRE DMDL', y='Fraction of TrackSig samples with some changepoint')+
```

```

  scale_color_manual(values = pcawg_palette)+theme(legend.position = "bottom")+
# scale_x_continuous(trans = "log2")+
  theme_bw()+theme(legend.position = "bottom")

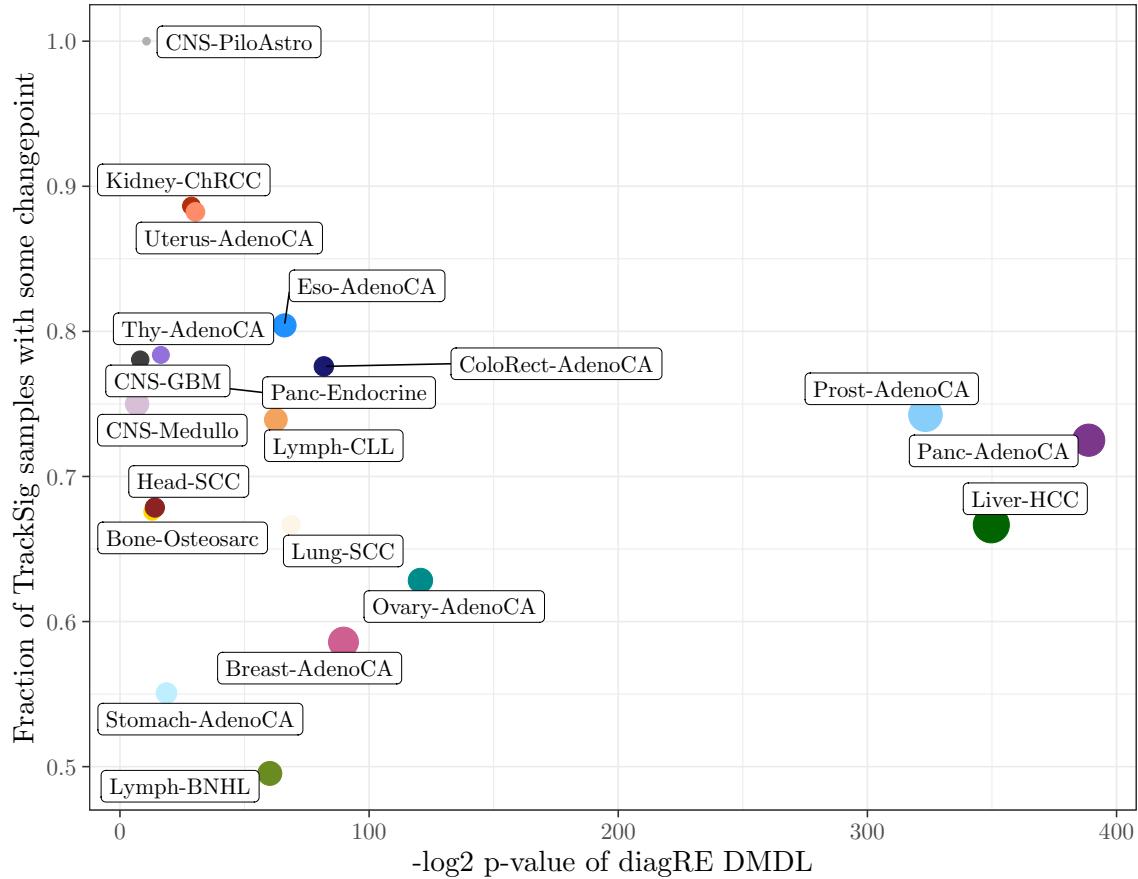
```

```

## Warning: Removed 3 rows containing missing values (geom_point).

## Warning: Removed 3 rows containing missing values (geom_label_repel).

```



```

  ggplot(tracksig, aes(x=-log2(pvals_diagRE_DMDL_nonexo_SP_adj), y=tracksig_frac, label=ct, size=count))+ge
  labs(x=' -log2 p-value of diagRE DMDL (nonexo)', y='Fraction of TrackSig samples with some changepoint')
  scale_color_manual(values = pcawg_palette)+theme(legend.position = "bottom")+
  theme_bw()+theme(legend.position = "bottom")

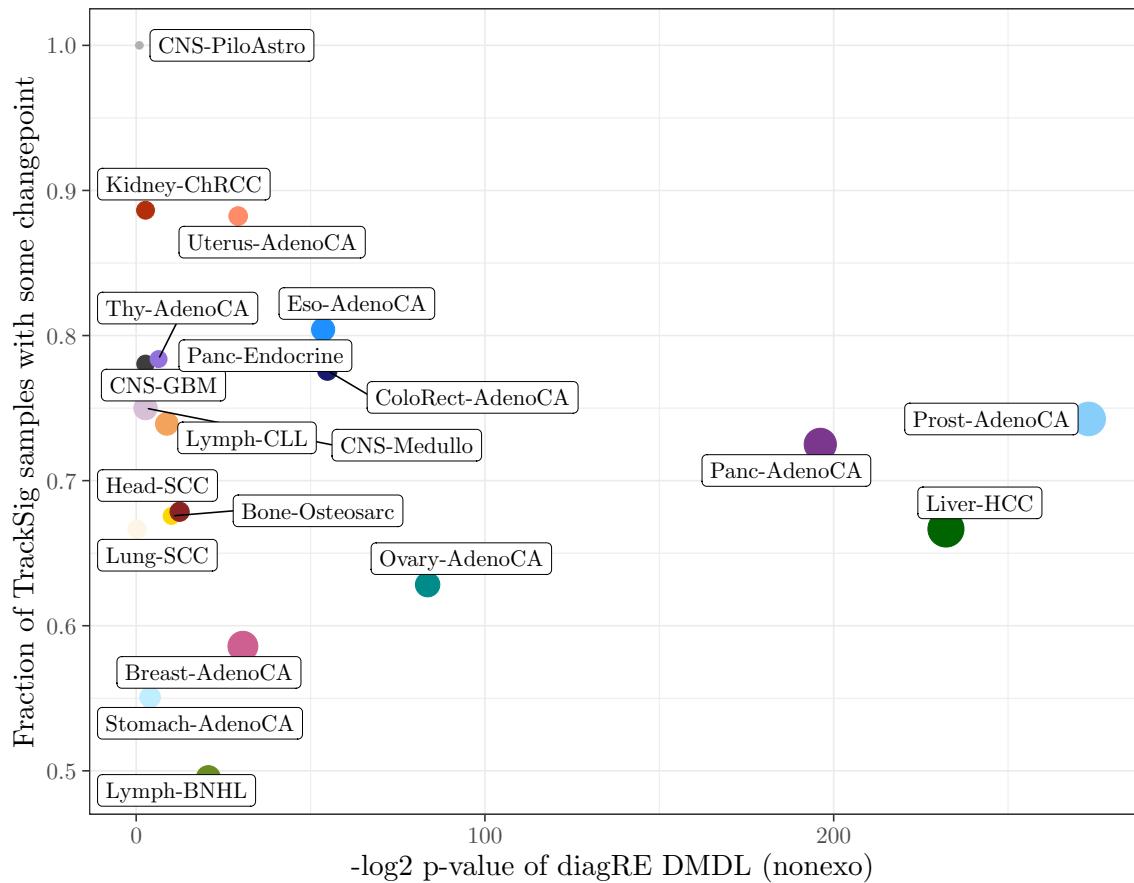
```

```

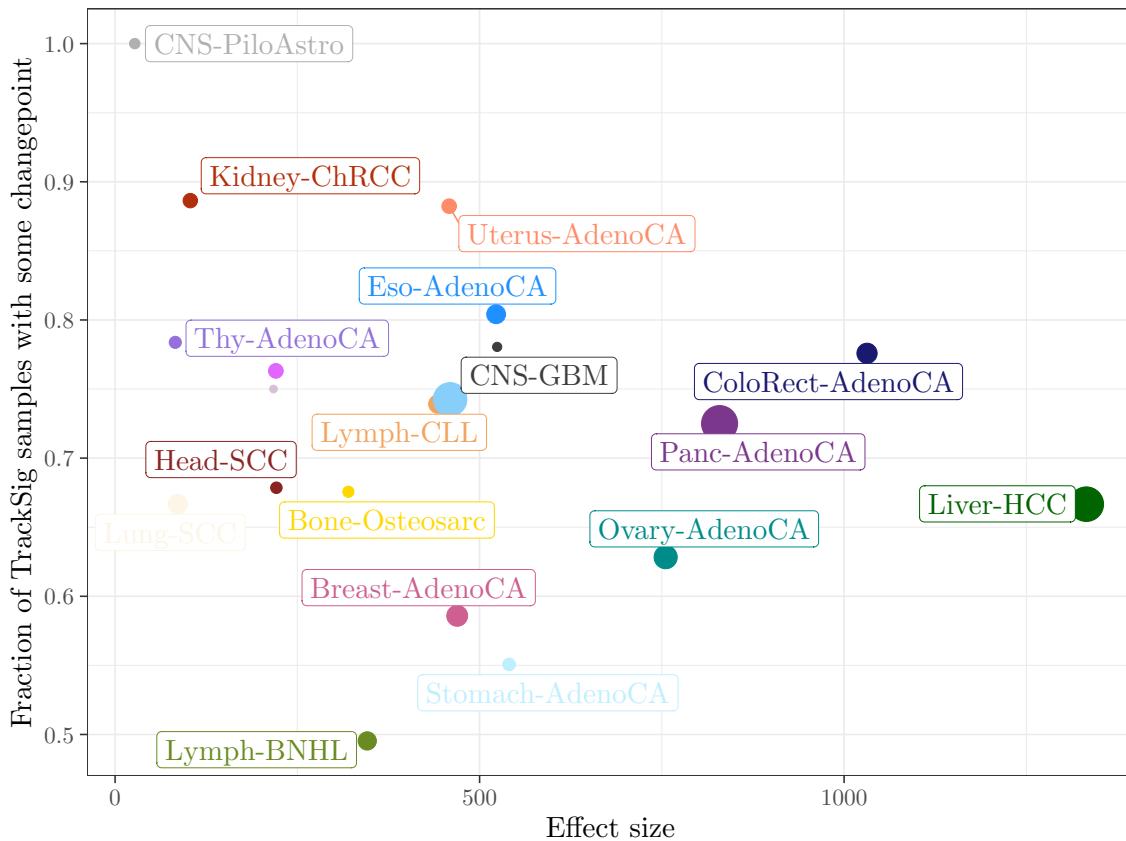
## Warning: Removed 3 rows containing missing values (geom_point).

## Warning: Removed 3 rows containing missing values (geom_label_repel).

```



```
ggplot(tracksig, aes(x=effect_size3_SP, y=tracksig_frac, label=ct, col=ct))+  
  geom_point(aes(size=minpvals))+geom_label_repel(max.overlaps = 5)+  
  labs(x='Effect size', y='Fraction of TrackSig samples with some changepoint', col="") + theme_bw() +  
  scale_color_manual(values = pcawg_palette)+theme(legend.position = "bottom") +  
  guides(col=guide_legend(ncol=4), size=FALSE)  
  
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =  
## "none")` instead.  
  
## Warning: Removed 3 rows containing missing values (geom_point).  
  
## Warning: Removed 3 rows containing missing values (geom_label_repel).  
  
## Warning: ggrepel: 3 unlabeled data points (too many overlaps). Consider  
## increasing max.overlaps
```



|   |                  |   |                      |   |                |   |                       |
|---|------------------|---|----------------------|---|----------------|---|-----------------------|
| a | Bone-Osteosarc   | a | Eso-AdenoCA          | a | Lung-SCC       | a | Prost-AdenoCA         |
| a | Breast-AdenoCA   | a | Head-SCC             | a | Lymph-BNHL     | a | Skin-Melanoma.cutaneo |
| a | CNS-GBM          | a | Kidney-ChRCC         | a | Lymph-CLL      | a | Stomach-AdenoCA       |
| a | CNS-Medullo      | a | Kidney-RCC.clearcell | a | Ovary-AdenoCA  | a | Thy-AdenoCA           |
| a | CNS-PiloAstro    | a | Kidney-RCC.papillary | a | Panc-AdenoCA   | a | Uterus-AdenoCA        |
| a | ColoRect-AdenoCA | a | Liver-HCC            | a | Panc-Endocrine |   |                       |

Same plots, but smaller, for images

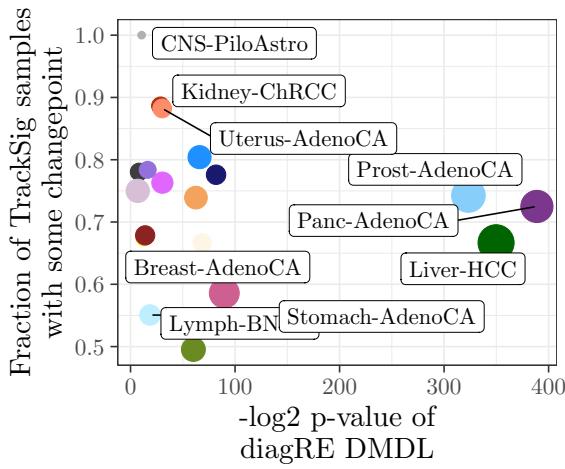
```
ggplot(tracksig, aes(x=-log2(pvals_diagRE_DMDL_SP_adj), y=tracksig_frac, label=ct, size=count))+geom_point()
  labs(x='-log2 p-value of\n diagRE DMDL', y='Fraction of TrackSig samples\n with some changepoint')+ 
  scale_color_manual(values = pcawg_palette)+theme(legend.position = "bottom")+
  # scale_x_continuous(trans = "log2")+
  theme_bw()+theme(legend.position = "bottom")+guides(col=FALSE)+labs(size='N. obs')

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 3 rows containing missing values (geom_point).

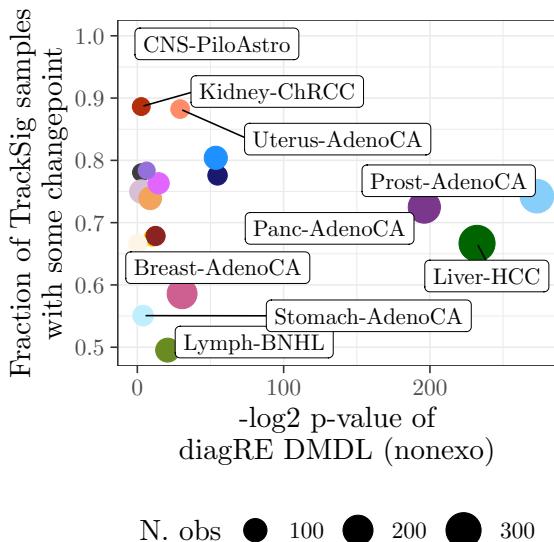
## Warning: Removed 3 rows containing missing values (geom_label_repel).

## Warning: ggrepel: 11 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps
```



```
ggplot(tracksig, aes(x=-log2(pvals_diagRE_DMDL_nonexo_SP_adj), y=tracksig_frac, label=ct, size=count))+
  geom_label_repel(size=3, col='black', max.overlaps = 4) +
  labs(x='-\log2 p-value of\n diagRE DMDL (nonexo)', y='Fraction of TrackSig samples\n with some changepoint') +
  scale_color_manual(values = pcawg_palette) + theme(legend.position = "bottom") +
  theme_bw() + theme(legend.position = "bottom") + guides(col=FALSE) + labs(size='N. obs')
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =  
## "none")` instead.  
  
## Warning: Removed 3 rows containing missing values (geom_point).  
  
## Warning: Removed 3 rows containing missing values (geom_label_repel).  
  
## Warning: ggrepel: 11 unlabeled data points (too many overlaps). Consider  
## increasing max.overlaps
```



```
plot_for_ct_legend <- ggplot(tracksig, aes(x=-log2(pvals_diagRE_DMDL_nonexo_SP_adj), y=tracksig_frac, label=ct, size=count))+
  geom_label_repel(size=3, col='black', max.overlaps = 2) +
```

```

  labs(x=-log2 p-value of\n diagRE DMDL (nonexo)', y='Fraction of TrackSig samples\n with some changepoi
    scale_color_manual(values = pcawg_palette)+theme(legend.position = "bottom")+
  theme_bw()+theme(legend.position = "bottom")+labs(size='N. observations')+guides(size=FALSE)+labs(col='')

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

legend_ct <- (cowplot::get_legend(plot_for_ct_legend))

## Warning: Removed 3 rows containing missing values (geom_point).

## Warning: Removed 3 rows containing missing values (geom_label_repel).

# pdf("../results/results_TMB/pcawg/legend_cts.pdf", height = 1, width = 6.5)
grid.newpage()
grid.draw(legend_ct)

  ● Bone-Osteosarc      ● ColoRect-AdenoCA      ● Kidney-RCC.papillary      ● Ovary-AdenoCA      ● Stomach-AdenoCA
  ● Breast-AdenoCA     ● Eso-AdenoCA        ● Liver-HCC            ● Panc-AdenoCA       ● Thy-AdenoCA
  ● CNS-GBM             ● Head-SCC          ● Lung-SCC           ● Panc-Endocrine     ● Uterus-AdenoCA
  ● CNS-Medullo         ● Kidney-ChRCC        ● Lymph-BNHL          ● Prost-AdenoCA
  ● CNS-PiloAstro       ● Kidney-RCC.clearcell ● Lymph-CLL           ● Skin-Melanoma.cutaneous

# dev.off()

tracksig

##                                     pvals_diagRE_DMDL_SP_adj      type count
## Bone-Osteosarc                  1.251484e-04 Bone-Osteosarc 37
## Breast-AdenoCA                 9.854928e-28 Breast-AdenoCA 198
## CNS-GBM                         3.551572e-03 CNS-GBM        41
## CNS-Medullo                     8.431463e-03 CNS-Medullo   100
## CNS-PiloAstro                   6.176762e-04 CNS-PiloAstro  3
## ColoRect-AdenoCA                2.330581e-25 ColoRect-AdenoCA 58
## Eso-AdenoCA                     1.302667e-20 Eso-AdenoCA   97
## Head-SCC                        6.081301e-05 Head-SCC        56
## Kidney-ChRCC                    2.291117e-09 Kidney-ChRCC  44
## Kidney-RCC.clearcell           7.383723e-18 <NA>           NA
## Kidney-RCC.papillary            NA               <NA>           NA
## Liver-HCC                       5.222605e-106 Liver-HCC      321
## Lung-SCC                        2.130510e-21 Lung-SCC        48
## Lymph-BNHL                      7.817274e-19 Lymph-BNHL     107
## Lymph-CLL                        1.454624e-19 Lymph-CLL        92
## Ovary-AdenoCA                   4.930852e-37 Ovary-AdenoCA 113
## Panc-AdenoCA                    9.012085e-118 Panc-AdenoCA 240
## Panc-Endocrine                  6.747398e-10 Panc-Endocrine 76
## Prost-AdenoCA                   4.747685e-98 Prost-AdenoCA 268
## Skin-Melanoma.cutaneous         2.914093e-24 <NA>           NA
## Stomach-AdenoCA                 2.358331e-06 Stomach-AdenoCA 69
## Thy-AdenoCA                     1.141617e-05 Thy-AdenoCA   37
## Uterus-AdenoCA                  7.574077e-10 Uterus-AdenoCA 51
##                                     bool_changepoints tracksig_frac effect_size3_SP
## Bone-Osteosarc                  25          0.6756757      320.02704

```

```

## Breast-AdenoCA           116   0.5858586   469.29125
## CNS-GBM                  32    0.7804878   524.08517
## CNS-Medullo              75    0.7500000   217.31161
## CNS-PiloAstro             3     1.0000000   27.02067
## ColoRect-AdenoCA          45    0.7758621   1031.46320
## Eso-AdenoCA               78    0.8041237   522.66804
## Head-SCC                  38    0.6785714   221.26052
## Kidney-ChRCC              39    0.8863636   103.16727
## Kidney-RCC.clearcell       NA    NA           247.53963
## Kidney-RCC.papillary       NA    NA           156.30958
## Liver-HCC                 214   0.6666667   1332.22216
## Lung-SCC                  32    0.6666667   86.07143
## Lymph-BNHL                53    0.4953271   345.88535
## Lymph-CLL                  68    0.7391304   442.78303
## Ovary-AdenoCA              71    0.6283186   755.21919
## Panc-AdenoCA               174   0.7250000   829.19711
## Panc-Endocrine              58    0.7631579   220.55650
## Prost-AdenoCA              199   0.7425373   459.55271
## Skin-Melanoma.cutaneous     NA    NA           1017.96421
## Stomach-AdenoCA             38    0.5507246   540.50633
## Thy-AdenoCA                29    0.7837838   82.57481
## Uterus-AdenoCA              45    0.8823529   458.24059
##                                         ct   minpvals
## Bone-Osteosarc              Bone-Osteosarc 12.964072
## Breast-AdenoCA              Breast-AdenoCA 89.713141
## CNS-GBM                      CNS-GBM        8.137327
## CNS-Medullo                 CNS-Medullo   6.890001
## CNS-PiloAstro                CNS-PiloAstro 10.660862
## ColoRect-AdenoCA             ColoRect-AdenoCA 81.827512
## Eso-AdenoCA                  Eso-AdenoCA   66.057093
## Head-SCC                      Head-SCC      14.005260
## Kidney-ChRCC                 Kidney-ChRCC  28.701302
## Kidney-RCC.clearcell         Kidney-RCC.clearcell 56.910357
## Kidney-RCC.papillary         Kidney-RCC.papillary NA
## Liver-HCC                      Liver-HCC    349.739609
## Lung-SCC                      Lung-SCC     68.669291
## Lymph-BNHL                     Lymph-BNHL   60.149968
## Lymph-CLL                      Lymph-CLL    62.575988
## Ovary-AdenoCA                 Ovary-AdenoCA 120.609503
## Panc-AdenoCA                  Panc-AdenoCA 388.815654
## Panc-Endocrine                 Panc-Endocrine 30.464950
## Prost-AdenoCA                  Prost-AdenoCA 323.301729
## Skin-Melanoma.cutaneous       Skin-Melanoma.cutaneous 78.183228
## Stomach-AdenoCA                Stomach-AdenoCA 18.693802
## Thy-AdenoCA                   Thy-AdenoCA   16.418562
## Uterus-AdenoCA                 Uterus-AdenoCA 30.298211
gerstung_changing_sigs_early_late <- readxl::read_excel("/Users/morril01/Documents/PhD/GlobalDA/data/rest

## New names:
## * `` -> ...

```



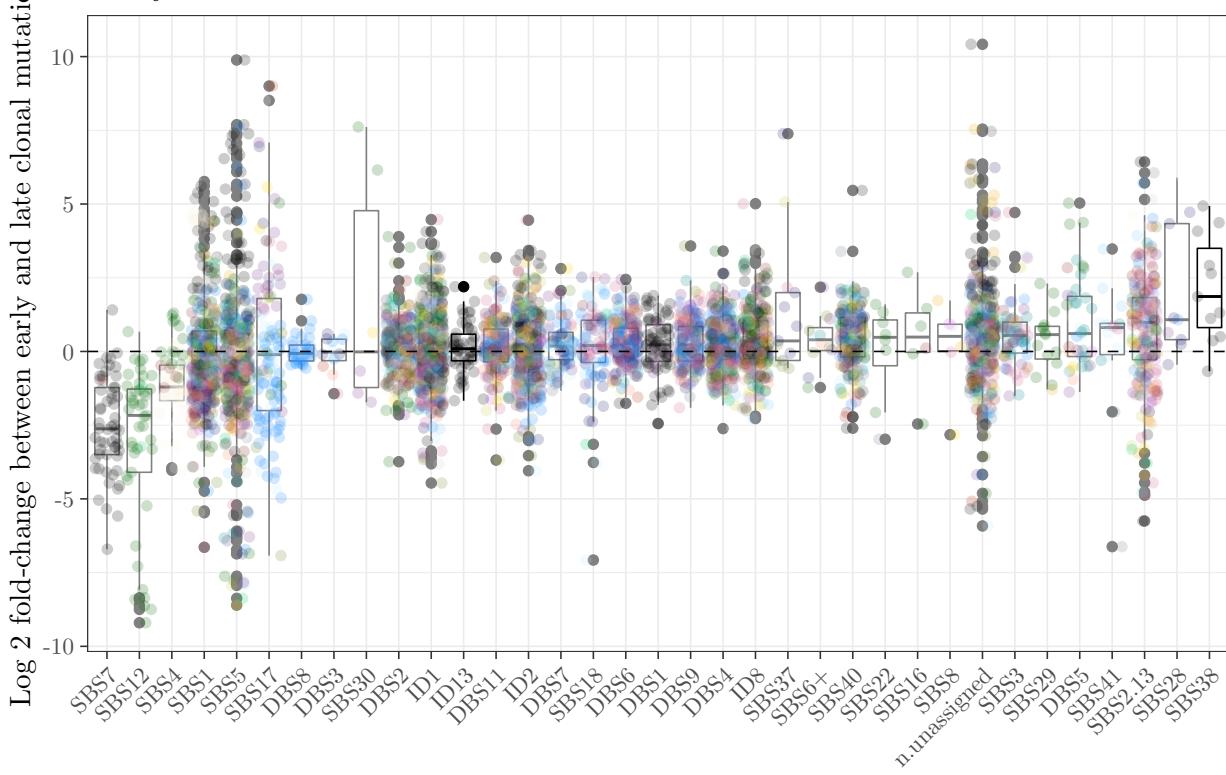
```

gerstung_changing_sigs_earlylate$signature <- factor(gerstung_changing_sigs_earlylate$signature,
                                                       levels=df_changes_el$signature[order(df_changes_el$signat
gerstung_changing_sigs_clonalsubclonal$signature <- factor(gerstung_changing_sigs_clonalsubclonal$signature,
                                                       levels=df_changes_cs$signature[order(df_change
# grid.arrange(ggplot(gerstung_changing_sigs_earlylate, aes(x=signature,
#                                         y=log2fc_earlyLate, group=signature,col=tumour_
#                                         geom_hline(yintercept = 0, lty='dashed')+ 
#                                         guides(col=FALSE)+theme_bw()+
#                                         theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Early vs late')+
#                                         scale_color_manual(values = pcawg_palette)+labs(x='', y='Log 2 fold-change between early
#                                         ggplot(gerstung_changing_sigs_clonalsubclonal, aes(x=signature,
#                                         y=log2fc_clonalsubclonal, group=signature)
#                                         geom_hline(yintercept = 0, lty='dashed')+ 
#                                         geom_boxplot()+ geom_jitter(alpha=0.2)+guides(col=FALSE)+theme_bw()+
#                                         theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Clonal vs subclonal')+
#                                         scale_color_manual(values = pcawg_palette)+labs(x='', y='Log 2 fold-change between clonal and subclonal')
#                                         nrow=2)
ggplot(gerstung_changing_sigs_earlylate, aes(x=signature,
                                               y=log2fc_earlyLate, group=signature,col=tumour_
                                               geom_hline(yintercept = 0, lty='dashed')+ 
                                               guides(col=FALSE)+theme_bw()+
                                               theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Early vs late')+
                                               scale_color_manual(values = pcawg_palette)+labs(x=' ', y='Log 2 fold-change between early and late')
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

```

Log 2 fold-change between early and late clonal mutations

Early vs late

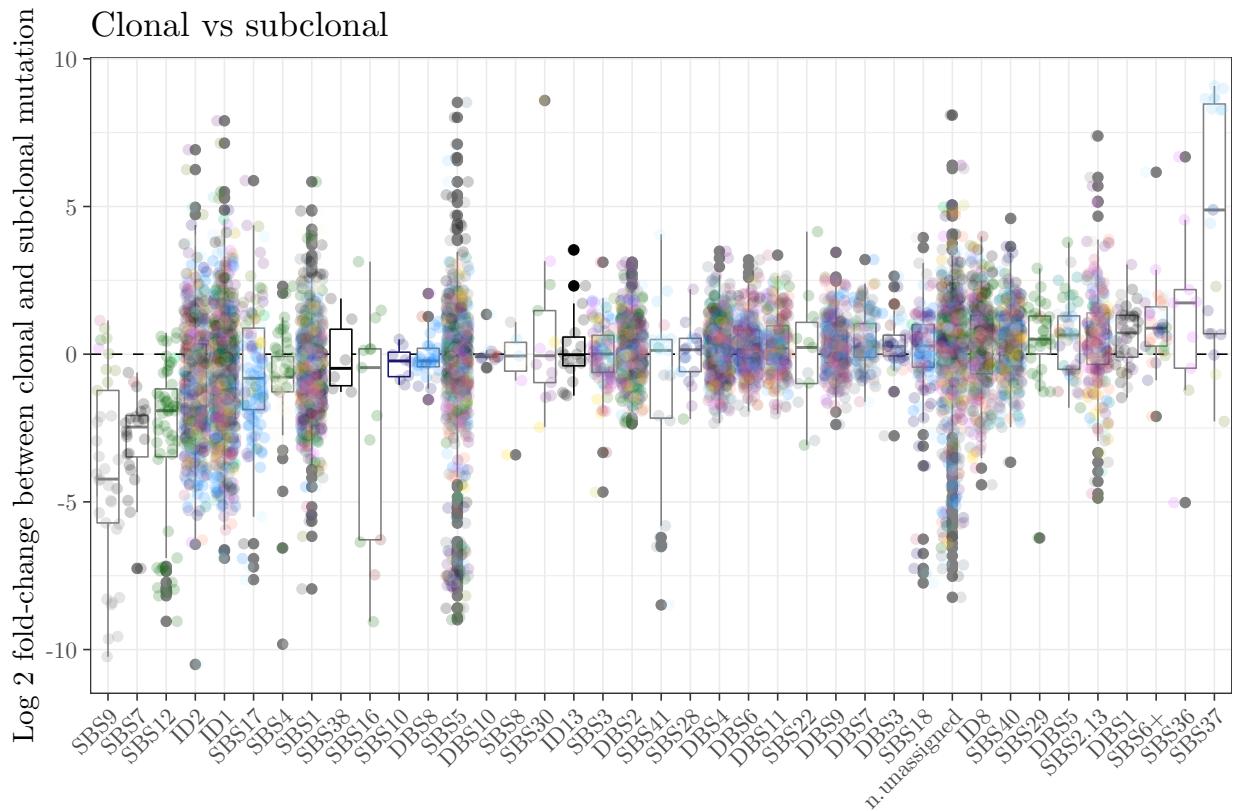


```
ggplot(gerstung_changing_sigs_clonalsubclonal, aes(x=signature,
                                                    y=log2fc_clonalSubclonal, group=signature)
      + geom_hline(yintercept = 0, lty='dashed')+
      geom_boxplot() + geom_jitter(alpha=0.2)+guides(col=FALSE)+theme_bw()+
      theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Clonal vs subclonal')
      + scale_color_manual(values = pcawg_palette)+labs(x=' ', y='Log 2 fold-change between clonal
      and subclonal mutations')

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

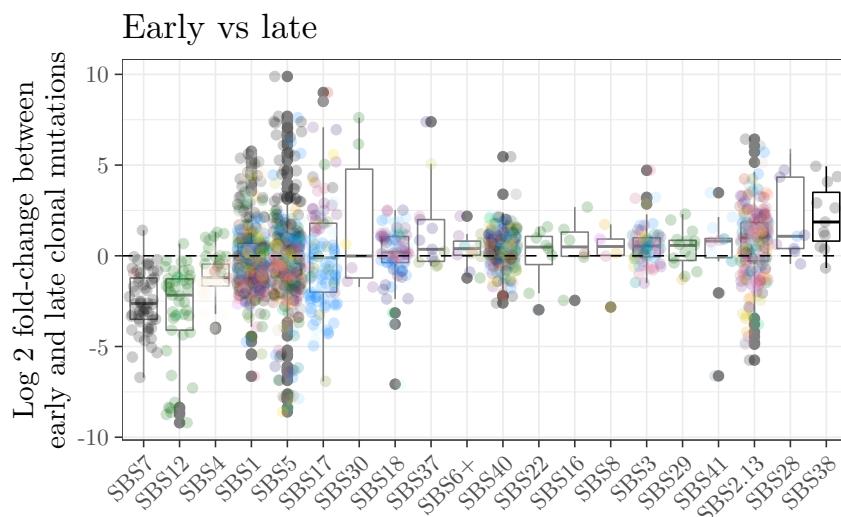
## Warning: Removed 38 rows containing non-finite values (stat_boxplot).

## Warning: Removed 38 rows containing missing values (geom_point).
```



```
ggplot(gerstung_changing_sigs_earlylate[grep('SBS', gerstung_changing_sigs_earlylate$signature),], aes(x=tumour, y=log2fc_earlyLate, group=signature, col=tumour))
  geom_hline(yintercept = 0, lty='dashed')+
  guides(col=FALSE)+theme_bw()+
  theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Early vs late')+
  scale_color_manual(values = pcawg_palette)+labs(x='', y='Log 2 fold-change between \nearly and late mutations')
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> = ## "none")` instead.
```



```

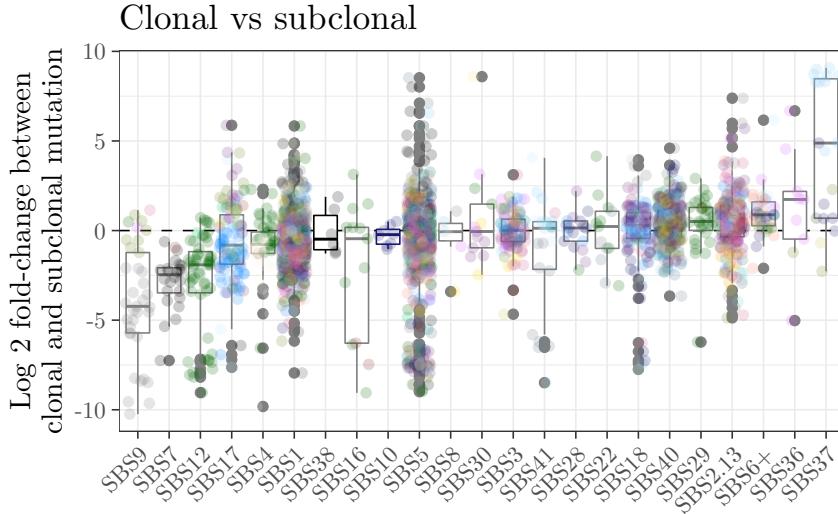
ggplot(gerstung_changing_sigs_clonalsubclonal[grepl('SBS', gerstung_changing_sigs_clonalsubclonal$signature),
                                              y=log2fc_clonalSubclonal, group=signature]
      geom_hline(yintercept = 0, lty='dashed')+
      geom_boxplot()+
      geom_jitter(alpha=0.2)+guides(col=FALSE)+theme_bw()+
      theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Clonal vs subclonal')
      scale_color_manual(values = pcawg_palette)+labs(x='', y='Log 2 fold-change between \nclonal\nand subclonal mutation')

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 13 rows containing non-finite values (stat_boxplot).

## Warning: Removed 13 rows containing missing values (geom_point).

```



```

df_changes_el_persample <- gerstung_changing_sigs_earlylate %>% group_by(samplename) %>% dplyr::summarise
df_changes_cs_persample <- gerstung_changing_sigs_clonalsubclonal %>% group_by(samplename) %>% dplyr::summarise
gerstung_changing_sigs_earlylate$samplename <- factor(gerstung_changing_sigs_earlylate$samplename,
                                                       levels=df_changes_el_persample$samplename[order(df_changes_el_persample$n)])
gerstung_changing_sigs_clonalsubclonal$samplename <- factor(gerstung_changing_sigs_clonalsubclonal$samplename,
                                                               levels=df_changes_cs_persample$samplename[order(df_changes_cs_persample$n)])
table(is.na(gerstung_changing_sigs_earlylate$samplename))

```

```

##  
## FALSE  
## 5347

```

```
table(is.na(gerstung_changing_sigs_clonalsubclonal$samplename))
```

```

##  
## FALSE  
## 7216

```

```

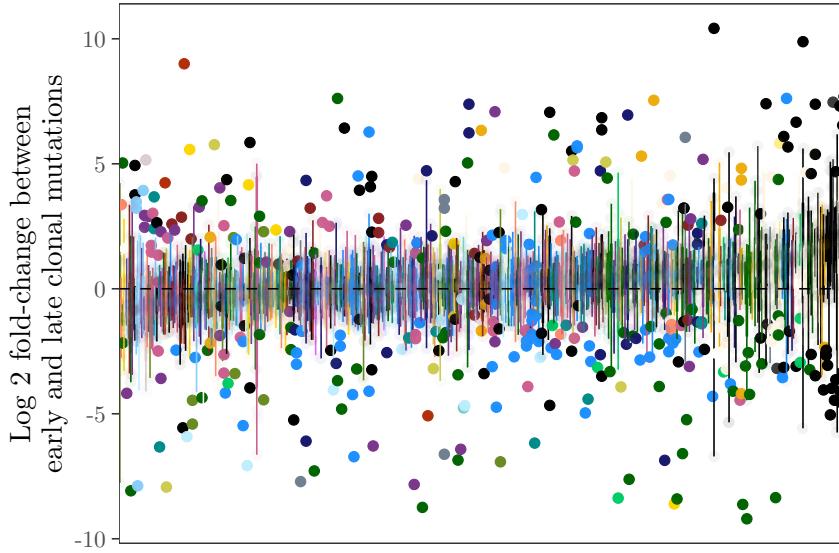
ggplot(gerstung_changing_sigs_earlylate, aes(x=samplename,
                                               y=log2fc_earlyLate, group=samplename,col=tumour_type))+geom_
      geom_hline(yintercept = 0, lty='dashed')+
      guides(col=FALSE)+theme_bw()+
      theme(axis.title.x=element_blank(),
```

```

    axis.text.x=element_blank(),
    axis.ticks.x=element_blank())+
scale_color_manual(values = pcawg_palette)+labs(x='', y='Log 2 fold-change between\nnearly and late clonal mutations')
theme(panel.grid.major = element_blank(), panel.grid.minor = element_blank())

```

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> = "none")` instead.



```

ggplot(gerstung_changing_sigs_clonalsubclonal, aes(x=samplename,
                                                    y=log2fc_clonalSubclonal, group=samplename, col=tumour_...
geom_hline(yintercept = 0, lty='dashed')+
geom_boxplot()+
geom_jitter(alpha=0.05)+guides(col=FALSE)+theme_bw()+
theme(axis.title.x=element_blank(),
      axis.text.x=element_blank(),
      axis.ticks.x=element_blank())+ggtitle('Clonal vs subclonal')+
scale_color_manual(values = pcawg_palette)+labs(x='', y='Log 2 fold-change between\nnclonal and subclonal mutations')
theme(panel.grid.major = element_blank(), panel.grid.minor = element_blank())

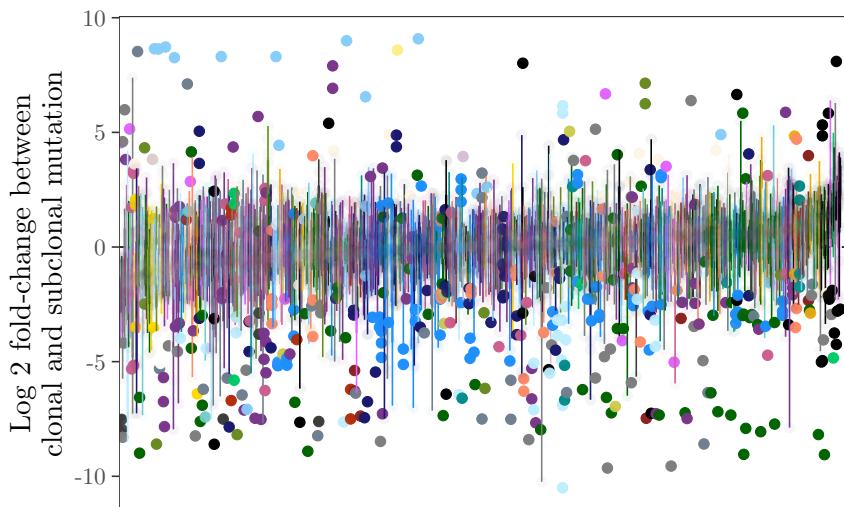
```

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> = "none")` instead.

## Warning: Removed 38 rows containing non-finite values (stat\_boxplot).

## Warning: Removed 38 rows containing missing values (geom\_point).

### Clonal vs subclonal



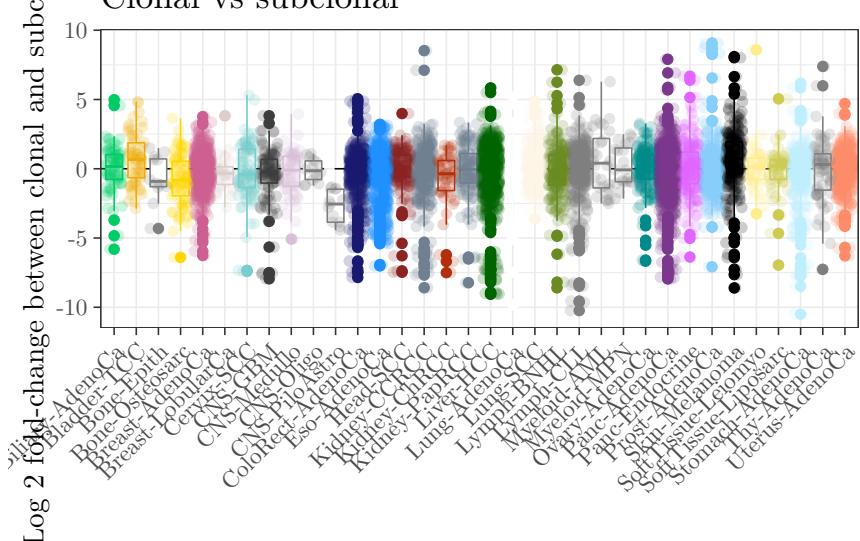
```
ggplot(gerstung_changing_sigs_clonalsubclonal, aes(x=tumour_type,
                                                    y=log2fc_clonalSubclonal, group=tumour_type,col=tumour_type))
  geom_hline(yintercept = 0, lty='dashed')+
  geom_boxplot() + geom_jitter(alpha=0.2)+guides(col=FALSE)+theme_bw()+
  theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Early vs late')+
  ggtitle('Clonal vs subclonal')+
  scale_color_manual(values = pcawg_palette)+labs(x='', y='Log 2 fold-change between clonal and subclonal')

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> = "none")` instead.

## Warning: Removed 38 rows containing non-finite values (stat_boxplot).

## Warning: Removed 38 rows containing missing values (geom_point).
```

### Clonal vs subclonal

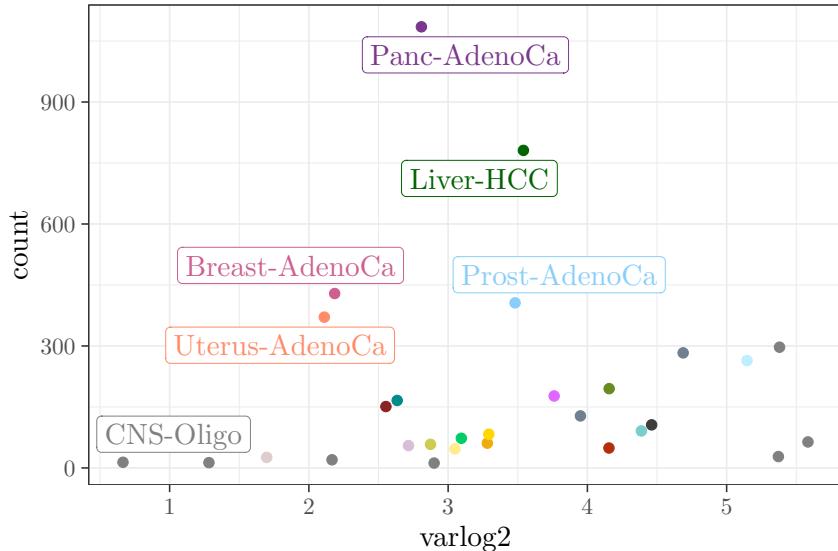


```
gerstung_changing_sigs_clonalsubclonal_var <- gerstung_changing_sigs_clonalsubclonal %>%
  dplyr::group_by(tumour_type) %>% summarise(varlog2=var(log2fc_clonalSubclonal), count=n())
```

```

ggplot(gerstung_changing_sigs_clonalsubclonal_var,
       aes(x=varlog2, y=count, label=tumour_type, col=tumour_type)) + geom_point() +
  scale_color_manual(values = pcawg_palette) + guides(col=FALSE) + theme_bw() + geom_label_repel(max.overlaps =
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
## Warning: Removed 4 rows containing missing values (geom_point).
## Warning: Removed 4 rows containing missing values (geom_label_repel).
## Warning: ggrepel: 24 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

```



```
labs(x='Variance of log2 fold change in cancer type', y='Number of observations')
```

```

## $x
## [1] "Variance of log2 fold change in cancer type"
##
## $y
## [1] "Number of observations"
##
## attr(,"class")
## [1] "labels"

```

Gerstung: comparison with minimal perturbation

```

perturb_to_vals <- function(i){
  sapply(i, function(j){
    if(j == 'FALSE'){
      0
    }else if(j == 'increase'){
      1
    }else if(j == 'decrease'){
      -1
    }else{

```

```

    stop('Wrong perturbation value')
  }
})
}
perturbed_betas_diagRE_DMDL_nonexo_SP_df_summary <- perturbed_betas_diagRE_DMDL_nonexo_SP_df %>% dplyr::g
  summarise(meanperturbed=mean( !(perturbed == 'FALSE')),
            mean_direction_perturb = mean(perturb_to_vals(perturbed)))
perturbed_betas_diagRE_DMDL_nonexo_SP_df_summary

## # A tibble: 32 x 3
##   sig     meanperturbed mean_direction_perturb
##   <chr>      <dbl>                  <dbl>
## 1 SBS10a      0                      0
## 2 SBS10b      0                      0
## 3 SBS12       1                     -1
## 4 SBS13      0.25                   0.25
## 5 SBS14       0.5                    0.5
## 6 SBS15      0.333                 -0.333
## 7 SBS16       0.5                   -0.5
## 8 SBS17a     0.364                  0.182
## 9 SBS17b     0.0909                -0.0909
## 10 SBS18      0.3                   -0.1
## # ... with 22 more rows
comparison_with_gerstung_earlylate <- cbind.data.frame(perturbed_betas_diagRE_DMDL_nonexo_SP_df_summary,
                                                       df_changes_el[match(perturbed_betas_diagRE_DM
                                                       df_changes_el$signature),
comparison_with_gerstung_clonalsubclonal <- cbind.data.frame(perturbed_betas_diagRE_DMDL_nonexo_SP_df_sum
                                                       df_changes_cs[match(perturbed_betas_diagRE_DM
                                                       df_changes_cs$signature),
comparison_with_gerstung_earlylate

##       sig meanperturbed mean_direction_perturb signature      median
## 1 SBS10a 0.00000000 0.00000000 <NA>          NA
## 2 SBS10b 0.00000000 0.00000000 <NA>          NA
## 3 SBS12 1.00000000 -1.00000000 SBS12 -2.16839553
## 4 SBS13 0.25000000 0.25000000 <NA>          NA
## 5 SBS14 0.50000000 0.50000000 <NA>          NA
## 6 SBS15 0.33333333 -0.33333333 <NA>          NA
## 7 SBS16 0.50000000 -0.50000000 SBS16  0.48743401
## 8 SBS17a 0.36363636 0.18181818 <NA>          NA
## 9 SBS17b 0.09090909 -0.09090909 <NA>          NA
## 10 SBS18 0.30000000 -0.10000000 SBS18  0.19987446
## 11 SBS19 0.50000000 -0.50000000 SBS19 -1.96353701
## 12 SBS2  0.17647059 0.17647059 <NA>          NA
## 13 SBS20 1.00000000 1.00000000 <NA>          NA
## 14 SBS21 0.00000000 0.00000000 <NA>          NA
## 15 SBS22 0.00000000 0.00000000 SBS22  0.47923554
## 16 SBS23 0.00000000 0.00000000 <NA>          NA
## 17 SBS24 0.00000000 0.00000000 SBS24 -10.24985022
## 18 SBS26 0.33333333 0.00000000 <NA>          NA

```

```

## 19 SBS28 0.50000000 0.50000000 SBS28 1.07561394
## 20 SBS3 0.09090909 -0.09090909 SBS3 0.53915013
## 21 SBS30 0.20000000 -0.20000000 SBS30 -0.01377077
## 22 SBS33 0.50000000 0.50000000 <NA> NA
## 23 SBS34 0.00000000 0.00000000 SBS34 -0.20973256
## 24 SBS36 0.50000000 -0.50000000 SBS36 0.99203837
## 25 SBS37 0.40000000 0.40000000 SBS37 0.35693398
## 26 SBS38 0.00000000 0.00000000 SBS38 1.86314214
## 27 SBS39 0.50000000 0.50000000 SBS39 -0.28583208
## 28 SBS40 0.25000000 -0.25000000 SBS40 0.46436260
## 29 SBS41 0.00000000 0.00000000 SBS41 0.80987484
## 30 SBS6 0.20000000 -0.20000000 <NA> NA
## 31 SBS8 0.25000000 -0.25000000 SBS8 0.51226887
## 32 SBS9 0.33333333 0.00000000 SBS9 1.61493581

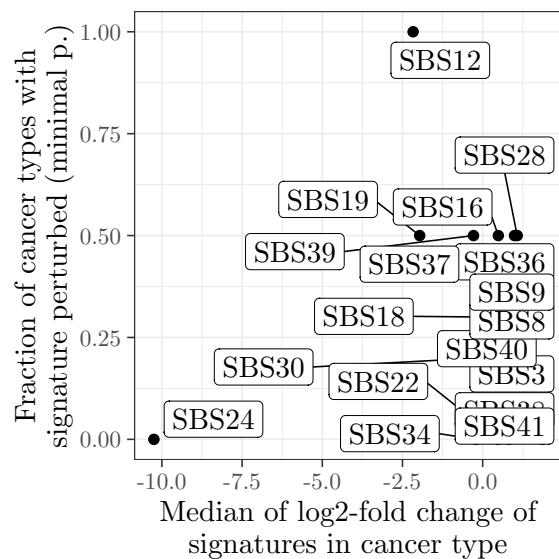
```

```
comparison_with_gerstung_earlylate$medianlog2fcearlylate = comparison_with_gerstung_earlylate$median  
comparison with gerstung clonalsubclonal$medianlog2fcclonalsubclonal = comparison with gerstung clonalsub
```

```
ggplot(comparison_with_gerstung_earlylate, aes(x=medianlog2fcearlylate, y=meanperturbed, label=signature))  
  labs(x='Median of log2-fold change of\nsignatures in cancer type', y='Fraction of cancer types with\nsignatures')
```

## Warning: Removed 14 rows containing missing values (geom\_point).

## Warning: Removed 14 rows containing missing values (geom\_label\_repel).



```
comparison_with_gerstung_clonalsubclonal[order(comparison_with_gerstung_clonalsubclonal$medianlog2fcclonal
```

```

##      sig meanperturbed mean_direction_perturb signature      median
## 32   SBS9    0.333333333            0.000000000  SBS9 -4.227968613
## 17   SBS24   0.000000000            0.000000000  SBS24 -2.456201536
##  3   SBS12   1.000000000           -1.000000000  SBS12 -1.914582675
## 26   SBS38   0.000000000            0.000000000  SBS38 -0.479756396
##  7   SBS16   0.500000000           -0.500000000  SBS16 -0.454004317
## 31   SBS8    0.250000000           -0.250000000  SBS8 -0.060487417
## 21   SBS30   0.200000000           -0.200000000  SBS30 -0.052668750

```

```

## 20   SBS3    0.09090909      -0.09090909      SBS3    0.007051629
## 29   SBS41   0.00000000      0.00000000      SBS41   0.127382663
## 23   SBS34   0.00000000      0.00000000      SBS34   0.144251796
## 19   SBS28   0.50000000      0.50000000      SBS28   0.148174746
## 15   SBS22   0.00000000      0.00000000      SBS22   0.227192828
## 10   SBS18   0.30000000      -0.10000000      SBS18   0.279900698
## 28   SBS40   0.25000000      -0.25000000      SBS40   0.453463859
## 27   SBS39   0.50000000      0.50000000      SBS39   1.647103892
## 24   SBS36   0.50000000      -0.50000000      SBS36   1.736408100
## 22   SBS33   0.50000000      0.50000000      SBS33   2.479041333
## 11   SBS19   0.50000000      -0.50000000      SBS19   3.654440550
## 25   SBS37   0.40000000      0.40000000      SBS37   4.882587271
## 16   SBS23   0.00000000      0.00000000      SBS23   6.934448614
## 1    SBS10a  0.00000000      0.00000000      <NA>    NA
## 2    SBS10b  0.00000000      0.00000000      <NA>    NA
## 4    SBS13   0.25000000      0.25000000      <NA>    NA
## 5    SBS14   0.50000000      0.50000000      <NA>    NA
## 6    SBS15   0.33333333      -0.33333333      <NA>    NA
## 8    SBS17a  0.36363636      0.18181818      <NA>    NA
## 9    SBS17b  0.09090909      -0.09090909      <NA>    NA
## 12   SBS2    0.17647059      0.17647059      <NA>    NA
## 13   SBS20   1.00000000      1.00000000      <NA>    NA
## 14   SBS21   0.00000000      0.00000000      <NA>    NA
## 18   SBS26   0.33333333      0.00000000      <NA>    NA
## 30   SBS6    0.20000000      -0.20000000      <NA>    NA
## medianlog2fcclonalsubclonal
## 32              -4.227968613
## 17              -2.456201536
## 3               -1.914582675
## 26              -0.479756396
## 7               -0.454004317
## 31              -0.060487417
## 21              -0.052668750
## 20              0.007051629
## 29              0.127382663
## 23              0.144251796
## 19              0.148174746
## 15              0.227192828
## 10              0.279900698
## 28              0.453463859
## 27              1.647103892
## 24              1.736408100
## 22              2.479041333
## 11              3.654440550
## 25              4.882587271
## 16              6.934448614
## 1                  NA
## 2                  NA
## 4                  NA
## 5                  NA
## 6                  NA

```

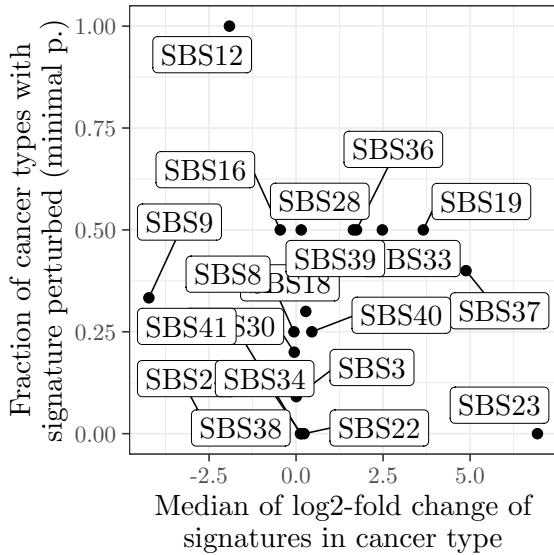
```

## 8 NA
## 9 NA
## 12 NA
## 13 NA
## 14 NA
## 18 NA
## 30 NA

ggplot(comparison_with_gerstung_clonalsubclonal, aes(x=medianlog2fcclonalsubclonal, y=meanperturbed, label=signature)
  geom_point() + geom_label_repel() + theme_bw()
  labs(x='Median of log2-fold change of\nsignatures in cancer type', y='Fraction of cancer types with\nsignature perturbed (minimal p.)')

## Warning: Removed 12 rows containing missing values (geom_point).
## Warning: Removed 12 rows containing missing values (geom_label_repel).

```

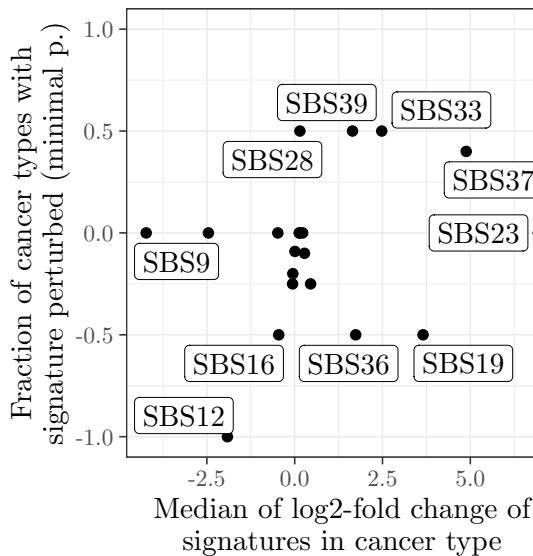


```

ggplot(comparison_with_gerstung_clonalsubclonal, aes(x=medianlog2fcclonalsubclonal, y=mean_direction_perturbed, label=signature)
  geom_point() + geom_label_repel() + theme_bw()
  labs(x='Median of log2-fold change of\nsignatures in cancer type', y='Fraction of cancer types with\nsignature perturbed (minimal p.)')

## Warning: Removed 12 rows containing missing values (geom_point).
## Warning: Removed 12 rows containing missing values (geom_label_repel).
## Warning: ggrepel: 10 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

```



Barplots of cancer types with and without differential abundance

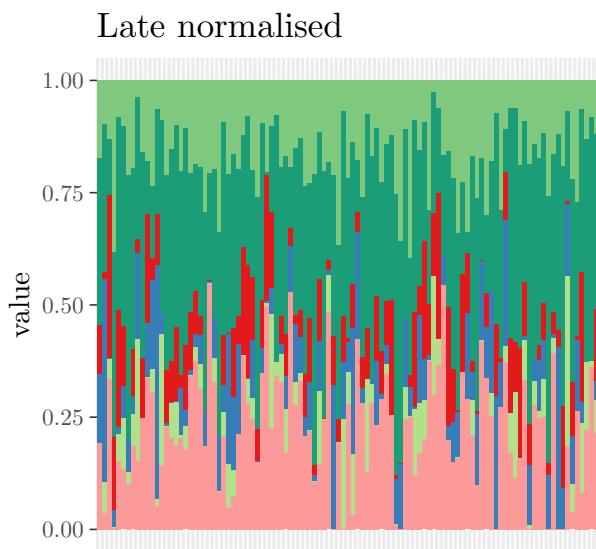
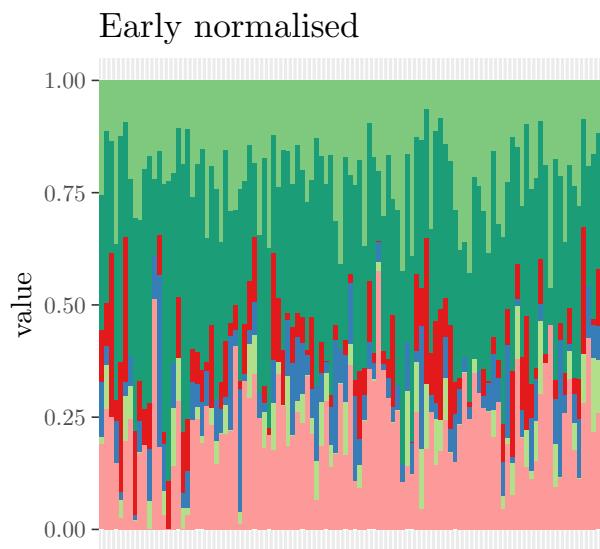
```
give_barplot_from_obj(obj = signatures_PCAWG[['CNS-Medullo']], legend_on = F,
                      nrow=1, verbose=F,
                      only_normalised=T, levels_signatures=sigs_cosmic)
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
```



```

give_barplot_from_obj(obj = signatures_PCAWG[['Uterus-AdenoCA']], legend_on = F,
                      nrow=1, verbose=F,
                      only_normalised=T, levels_signatures=sigs_cosmic)

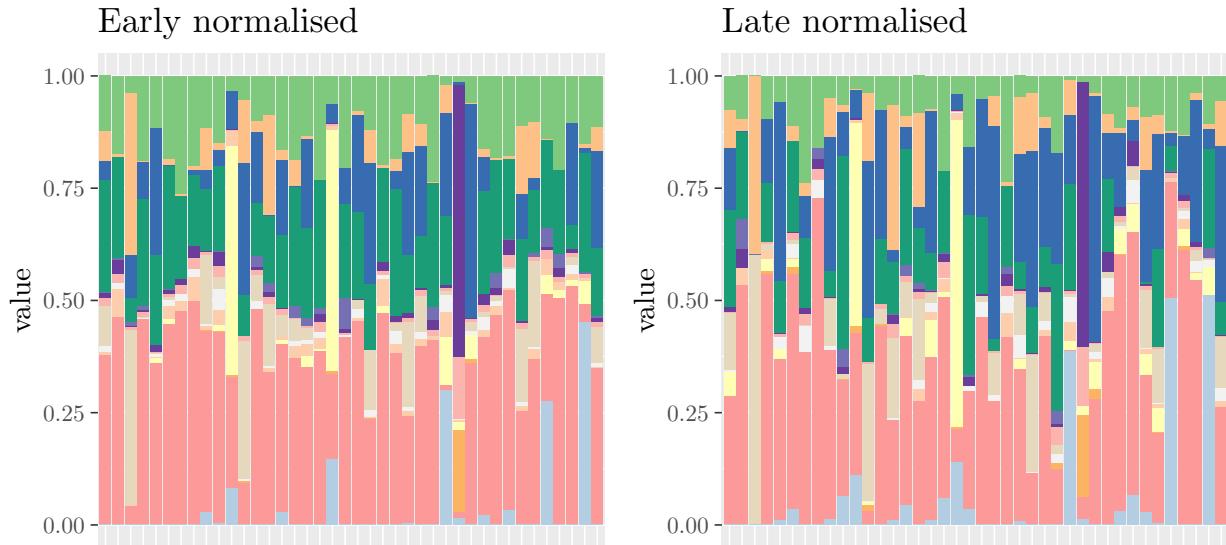
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

```



```

give_barplot_from_obj(obj = signatures_PCAWG[['Ovary-AdenoCA']], legend_on = F,
                      nrow=1, verbose=F,
                      only_normalised=T, levels_signatures=sigs_cosmic)

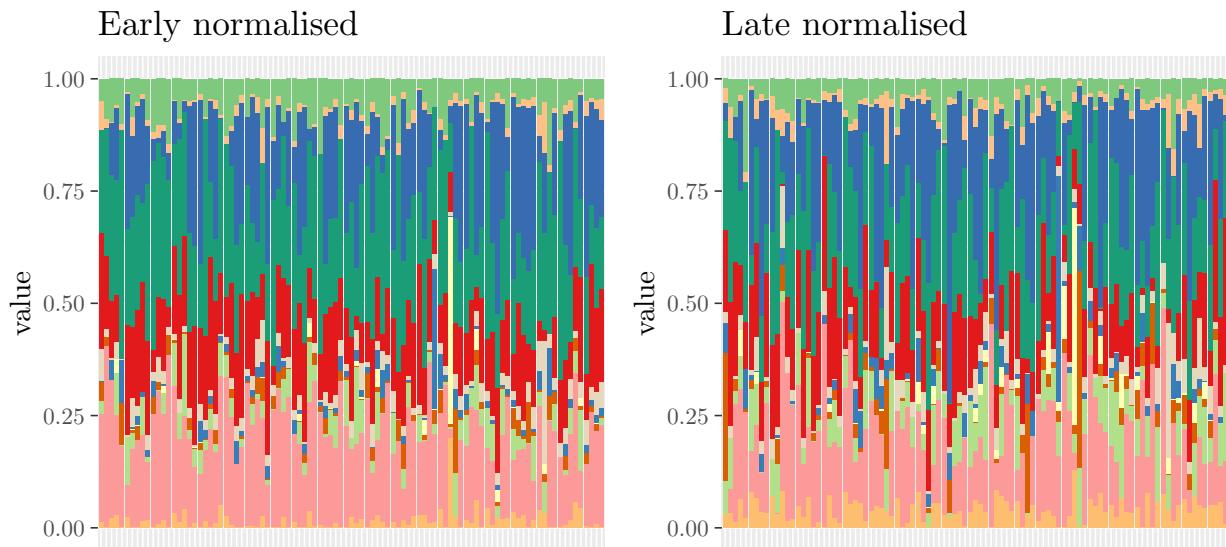
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

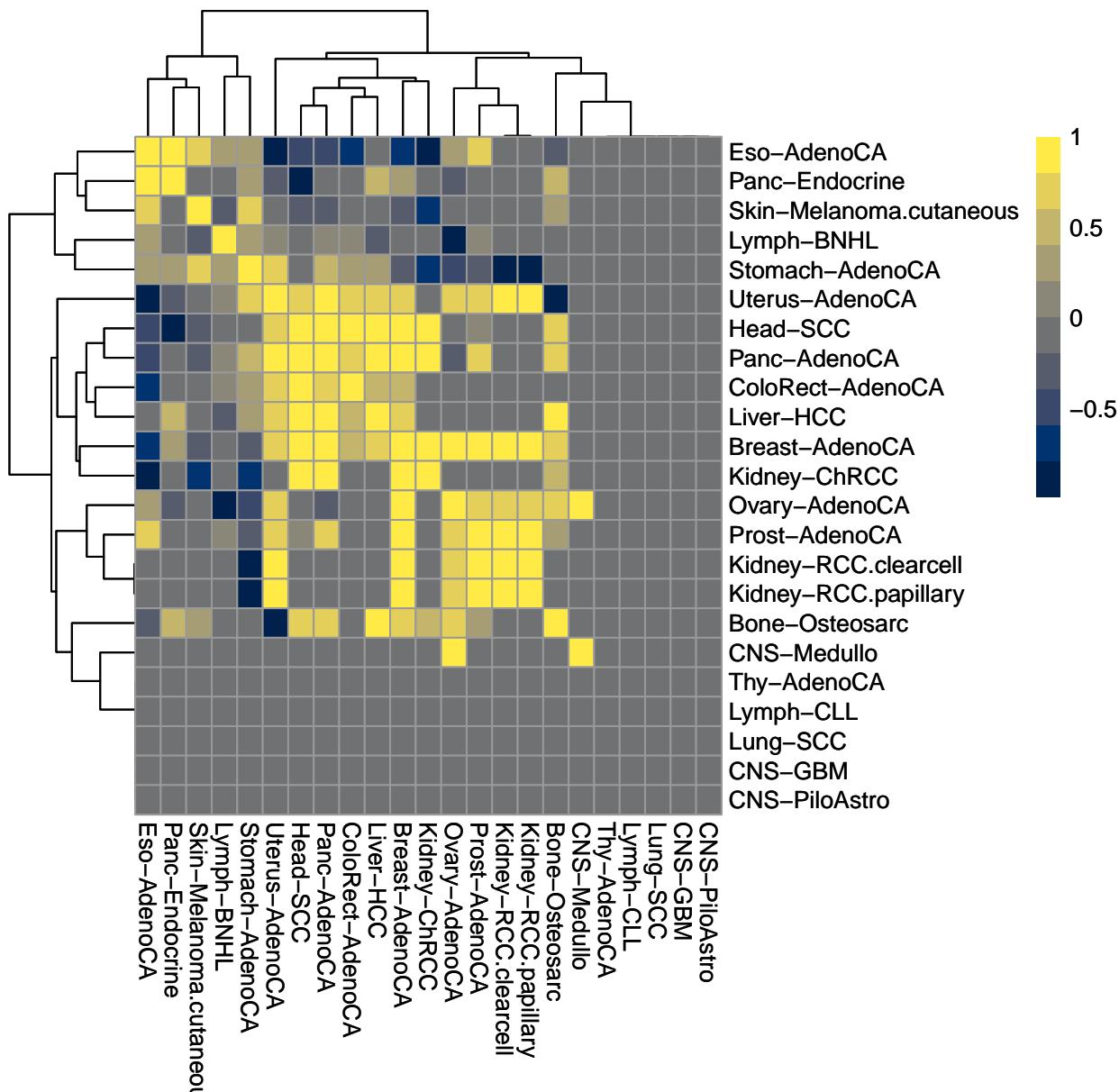
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

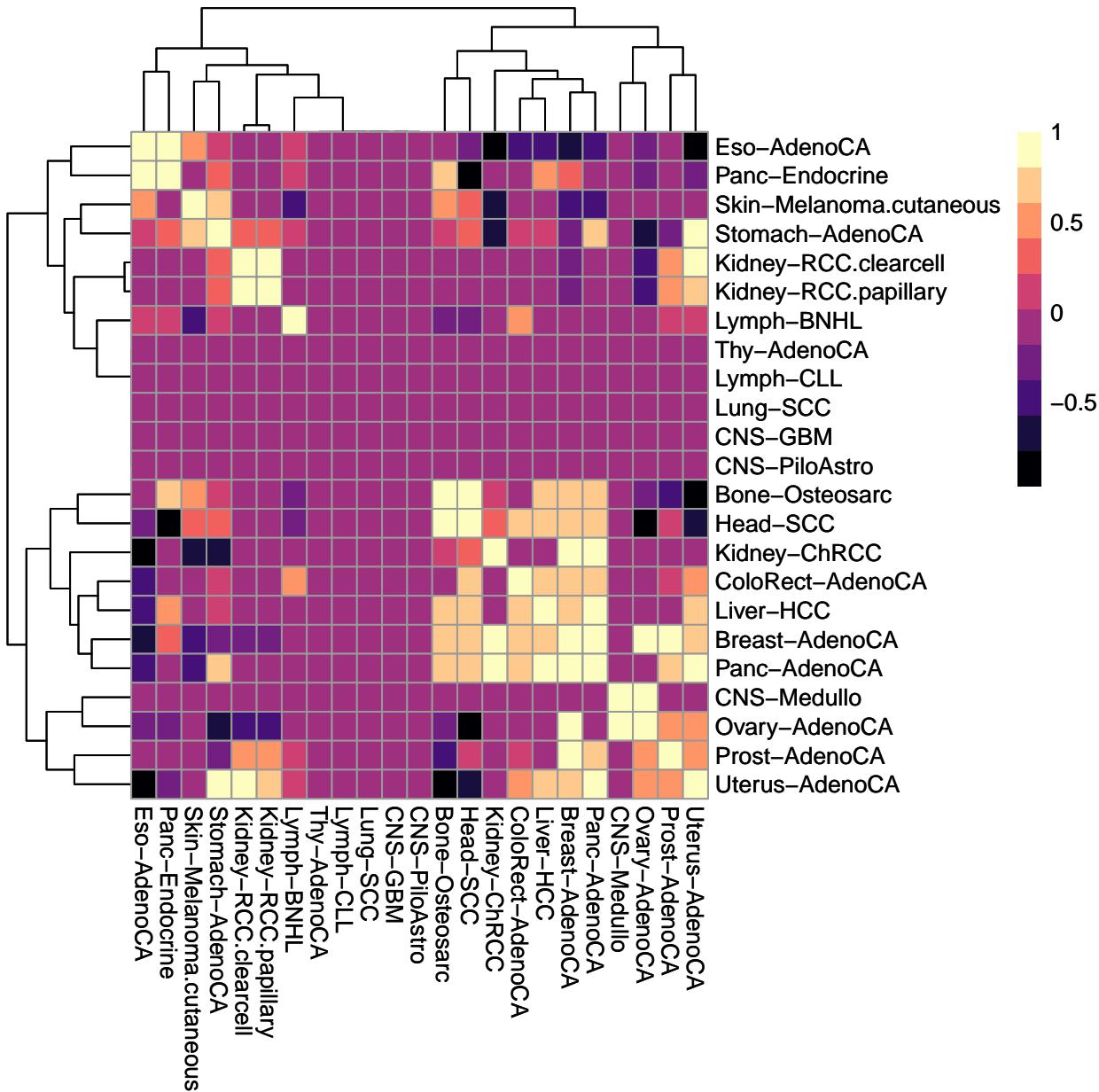
```



## Correlations of cancer types and of signatures based on betas



```
## null device
##      1
## null device
##      1
```



```

## null device
##      1

## null device
##      1

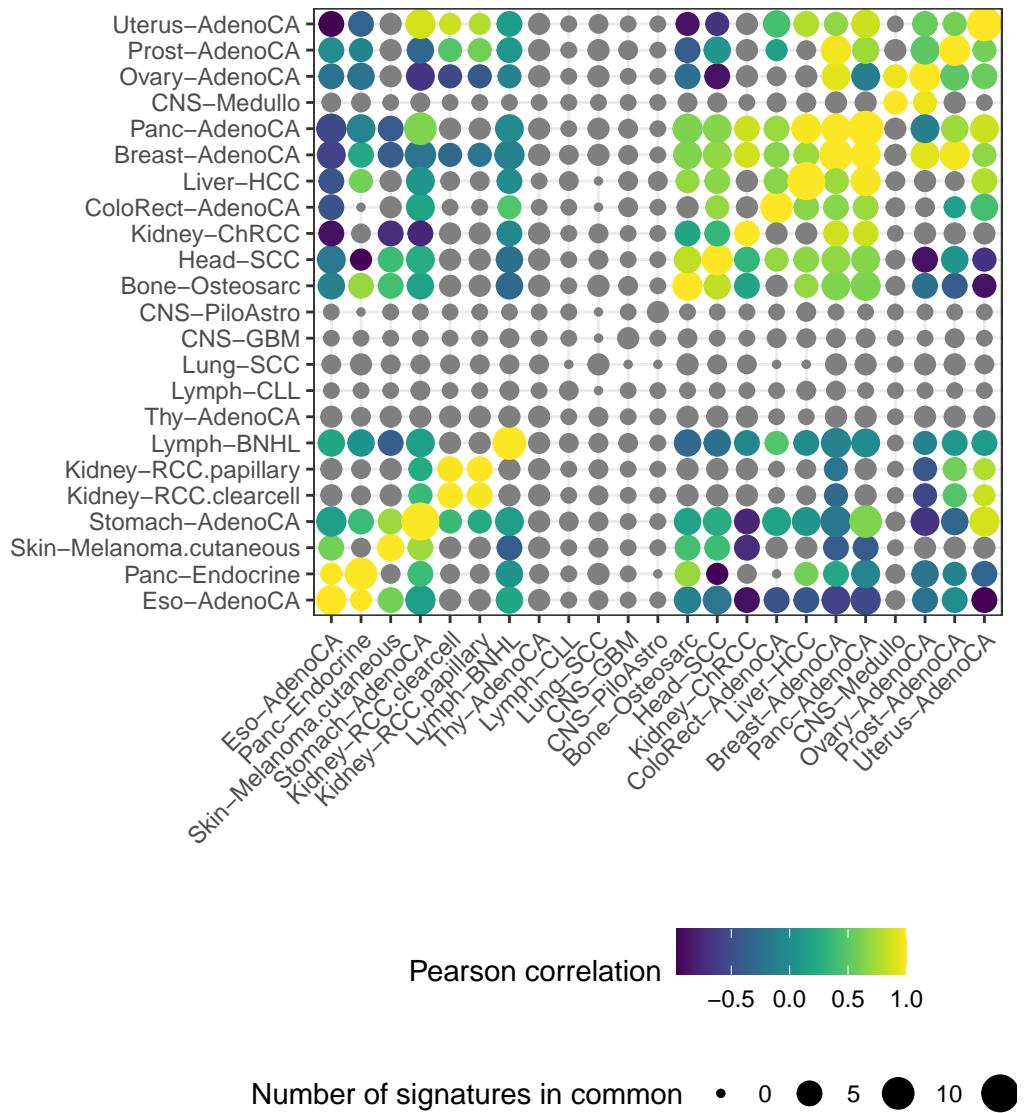
##   cors_softmax.Var1 cors_softmax.Var2 cors_softmax.value num_common_sigs.Var1
## 1                  1                  1 1.0000000      Bone-Osteosarc
## 2                  2                  1 0.6269273      Breast-AdenoCA
## 3                  3                  1        NA          CNS-GBM
## 4                  4                  1        NA          CNS-Medullo
## 5                  5                  1        NA      CNS-PiloAstro
## 6                  6                  1        NA      ColoRect-AdenoCA

```

```

##   num_common_sigs.Var2 num_common_sigs.value
## 1      Bone-Osteosarc          8
## 2      Bone-Osteosarc          7
## 3      Bone-Osteosarc          2
## 4      Bone-Osteosarc          2
## 5      Bone-Osteosarc          1
## 6      Bone-Osteosarc          3

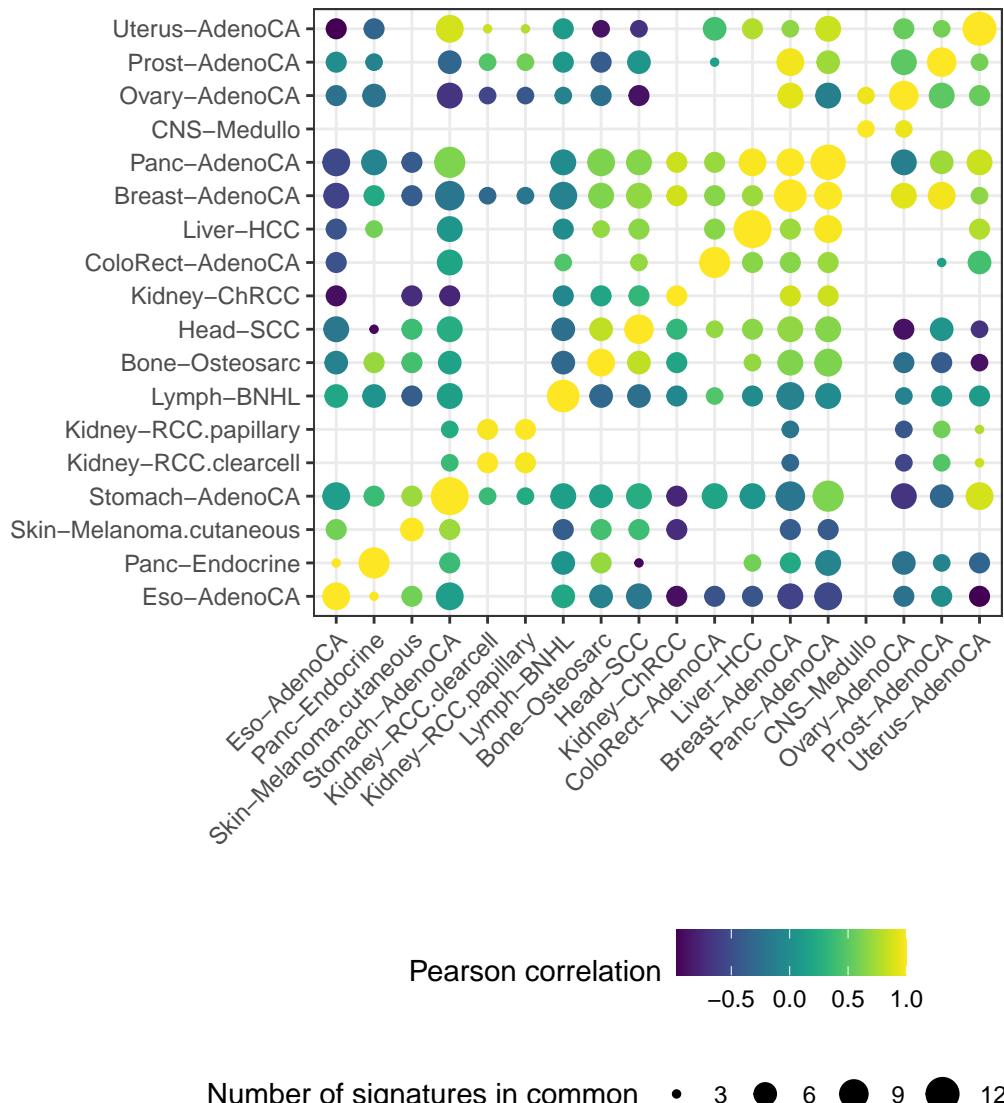
```



```

## Saving 5.5 x 6 in image

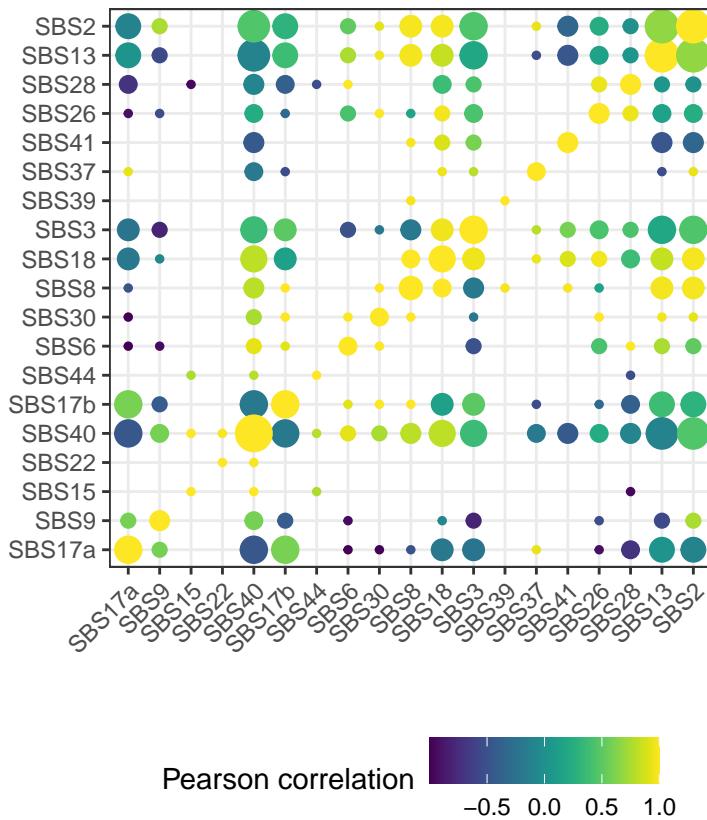
```



```
## Saving 5.5 x 6 in image
```

Correlation of signatures based on betas (softmaxed betas)

```
## [1] cors_softmax.Var1      cors_softmax.Var2      cors_softmax.value
## [4] num_common_samples.Var1 num_common_samples.Var2 num_common_samples.value
## <0 rows> (or 0-length row.names)
```



```
# pcawg_palette <- pcawg.colour.palette(gsub("\\..*", "", all_pvals$ct),
#                                         scheme = "tumour.subtype")
#
# names(pcawg_palette) <- all_pvals$ct
#
# pcawg_palette
pcawg_palette[names(pcawg_palette) == 'Lung-SCC'] <- '#ffff29'
```

pcawg\_palette

|    |                  |               |                |                    |
|----|------------------|---------------|----------------|--------------------|
| ## | Biliary-AdenoCa  | Bladder-TCC   | Bone-Osteosarc | Breast-AdenoCa     |
| ## | "#00CD66"        | "#EEAOE"      | "#FFD700"      | "#CD6090"          |
| ## | Breast-LobularCa | Cervix-SCC    | CNS-GBM        | CNS-Medullo        |
| ## | "#DDCDCD"        | "#79CDCD"     | "#3D3D3D"      | "#D8BFD8"          |
| ## | ColoRect-AdenoCa | Eso-AdenoCa   | Head-SCC       | Kidney-CCRCC       |
| ## | "#191970"        | "#1E90FF"     | "#8B2323"      | "slategrey"        |
| ## | Kidney-ChRCC     | Kidney-PapRCC | Liver-HCC      | Lung-AdenoCa       |
| ## | "#B32F0B"        | "slategrey"   | "#006400"      | "#FFFFFF"          |
| ## | Lung-SCC         | Lymph-BNHL    | Ovary-AdenoCa  | Panc-AdenoCa       |
| ## | "#ffff29"        | "#698B22"     | "#008B8B"      | "#7A378B"          |
| ## | Panc-Endocrine   | Prost-AdenoCa | Skin-Melanoma  | SoftTissue-Leiomyo |
| ## | "#E066FF"        | "#87CEFA"     | "#000000"      | "#FFEC8B"          |

```

## SoftTissue-Liposarc      Stomach-AdenoCa       Uterus-AdenoCa
##                      "#CDCB50"          "#BFFFFF"          "#FF8C69"
df_cor_pvals_n <- data.frame(num_samples=num_samples_all_SP,
                               pvalue=pvals_diagRE_DMDL_SP,
                               ct=gsub("CA$", "Ca", gsub("\\\..*", "", enough_samples)))
df_cor_pvals_n

##                                     num_samples     pvalue           ct
## Bone-Osteosarc                  27 1.080828e-04 Bone-Osteosarc
## Breast-AdenoCA                 136 2.239756e-28 Breast-AdenoCa
## CNS-GBM                          34 3.390137e-03 CNS-GBM
## CNS-Medullo                     106 8.431463e-03 CNS-Medullo
## CNS-PiloAstro                   42 5.615238e-04 CNS-PiloAstro
## ColoRect-AdenoCA                37 6.356131e-26 ColoRect-AdenoCa
## Eso-AdenoCA                     65 5.329093e-21 Eso-AdenoCa
## Head-SCC                         32 4.975610e-05 Head-SCC
## Kidney-ChRCC                    38 1.562125e-09 Kidney-ChRCC
## Kidney-RCC.clearcell            86 4.027485e-18 Kidney-RCC
## Kidney-RCC.papillary             30 NA                 Kidney-RCC
## Liver-HCC                        207 4.747822e-107 Liver-HCC
## Lung-SCC                          34 7.747310e-22 Lung-SCC
## Lymph-BNHL                        51 3.908637e-19 Lymph-BNHL
## Lymph-CLL                          53 6.611927e-20 Lymph-CLL
## Ovary-AdenoCA                    97 8.965185e-38 Ovary-AdenoCa
## Panc-AdenoCA                     193 4.096402e-119 Panc-AdenoCa
## Panc-Endocrine                   70 3.987099e-10 Panc-Endocrine
## Prost-AdenoCA                    208 6.474116e-99 Prost-AdenoCa
## Skin-Melanoma.cutaneous          30 9.272113e-25 Skin-Melanoma
## Stomach-AdenoCA                  30 1.715150e-06 Stomach-AdenoCa
## Thy-AdenoCA                      41 8.821583e-06 Thy-AdenoCa
## Uterus-AdenoCA                   40 4.819867e-10 Uterus-AdenoCa

ggplot(df_cor_pvals_n, aes(x=num_samples, y=pvalue, label=ct, col=ct, group=1))+
  geom_point() + scale_y_continuous(trans = "log2") +
  geom_smooth(method = lm) + theme_bw() +
  geom_label_repel() + geom_hline(yintercept = log2(0.05), lty='dashed') +
  labs(x='Number of samples', y = 'p-value (log2)') +
  scale_color_manual(values = pcawg_palette) +
  guides(col=FALSE)

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> = "none")` instead.

## Warning in log(x, base): NaNs produced

## Warning: Transformation introduced infinite values in continuous y-axis

## `geom_smooth()` using formula 'y ~ x'

## Warning: Removed 1 rows containing non-finite values (stat_smooth).

## Warning: Removed 1 rows containing missing values (geom_point).

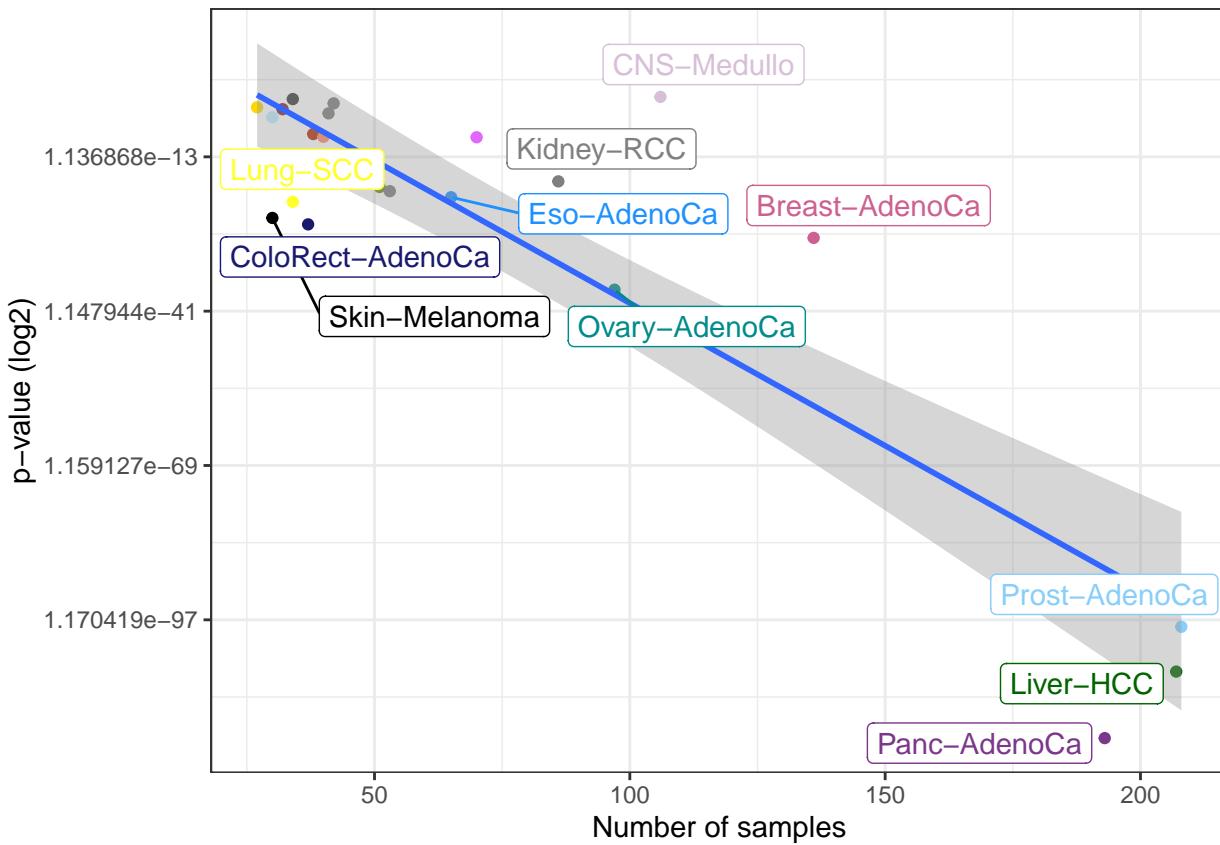
## Warning: Removed 1 rows containing missing values (geom_label_repel).

```

```

## Warning: Removed 1 rows containing missing values (geom_hline).
## Warning: ggrepel: 11 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

```



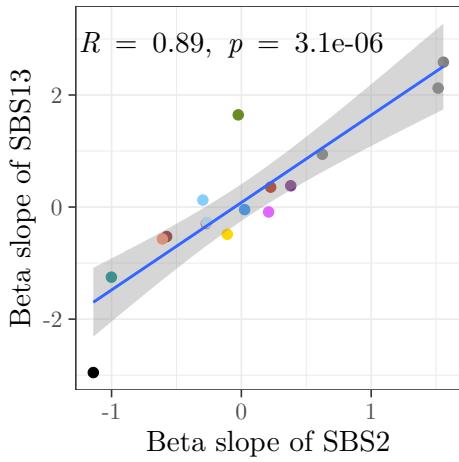
|             | Estimate numerator_LogR | ct                      |
|-------------|-------------------------|-------------------------|
| ## beta.1   | -0.10868535             | 2 Bone-Osteosarc        |
| ## beta.7   | -0.48518518             | 13 Bone-Osteosarc       |
| ## beta.12  | -0.27064004             | 2 Breast-AdenoCA        |
| ## beta.91  | -0.29393557             | 13 Breast-AdenoCA       |
| ## beta.113 | 0.02518066              | 2 Eso-AdenoCA           |
| ## beta.54  | -0.04596199             | 13 Eso-AdenoCA          |
| ## beta.115 | -0.57582551             | 2 Head-SCC              |
| ## beta.55  | -0.52635385             | 13 Head-SCC             |
| ## beta.117 | 0.22566046              | 2 Kidney-ChRCC          |
| ## beta.38  | 0.35508274              | 13 Kidney-ChRCC         |
| ## beta.118 | 1.51557028              | 2 Kidney-RCC.clearcell  |
| ## beta.39  | 2.12303828              | 13 Kidney-RCC.clearcell |
| ## beta.119 | 1.55643670              | 2 Kidney-RCC.papillary  |
| ## beta.310 | 2.58590299              | 13 Kidney-RCC.papillary |
| ## beta.121 | 0.05062637              | 2 Lung-SCC              |
| ## beta.122 | -0.02400179             | 2 Lymph-BNHL            |
| ## beta.96  | 1.64560251              | 13 Lymph-BNHL           |
| ## beta.124 | -1.00151692             | 2 Ovary-AdenoCA         |
| ## beta.710 | -1.25120153             | 13 Ovary-AdenoCA        |

```

## beta.125  0.38030698      2      Panc-AdenoCA
## beta.98   0.37995820     13     Panc-AdenoCA
## beta.126  0.20999050      2      Panc-Endocrine
## beta.1114 -0.08708674     13     Panc-Endocrine
## beta.127  -0.29675703     2      Prost-AdenoCA
## beta.713   0.12467277     13     Prost-AdenoCA
## beta.128  -1.14063355      2 Skin-Melanoma.cutaneous
## beta.318  -2.95346899     13 Skin-Melanoma.cutaneous
## beta.129  -0.26552047      2      Stomach-AdenoCA
## beta.715  -0.27417496     13     Stomach-AdenoCA
## beta.130   0.62364260      2      Thy-AdenoCA
## beta.320   0.94221489     13     Thy-AdenoCA
## beta.140  -0.60872957      2 Uterus-AdenoCA
## beta.1117 -0.56888068     13 Uterus-AdenoCA

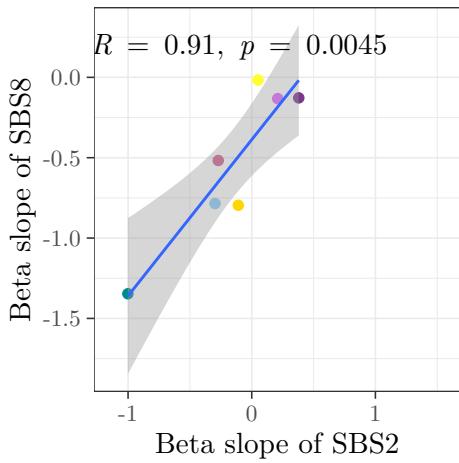
## `geom_smooth()` using formula 'y ~ x'

```

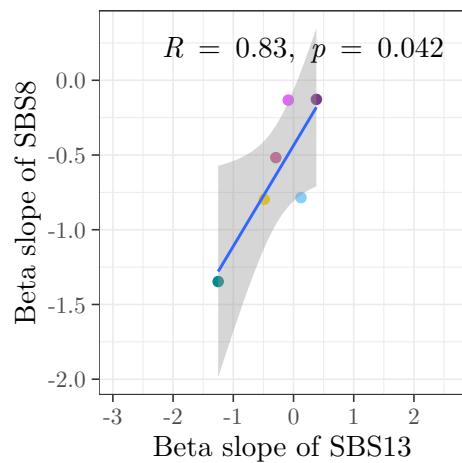


Correlations of beta slopes of SBS8 and APOBEC signatures

```
## `geom_smooth()` using formula 'y ~ x'
```

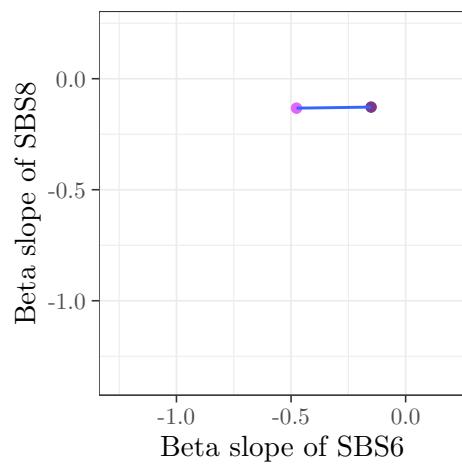


```
## `geom_smooth()` using formula 'y ~ x'
```

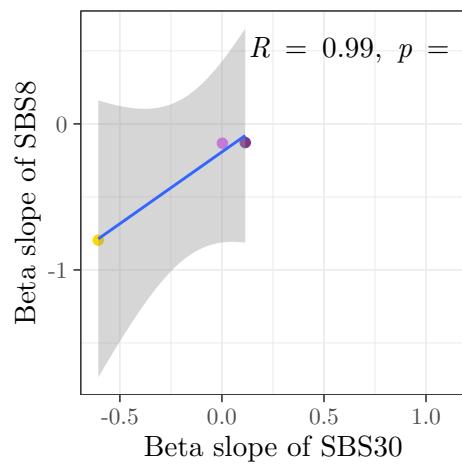


Correlations of beta slopes of SBS8 with SBS6, SBS18, SBS30

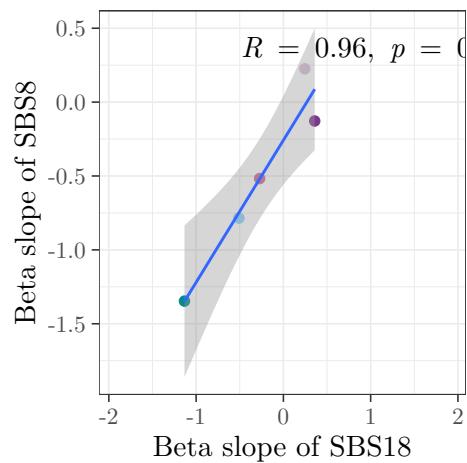
```
## `geom_smooth()` using formula 'y ~ x'
```



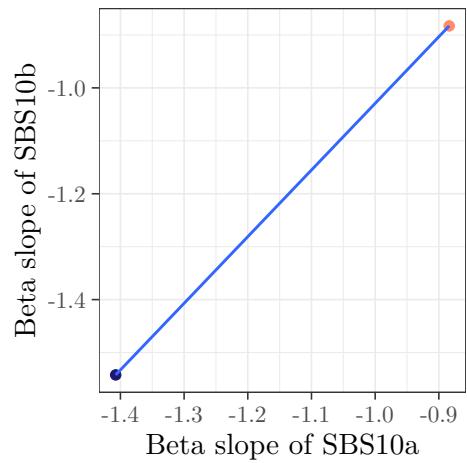
```
## `geom_smooth()` using formula 'y ~ x'
```



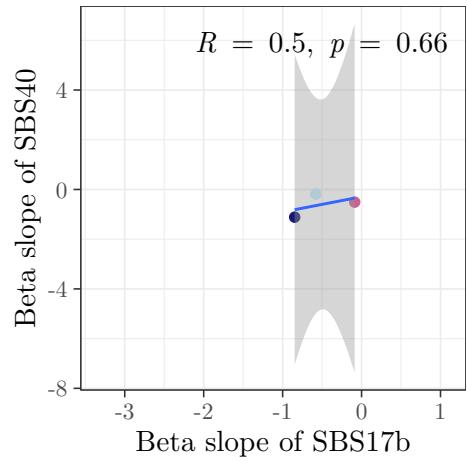
```
## `geom_smooth()` using formula 'y ~ x'
```

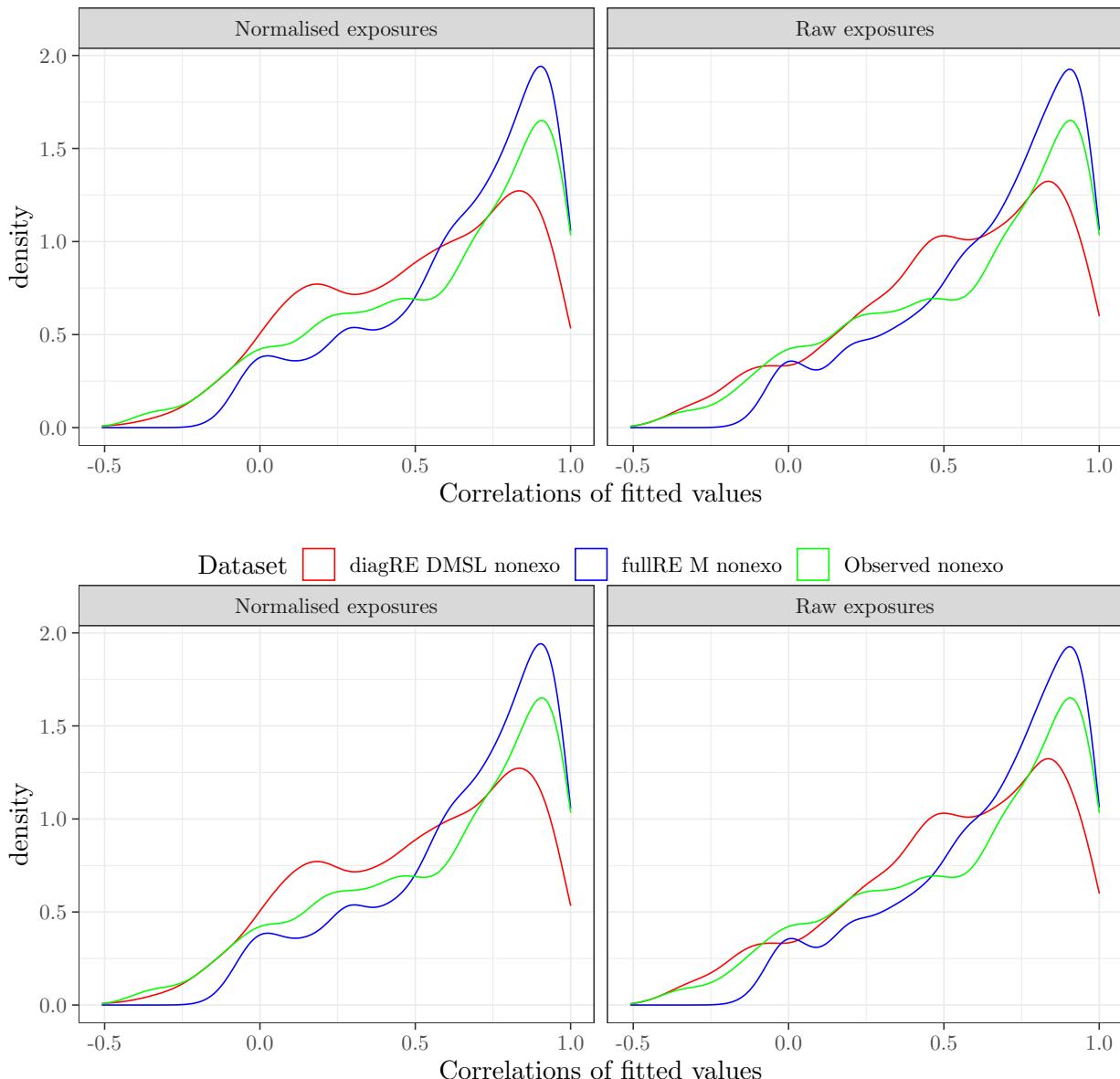


```
## `geom_smooth()` using formula 'y ~ x'
```



```
## `geom_smooth()` using formula 'y ~ x'
```





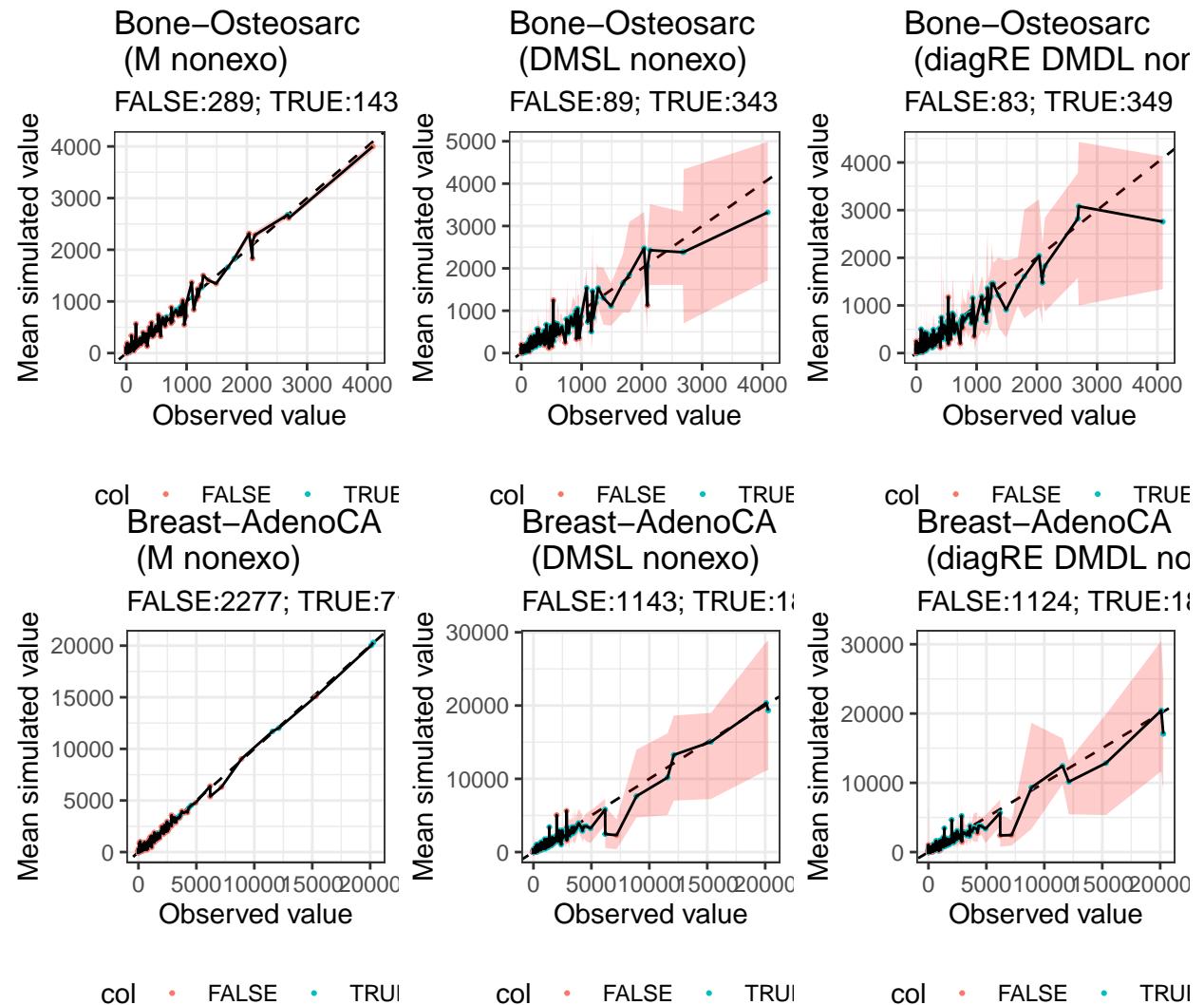
Ranked plots

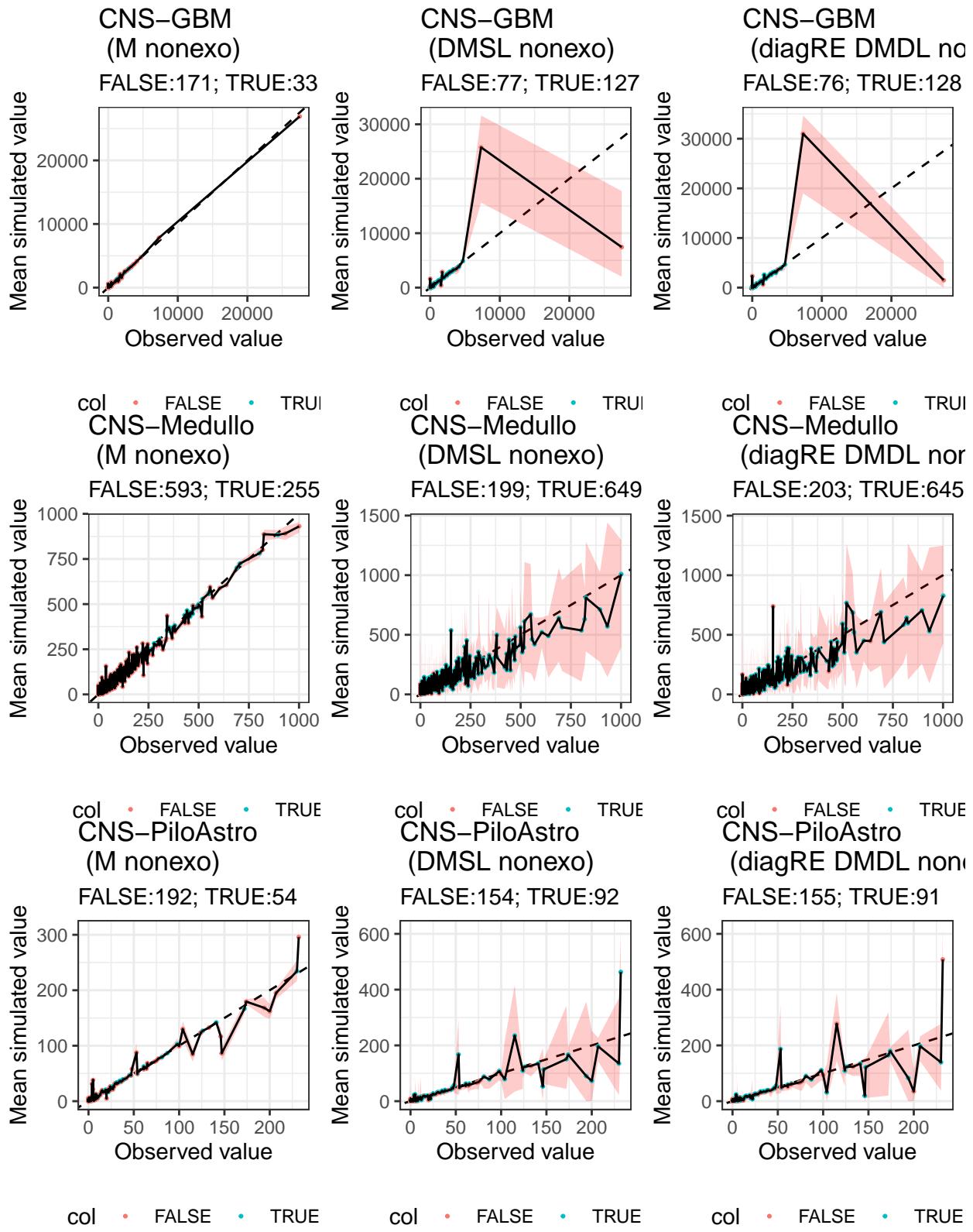
```
for(ct in enough_samples){
  integer_overdispersion_param_DMSL <- 1
  grid.arrange(give_interval_plots_2(df_rank = lapply(list(give_ranked_plot_simulation(tmb_fit_object =
    data_object = all_objects_nonexo_SP[[ct]],
    print_plot = F, nreps = 20, model = "M")), function(i){
    lapply(i, function(j) cbind.data.frame(sorted_value=as.vector(j),
      rank_number=1:length(j)) )}[[1]],
    data_object = all_objects_nonexo_SP[[ct]],
    loglog = F, title = paste0(ct, '\n (M nonexo)'), 
  give_interval_plots_2(df_rank = lapply(list(give_ranked_plot_simulation(tmb_fit_object = fullRE_DMSL_r
```

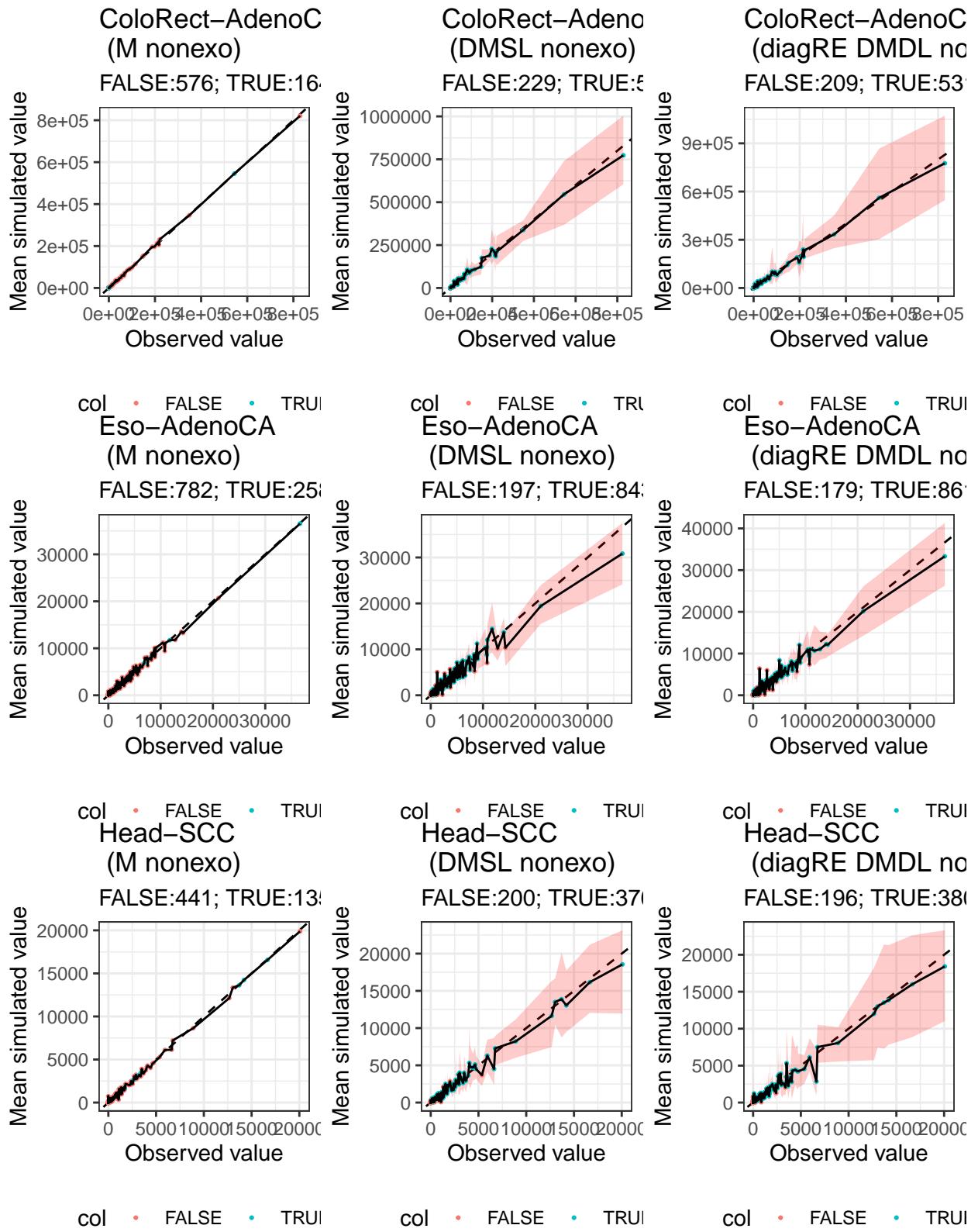
```

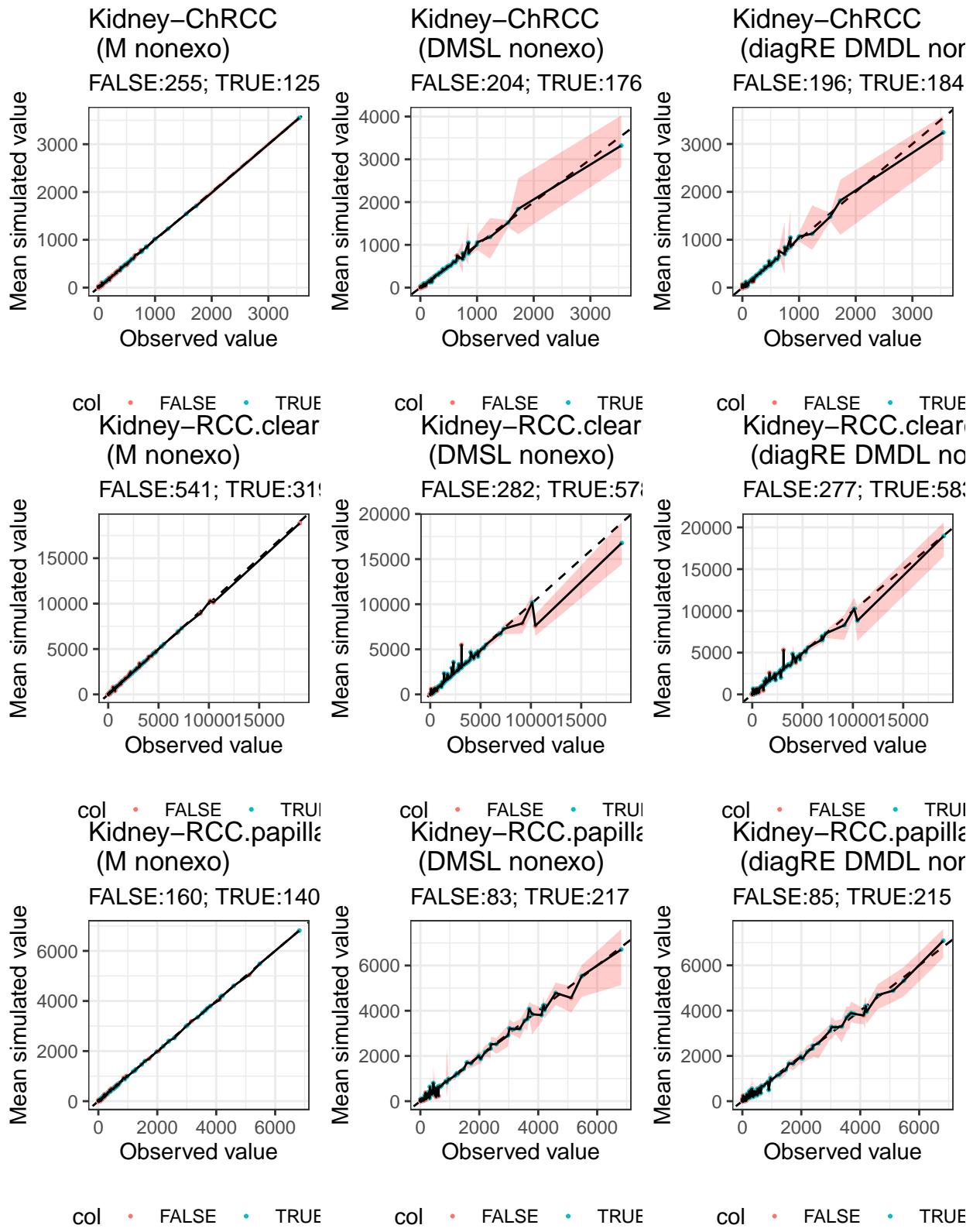
    data_object = all_objects_nonexo_SP[[ct]],
    print_plot = F, nreps = 20, model = "DMSL", integer_overdispersion_param = integer_overdispersion_param,
    lapply(i, function(j) cbind.data.frame(sorted_value=as.vector(j),
                                            rank_number=1:length(j)) )}[[1]],
    data_object = all_objects_nonexo_SP[[ct]],
    loglog = F, title = paste0(ct, '\n (DMSL nonexo)'), 
give_interval_plots_2(df_rank = lapply(list(give_ranked_plot_simulation(tmb_fit_object = diagRE_DMDL_nonexo_SP[[ct]]),
    data_object = all_objects_nonexo_SP[[ct]],
    print_plot = F, nreps = 20, model = "DM", integer_overdispersion_param = 1000)), function(j) cbind.data.frame(sorted_value=as.vector(j),
                                            rank_number=1:length(j)) )}[[1]],
    data_object = all_objects_nonexo_SP[[ct]],
    loglog = F, title = paste0(ct, '\n (diagRE DMDL nonexo)'), ncol=3)
}

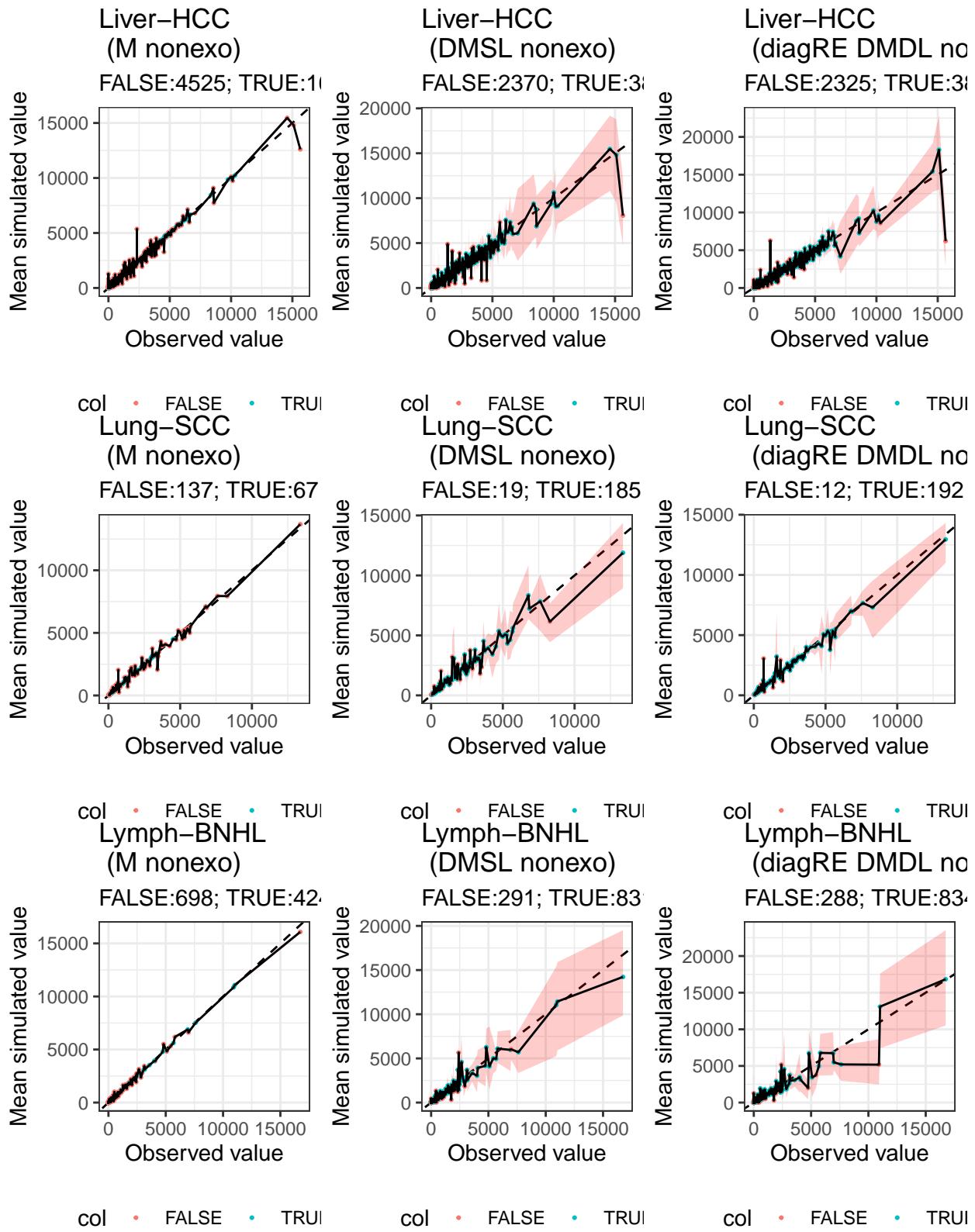
```

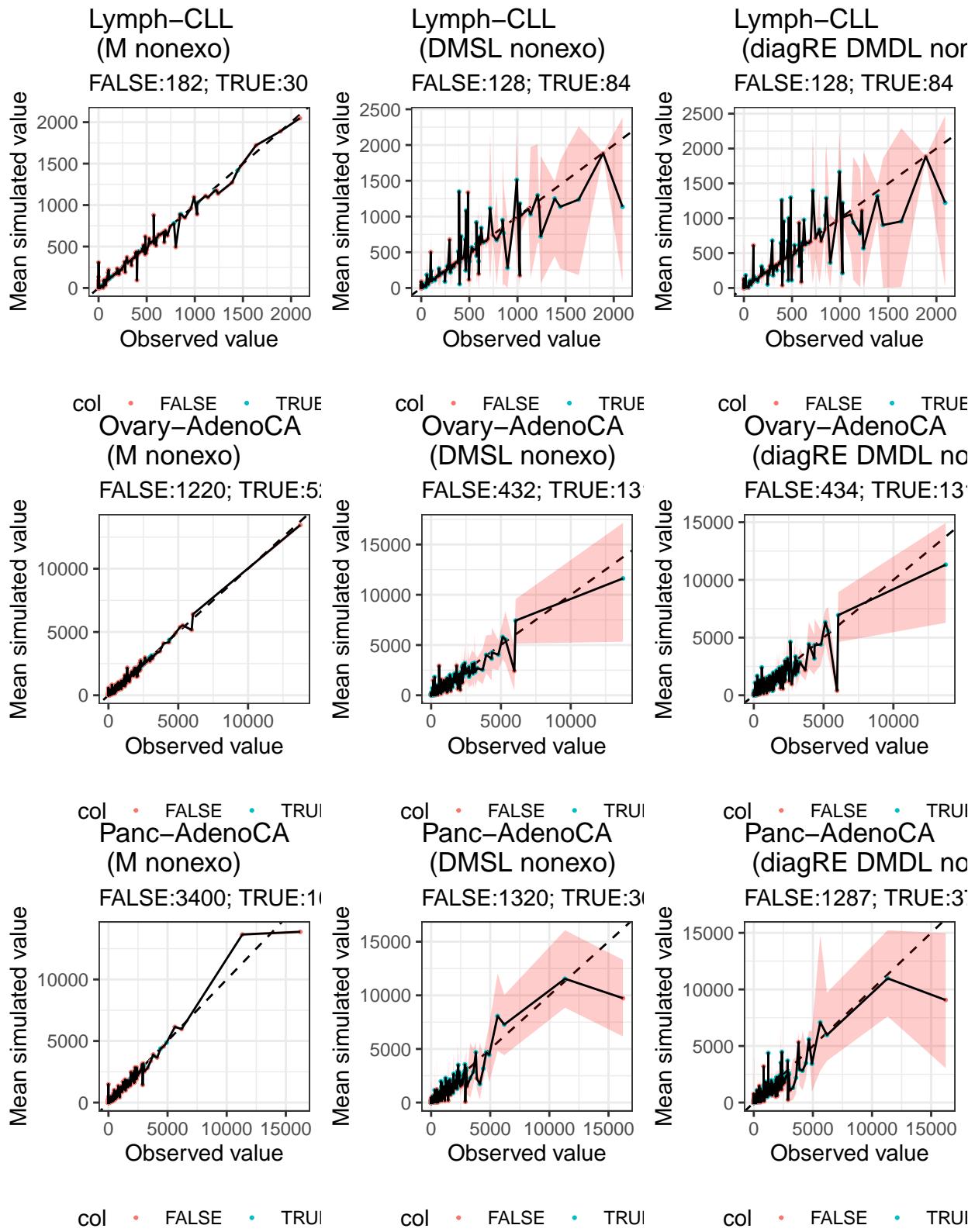


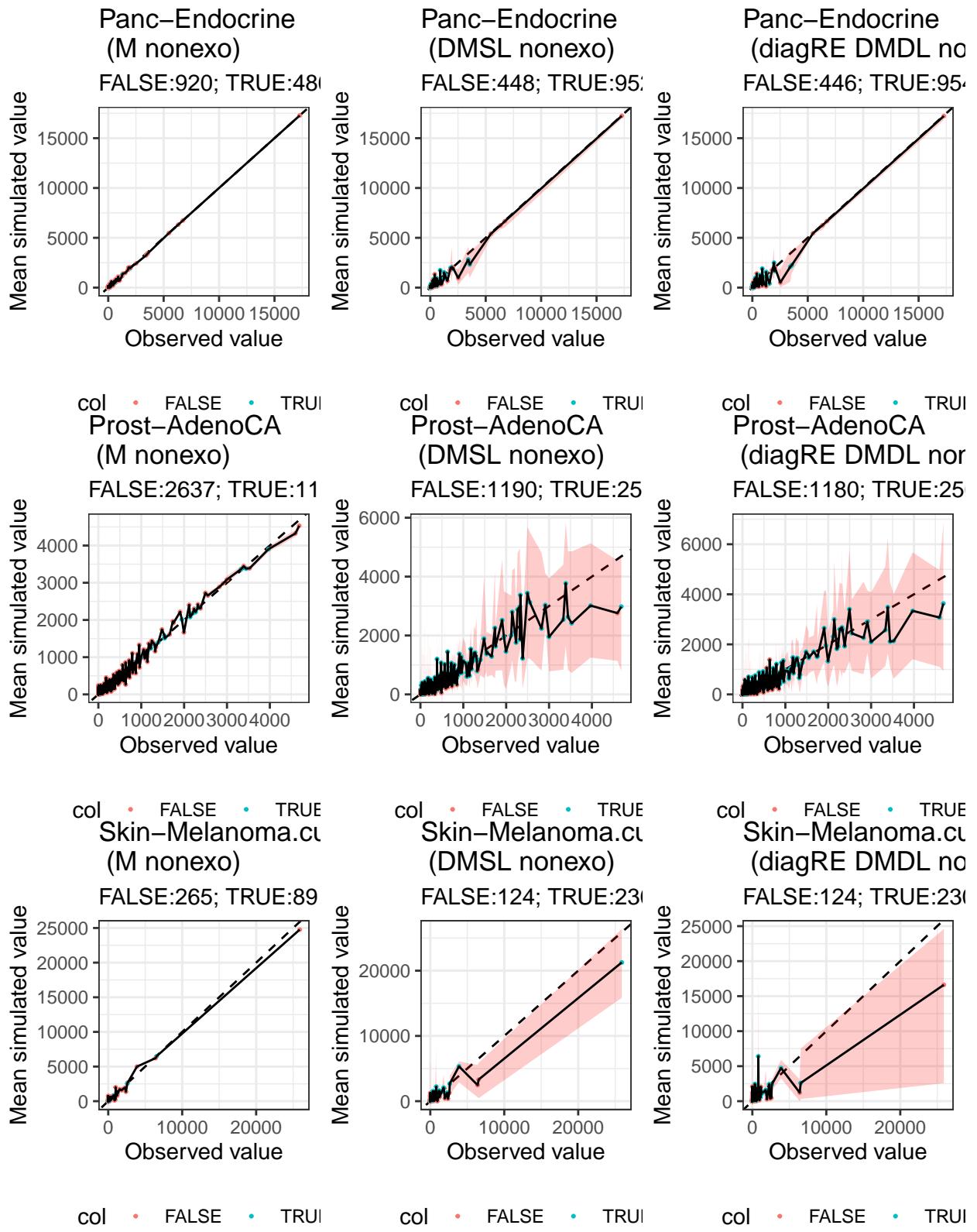


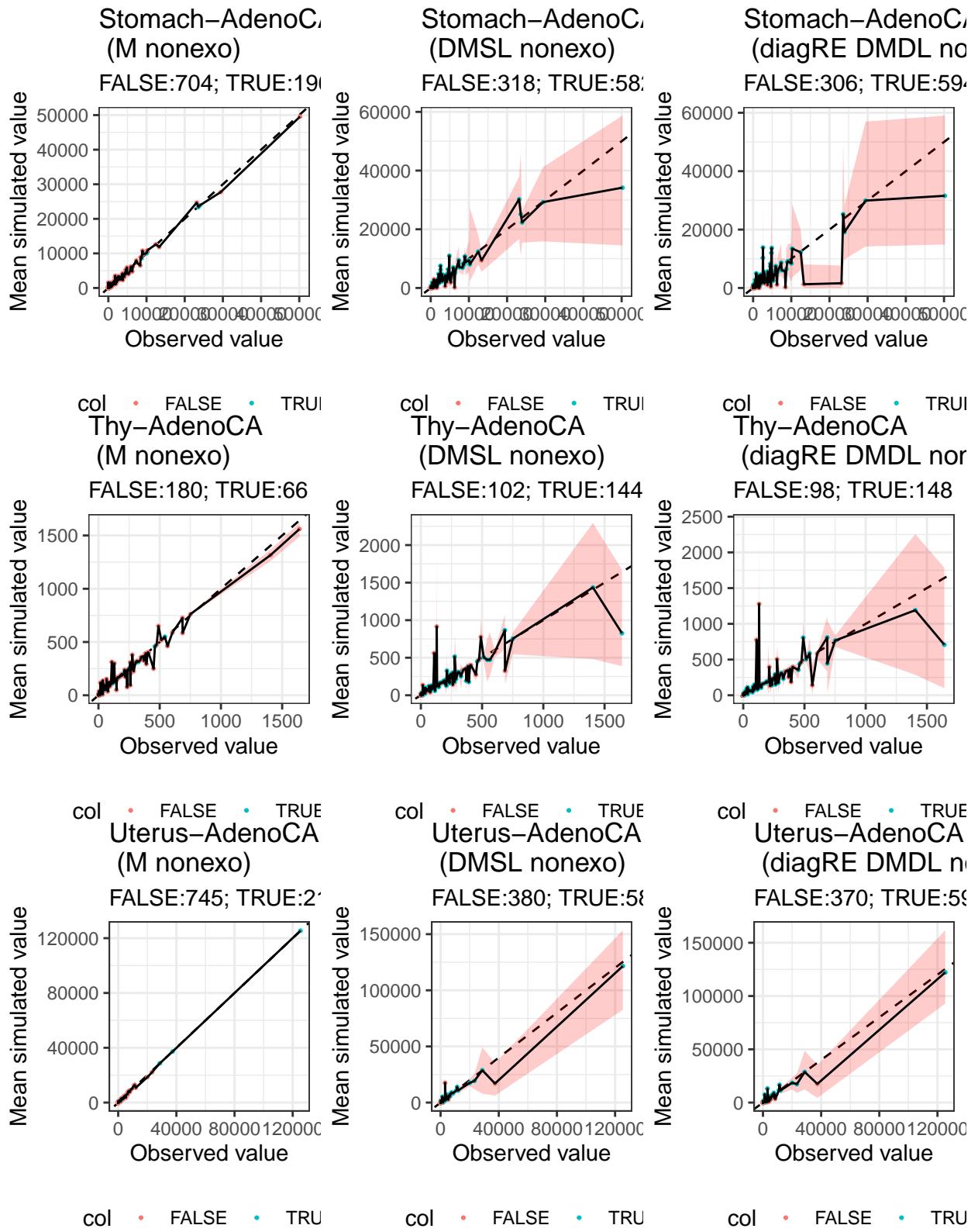












```

for(ct in enough_samples){
  try({
    grid.arrange(give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], ct=ct, typedata="signature",
                                         sigs_to_remove=unique(nonexogenous$V1),
                                         bool_give_PCA = T, path_to_data= "../..../data/",
                                         obj_data=all_objects_nonexo_SP[[ct]],
                                         sig_of_interest=colnames(all_objects_nonexo_SP[[ct]]$Y)[1],
                                         bool_nonexo=T,
                                         model="fullRE_DMSL", nrow_pca_plot=1)[[2]]+
      ggtile(paste0('Simulation of ', ct, ' fullRE_DMSL'))),
    give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], ct=ct, typedata="signature",
                            sigs_to_remove=unique(nonexogenous$V1),
                            bool_give_PCA = T, path_to_data= "../..../data/",
                            obj_data=all_objects_nonexo_SP[[ct]],
                            sig_of_interest=colnames(all_objects_nonexo_SP[[ct]]$Y)[1],
                            bool_nonexo=T,
                            model="diagRE_DMDL", integer_overdispersion_param=1000,
                            nrow_pca_plot=1)[[2]]+
      ggtile(paste0('Simulation of ', ct, ' diagRE_DMDL'))))
  })
}

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), : This
## function had been incorrect until now (30 july 2021)

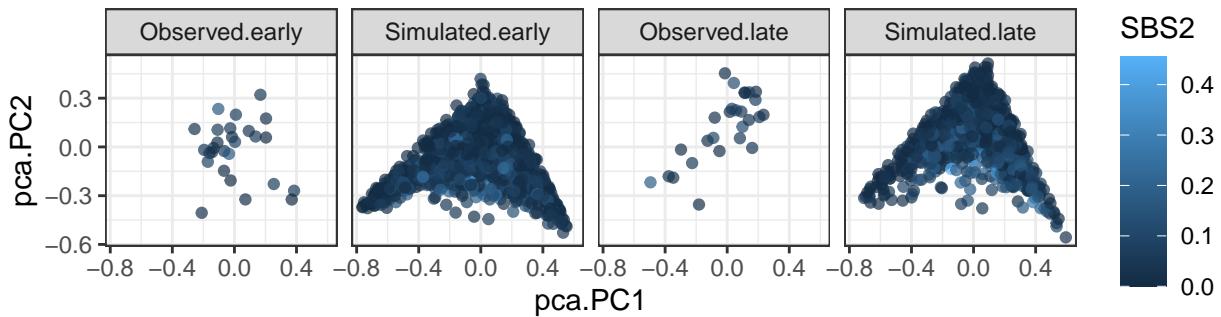
## Warning in mvtnorm:::rmvnorm(n = n_sim, mean = rep(0, dmin1), sigma = cov_mat):
## sigma is numerically not positive semidefinite

## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

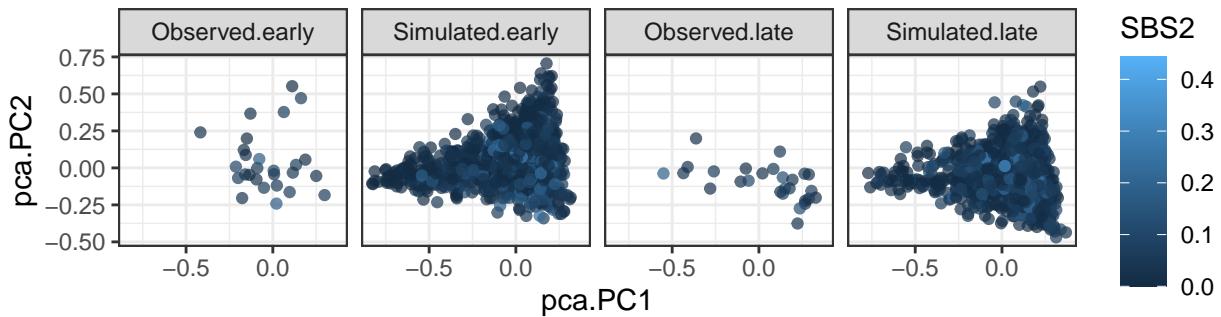
## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), : This
## function had been incorrect until now (30 july 2021)

```

### Simulation of Bone–Osteosarc fullRE\_DMSL



### Simulation of Bone–Osteosarc diagRE\_DMDL



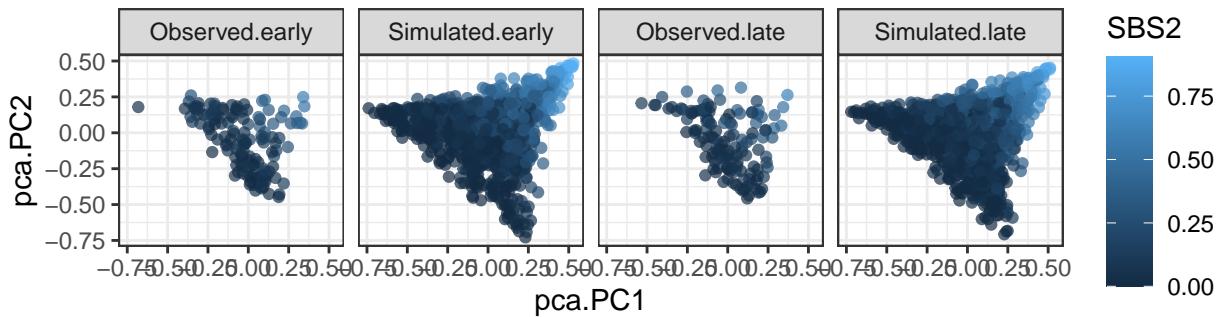
```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

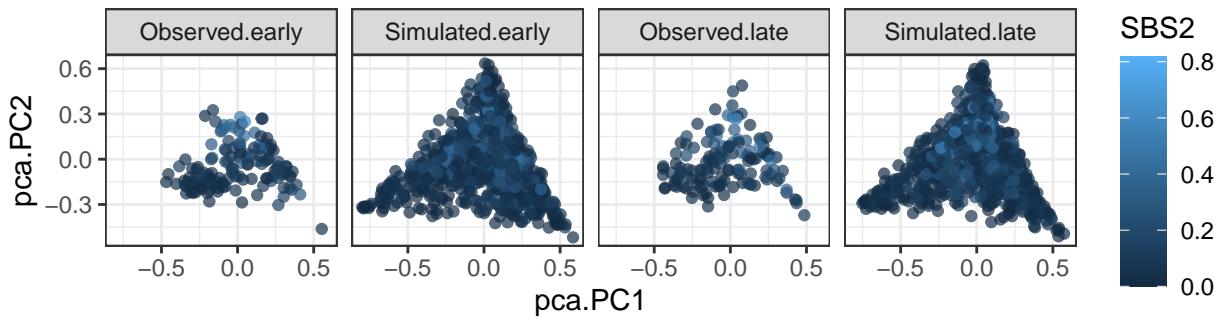
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of Breast–AdenoCA fullRE\_DMSL



### Simulation of Breast–AdenoCA diagRE\_DMDL



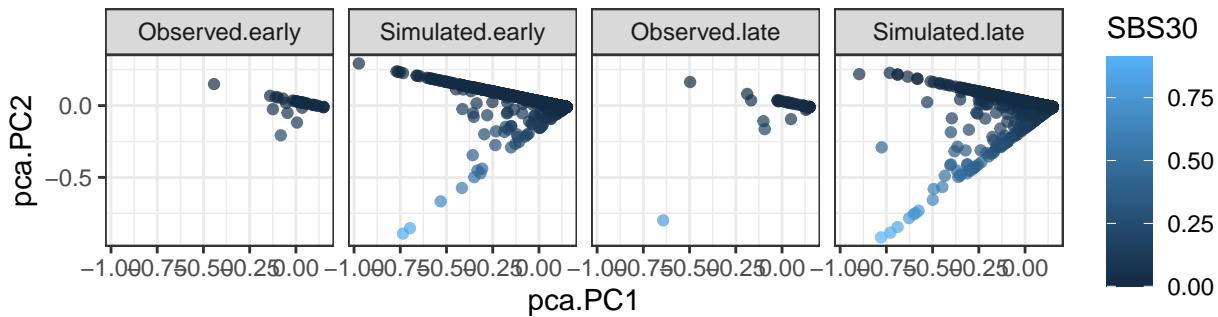
```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

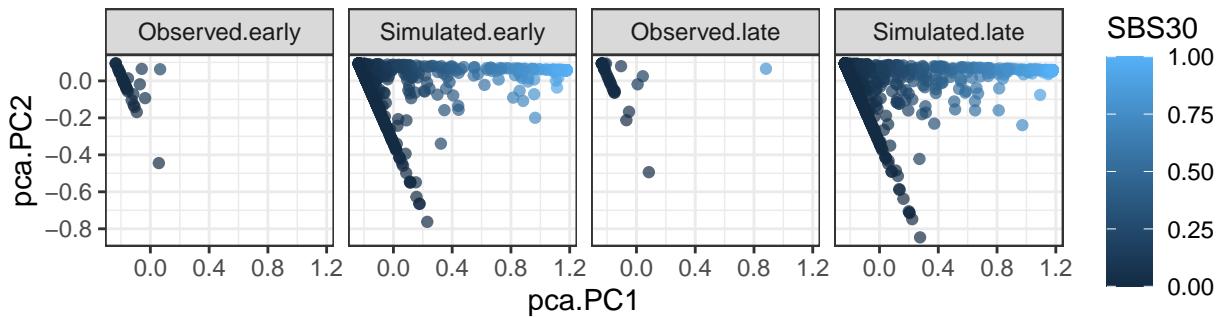
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of CNS–GBM fullRE\_DMSL



### Simulation of CNS–GBM diagRE\_DMDL



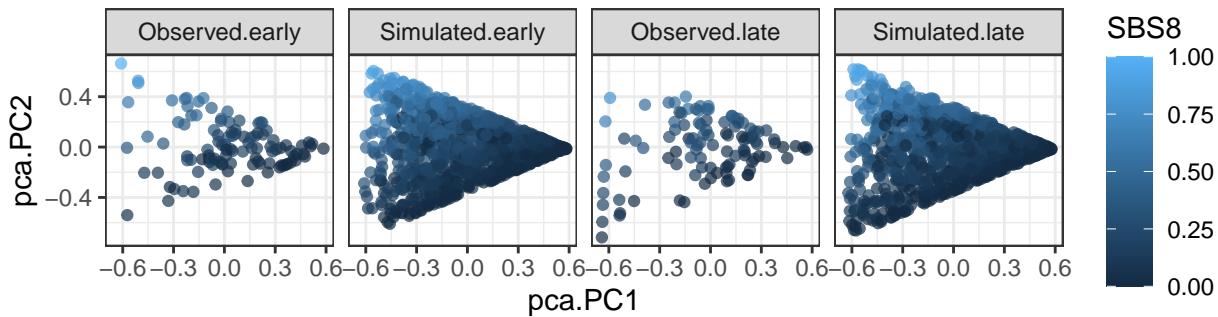
```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

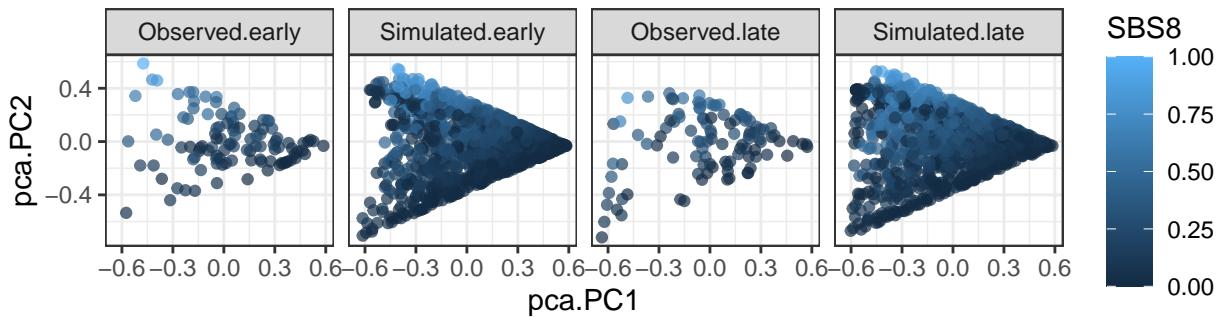
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of CNS–Medullo fullRE\_DMSL



### Simulation of CNS–Medullo diagRE\_DMDL



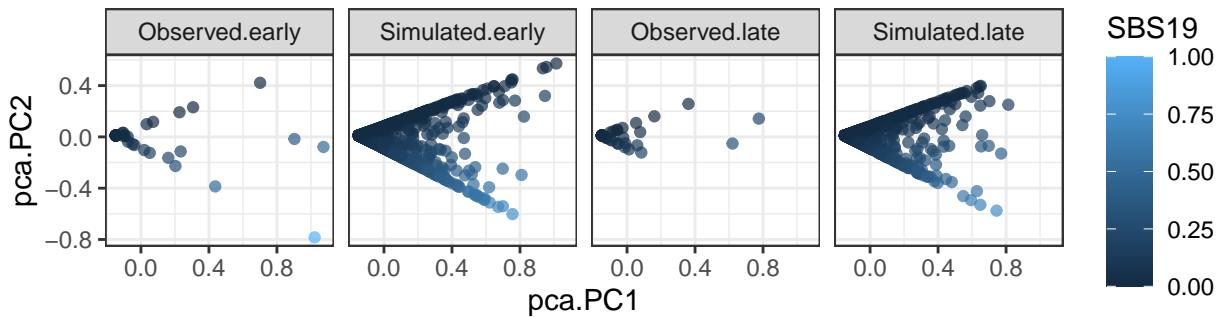
```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

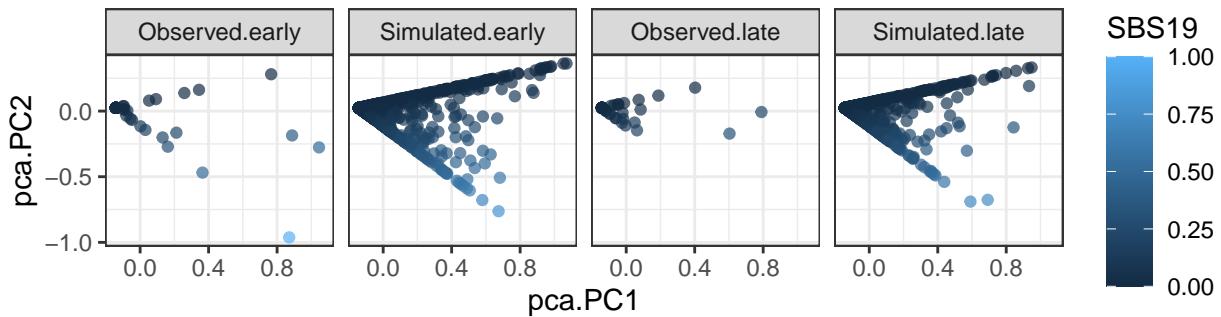
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of CNS–PiloAstro fullRE\_DMSL



### Simulation of CNS–PiloAstro diagRE\_DMDL



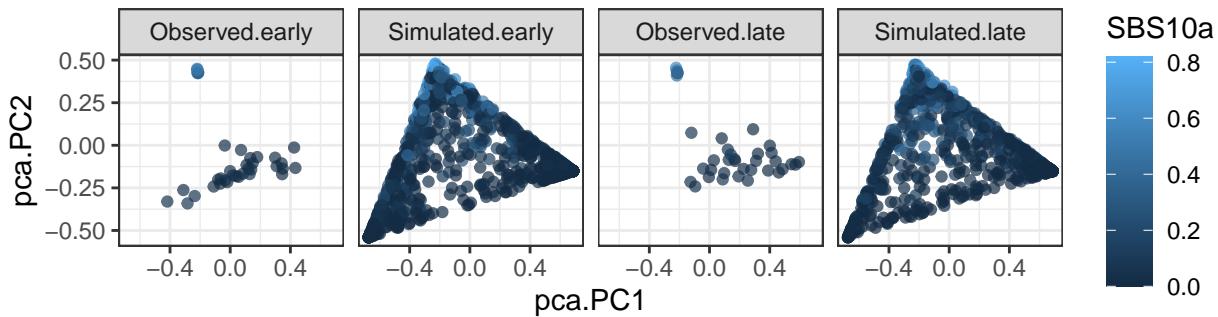
```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

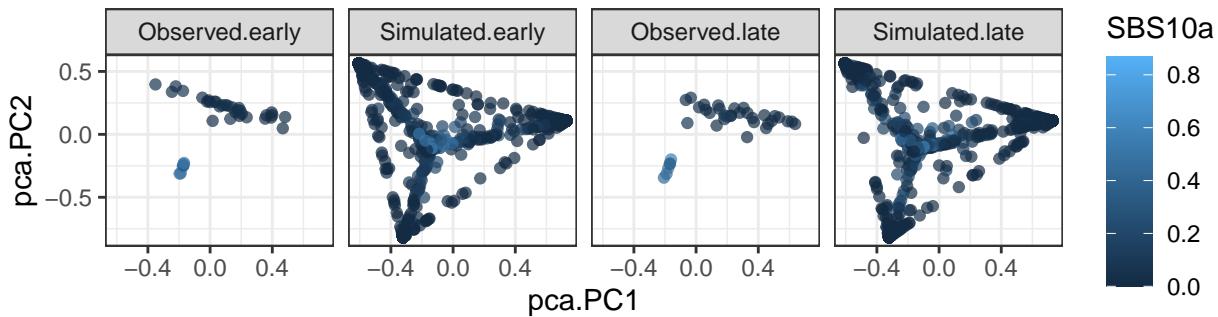
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of ColoRect–AdenoCA fullRE\_DMSL



### Simulation of ColoRect–AdenoCA diagRE\_DMDL



```

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

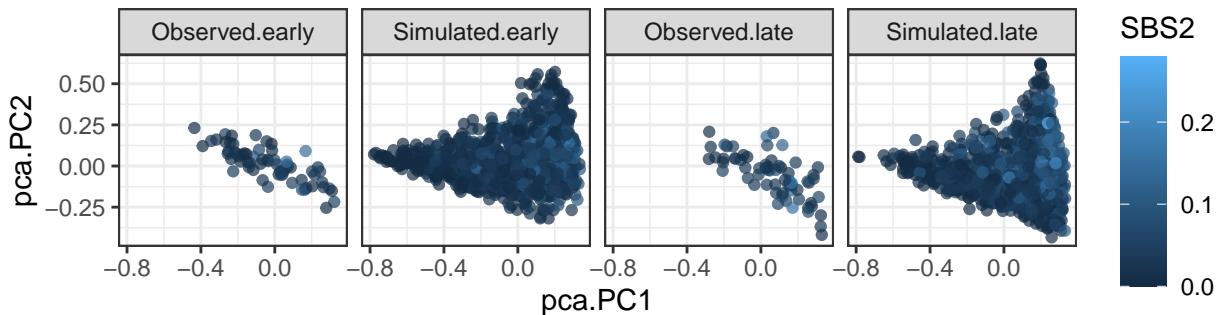
## Warning in mvtnorm:::rmvnorm(n = n_sim, mean = rep(0, dmin1), sigma = cov_mat):
## sigma is numerically not positive semidefinite

## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

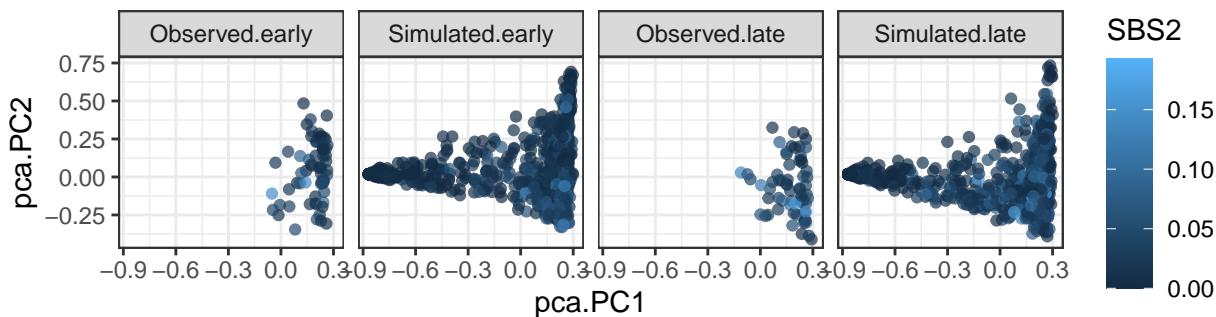
## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)

```

### Simulation of Eso–AdenoCA fullRE\_DMSL



### Simulation of Eso–AdenoCA diagRE\_DMDL



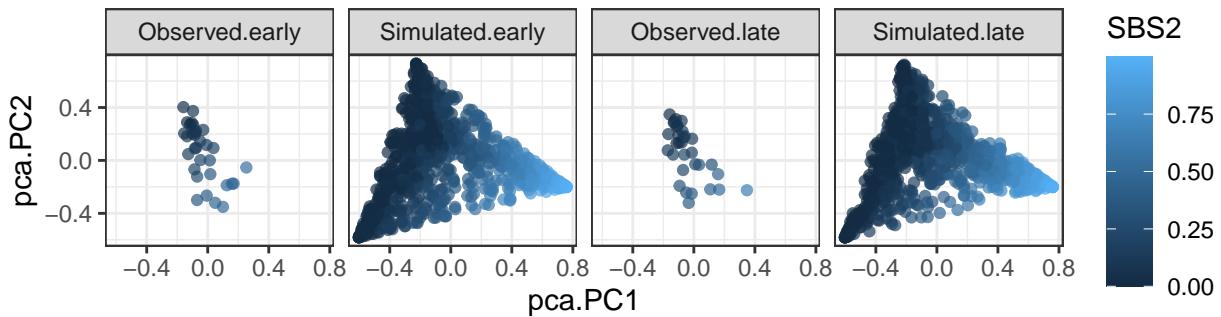
```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

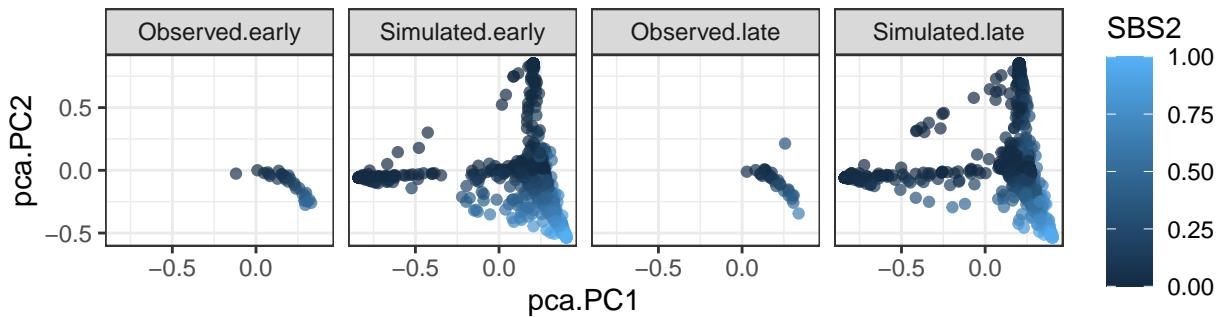
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of Head–SCC fullRE\_DMSL



### Simulation of Head–SCC diagRE\_DMDL



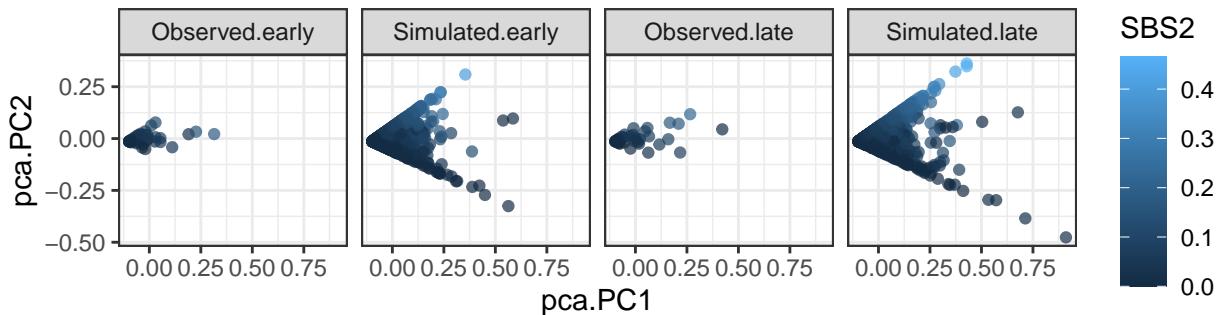
```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

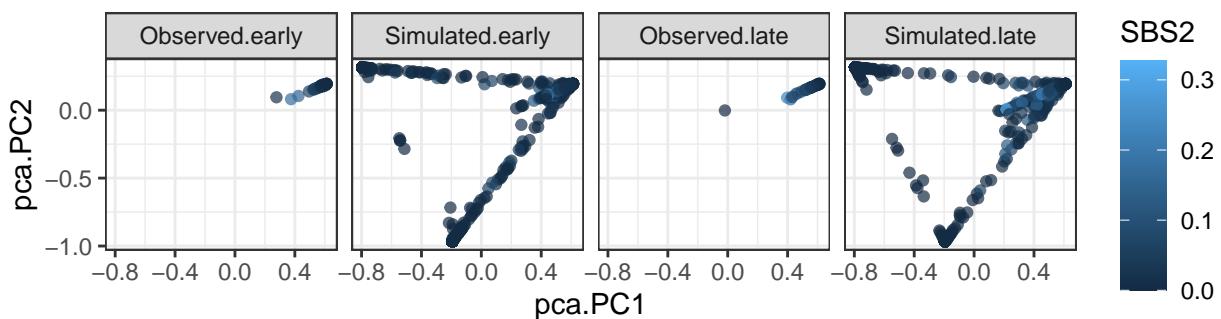
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of Kidney–ChRCC fullRE\_DMSL



### Simulation of Kidney–ChRCC diagRE\_DMDL



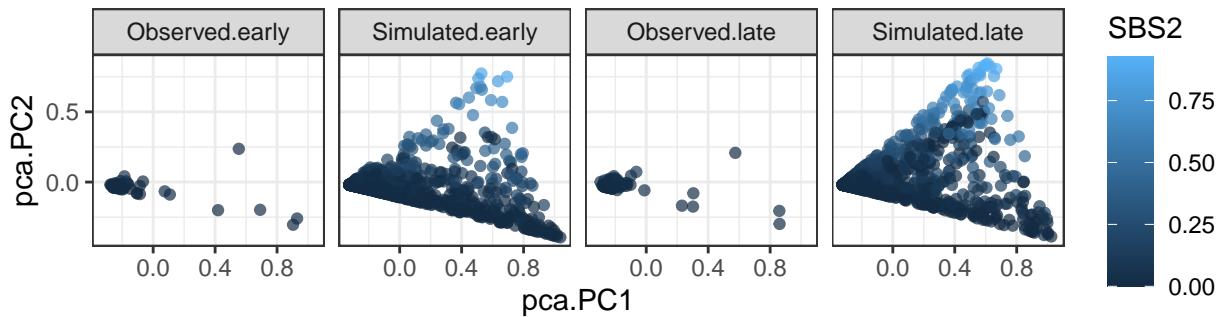
```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

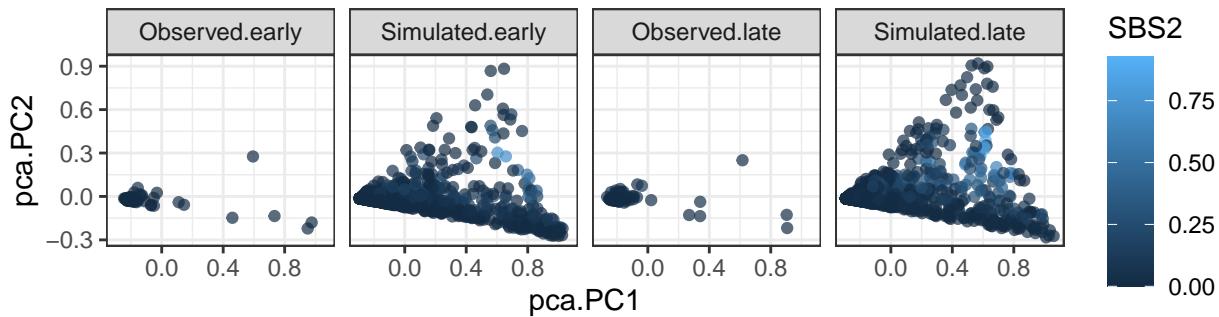
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of Kidney–RCC.clearcell fullRE\_DMSL



### Simulation of Kidney–RCC.clearcell diagRE\_DMDL



```

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

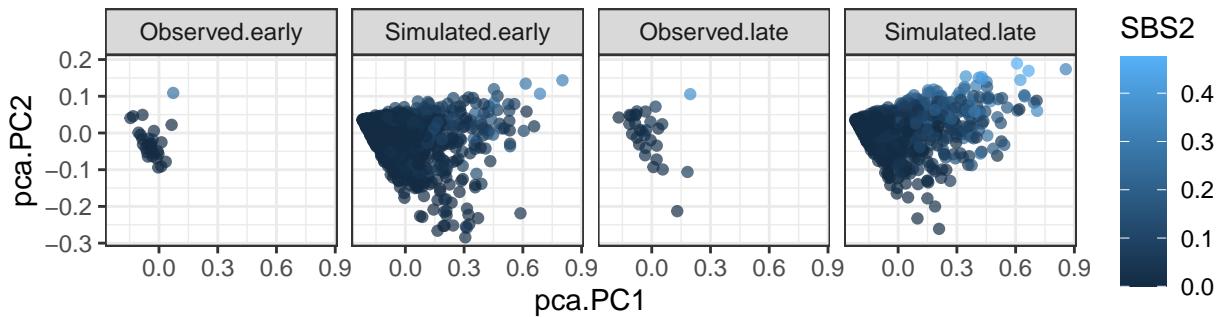
## Warning in mvtnorm:::rmvnorm(n = n_sim, mean = rep(0, dmin1), sigma = cov_mat):
## sigma is numerically not positive semidefinite

## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

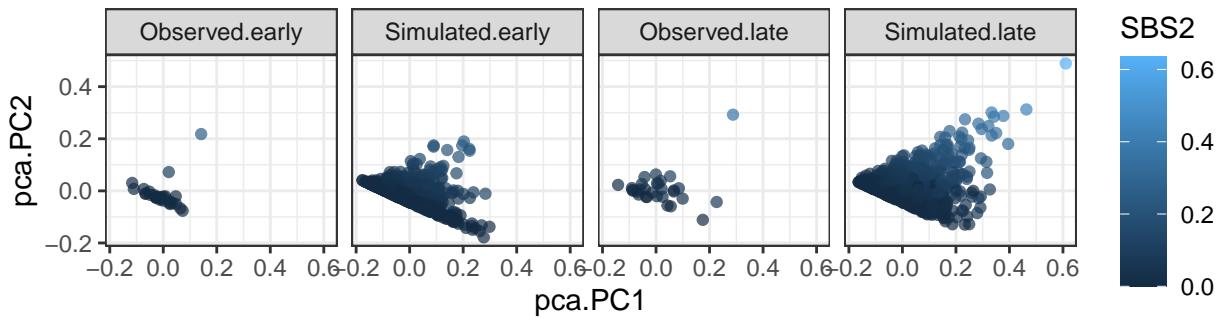
## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)

```

### Simulation of Kidney–RCC.papillary fullRE\_DMSL



### Simulation of Kidney–RCC.papillary diagRE\_DMDL



```

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

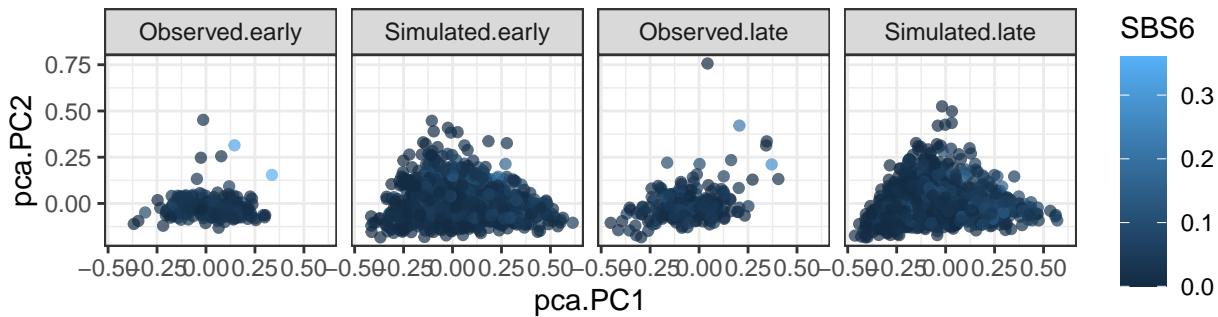
## Warning in mvtnorm:::rmvnorm(n = n_sim, mean = rep(0, dmin1), sigma = cov_mat):
## sigma is numerically not positive semidefinite

## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

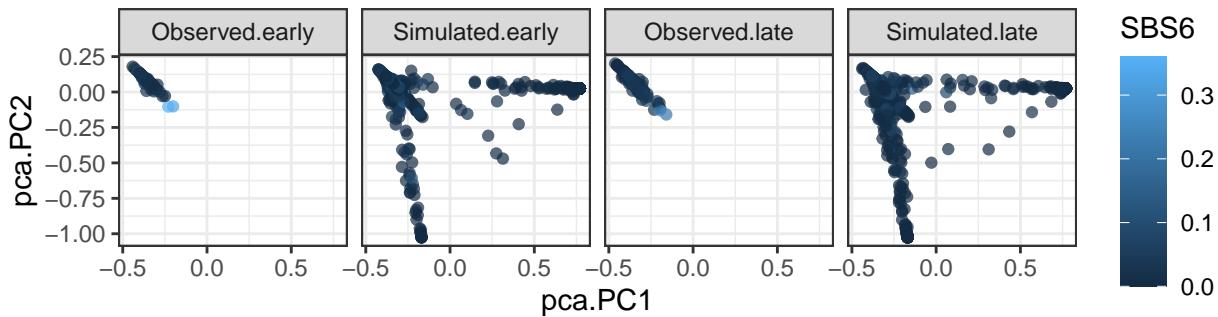
## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)

```

### Simulation of Liver–HCC fullRE\_DMSL



### Simulation of Liver–HCC diagRE\_DMDL



```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

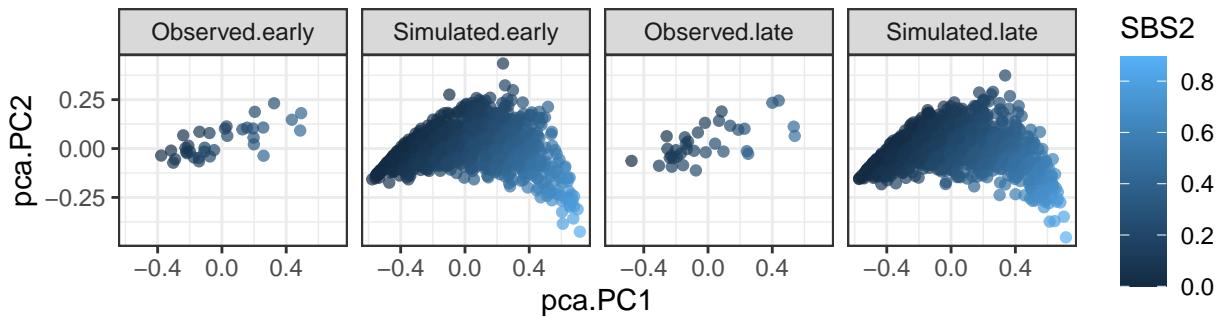
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

## Warning in mvtnorm:::rmvnorm(n = n_sim, mean = rep(0, dmin1), sigma = cov_mat):
## sigma is numerically not positive semidefinite

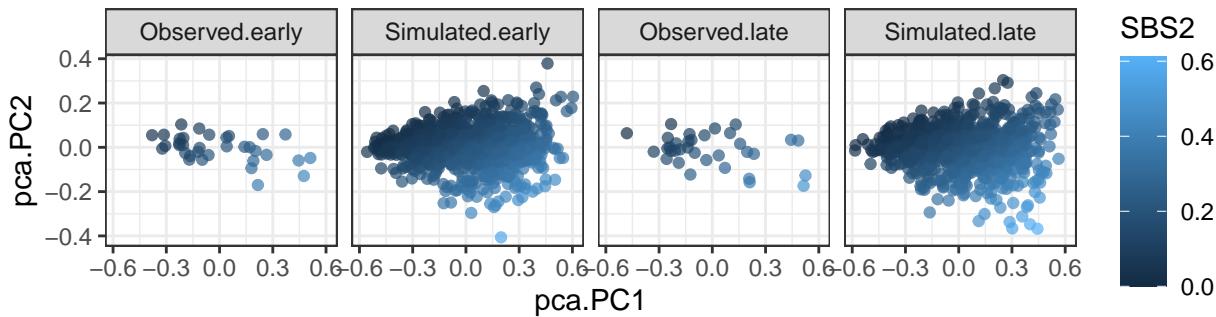
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## This
## function had been incorrect until now (30 july 2021)
```

### Simulation of Lung–SCC fullRE\_DMSL



### Simulation of Lung–SCC diagRE\_DMDL



```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

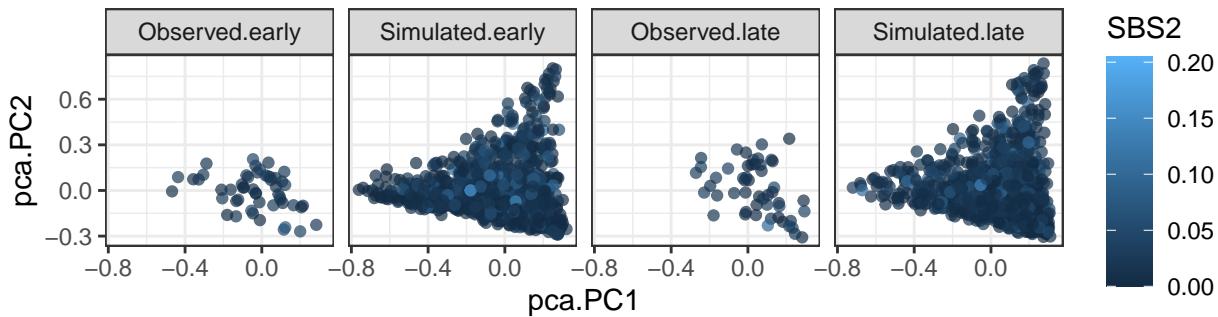
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

## Warning in mvtnorm:::rmvnorm(n = n_sim, mean = rep(0, dmin1), sigma = cov_mat):
## sigma is numerically not positive semidefinite

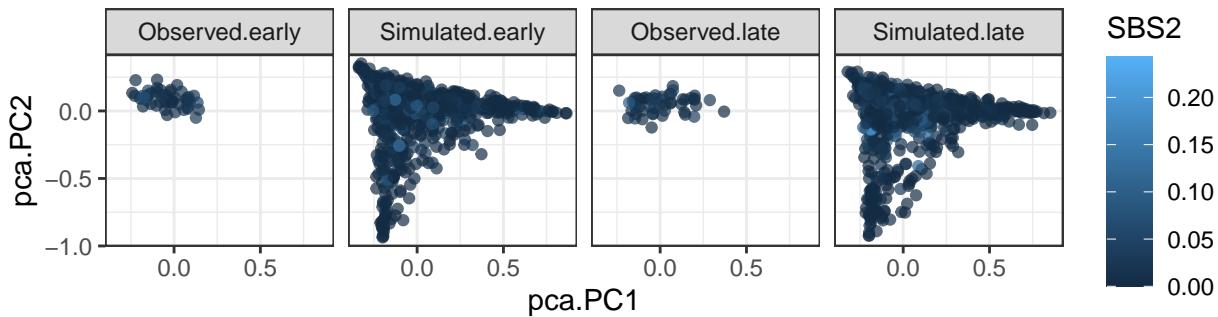
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of Lymph–BNHL fullRE\_DMSL



### Simulation of Lymph–BNHL diagRE\_DMDL



```

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

## Error in m[unlist(sapply(2:nrow(m), function(rw) seq(from = rw, length.out = (rw - :
##   replacement has length zero

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

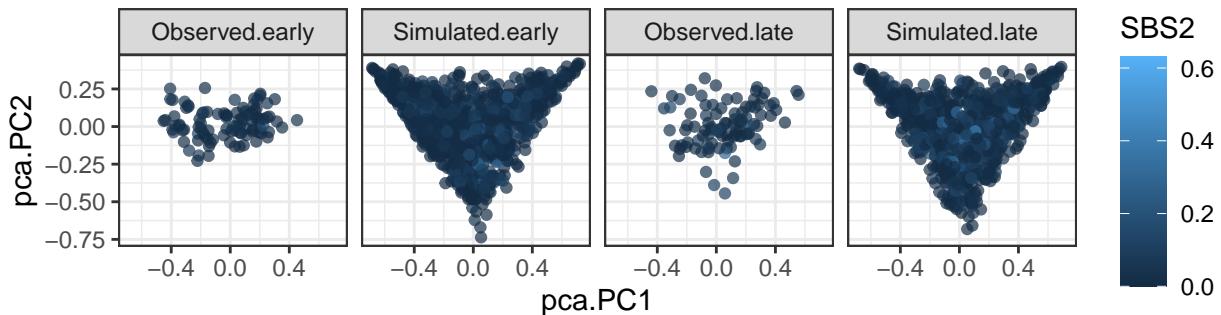
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

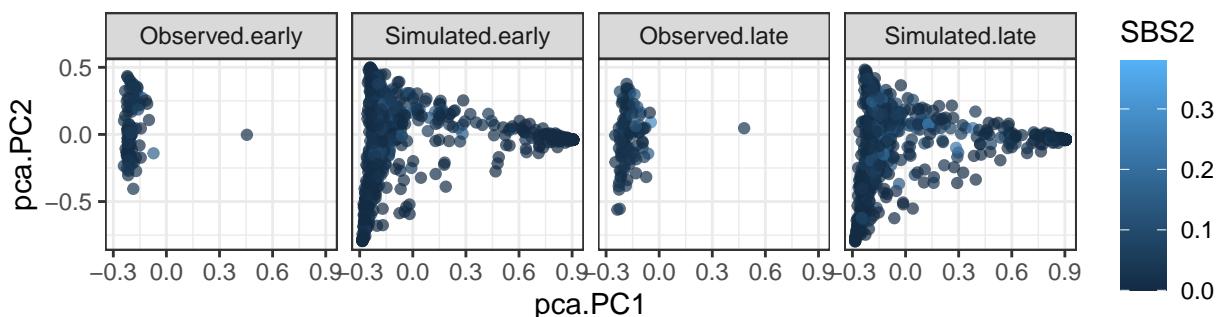
## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), : This
## function had been incorrect until now (30 july 2021)

```

### Simulation of Ovary–AdenoCA fullRE\_DMSL



### Simulation of Ovary–AdenoCA diagRE\_DMDL



```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

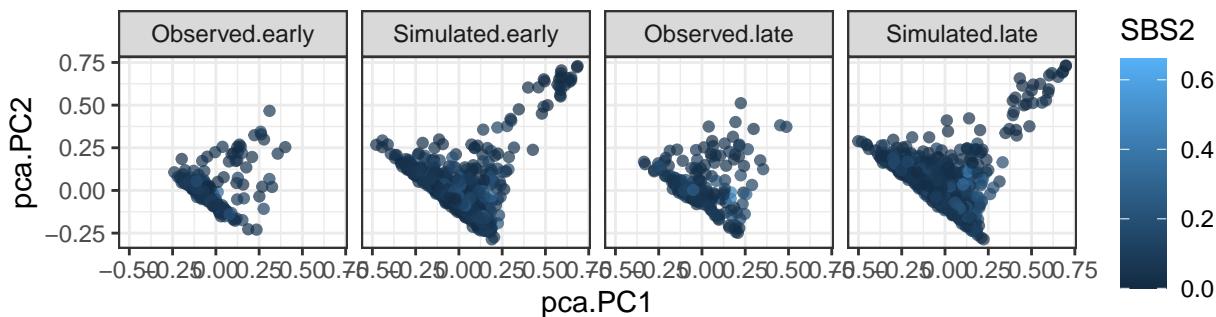
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

## Warning in mvtnorm:::rmvnorm(n = n_sim, mean = rep(0, dmin1), sigma = cov_mat):
## sigma is numerically not positive semidefinite

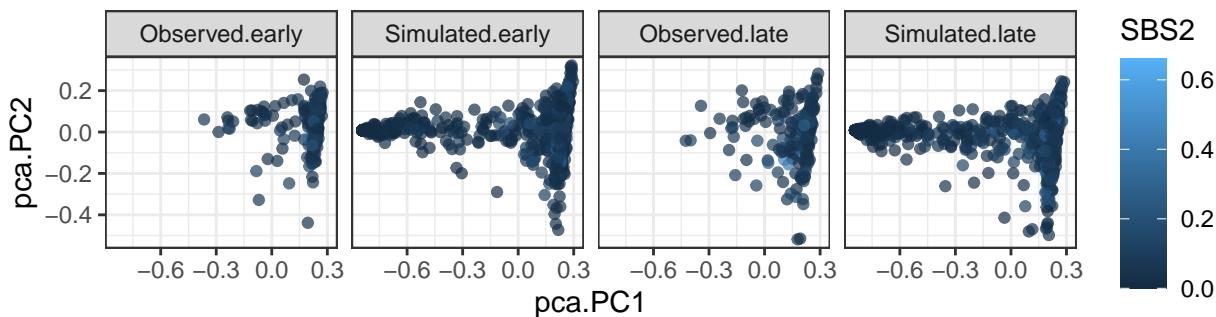
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of Panc–AdenoCA fullRE\_DMSL



### Simulation of Panc–AdenoCA diagRE\_DMDL



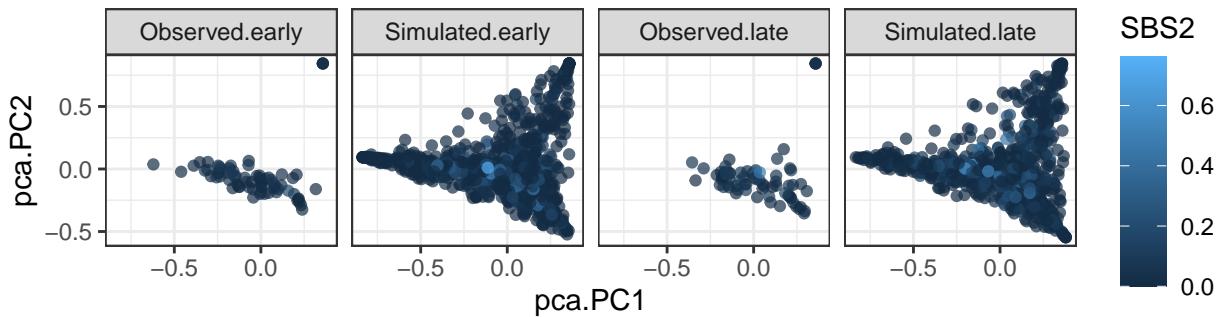
```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

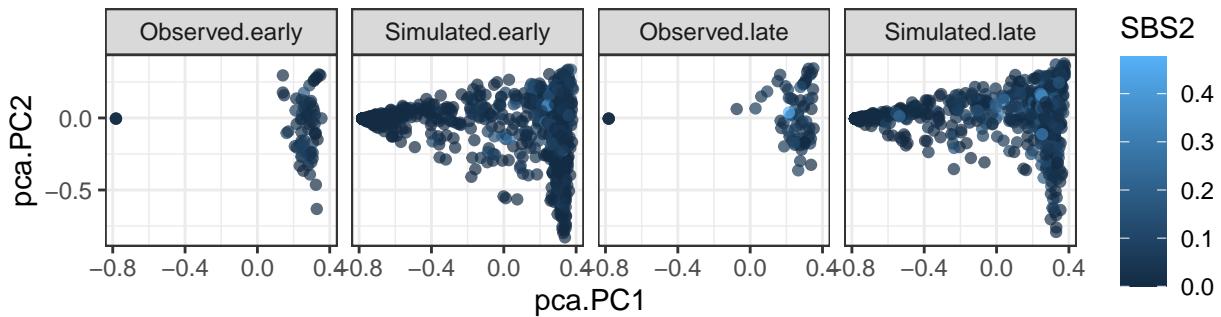
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), : This
## function had been incorrect until now (30 july 2021)
```

### Simulation of Panc–Endocrine fullRE\_DMSL



### Simulation of Panc–Endocrine diagRE\_DMDL



```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

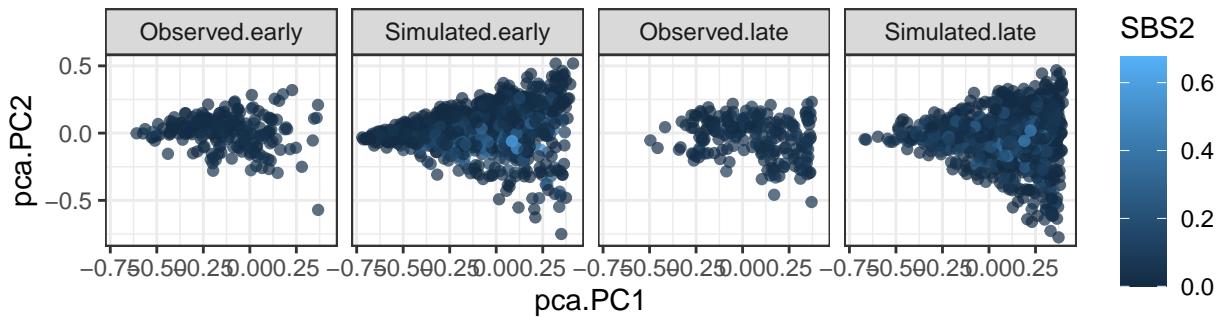
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

## Warning in mvtnorm:::rmvnorm(n = n_sim, mean = rep(0, dmin1), sigma = cov_mat):
## sigma is numerically not positive semidefinite

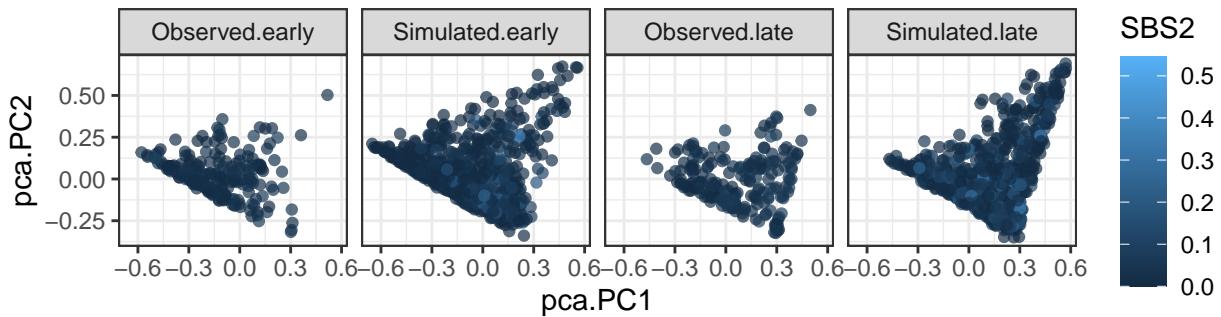
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of Prost–AdenoCA fullRE\_DMSL



### Simulation of Prost–AdenoCA diagRE\_DMDL



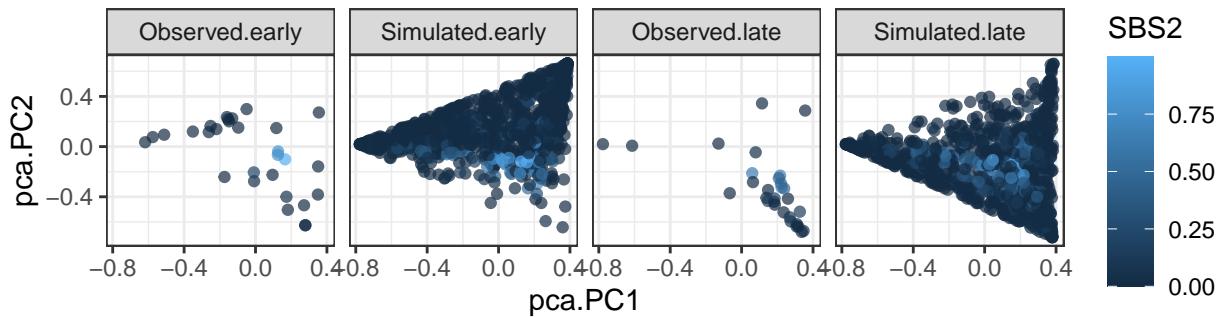
```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

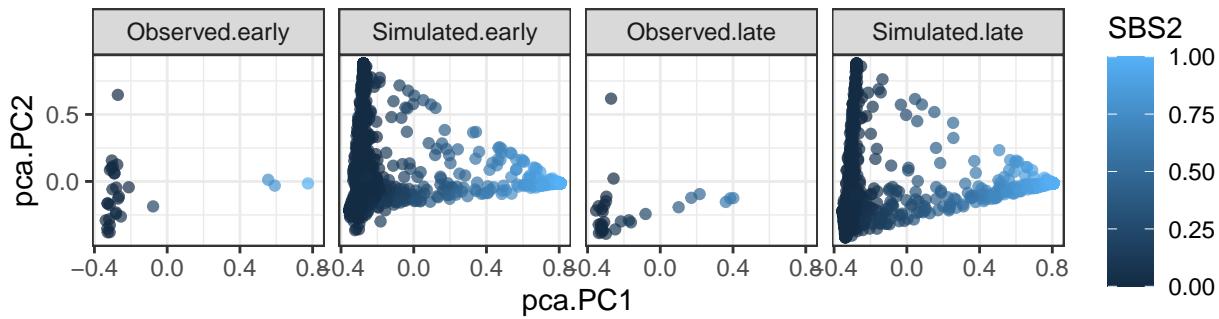
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of Skin–Melanoma.cutaneous fullRE\_DMSL



### Simulation of Skin–Melanoma.cutaneous diagRE\_DMDL



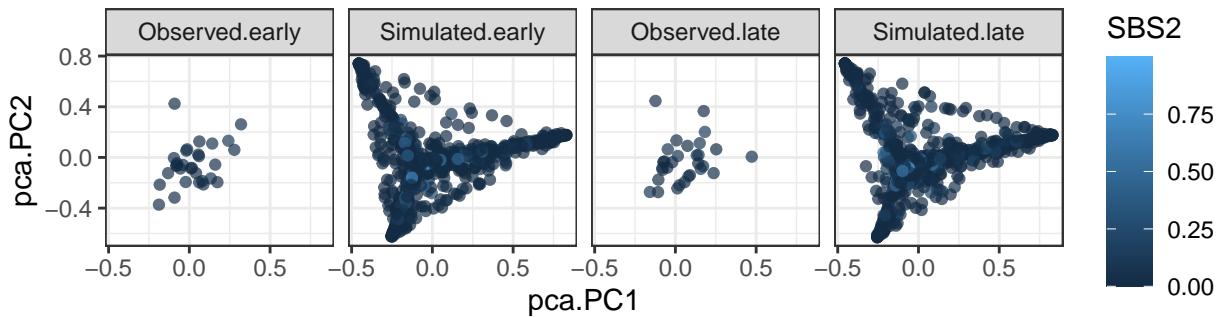
```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

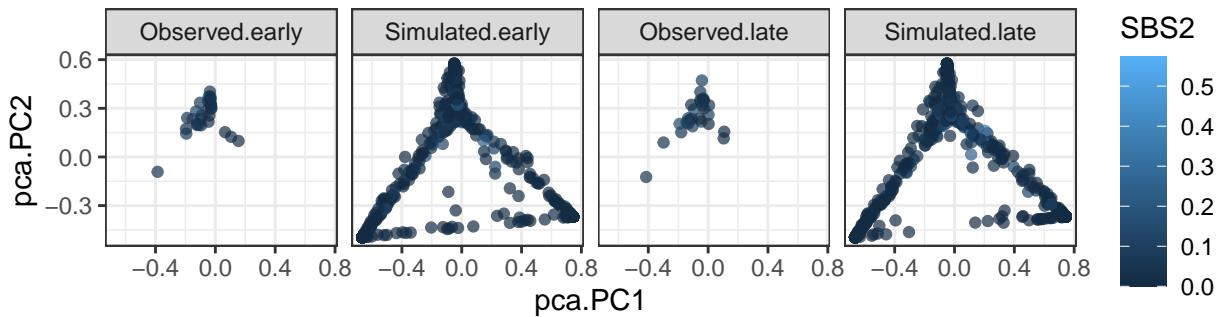
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of Stomach–AdenoCA fullRE\_DMSL



### Simulation of Stomach–AdenoCA diagRE\_DMDL



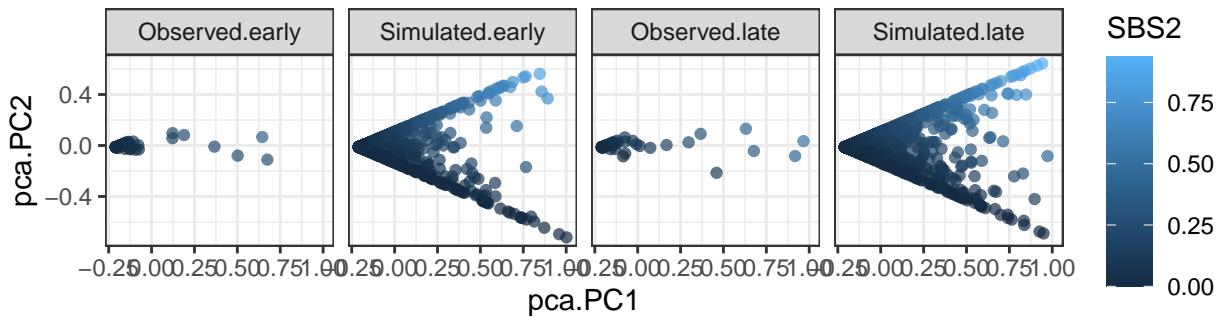
```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

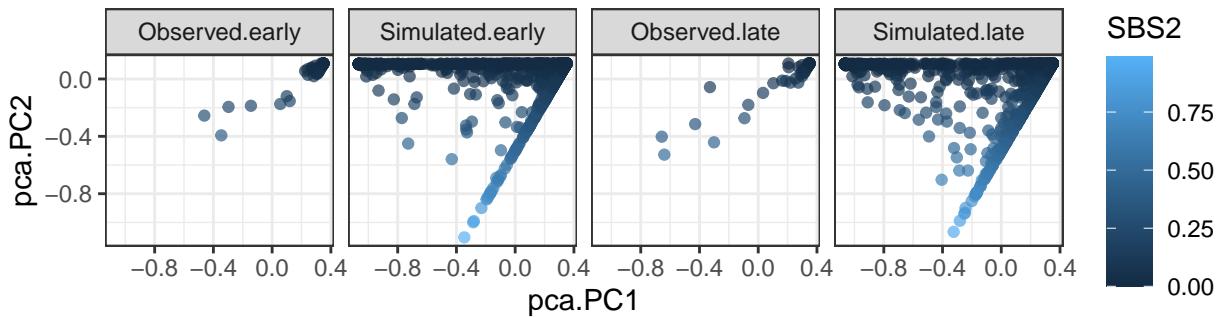
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of Thy–AdenoCA fullRE\_DMSL



### Simulation of Thy–AdenoCA diagRE\_DMDL



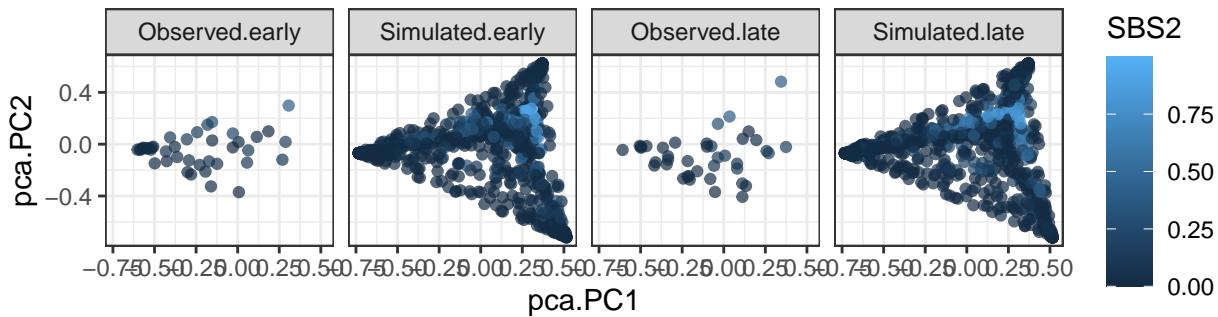
```
## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], :
## This function had been incorrect until now (30 july 2021)

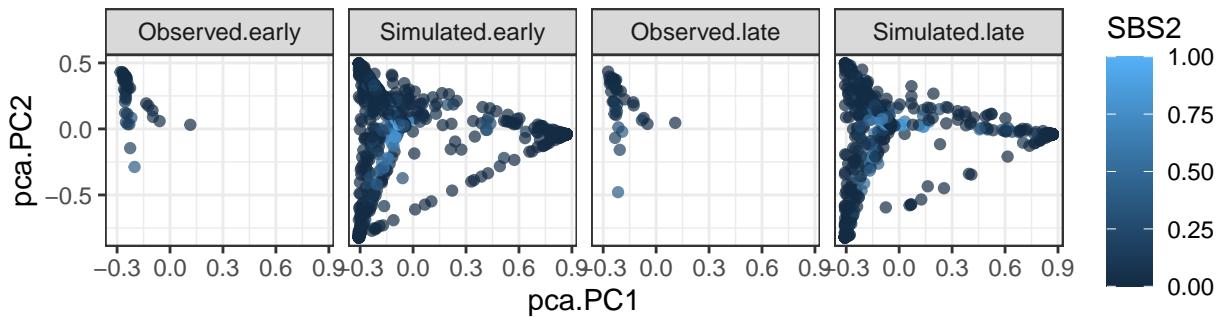
## Warning in give_sim_from_estimates(tmb_object = diagRE_DMDL_nonexo_SP[[ct]], :
## <fullRE_DMSL> and <fullRE_DM> used be to used interchangeably

## Warning in fill_covariance_matrix(arg_d = d, arg_entries_var = rep(1, d), :
## function had been incorrect until now (30 july 2021)
```

### Simulation of Uterus–AdenoCA fullRE\_DMSL

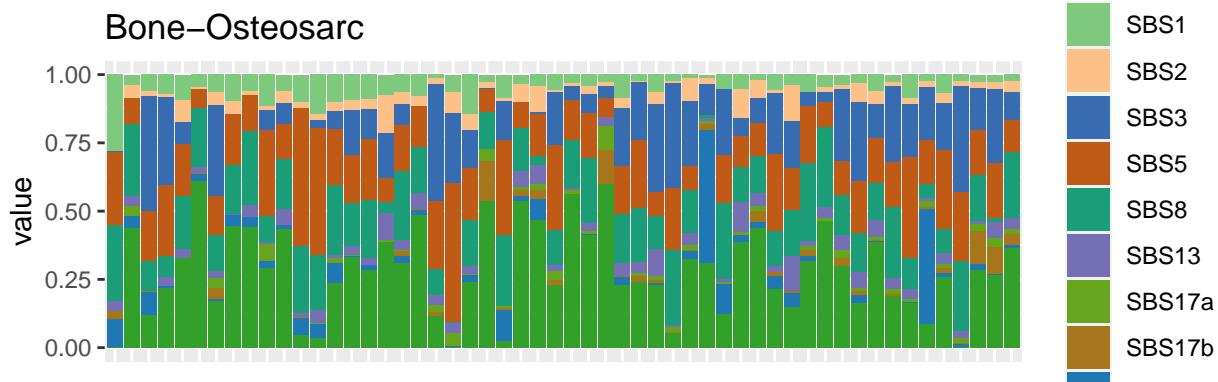


### Simulation of Uterus–AdenoCA diagRE\_DMDL

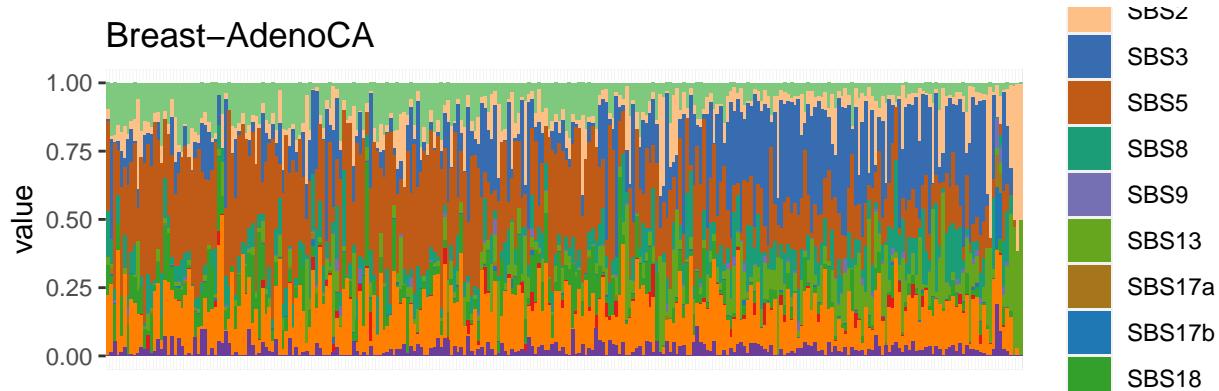


```
for(ct in enough_samples){
  print(createBarplot(normalise_rw(non_duplicated_rows(all_objects_SP[[ct]]$Y)),
    order_labels = names(sort(rowSums(non_duplicated_rows(all_objects_SP[[ct]]$Y)),
      decreasing = F)), remove_labels=T)+ggtitle(ct))
}
```

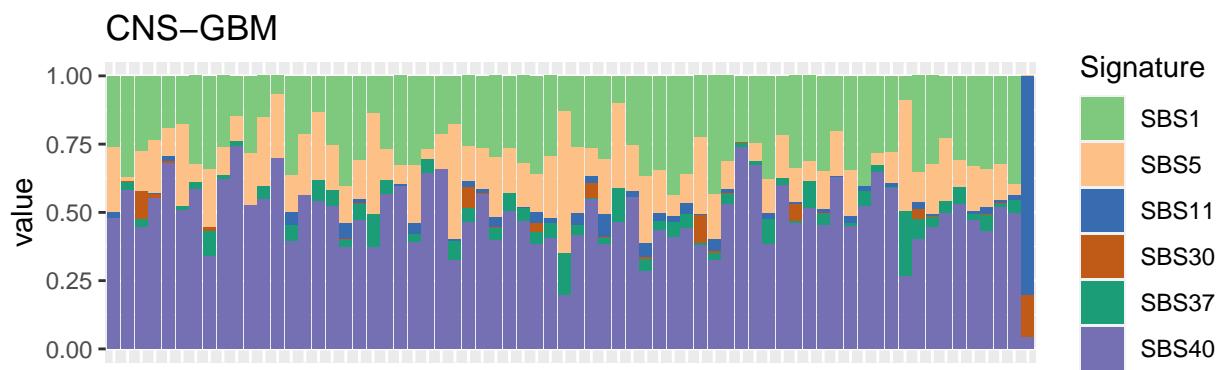
## Creating plot... it might take some time if the data are large. Number of samples: 54



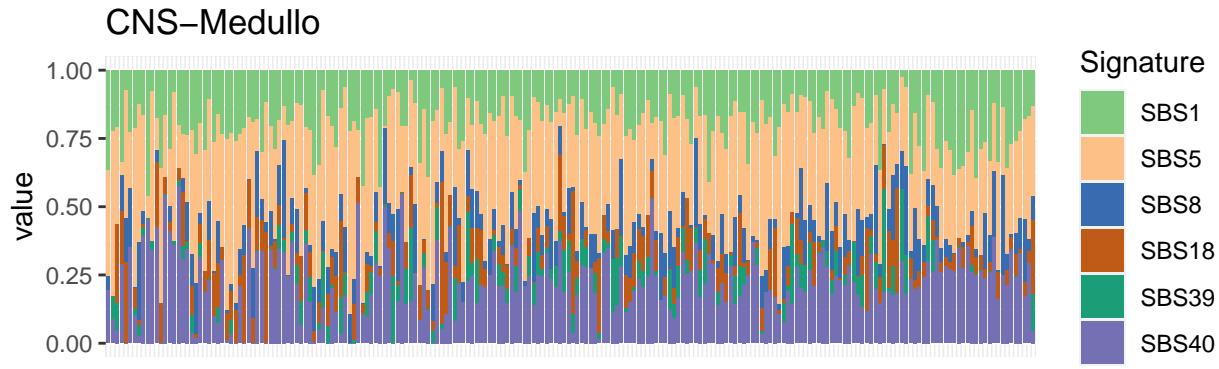
## Creating plot... it might take some time if the data are large. Number of samples: 272



```
## Creating plot... it might take some time if the data are large. Number of samples: 68
```

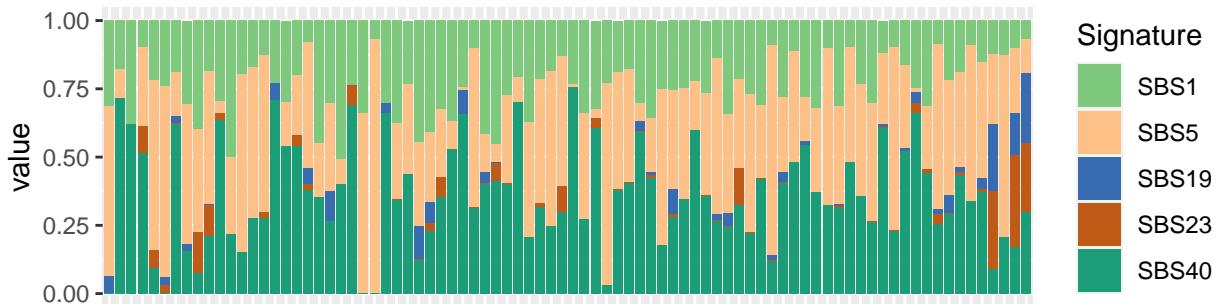


```
## Creating plot... it might take some time if the data are large. Number of samples: 212
```



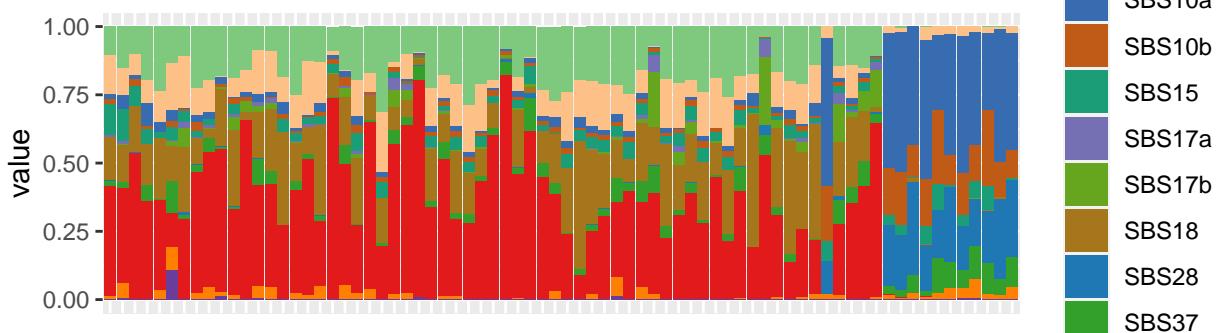
```
## Creating plot... it might take some time if the data are large. Number of samples: 84
```

### CNS–PiloAstro



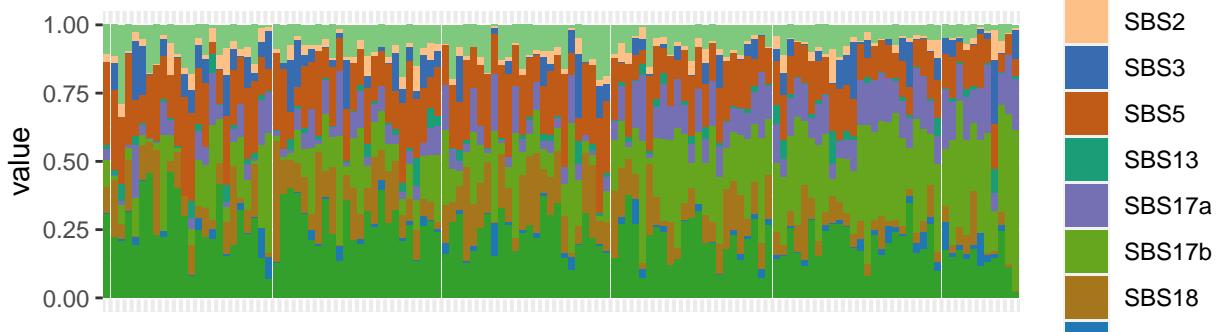
```
## Creating plot... it might take some time if the data are large. Number of samples: 74
```

### ColoRect–AdenoCA

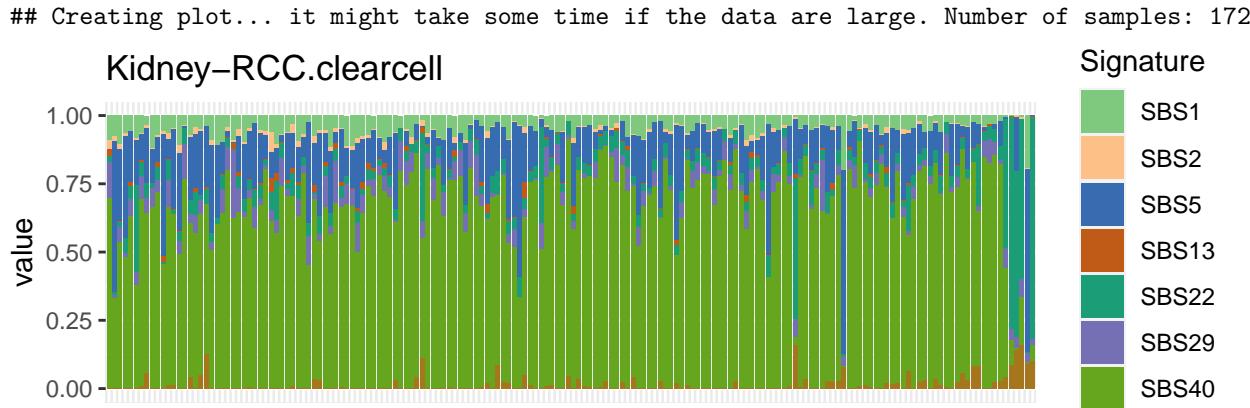
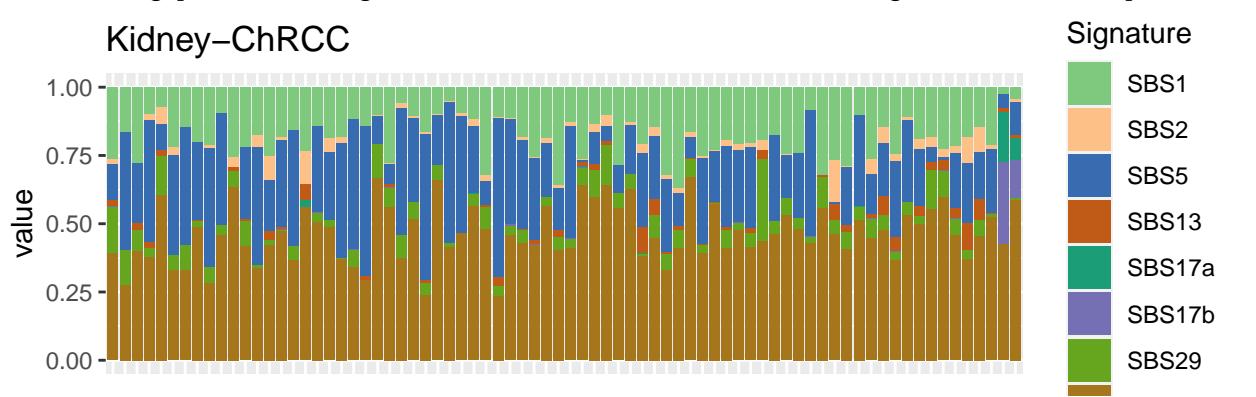
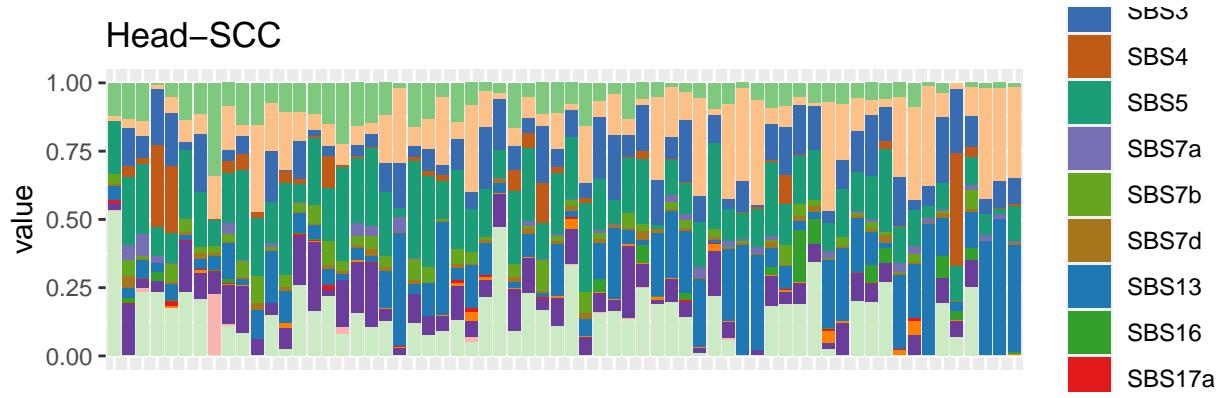


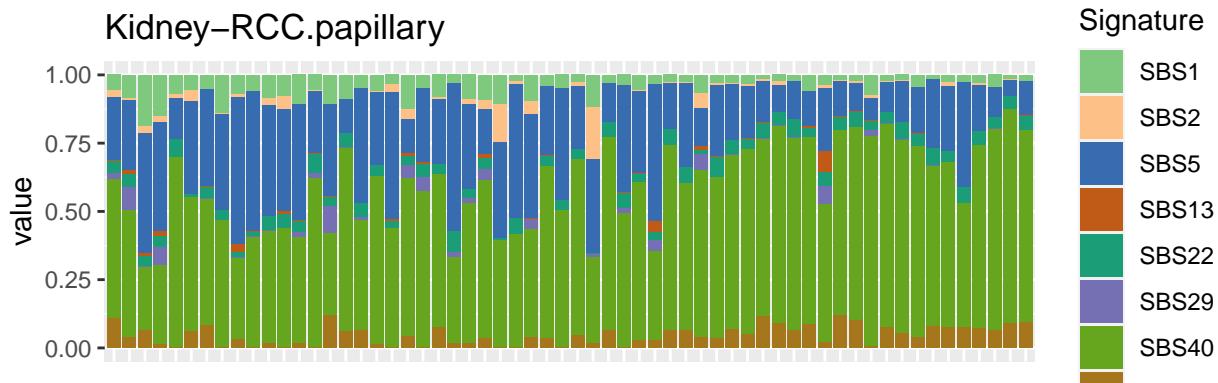
```
## Creating plot... it might take some time if the data are large. Number of samples: 130
```

### Eso–AdenoCA

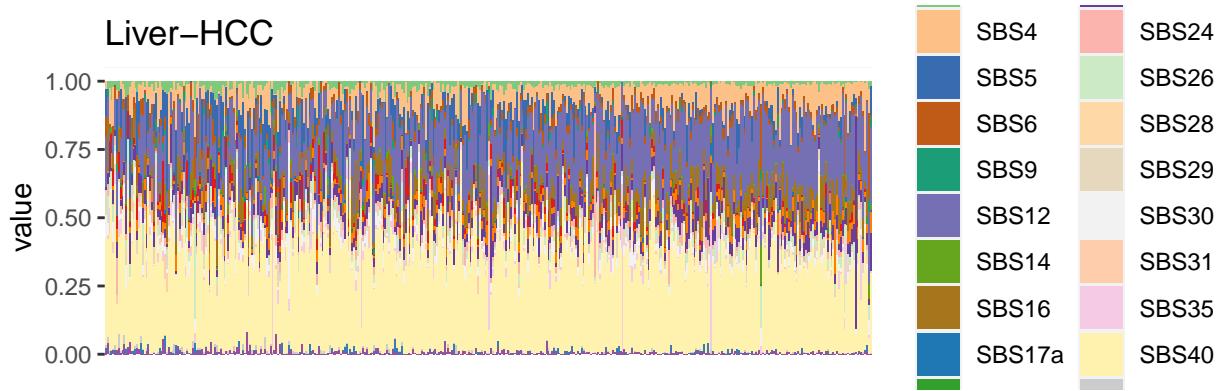


```
## Creating plot... it might take some time if the data are large. Number of samples: 64
```

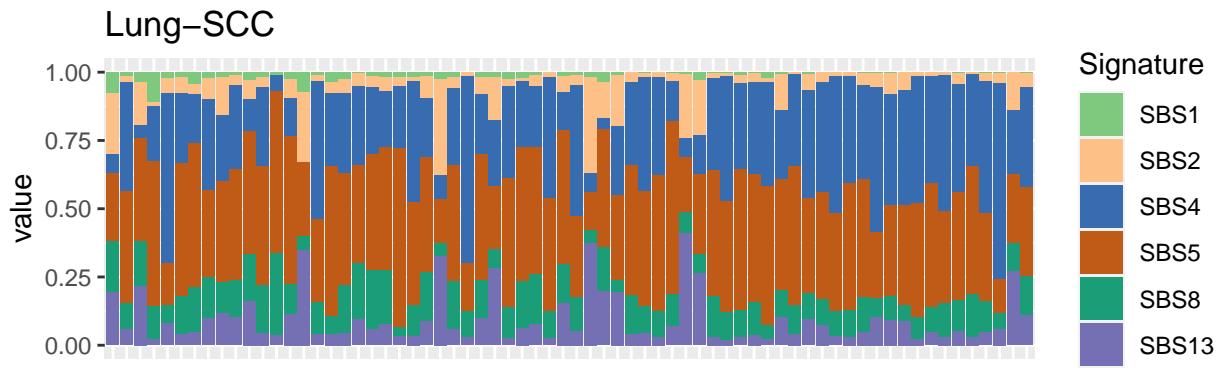




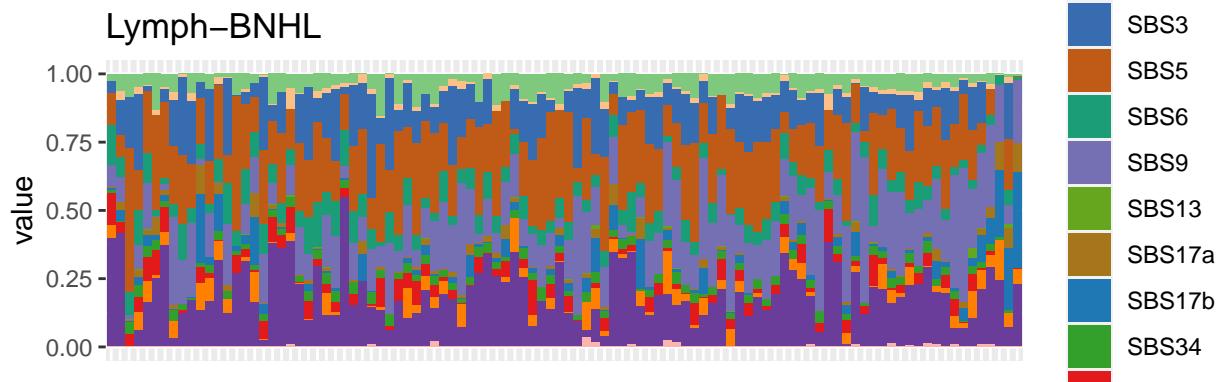
```
## Creating plot... it might take some time if the data are large. Number of samples: 414
```



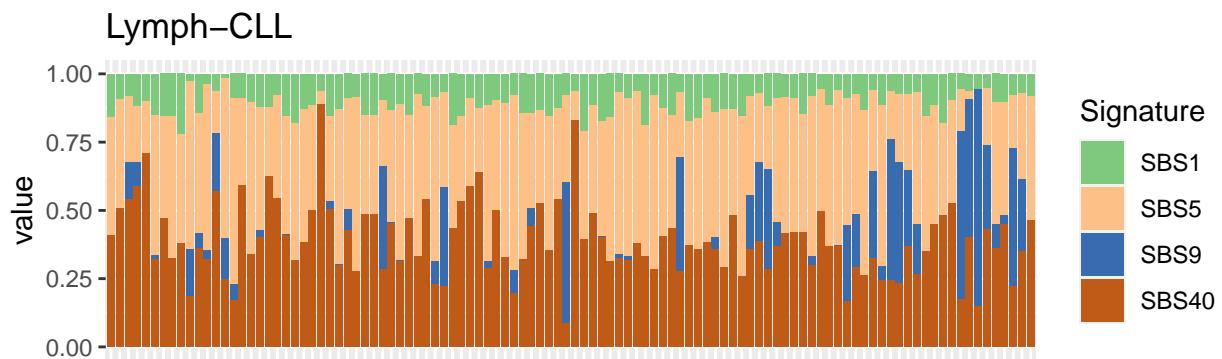
```
## Creating plot... it might take some time if the data are large. Number of samples: 68
```



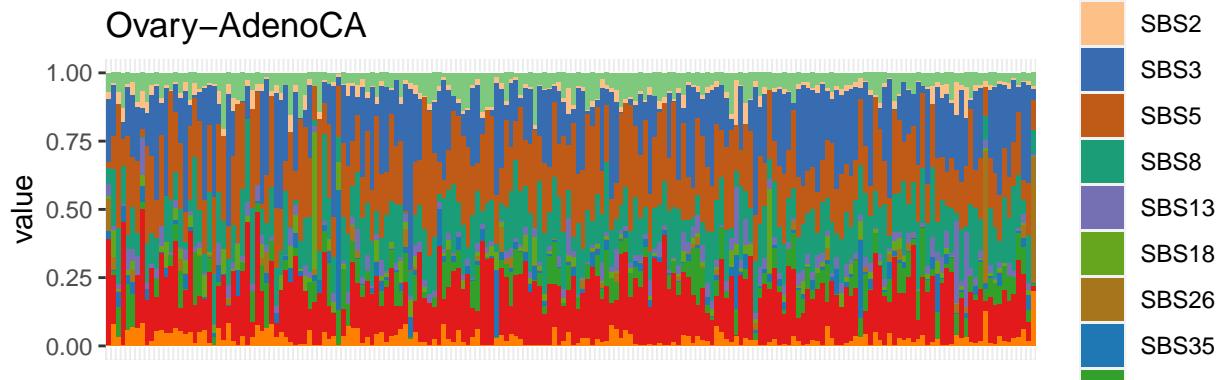
```
## Creating plot... it might take some time if the data are large. Number of samples: 102
```



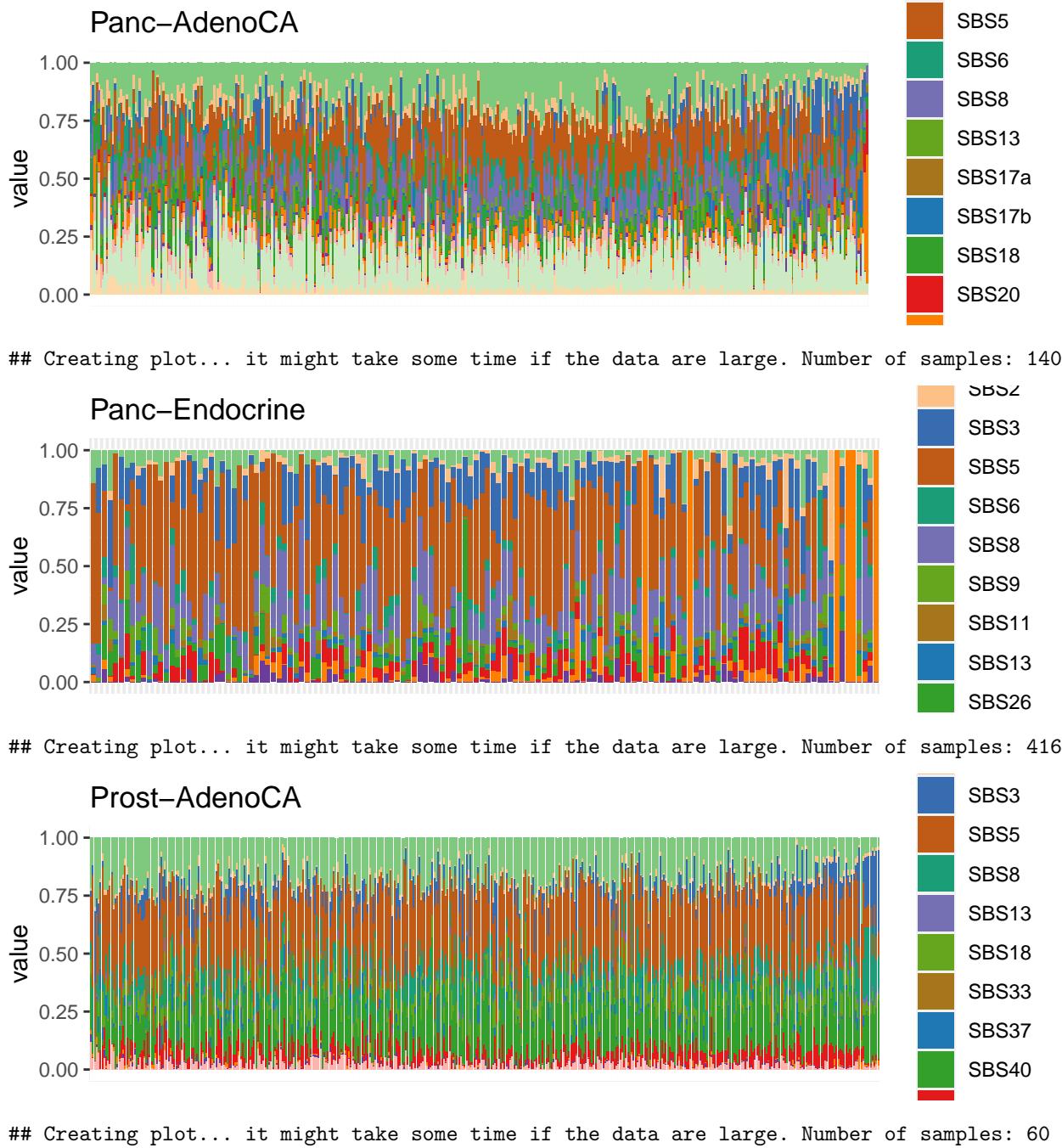
```
## Creating plot... it might take some time if the data are large. Number of samples: 106
```

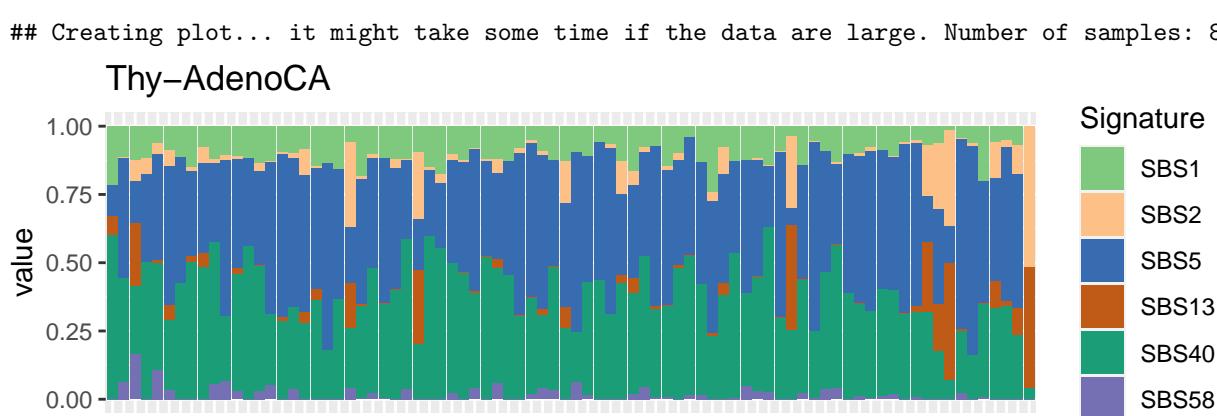
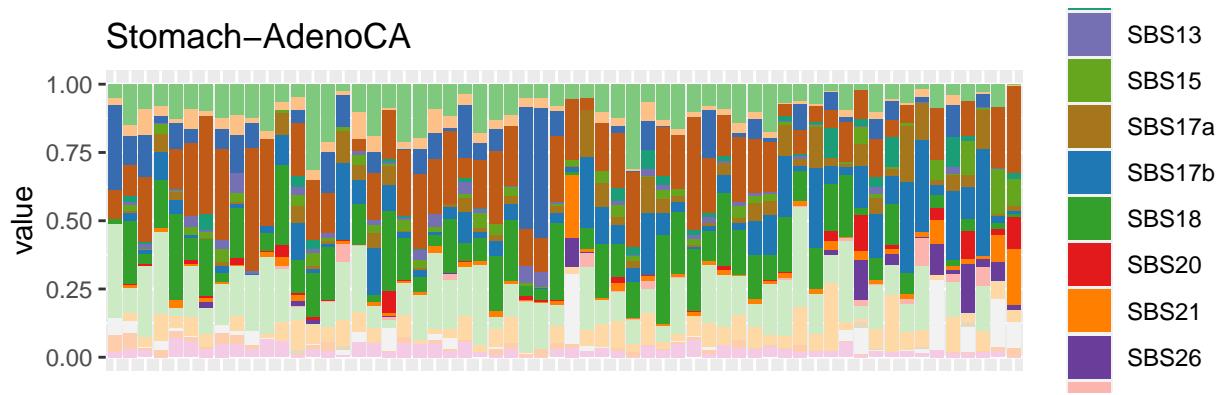
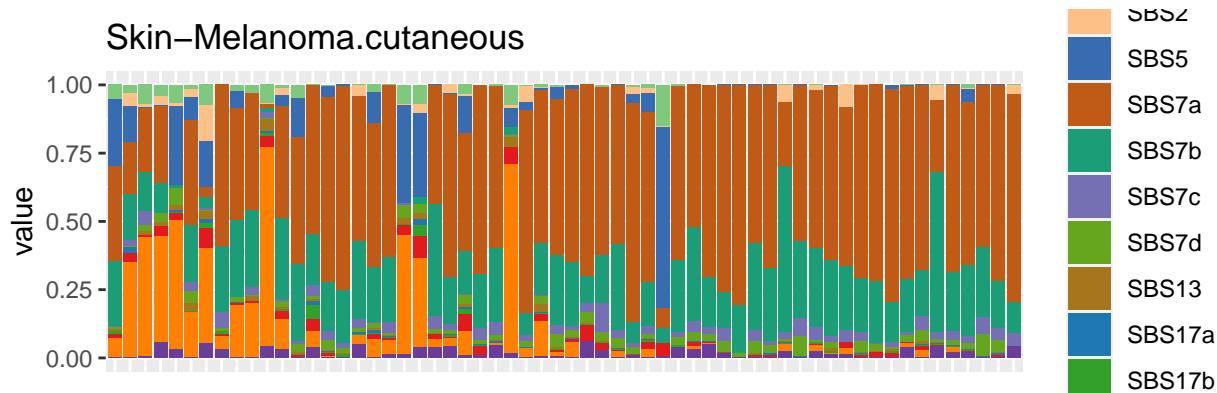


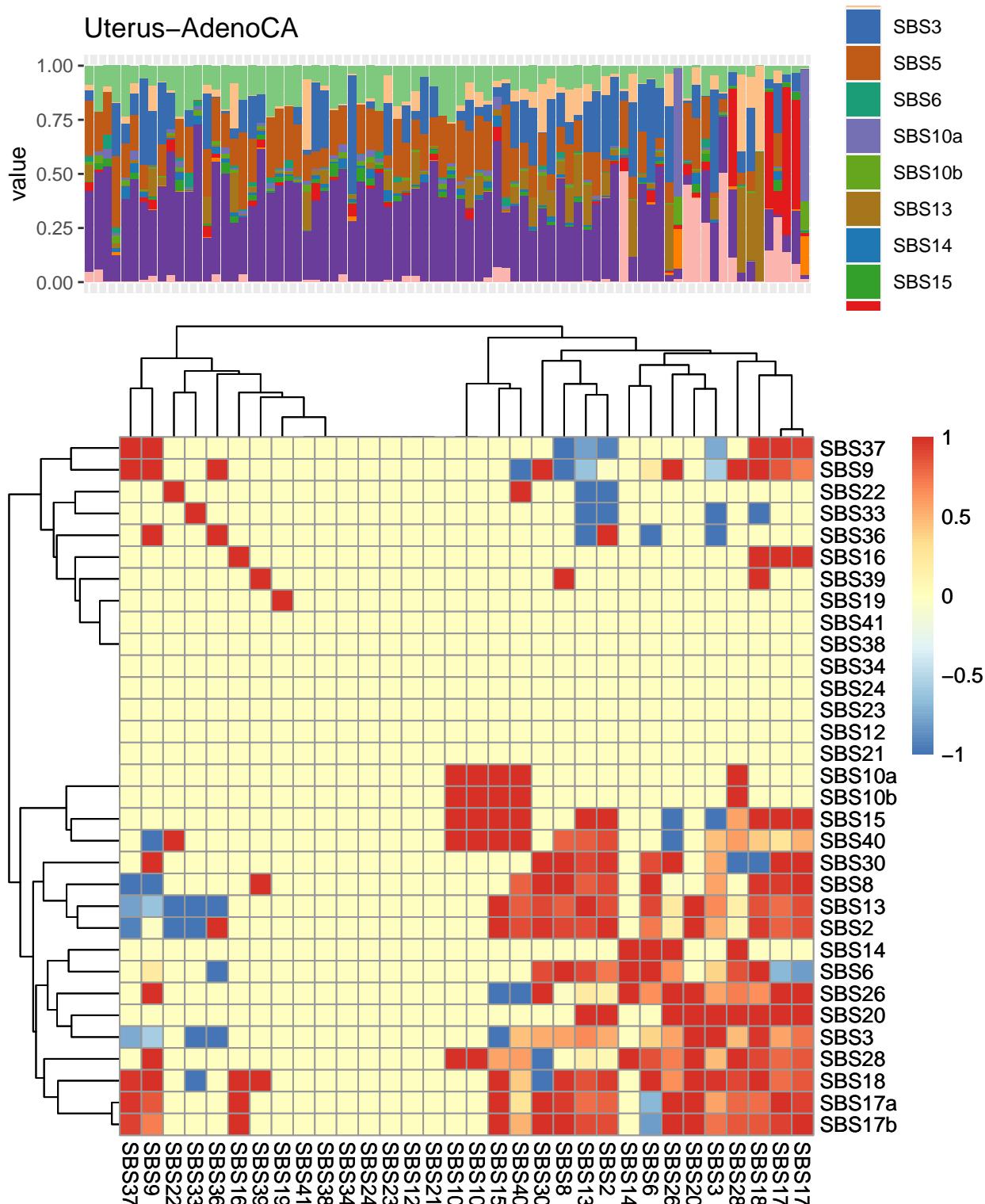
```
## Creating plot... it might take some time if the data are large. Number of samples: 194
```



```
## Creating plot... it might take some time if the data are large. Number of samples: 386
```







```
## null device
## 1
```

```

## null device
##           1

cors_sigs_v2 <- outer(1:nrow(aaa_dcast), 1:nrow(aaa_dcast), Vectorize(function(i,j){
  if( sum(!is.na(aaa_dcast[i,]) & !is.na(aaa_dcast[j,])) <=2){
    NA ## if there are 2 or fewer points in common. if there are 2 the correlation is possible but always
  }else{
    try(cor(x = unlist(aaa_dcast[i,]), y = unlist(aaa_dcast[j,]), use = "pairwise.complete.obs"))
  }
}))
cors_sigs_v2 <- apply(cors_sigs_v2, 2, as.numeric)

rownames(cors_sigs_v2) <- colnames(cors_sigs_v2) <- paste0('SBS', rownames(aaa_dcast))

# rownames(cors_sigs) <- colnames(cors) <- rownames(aaa_dcast)

hclust_correlation_betas_logR <- hclust(dist(cors_sigs))

num_common_samples_logR <- outer(1:nrow(aaa_dcast), 1:nrow(aaa_dcast), Vectorize(function(i,j){
  try(sum(!is.na(unlist(aaa_dcast[i,])+unlist(aaa_dcast[j,])))))})
rownames(num_common_samples_logR) <- colnames(num_common_samples_logR) <- paste0('SBS', rownames(aaa_dcast))

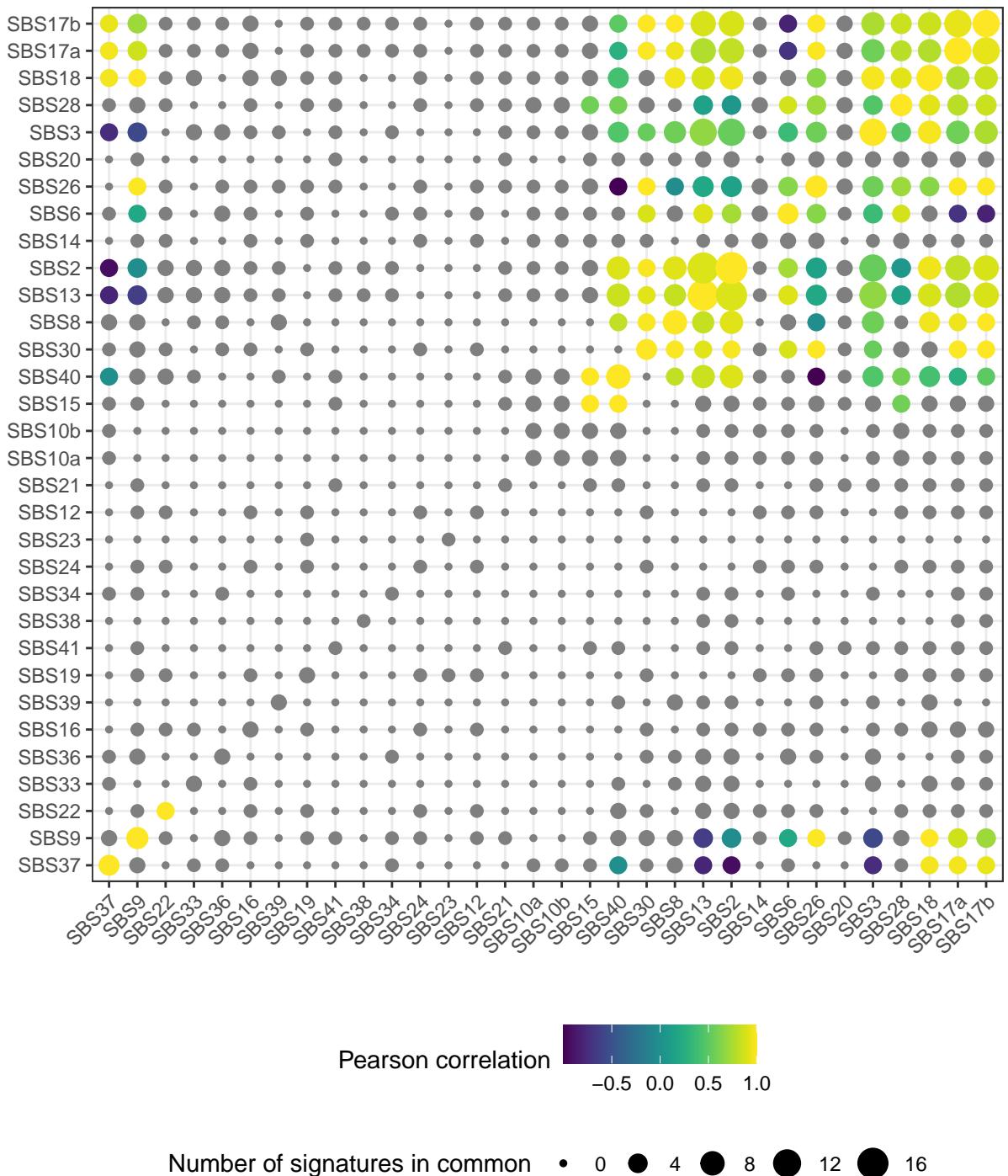
cors_melt_logR <- cbind.data.frame(cors=melt(cors_sigs_v2),
                                      num_common_samples=melt(num_common_samples_logR))

head(cors_melt_logR)

##   cors.Var1 cors.Var2 cors.value num_common_samples.Var1
## 1 SBS10a   SBS10a      NA        SBS10a
## 2 SBS10b   SBS10a      NA        SBS10b
## 3 SBS12    SBS10a      NA        SBS12
## 4 SBS13    SBS10a      NA        SBS13
## 5 SBS14    SBS10a      NA        SBS14
## 6 SBS15    SBS10a      NA        SBS15
##   num_common_samples.Var2 num_common_samples.value
## 1                      SBS10a                  2
## 2                      SBS10a                  2
## 3                      SBS10a                  0
## 4                      SBS10a                  1
## 5                      SBS10a                  1
## 6                      SBS10a                  2

ggplot(cors_melt_logR, aes(x=factor(num_common_samples.Var1,
                                         levels = hclust_correlation_betas_logR$labels[hclust_correlat
                                         y=factor(num_common_samples.Var2, levels=hclust_correlation_betas_logR$label
                                         col=cors.value, size=num_common_samples.value))+
                                         geom_point()+scale_color_viridis() + theme_bw() + theme(legend.position = "bottom", legend.box="vertical"
                                         theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+
                                         labs(x=' ',y=' ', size='Number of signatures in common', col='Pearson correlation')

```



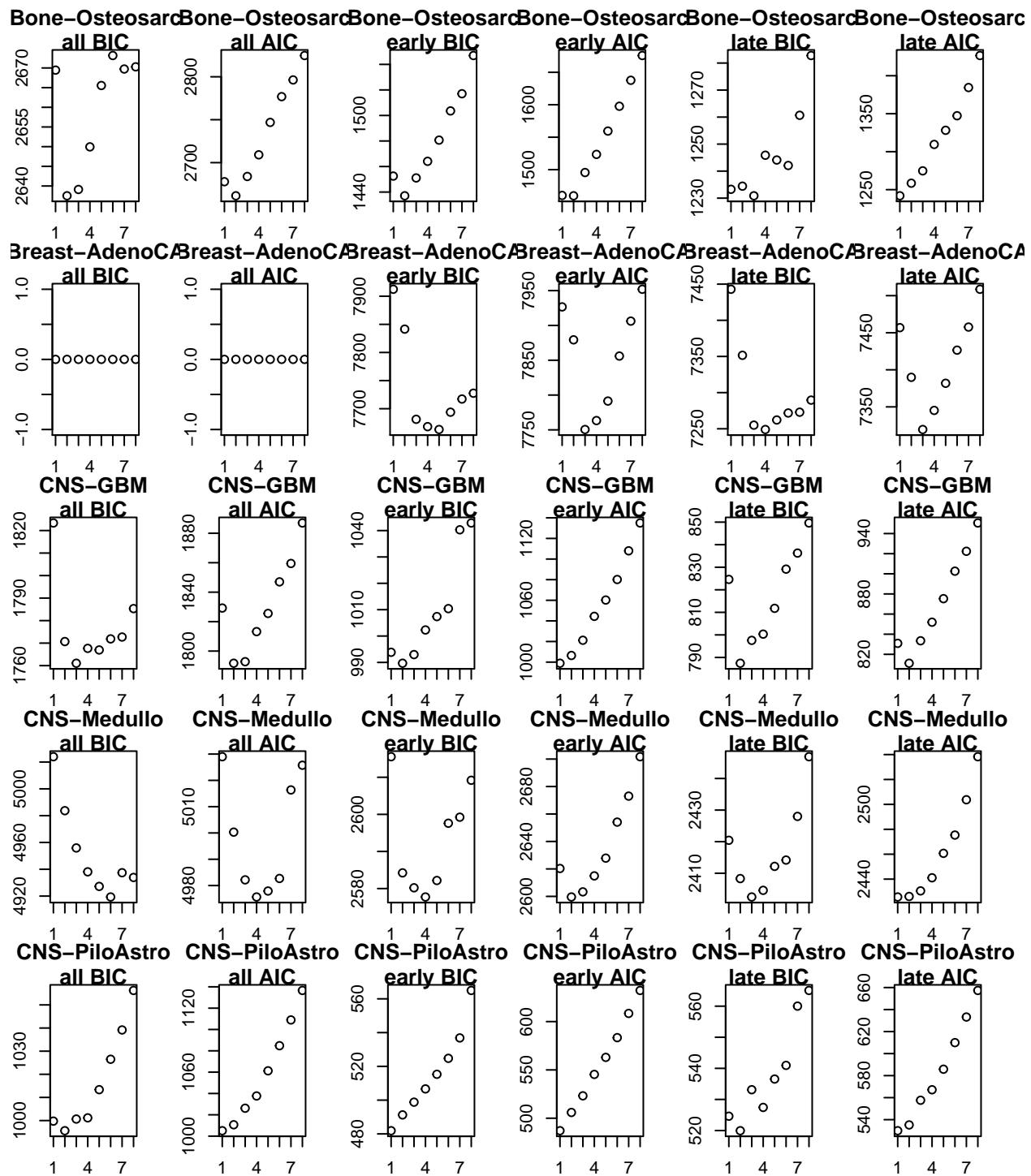
## Dirichlet-Multinomial Mixtures

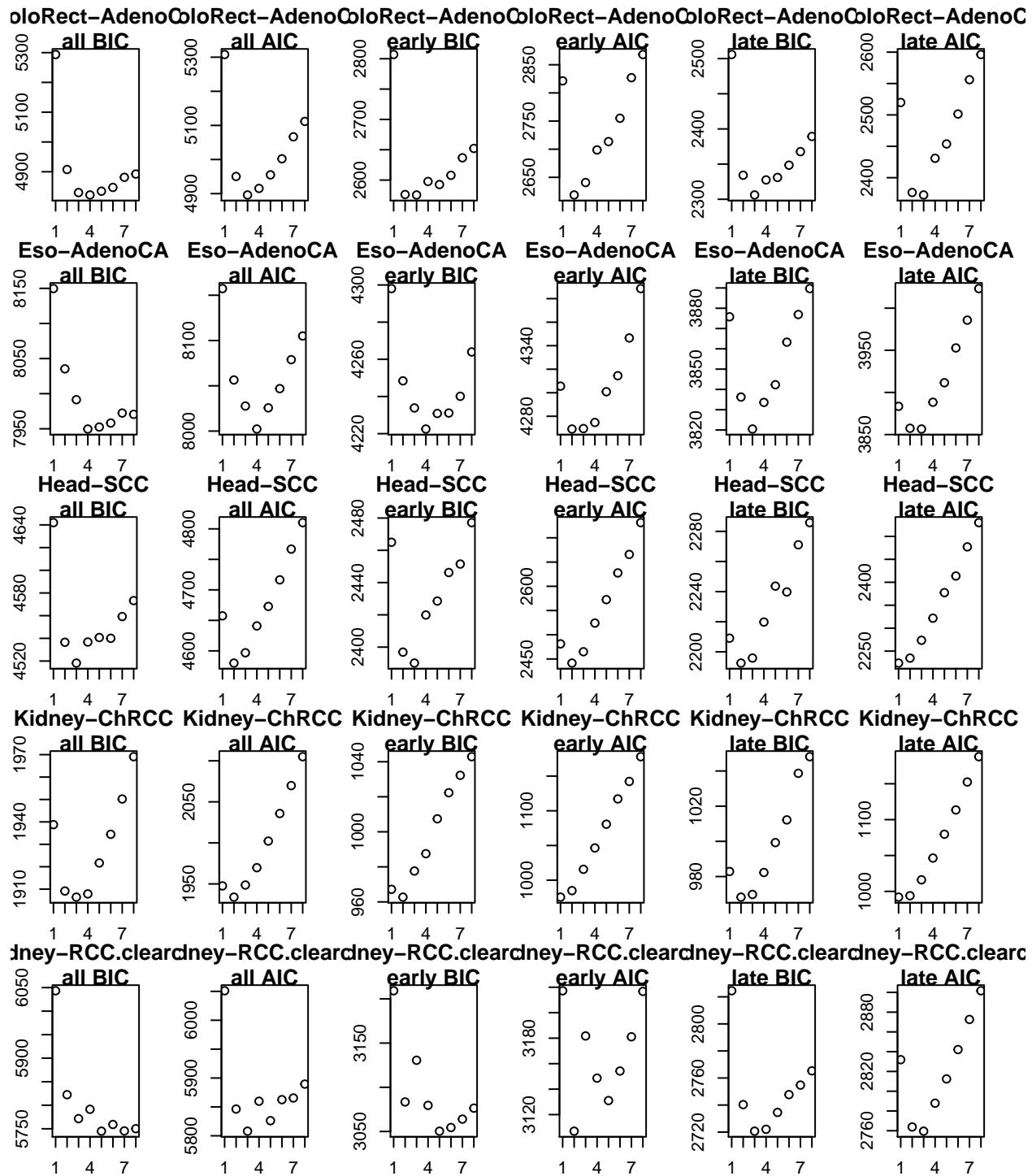
We run the software `MicrobeDMMv1.0` to determine whether we are facing DMM mixtures or not.

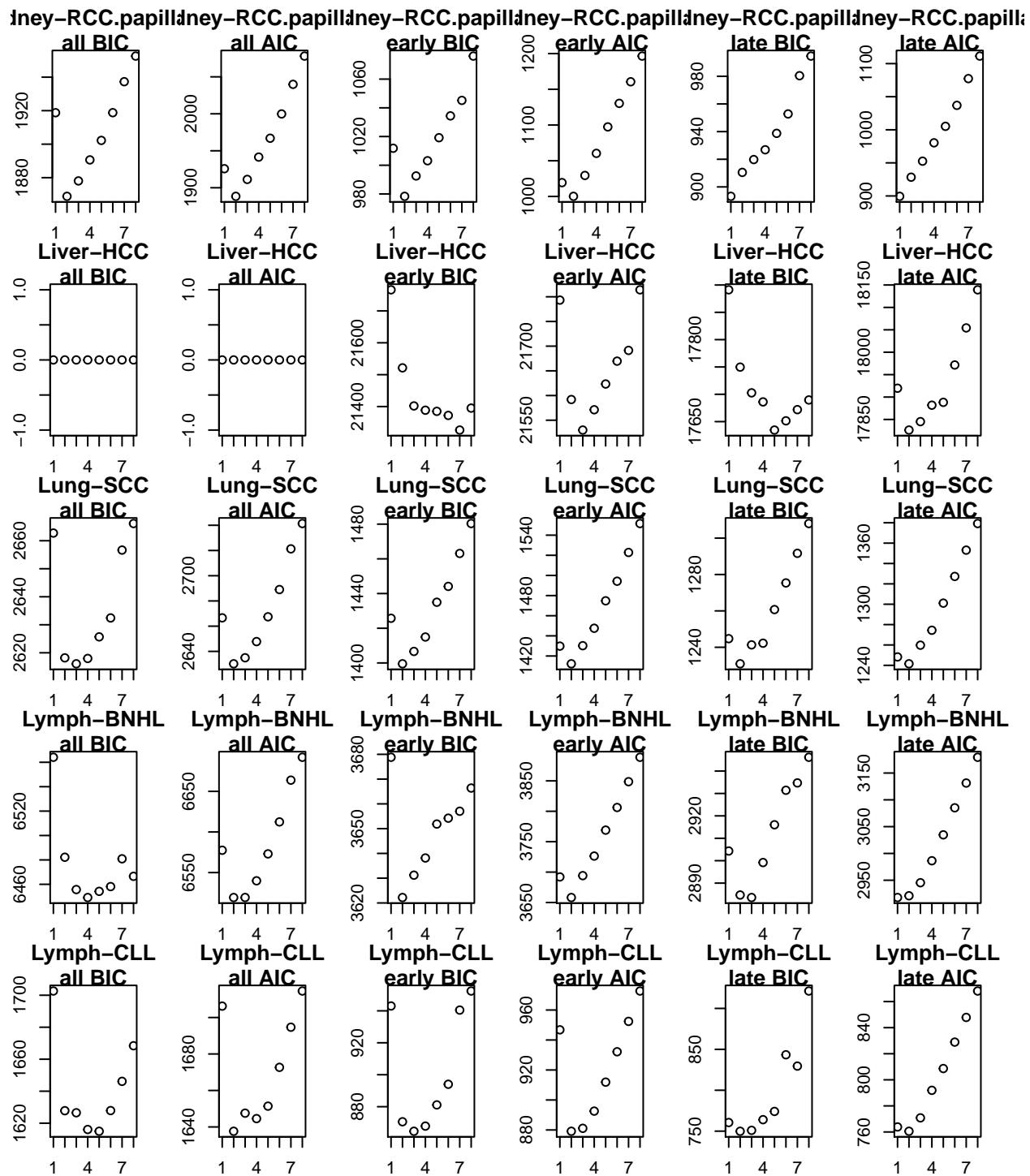
We save the files in two ways: all of the samples - early or not - together, and separately.

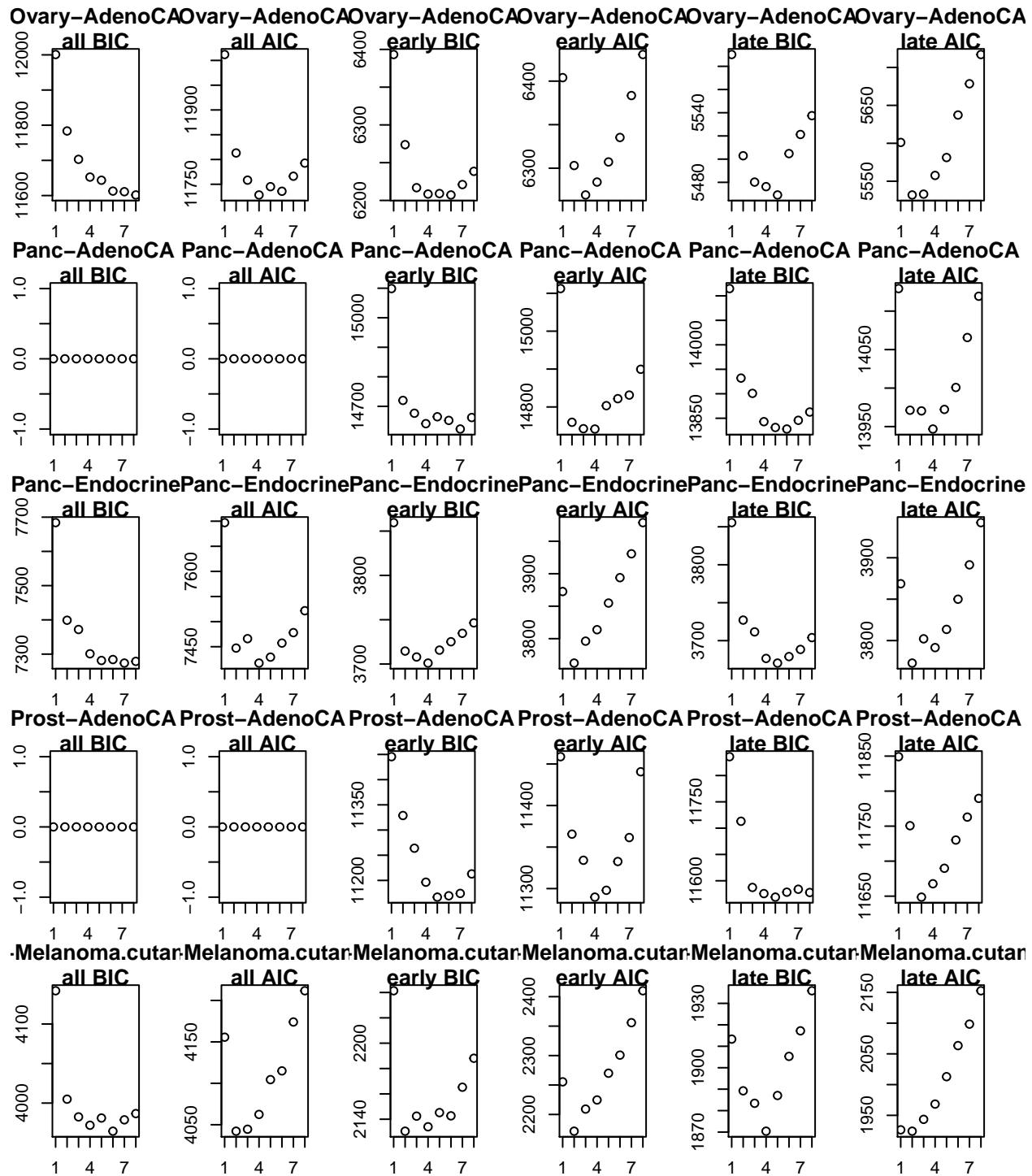
In some cases DMM says that there is an error with the input file - in this case the AIC or BIC is not plotted. If

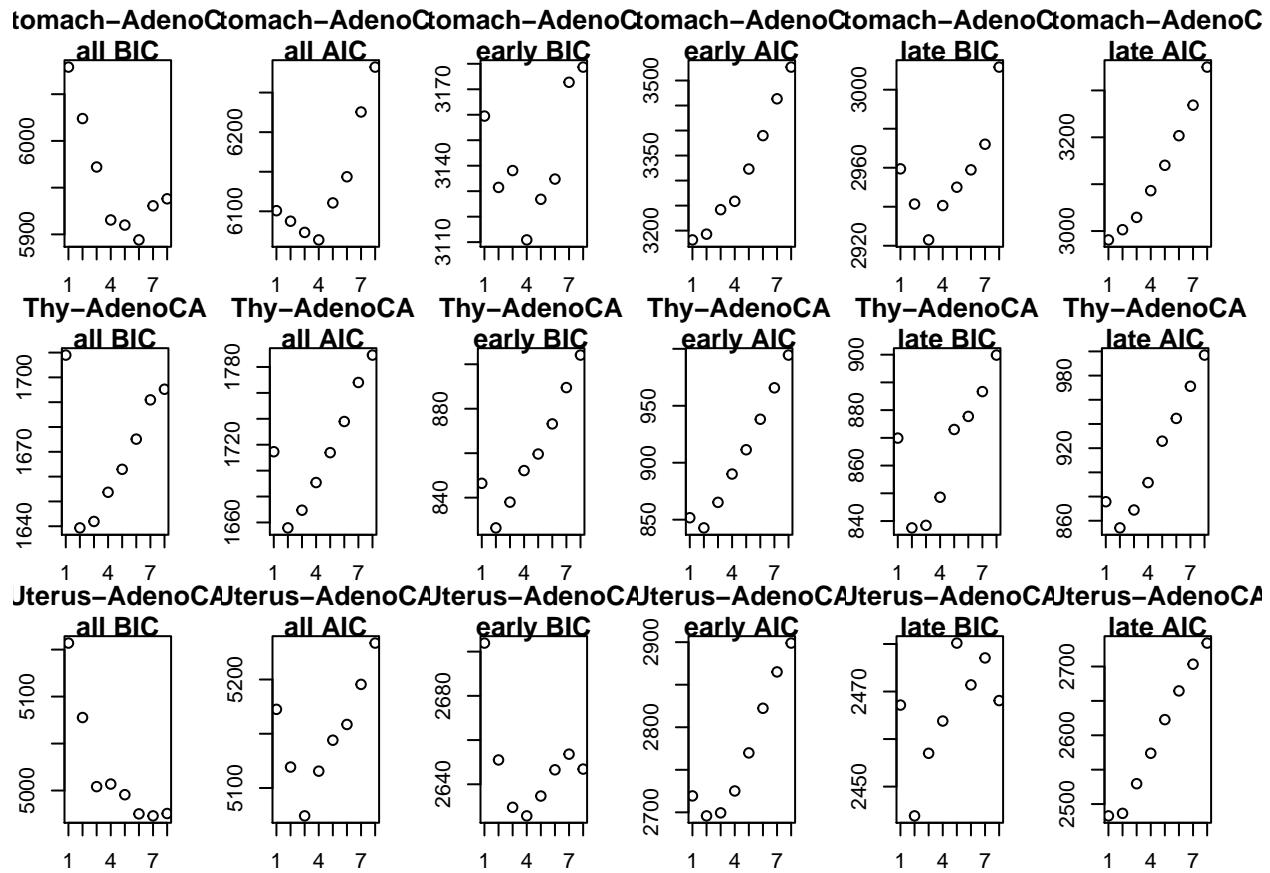
all of them are missing, all BIC and AIC are set to zero.







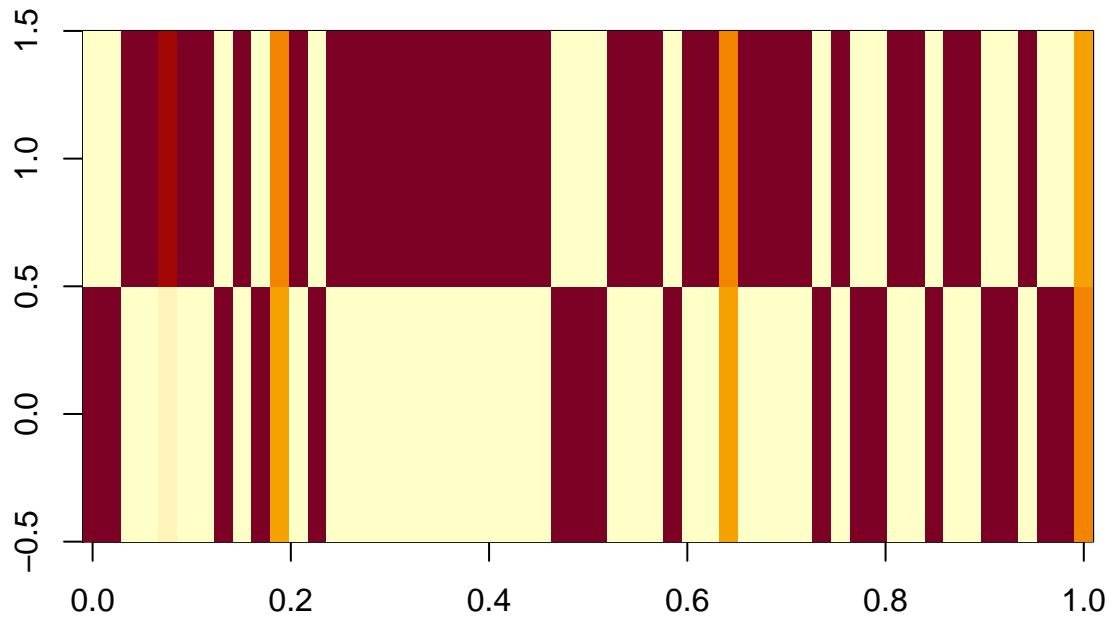




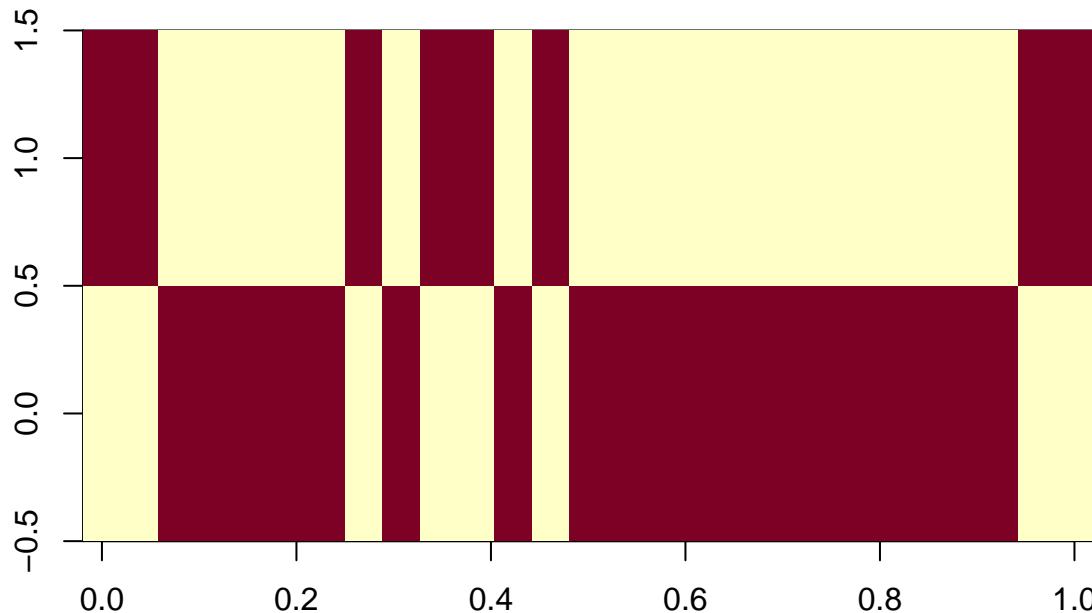
Now we have the optimal classes for each cancer type, both for early and late mutations separately, and for all of them together. We want to see if there is more than one group in general, and if the groups are maintained from early to late.

We look at the “all” mixtures, and look at the percentage of early/late paired observations that share group, and the percentage of early/late grouped samples that do.

```
image(as(z_DMM$`Bone-Osteosarc`$all[[2]][,-1], 'matrix'))
```



```
image(as(z_DMM$`Bone-Osteosarc`$early[[2]][,-1], 'matrix'))
```



```
give_matching_information_about_DMM <- function(ct, k){
  if(k!=2){stop('Only k==2 implemented')}
  .splitted_DMM <- split_matrix_in_half(as(z_DMM[[ct]]$all[[2]][,-1], 'matrix'))
  .whichmax1 <- apply(.splitted_DMM[[1]], 1, which.max)
  .whichmax2 <- apply(.splitted_DMM[[2]], 1, which.max)
  # percentage of early/late paired observations that share group
  .res1 <- max(c(mean(.whichmax1 == .whichmax2), mean(.whichmax1 != .whichmax2))) ## this is only for k==2
  #percentage of early/late grouped samples that share group
  .res2 <- mean(c(.whichmax1 == max(.whichmax1), .whichmax2 == max(.whichmax2)))
  return(list(pairedshared=.res1, groupshared=.res2))
}
```

```

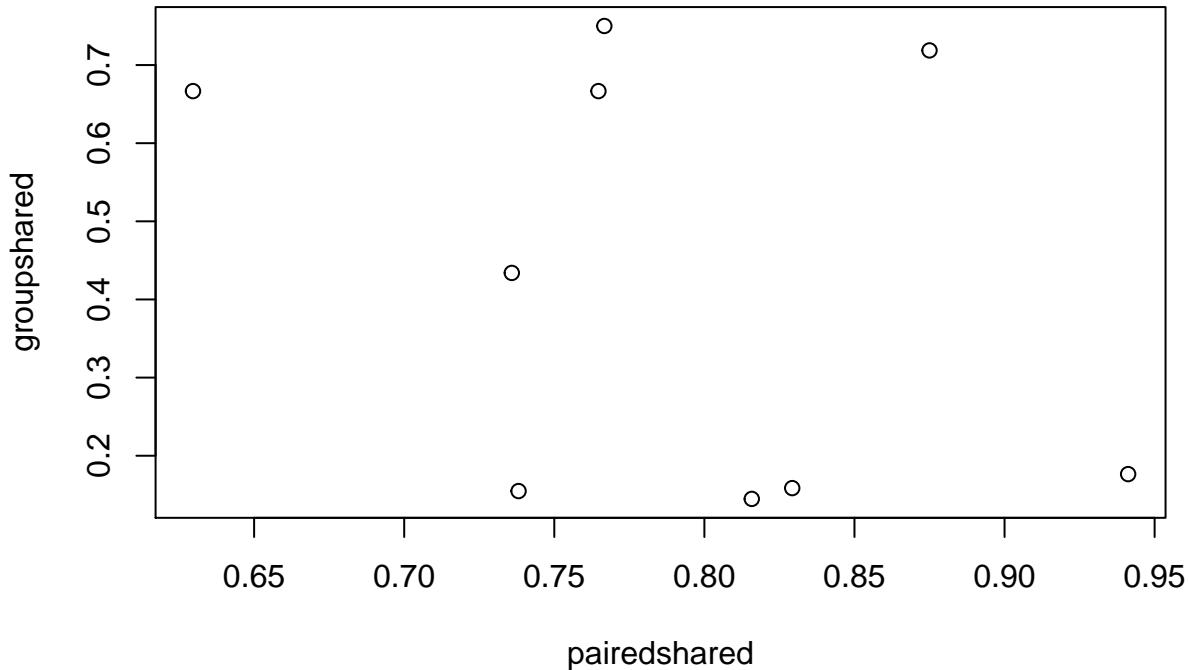
## for now, only the ones where there are two groups
matching_information_about_DMM_k2 <- sapply(c('Bone-Osteosarc', 'CNS-PiloAstro', 'Head-SCC', 'Kidney-ChRCC',
                                             'Lung-SCC', 'Lymph-BNHL', 'Lymph-CLL', 'Skin-Melanoma.cutaneous',
                                             'Thy-AdenoCA'), give_matching_information_about_DMM, k=2)

matching_information_about_DMM_k2

##          Bone-Osteosarc CNS-PiloAstro Head-SCC Kidney-ChRCC Lung-SCC
## pairedshared 0.6296296    0.7380952   0.875    0.8157895   0.9411765
## groupshared  0.6666667    0.1547619   0.71875   0.1447368   0.1764706
##          Lymph-BNHL Lymph-CLL Skin-Melanoma.cutaneous Thy-AdenoCA
## pairedshared 0.7647059   0.7358491   0.7666667   0.8292683
## groupshared  0.6666667   0.4339623   0.75        0.1585366

plot(t(matching_information_about_DMM_k2))

```



```

# ct = "Bone-Osteosarc"
# xxxx <- try(read.table(paste0("../data/roo_for_DMM/DMM_output/", ct, "_signatures_all.z"), sep = ','
# length(xxxx)
# table(apply(xxxx[grep('early', xxxx$V1), -1], 1, which.max),
#       apply(xxxx[grep('late', xxxx$V1), -1], 1, which.max))

\end{document}

```