

Cancer

Lieven Clement

statOmics, Ghent University (<https://statomics.github.io>)

Contents

1	Background	1
2	Data	2
2.1	Data exploration	4
3	Preprocessing	4
3.1	Log transform the data	4
3.2	Filtering	4
3.3	Normalize the data using median centering	5
3.4	Explore normalized data	5
3.5	Summarization to protein level	7
4	Data Analysis	8
4.1	Estimation	8
4.2	Inference	8
4.3	Plots	9
5	Session Info	227

This is part of the online course [Proteomics Data Analysis \(PDA\)](#)

1 Background

Eighteen Estrogen Receptor Positive Breast cancer tissues from from patients treated with tamoxifen upon recurrence have been assessed in a proteomics study. Nine patients had a good outcome (OR) and the other nine had a poor outcome (PD). The proteomes have been assessed using an LTQ-Orbitrap and the thermo output .RAW files were searched with MaxQuant (version 1.4.1.2) against the human proteome database (FASTA version 2012-09, human canonical proteome).

2 Data

We first import the data from peptide.txt file. This is the file containing your peptide-level intensities. For a MaxQuant search [6], this peptide.txt file can be found by default in the “path_to_raw_files/combined/txt/” folder from the MaxQuant output, with “path_to_raw_files” the folder where the raw files were saved.

We generate the object peptideFile with the path to the peptide.txt file. Using the `grepEcols` function, we find the columns that contain the expression data of the peptide in the peptide.txt file.

```
library(tidyverse)
library(limma)
library(QFeatures)
library(msqrob2)
library(plotly)

peptidesFile <- "https://raw.githubusercontent.com/statOmics/PDA22GTPB/data/quantification/cancer/peptide.txt"

ecols <- grep(
  "Intensity\\.\\.",
  names(read.delim(peptidesFile))
)
```

Next, we read the data and store it in QFeatures object

```
pe <- readQFeatures(
  table = peptidesFile,
  fnames = 1,
  ecol = ecols,
  name = "peptideRaw", sep="\t")
```

The QFeatures object `pe` currently contains a single assay, named `peptideRaw`.

We extract the column names from the `peptideRaw` assay and see that this contains information about the prognosis.

```
colnames(pe[["peptideRaw"]])
```

```
## [1] "Intensity.OR.01" "Intensity.OR.04" "Intensity.OR.07" "Intensity.OR.09"
## [5] "Intensity.OR.10" "Intensity.OR.13" "Intensity.OR.20" "Intensity.OR.23"
## [9] "Intensity.OR.25" "Intensity.PD.02" "Intensity.PD.03" "Intensity.PD.04"
## [13] "Intensity.PD.06" "Intensity.PD.07" "Intensity.PD.08" "Intensity.PD.09"
## [17] "Intensity.PD.10" "Intensity.PD.11"
```

We rename the colnames by dropping the “Intensity.” from the name.

```
(newNames <- sub(
  pattern = "Intensity\\.\\.",
  replacement = "",
  colnames(pe[["peptideRaw"]]))
)
```

```
## [1] "OR.01" "OR.04" "OR.07" "OR.09" "OR.10" "OR.13" "OR.20" "OR.23" "OR.25"
## [10] "PD.02" "PD.03" "PD.04" "PD.06" "PD.07" "PD.08" "PD.09" "PD.10" "PD.11"
```

```
pe <- renameColname(pe,
                    i = "peptideRaw",
                    newNames)
pe <- renamePrimary(pe, newNames)
colnames(pe[["peptideRaw"]])
```

```
## [1] "OR.01" "OR.04" "OR.07" "OR.09" "OR.10" "OR.13" "OR.20" "OR.23" "OR.25"
## [10] "PD.02" "PD.03" "PD.04" "PD.06" "PD.07" "PD.08" "PD.09" "PD.10" "PD.11"
```

In the following code chunk, we add the prognosis of the patients that we can read in the raw file name to the colData.

```
colData(pe)$prognosis <-
  colnames(pe[["peptideRaw"]]) %>%
  substr(start = 1, stop = 2) %>%
  as.factor
colData(pe)$prognosis
```

```
## [1] OR OR OR OR OR OR OR OR OR OR PD PD PD PD PD PD PD PD PD PD
## Levels: OR PD
```

We calculate how many non zero intensities we have per peptide and this will be useful for filtering.

```
rowData(pe[["peptideRaw"]])$nNonZero <- rowSums(assay(pe[["peptideRaw"]]) > 0)
```

Peptides with zero intensities are missing peptides and should be represent with a NA value rather than 0.

```
pe <- zeroIsNA(pe, "peptideRaw") # convert 0 to NA
```

Look at the column names of the data to know the variables that you can use for filtering.

```
pe[["peptideRaw"]] %>% rowData %>% names
```

```
## [1] "Sequence"          "Proteins"          "Leading.razor.protein"
## [4] "Gene.names"        "Protein.names"     "Unique..Groups."
## [7] "Unique..Proteins." "Charges"           "PEP"
## [10] "Score"             "Slice.Average"     "Slice.Std..Dev."
## [13] "Slice.1"           "Unique.Slice.Average" "Unique.Slice.Std..Dev."
## [16] "Unique.Slice.1"     "Experiment.OR.01"   "Experiment.OR.04"
## [19] "Experiment.OR.07"   "Experiment.OR.09"   "Experiment.OR.10"
## [22] "Experiment.OR.13"   "Experiment.OR.20"   "Experiment.OR.23"
## [25] "Experiment.OR.25"   "Experiment.PD.02"   "Experiment.PD.03"
## [28] "Experiment.PD.04"   "Experiment.PD.06"   "Experiment.PD.07"
## [31] "Experiment.PD.08"   "Experiment.PD.09"   "Experiment.PD.10"
## [34] "Experiment.PD.11"   "Intensity"          "Reverse"
## [37] "Contaminant"        "id"                 "Protein.group.IDs"
## [40] "Mod..peptide.IDs"   "Evidence.IDs"       "MS.MS.IDs"
## [43] "Best.MS.MS"         "Oxidation..M..site.IDs" "nNonZero"
```

So we will filter on the “Reverse”, “Contaminant” and “nNonZero” column.

2.1 Data exploration

47% of all peptide intensities are missing and for some peptides we do not even measure a signal in any sample.

3 Preprocessing

This section performs preprocessing for the peptide data. This includes

- log transformation,
- filtering and
- summarisation of the data.

3.1 Log transform the data

```
pe <- logTransform(pe, base = 2, i = "peptideRaw", name = "peptideLog")
```

3.2 Filtering

1. Handling overlapping protein groups

In our approach a peptide can map to multiple proteins, as long as there is none of these proteins present in a smaller subgroup.

```
pe <- filterFeatures(pe, ~ Proteins %in% smallestUniqueGroups(rowData(pe[["peptideLog"]])$Proteins))
```

2. Remove reverse sequences (decoys) and contaminants

We now remove the contaminants and peptides that map to decoy sequences.

```
pe <- filterFeatures(pe, ~Reverse != "+")  
pe <- filterFeatures(pe, ~Contaminant != "+")
```

3. Drop peptides that were only identified in one sample

We keep peptides that were observed at least twice.

```
pe <- filterFeatures(pe, ~ nNonZero >= 2)  
nrow(pe[["peptideLog"]])
```

```
## [1] 26696
```

We keep 26696 peptides upon filtering.

3.3 Normalize the data using median centering

We normalize the data by subtracting the sample median from every intensity for peptide p in a sample i :

$$y_{ip}^{\text{norm}} = y_{ip} - \hat{\mu}_i$$

with $\hat{\mu}_i$ the median intensity over all observed peptides in sample i .

```
pe <- normalize(pe,  
  i = "peptideLog",  
  name = "peptideNorm",  
  method = "center.median")
```

3.4 Explore normalized data

Upon the normalisation the density curves are nicely registered

```
pe[["peptideNorm"]] %>%  
  assay %>%  
  as.data.frame() %>%  
  gather(sample, intensity) %>%  
  mutate(prognosis = colData(pe)[sample, "prognosis"]) %>%  
  ggplot(aes(x = intensity, group = sample, color = prognosis)) +  
    geom_density()
```

```
## Warning: Removed 188395 rows containing non-finite values (stat_density).
```



We can visualize our data using a Multi Dimensional Scaling plot, eg. as provided by the `limma` package.

```
pe[["peptideNorm"]] %>%  
  assay %>%  
  limma::plotMDS(col = as.numeric(colData(pe)$prognosis))
```



The first axis in the plot is showing the leading log fold changes (differences on the log scale) between the samples. We observe one outlying sample. In the second dimension we observe a separation according to prognosis.

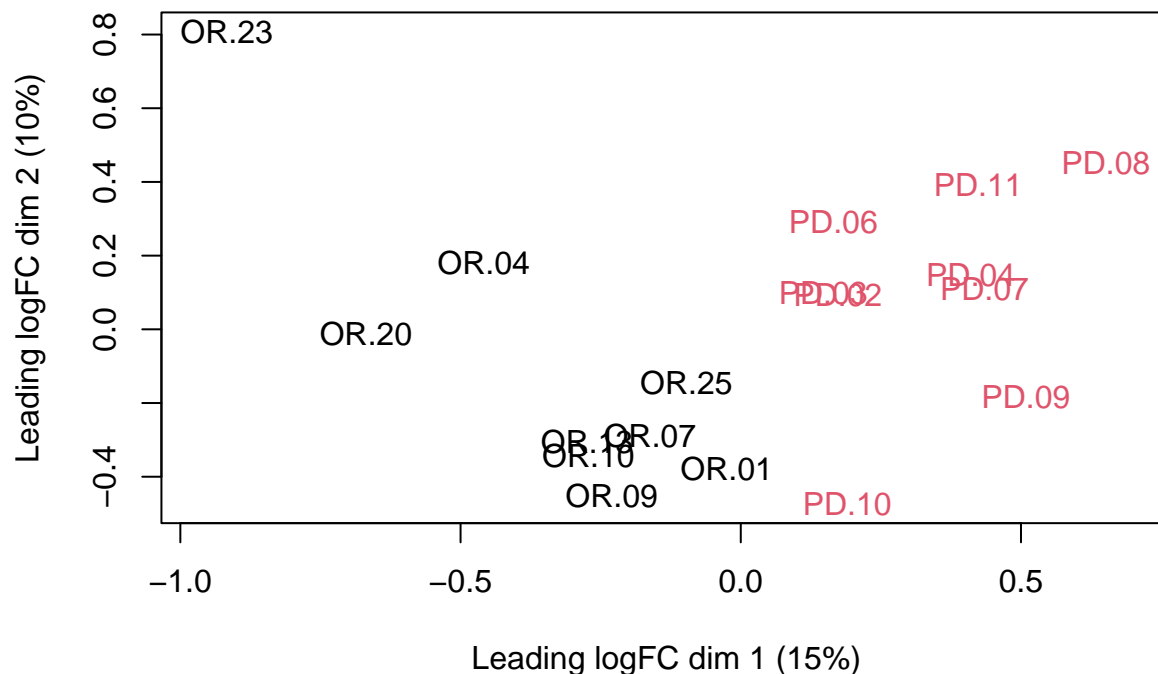
3.5 Summarization to protein level

- By default robust summarization is used: `fun = MsCoreUtils::robustSummary()`

```
pe <- aggregateFeatures(pe,
  i = "peptideNorm",
  fcol = "Proteins",
  na.rm = TRUE,
  name = "protein")
```

```
## Your quantitative and row data contain missing values. Please read the
## relevant section(s) in the aggregateFeatures manual page regarding the
## effects of missing values on data aggregation.
```

```
plotMDS(assay(pe[["protein"]]), col = as.numeric(colData(pe)$prognosis))
```



Note that the samples upon robust summarisation show a separation according to the prognosis.

4 Data Analysis

4.1 Estimation

We model the protein level expression values using `msqrob`. By default `msqrob2` estimates the model parameters using robust regression.

We will model the data with a different group mean. The group is incoded in the variable `prognosis` of the `colData`. We can specify this model by using a formula with the factor condition as its predictor: `formula = ~prognosis`.

Note, that a formula always starts with a symbol `~`.

```
pe <- msqrob(object = pe, i = "protein", formula = ~prognosis)
```

4.2 Inference

First, we extract the parameter names of the model by looking at the first model. The models are stored in the row data of the assay under the default name `msqrobModels`.

```
getCoef(rowData(pe[["protein"]])$msqrobModels[[1]])
```



```
## (Intercept) prognosisPD
## -1.1185468 0.4007461
```

We can also explore the design of the model that we specified using the the package `ExploreModelMatrix`

```
library(ExploreModelMatrix)
VisualizeDesign(colData(pe), ~prognosis)$plotlist
```

```
## [[1]]
```



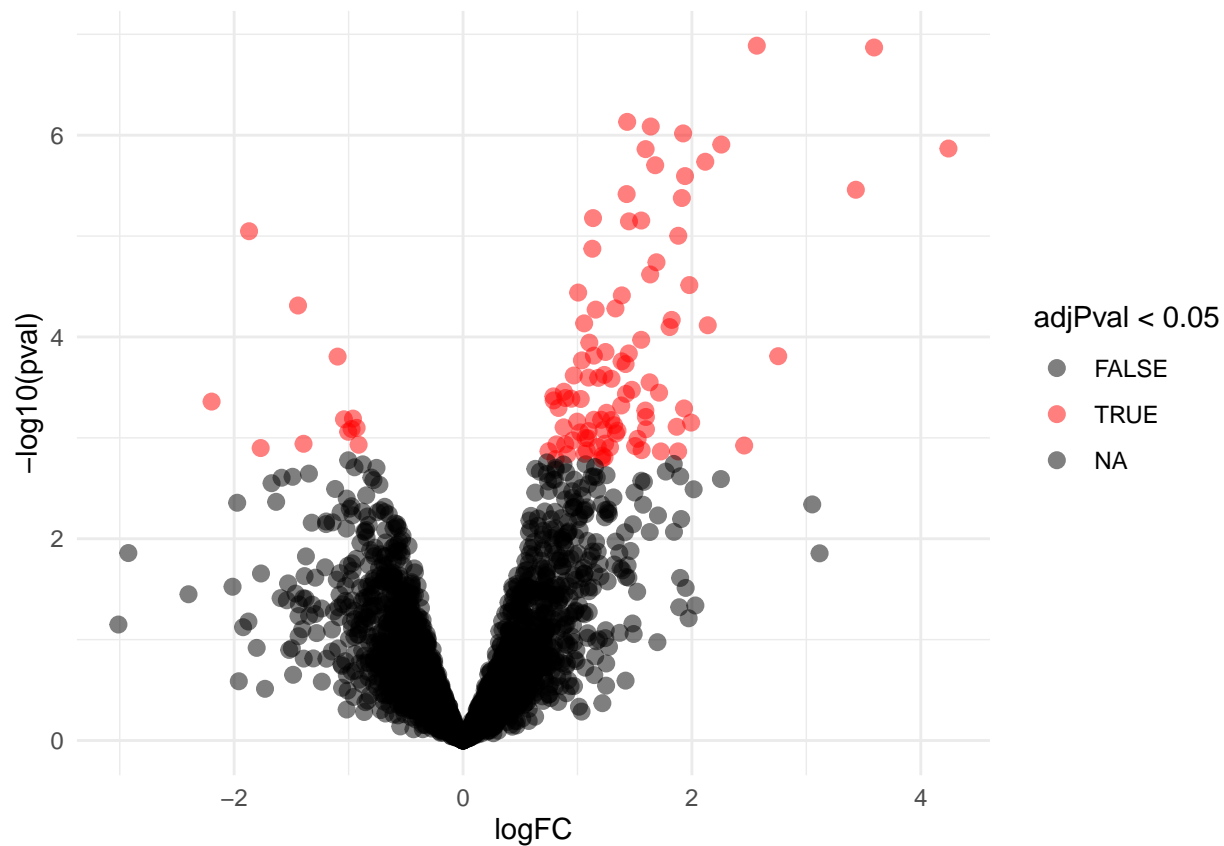
Spike-in condition A is the reference class. So the mean log2 expression for samples from good prognosis (OR) is '(Intercept)'. The mean log2 expression for samples from poor prognosis (PD) is '(Intercept)+prognosisPD'. Hence, the average log2 fold change between prognosis PD and prognosis OR is modelled using the parameter 'conditionPD'. Thus, we assess the contrast 'conditionPD = 0' with our statistical test.

```
L <- makeContrast("prognosisPD=0", parameterNames = c("prognosisPD"))
pe <- hypothesisTest(object = pe, i = "protein", contrast = L)
```

4.3 Plots

4.3.1 Volcano-plot

```
volcano <- ggplot(rowData(pe[["protein"]])$prognosisPD,
  aes(x = logFC, y = -log10(pval), color = adjPval < 0.05)) +
  geom_point(cex = 2.5) +
  scale_color_manual(values = alpha(c("black", "red"), 0.5)) + theme_minimal()
volcano
```



Note, that 108 proteins are found to be differentially abundant.

4.3.2 Heatmap

Note, that we also order the sigNames according to statistical significance.

```
sigNames <- rowData(pe[["protein"]])$prognosisPD %>%
  rownames_to_column("protein") %>%
  arrange(pval) %>%
  filter(adjPval<0.05) %>%
  pull(protein)
heatmap(assay(pe[["protein"]])[sigNames, ])
```



4.3.3 Detail plots

We make detail plots for the top 10 proteins to restrict the number of detail plots.

```
for (protName in sigNames)
#for (protName in orderProt[1:10])
{
  pePlot <- pe[protName, , c("peptideNorm","protein")]
  pePlotDf <- data.frame(longFormat(pePlot))
  pePlotDf$assay <- factor(pePlotDf$assay,
                          levels = c("peptideNorm", "protein"))
  pePlotDf$prognosis <- as.factor(colData(pePlot)[pePlotDf$colname, "prognosis"])

  # plotting
  p1 <- ggplot(data = pePlotDf,
               aes(x = colname, y = value, group = rowname)) +
    geom_line() +
    geom_point() +
    theme(axis.text.x = element_text(angle = 70, hjust = 1, vjust = 0.5)) +
    facet_grid(~assay) +
    ggtitle(protName)
  print(p1)

  # plotting 2
  p2 <- ggplot(pePlotDf, aes(x = colname, y = value, fill = prognosis)) +
```

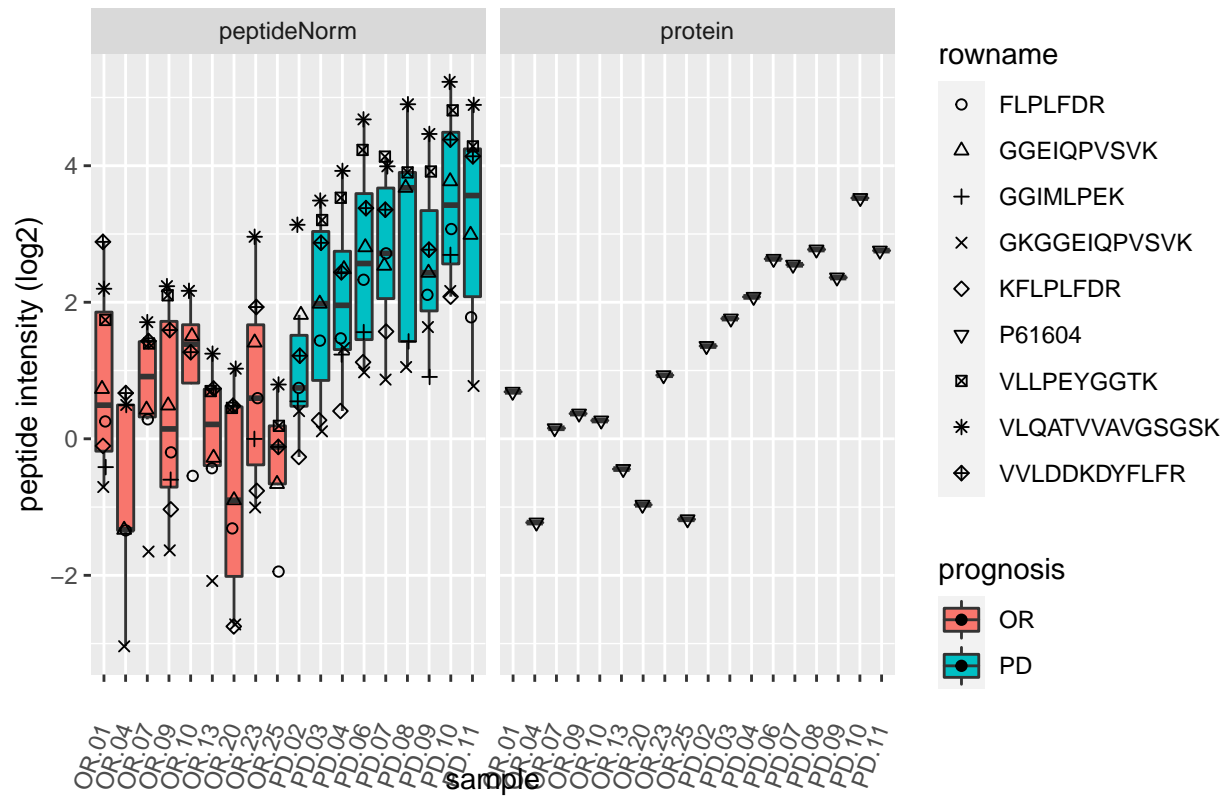
```

geom_boxplot(outlier.shape = NA) +
geom_point(
  position = position_jitter(width = .1),
  aes(shape = rowname)) +
scale_shape_manual(values = 1:nrow(pePlotDf)) +
labs(title = protName, x = "sample", y = "peptide intensity (log2)") +
theme(axis.text.x = element_text(angle = 70, hjust = 1, vjust = 0.5)) +
facet_grid(~assay)
print(p2)
}

```



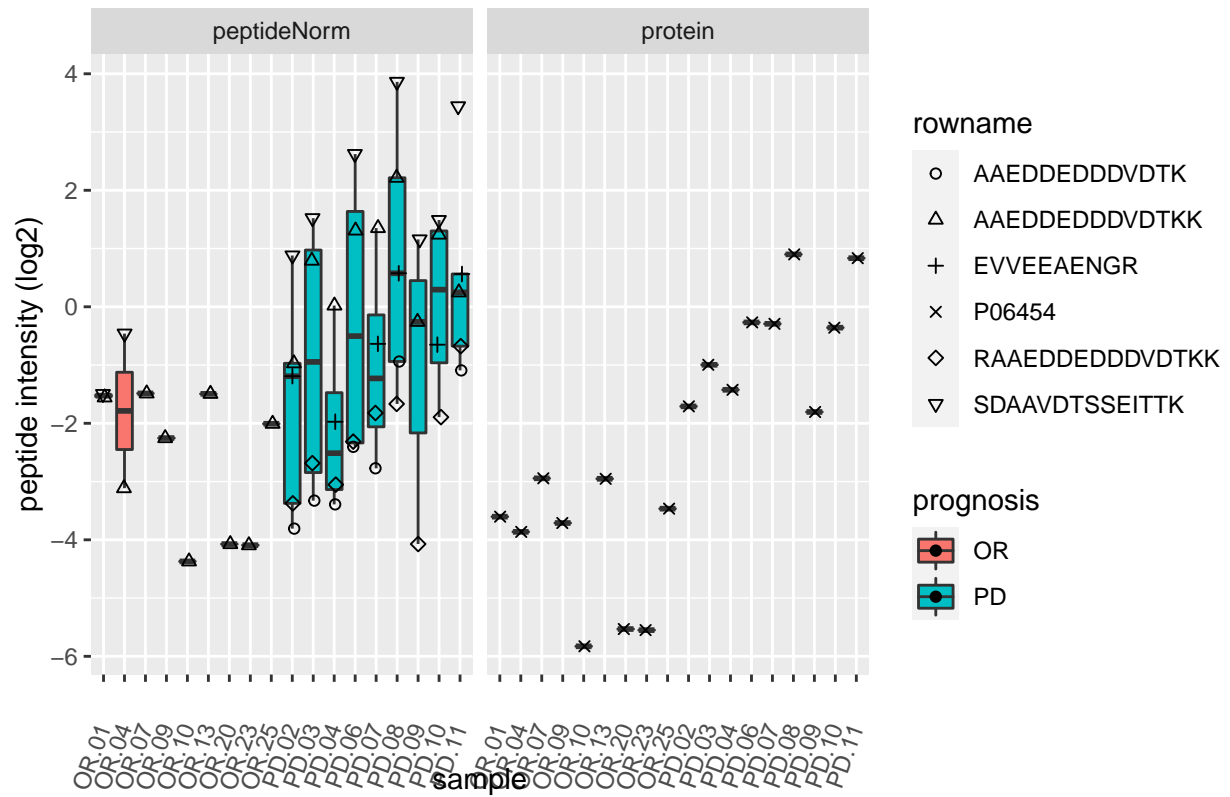
P61604



P06454



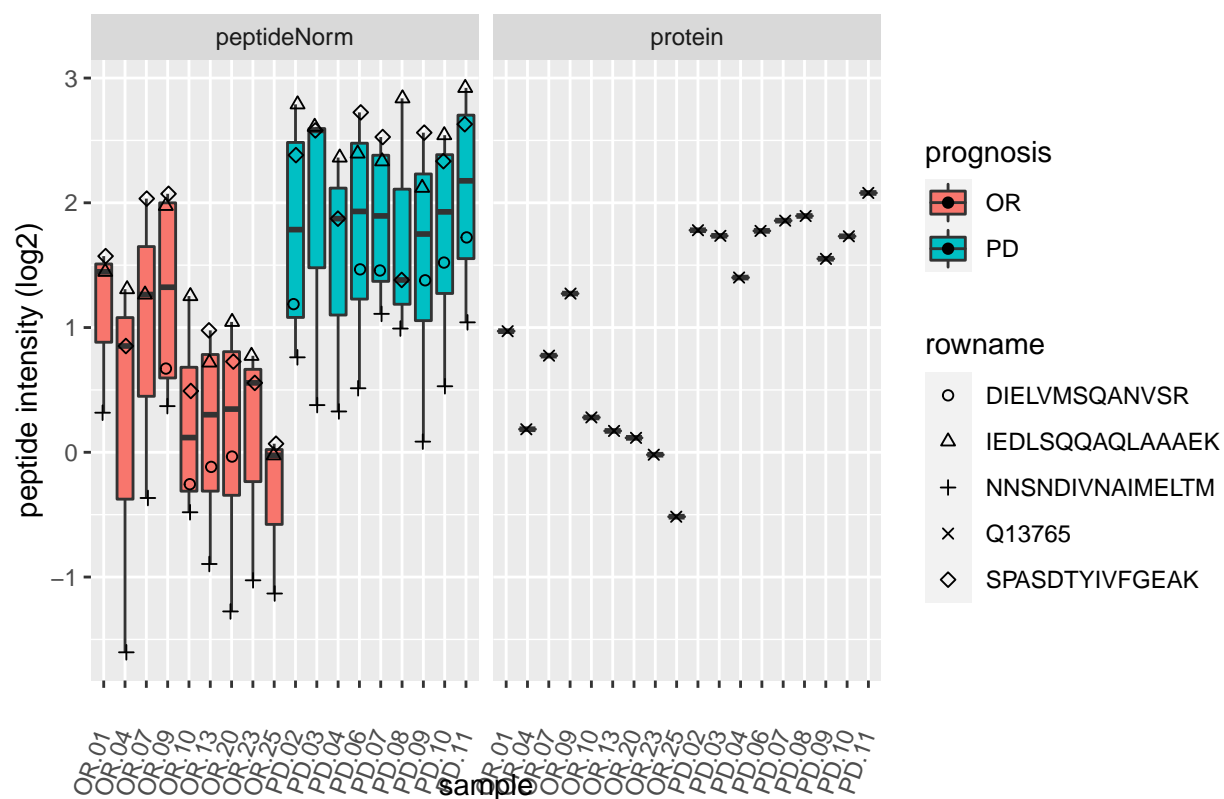
P06454



Q13765



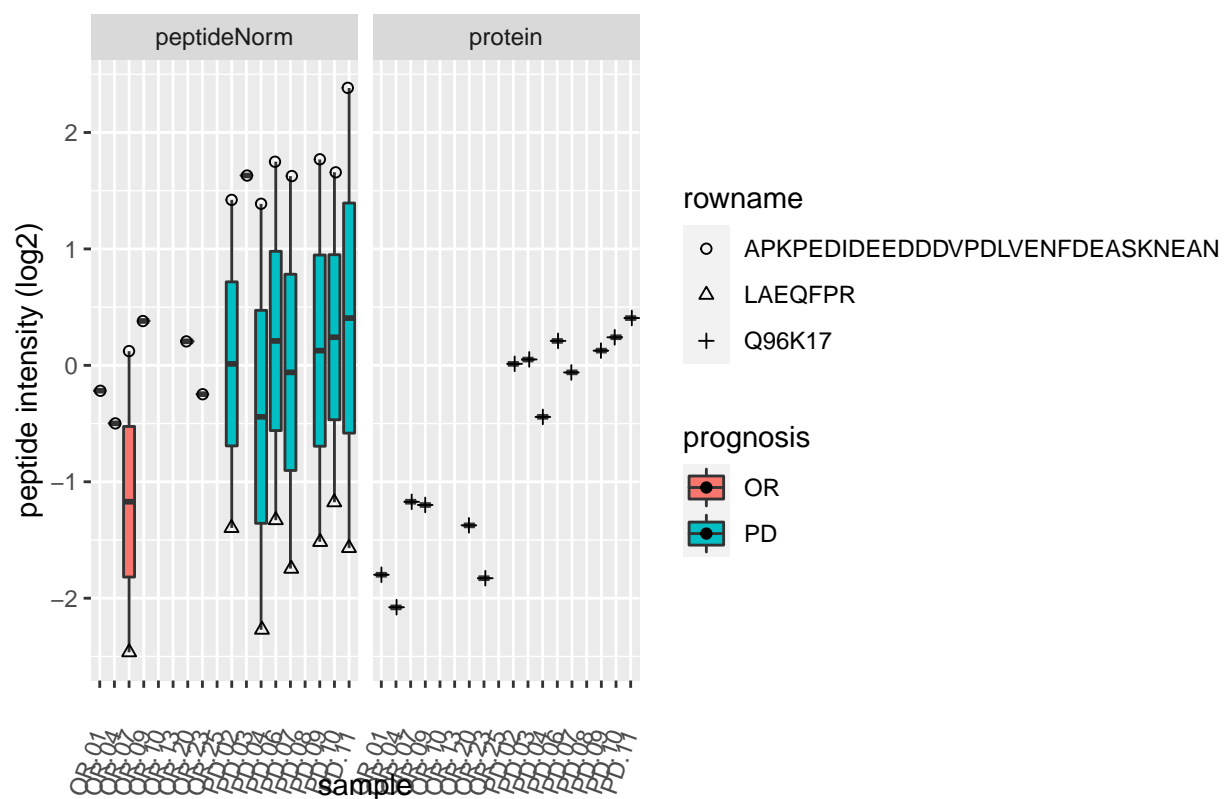
Q13765



Q96K17

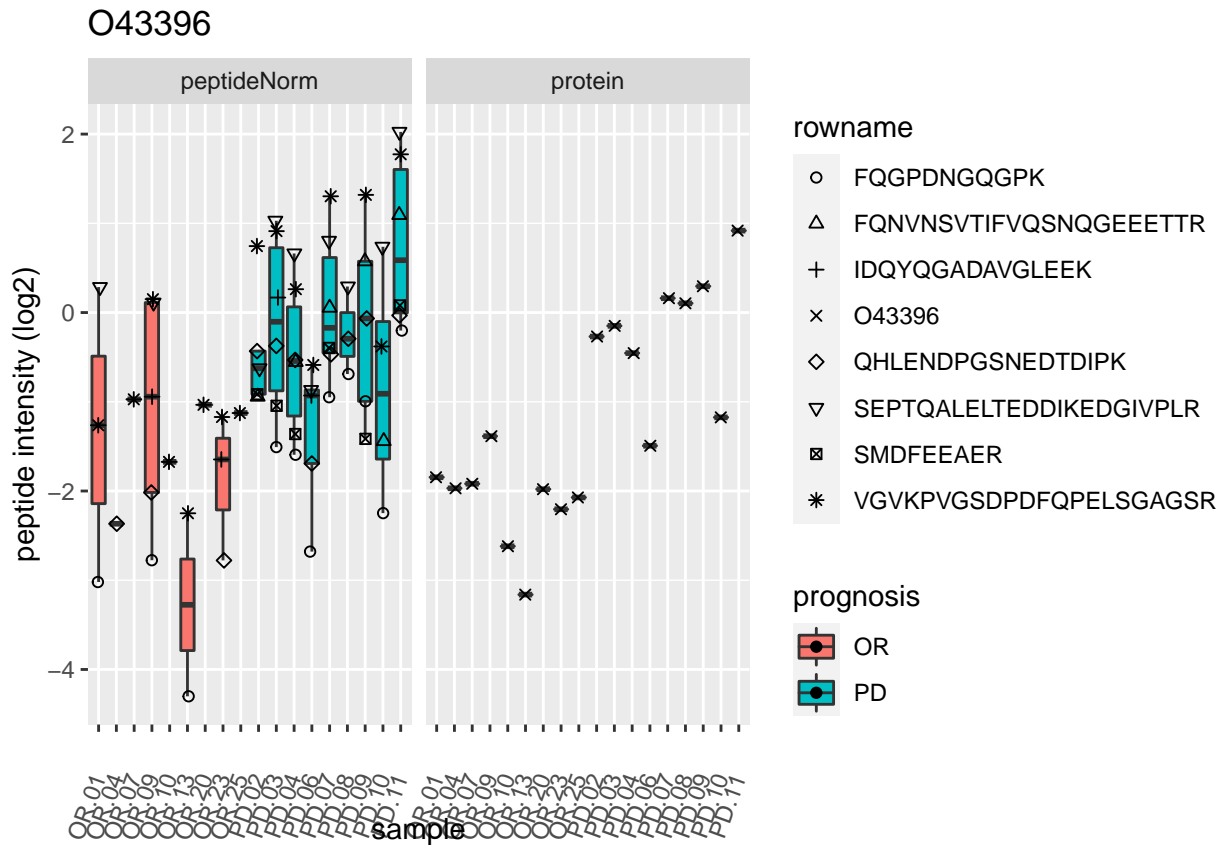


Q96K17



O43396

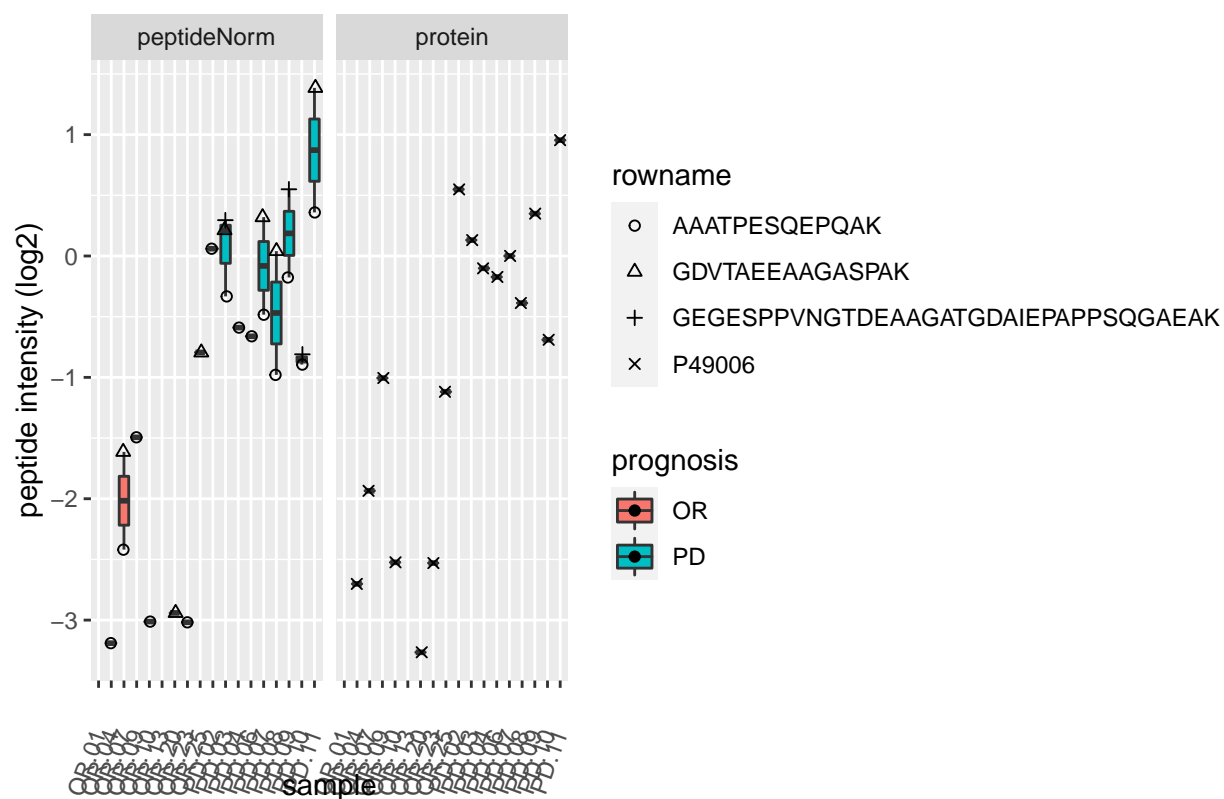




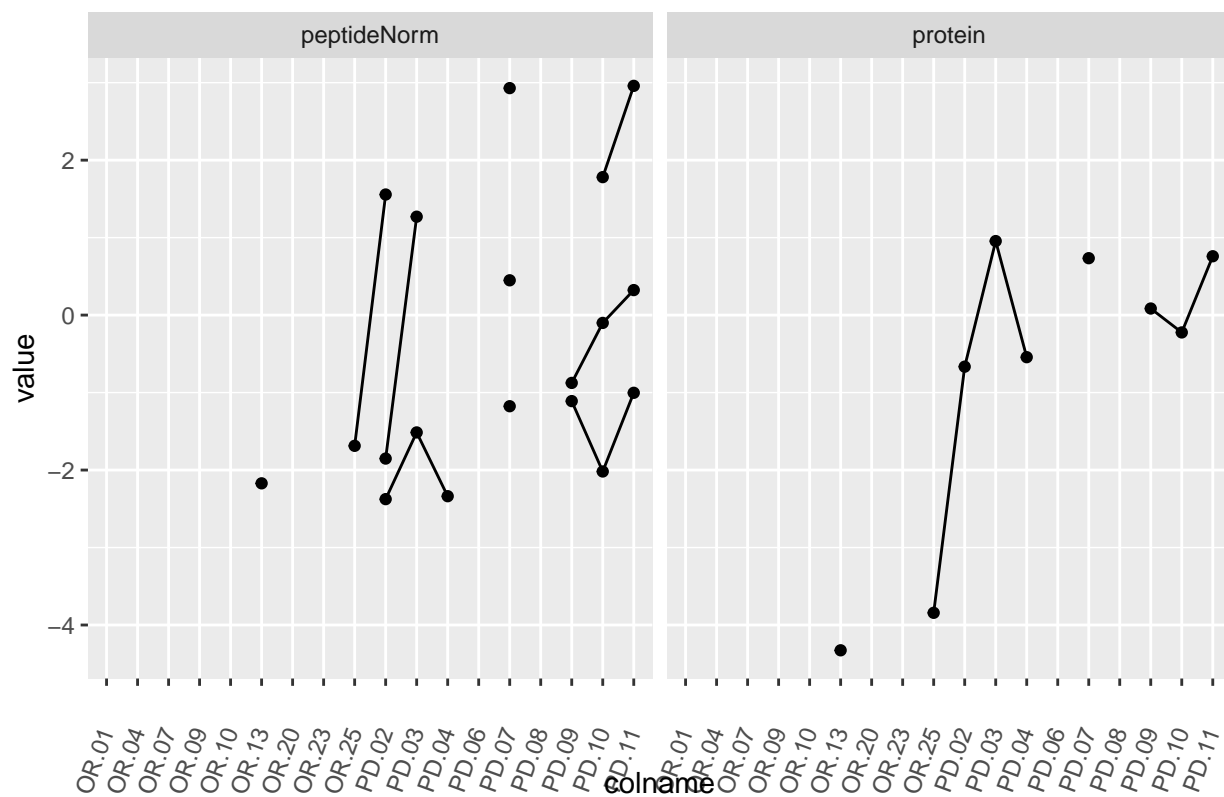
P49006



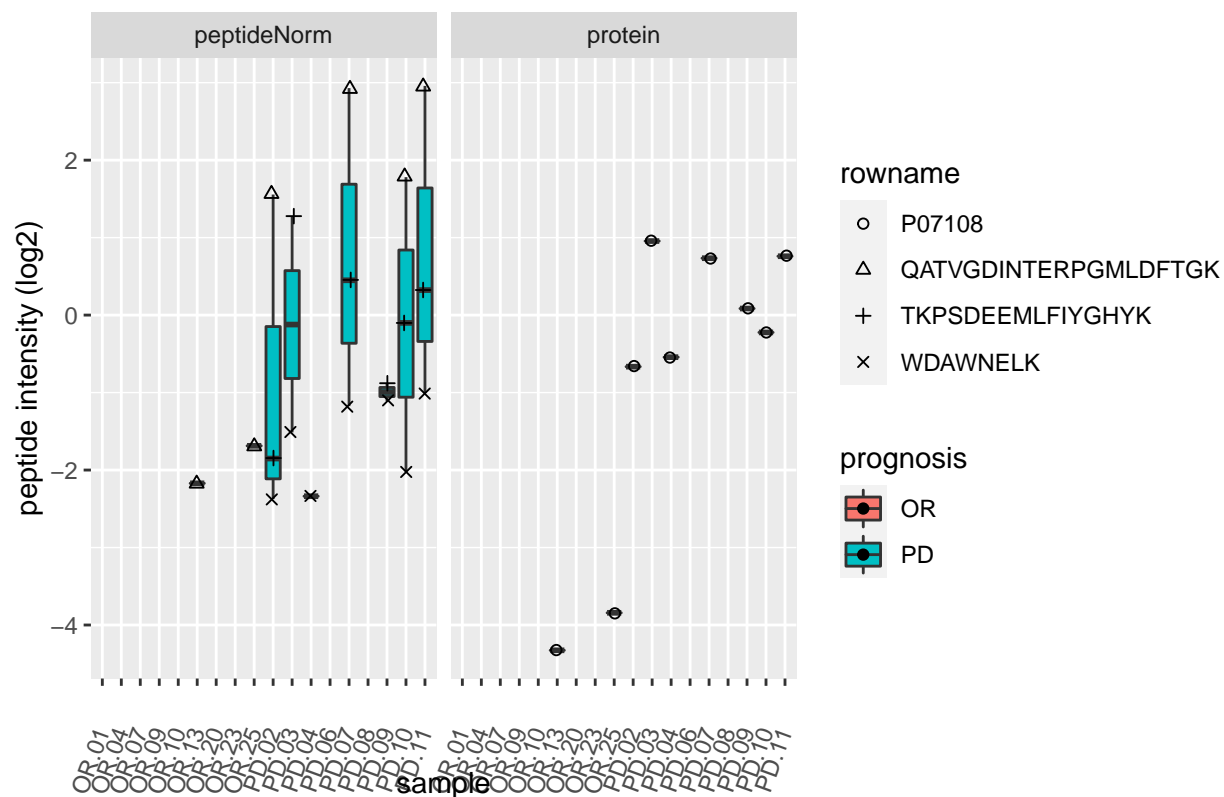
P49006



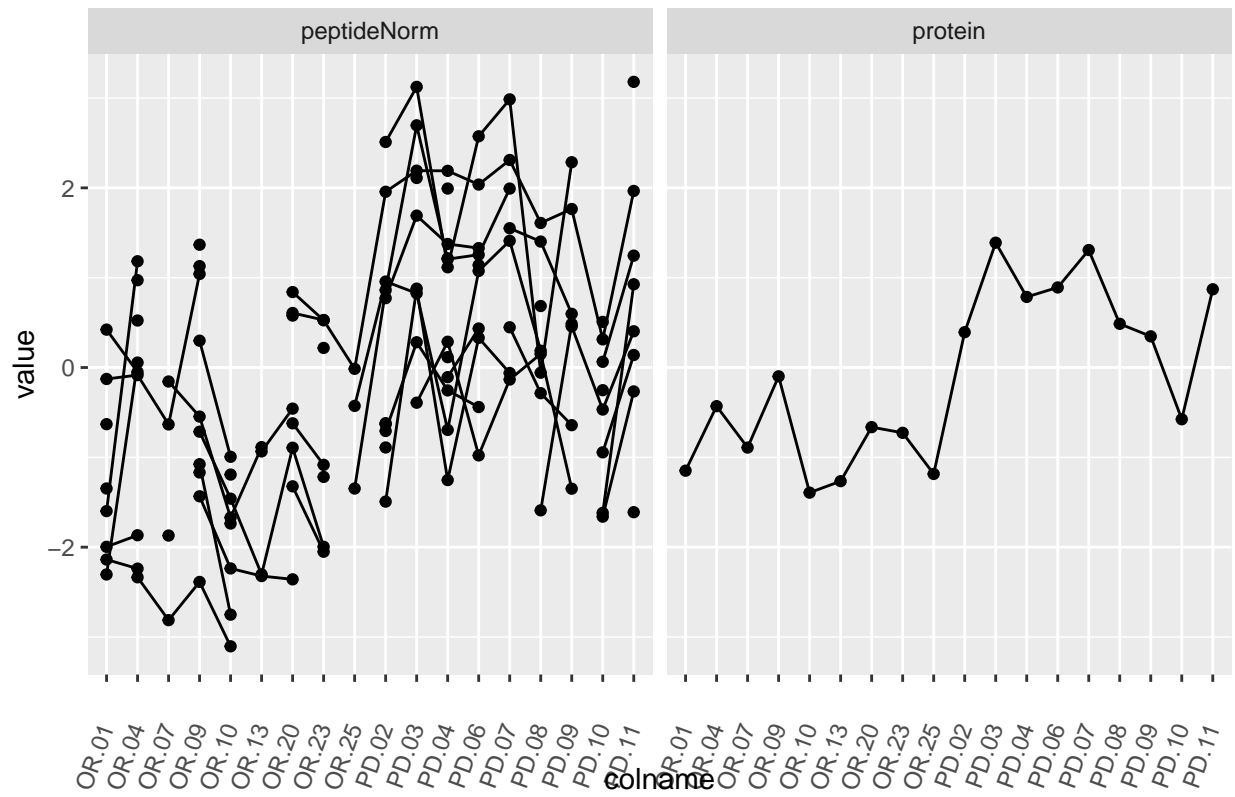
P07108

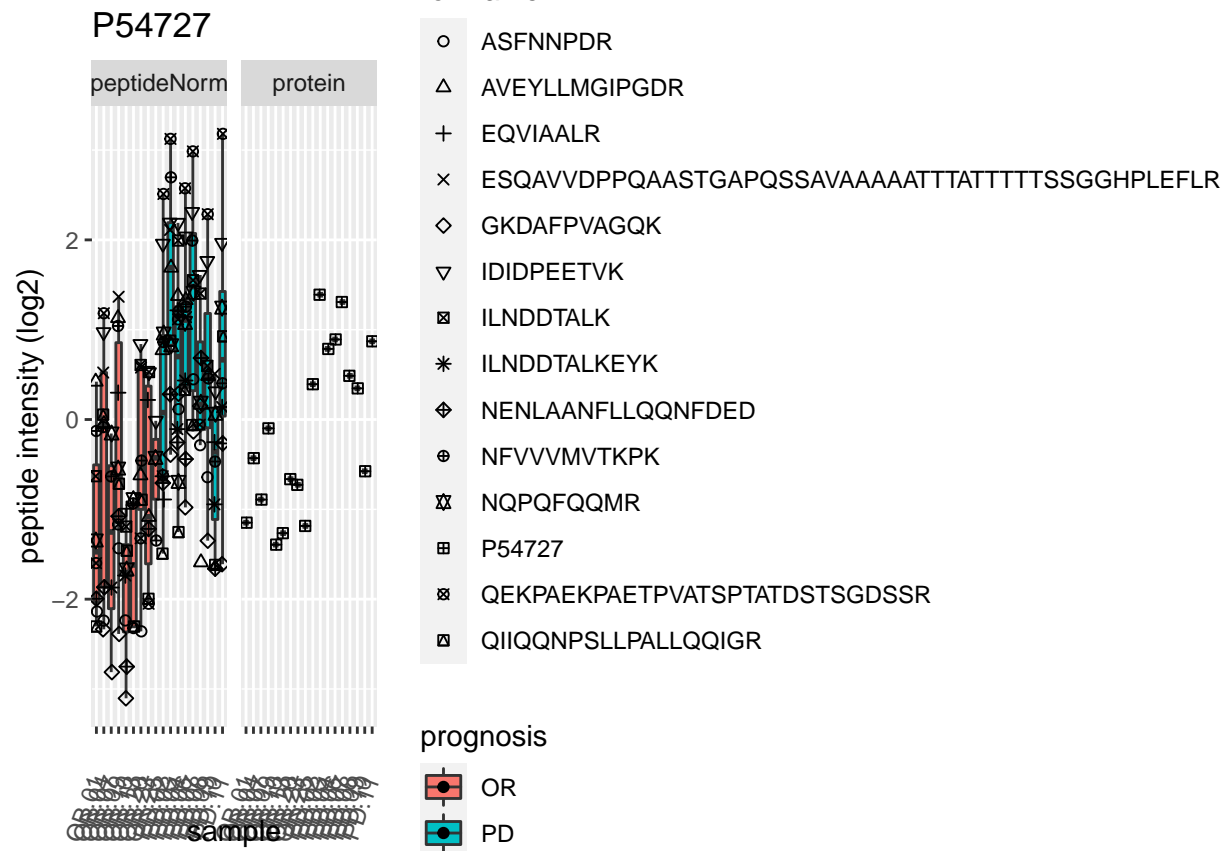


P07108

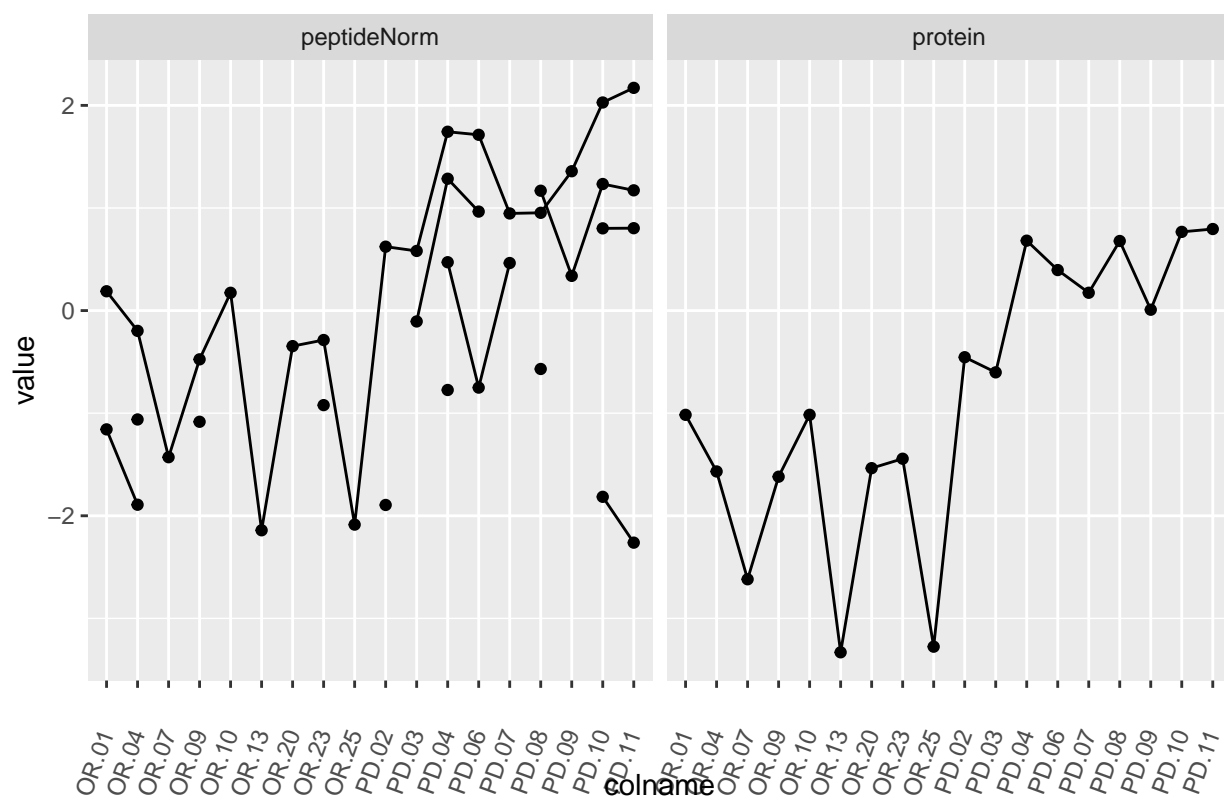


P54727

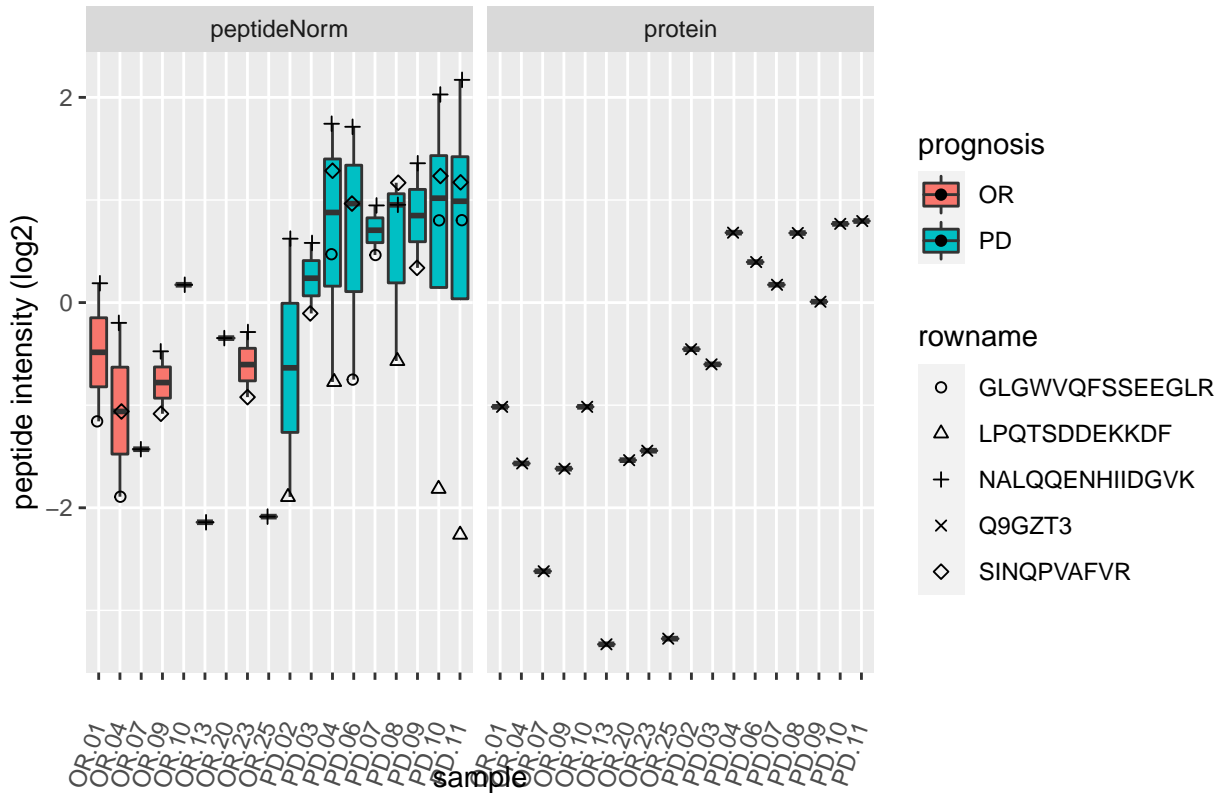




Q9GZT3

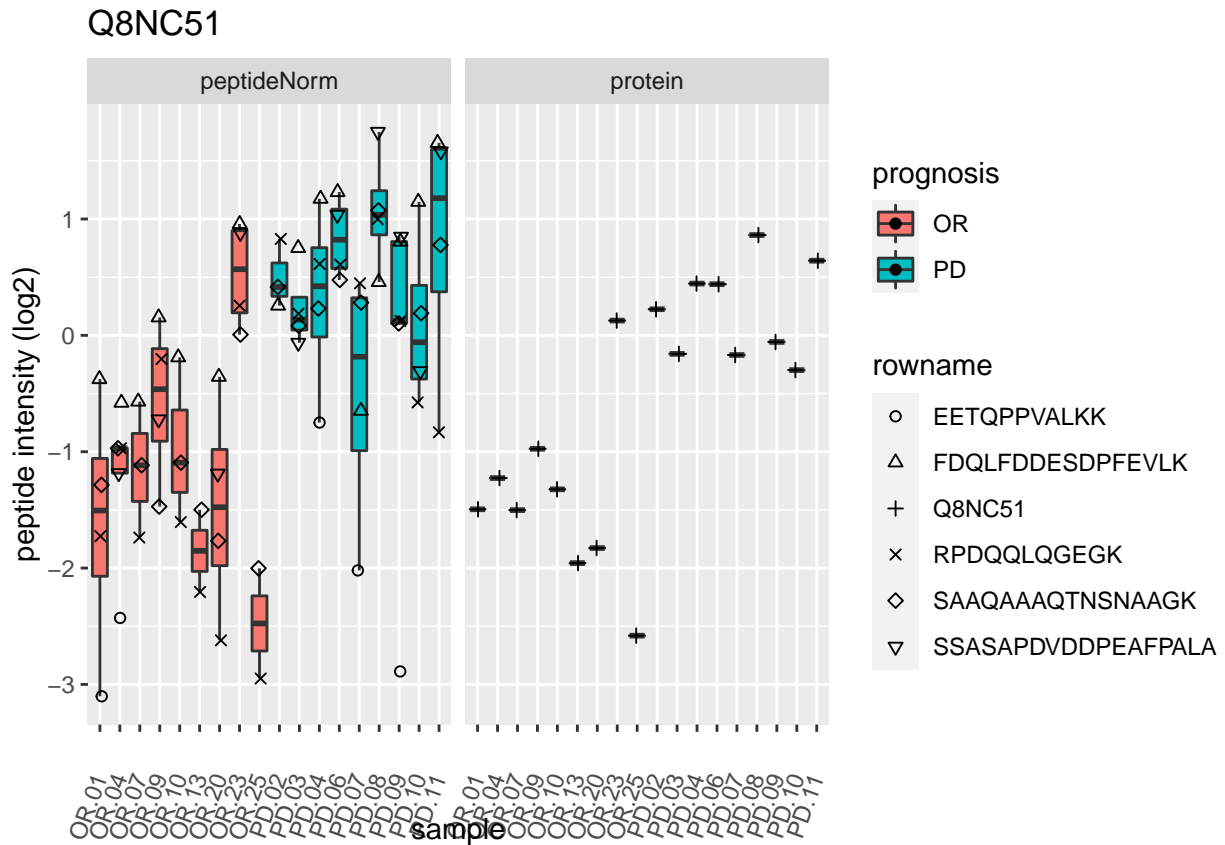


Q9GZT3



Q8NC51

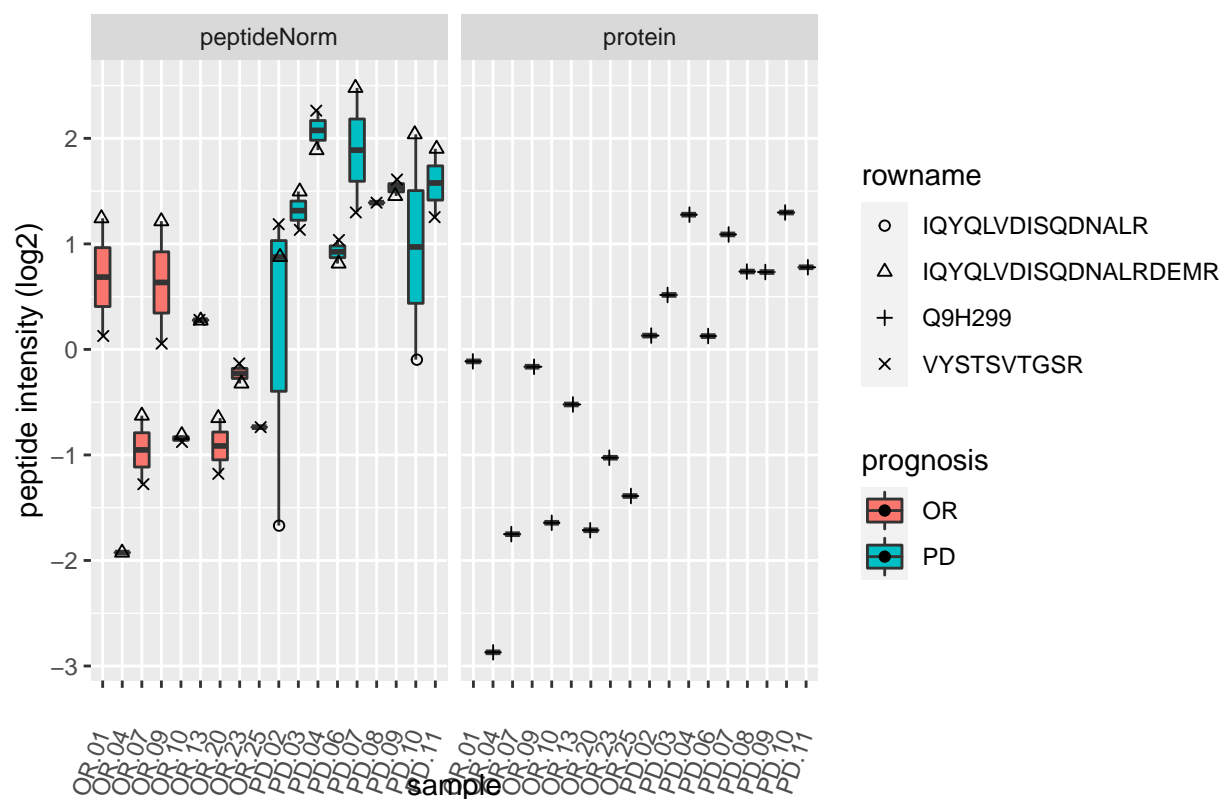




Q9H299



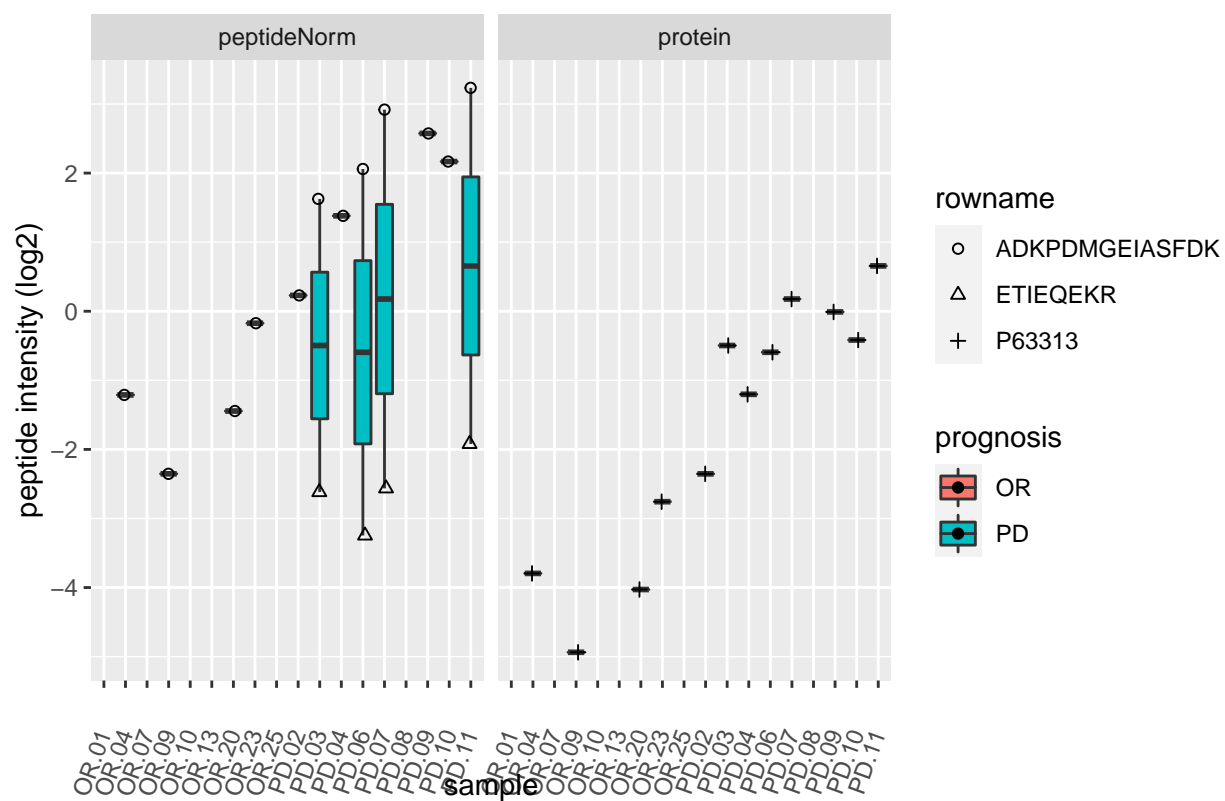
Q9H299



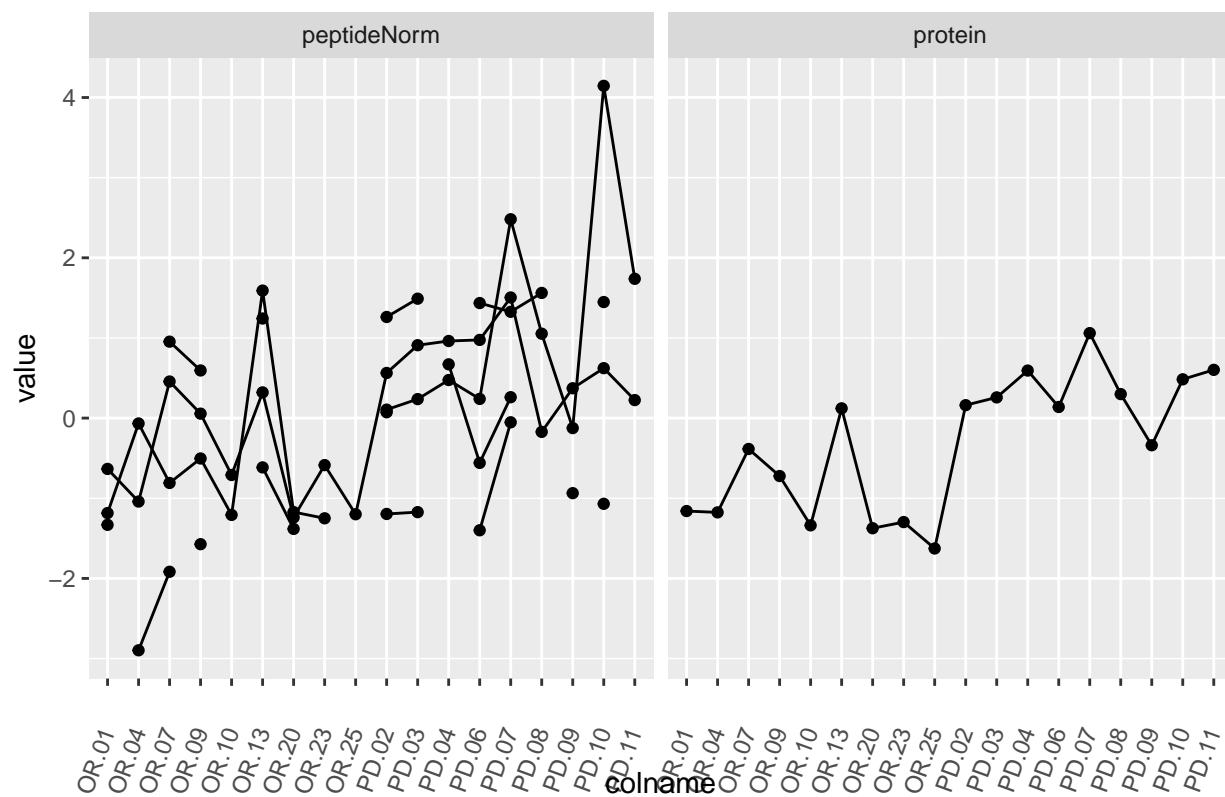
P63313



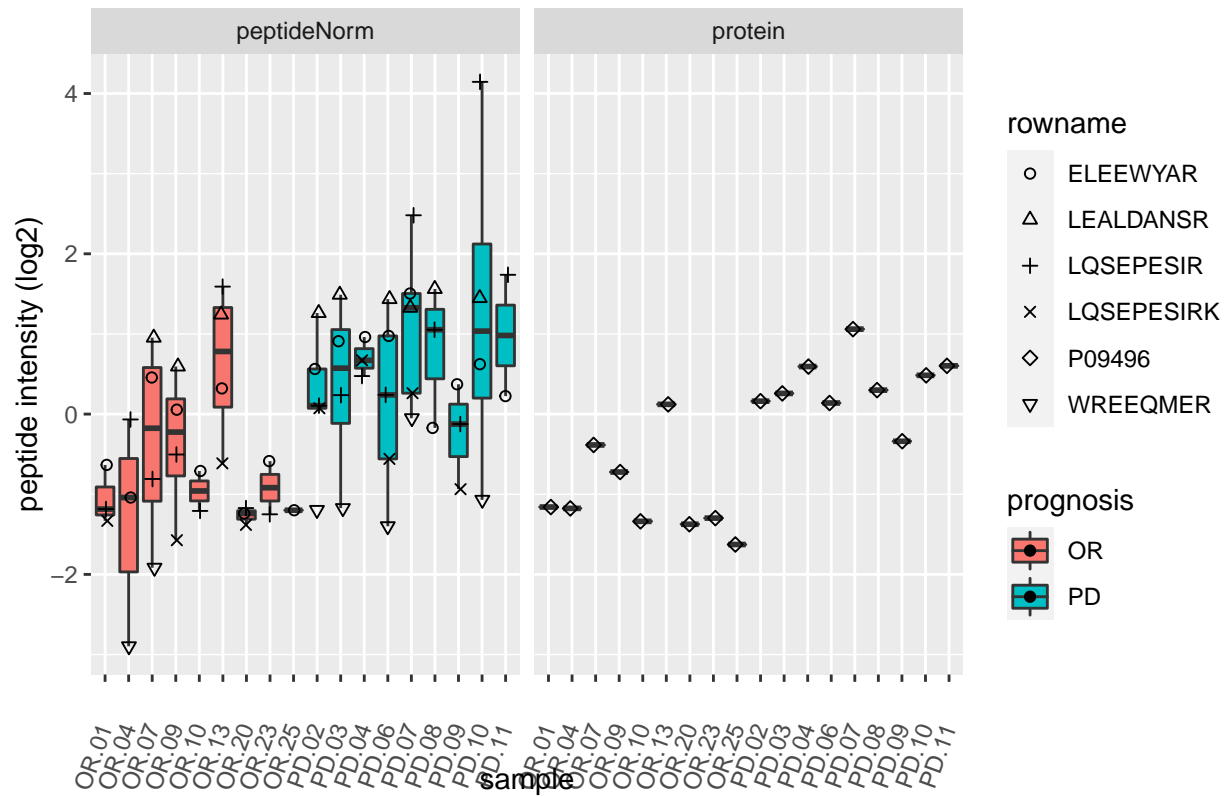
P63313



P09496

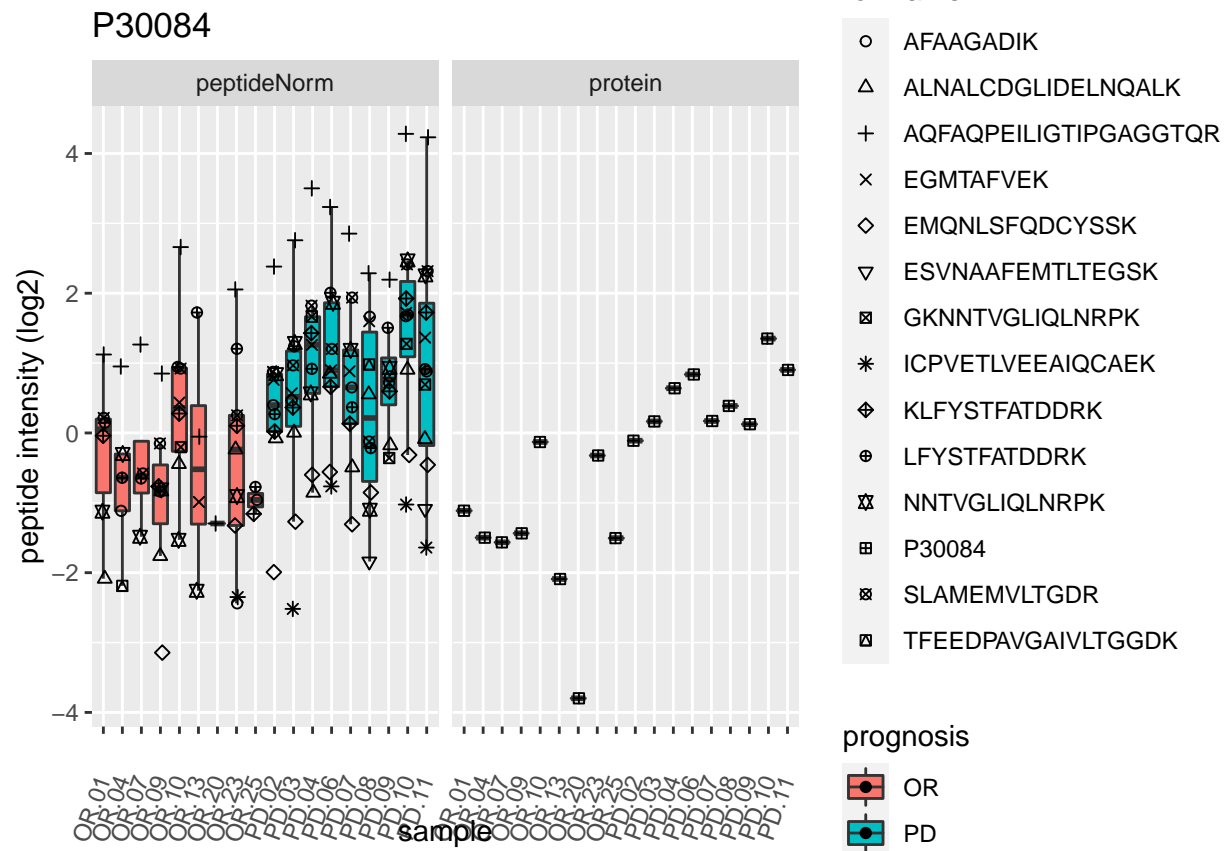


P09496



P30084

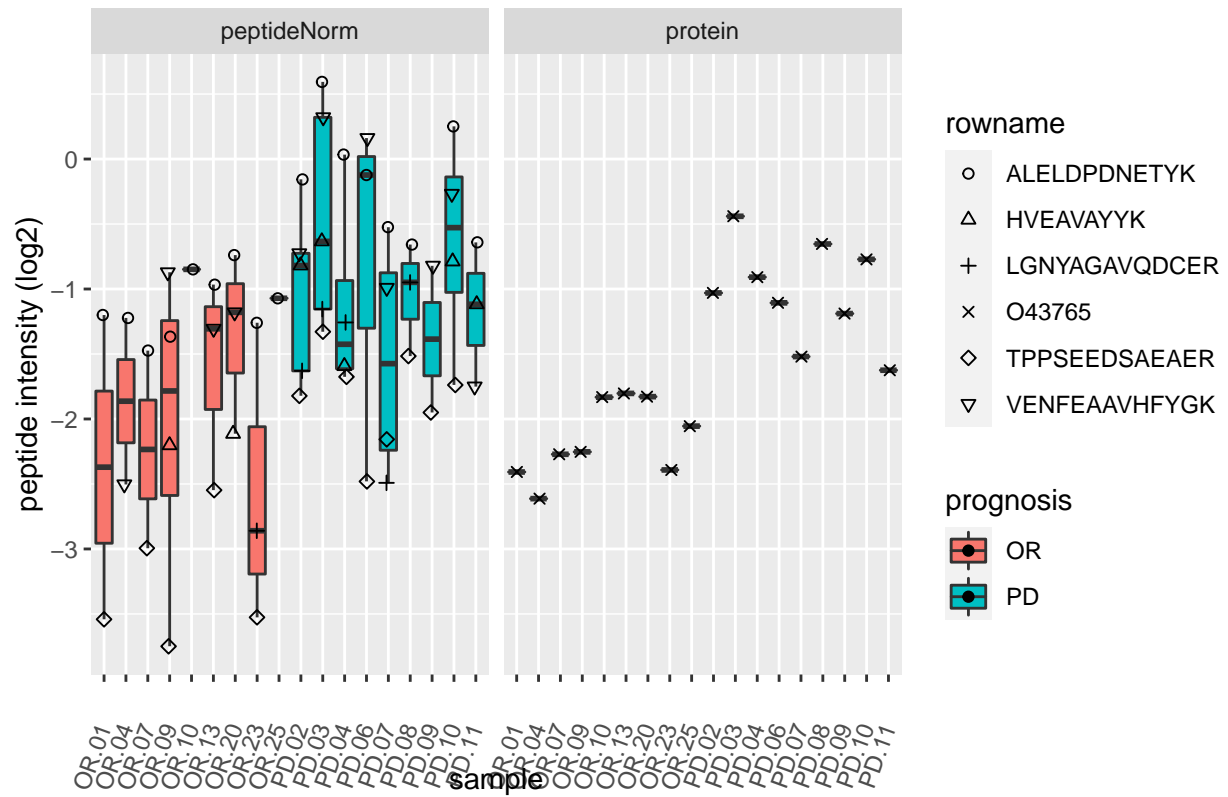




O43765

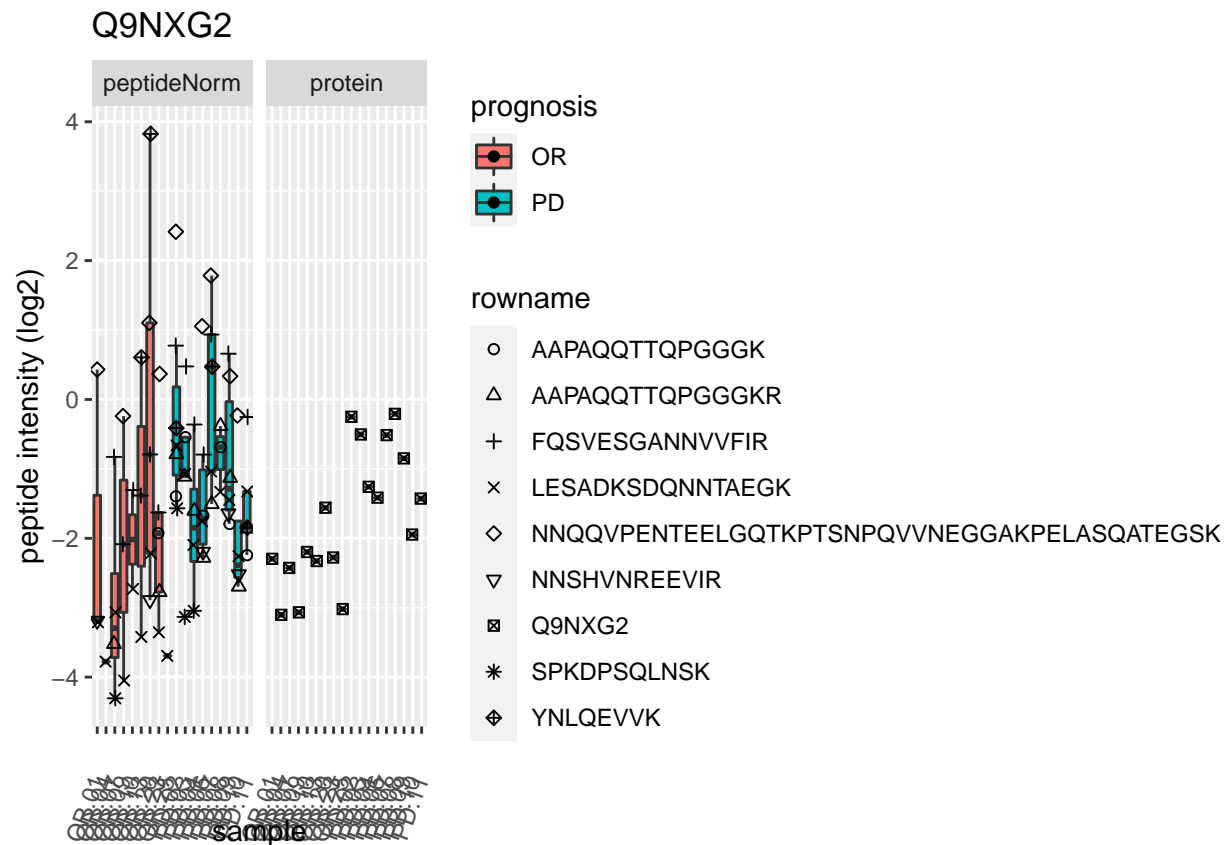


O43765



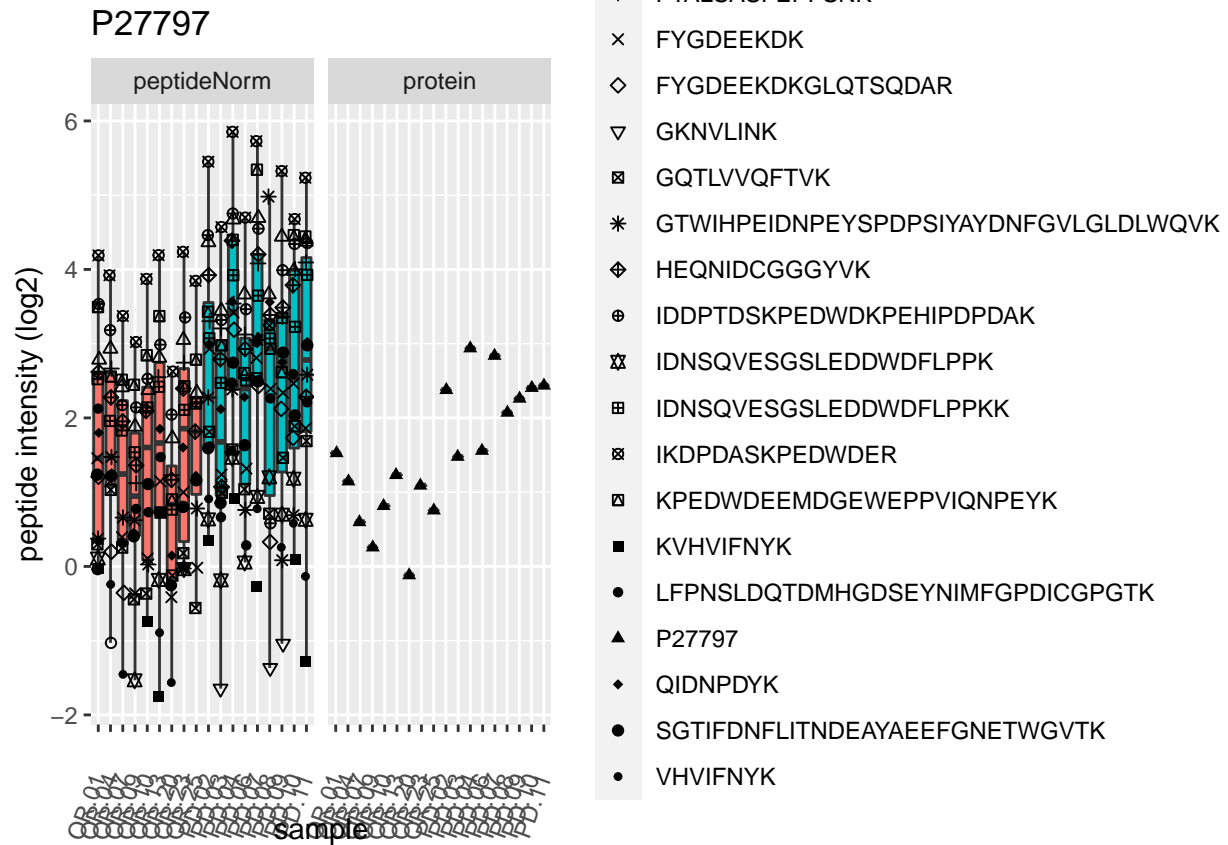
Q9NXG2



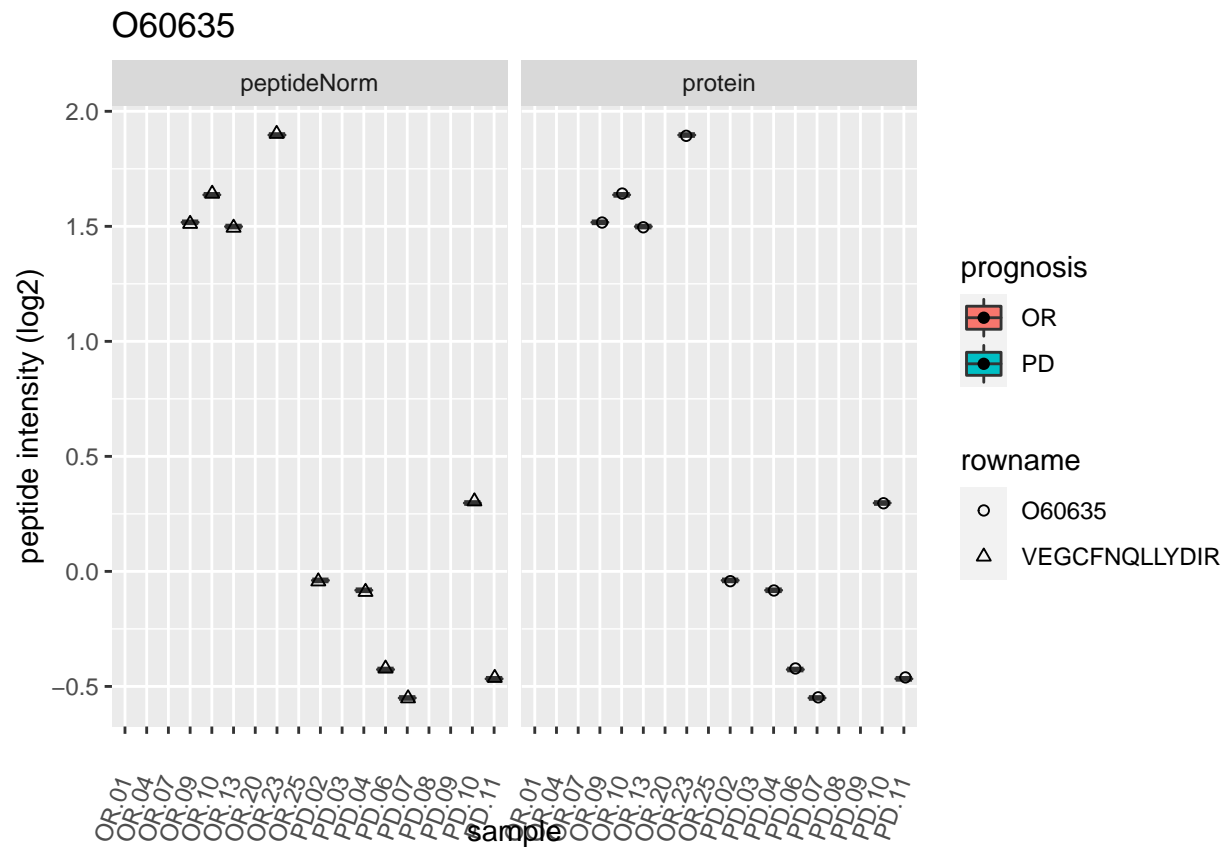


P27797





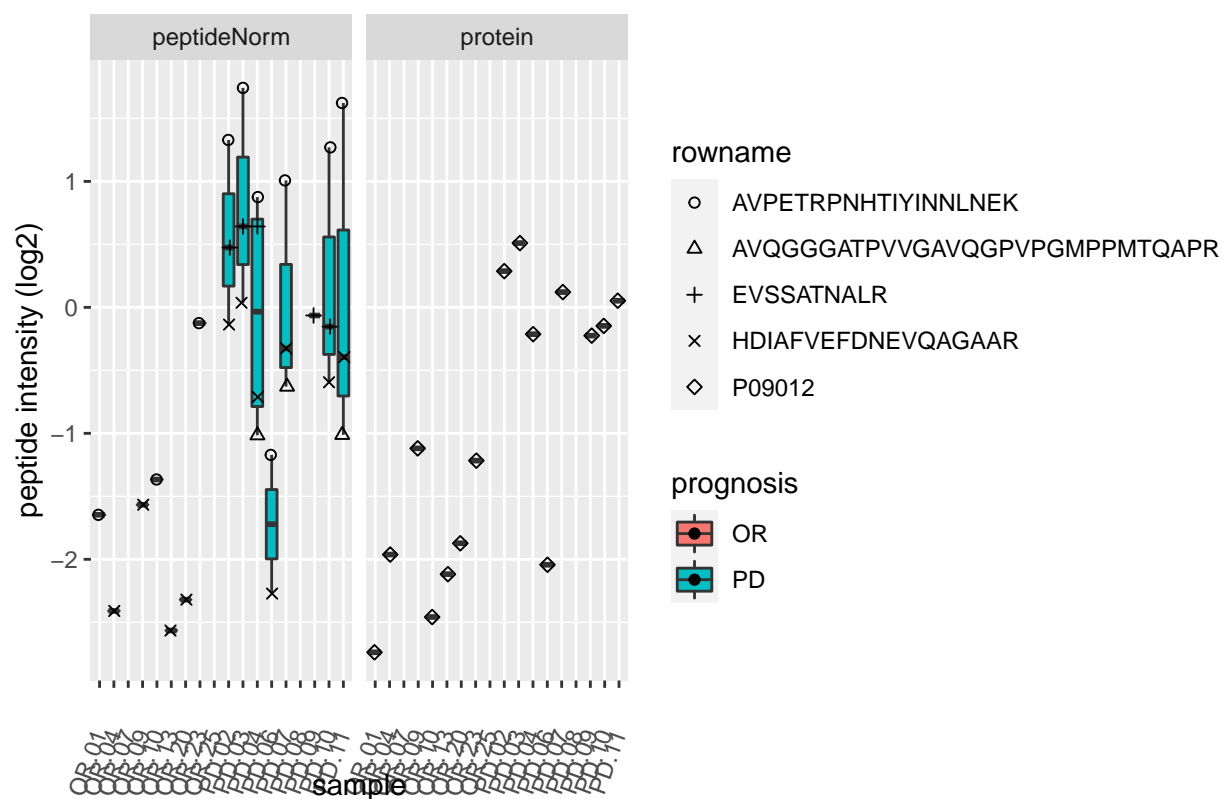




P09012

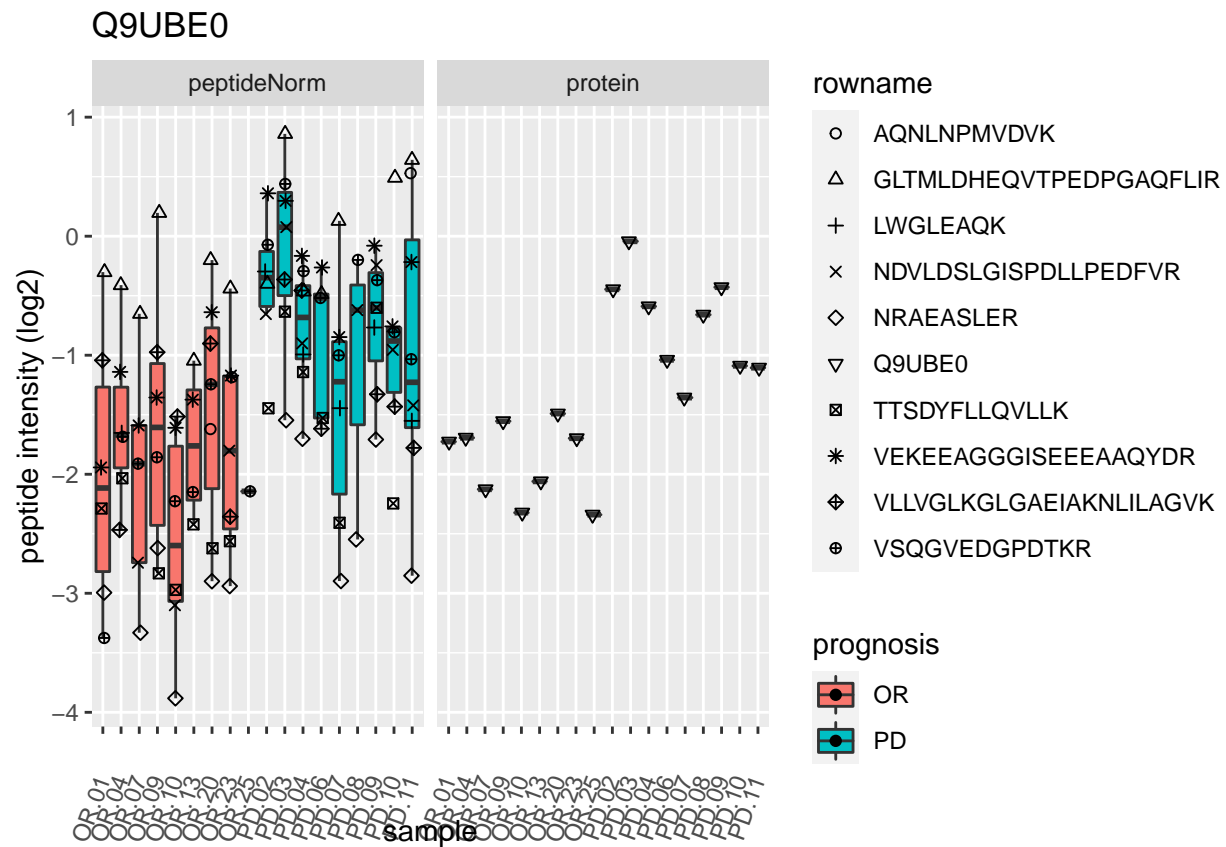


P09012



Q9UBE0

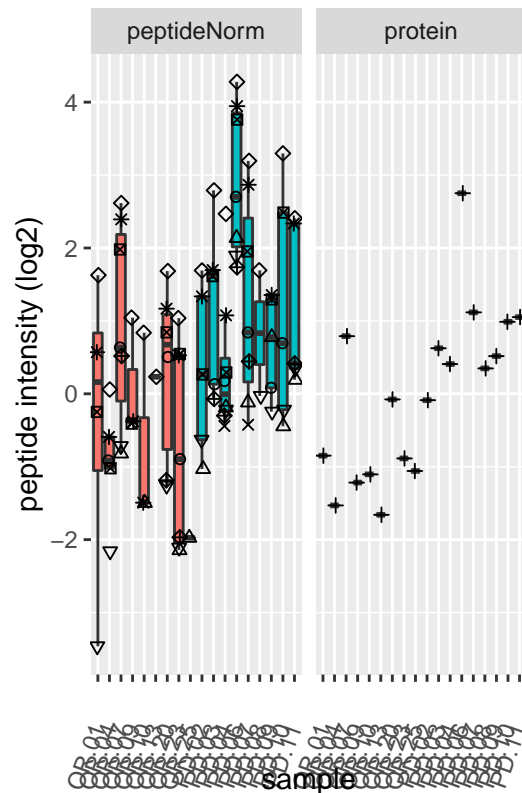




P55327



P55327



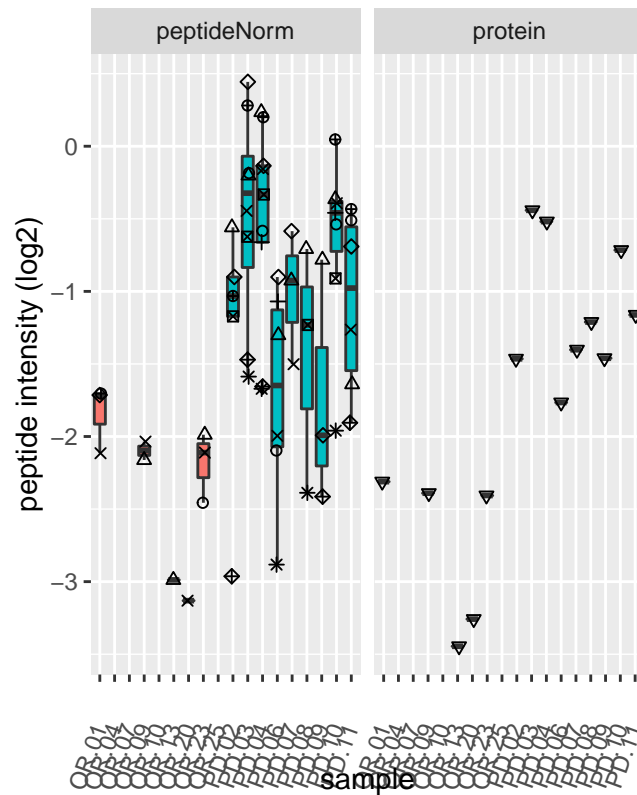
rowname

- ASAAFSSVGSVITK
- △ ELAKVEEEIQTLTSQVLAAG
- + P55327
- × SFEEKVENLK
- ◇ TDPVPEEGEDVAATISATETLSEEEQEELRR
- ▽ TSETLSQAGQK
- ⊠ VEEIQTLTSQVLAAG
- * VGGTKPAGGDFGEVLNSAANASATTEPLPEK
- ⬠ VGGTKPAGGDFGEVLNSAANASATTEPLPEKTQESL

P46108



P46108



rowname

- ALFDFNGNDEEDLPFK
- △ DSSTSPGDYVLSVSENSR
- + HGVFLVR
- × IGDQEFDSLPALEFYK
- ◇ IHYLDTTTLIEPVSR
- ▽ P46108
- ⊠ QEAVALQQR
- * QGSGVILR
- ⊞ TALAELVGELVK
- ⊕ VSHYIINSSGPRPPVPPSPAQPPPGVSPSR

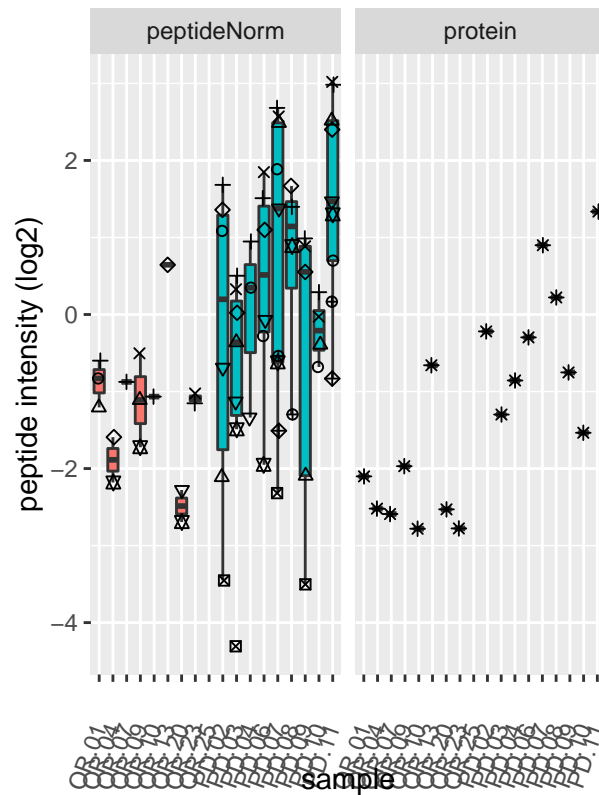
prognosis

- OR
- PD

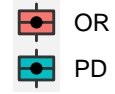
P51858



P51858



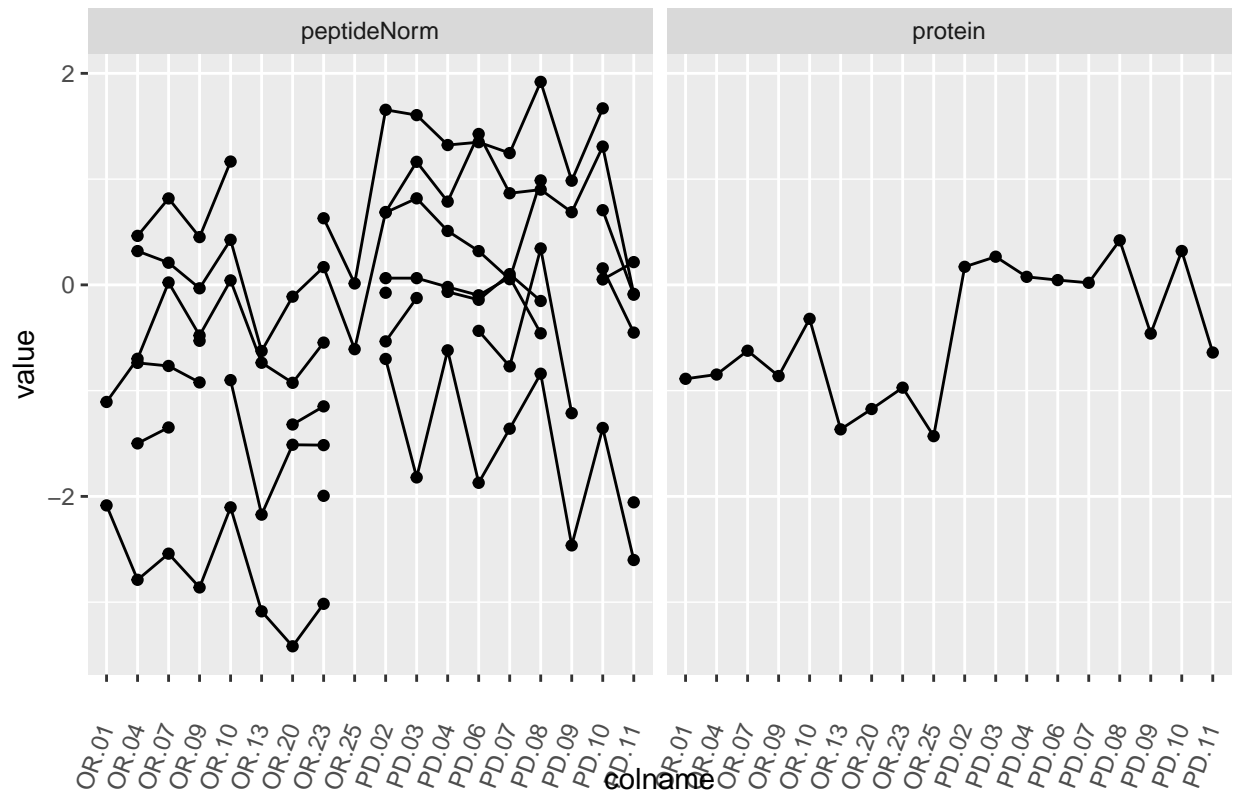
prognosis



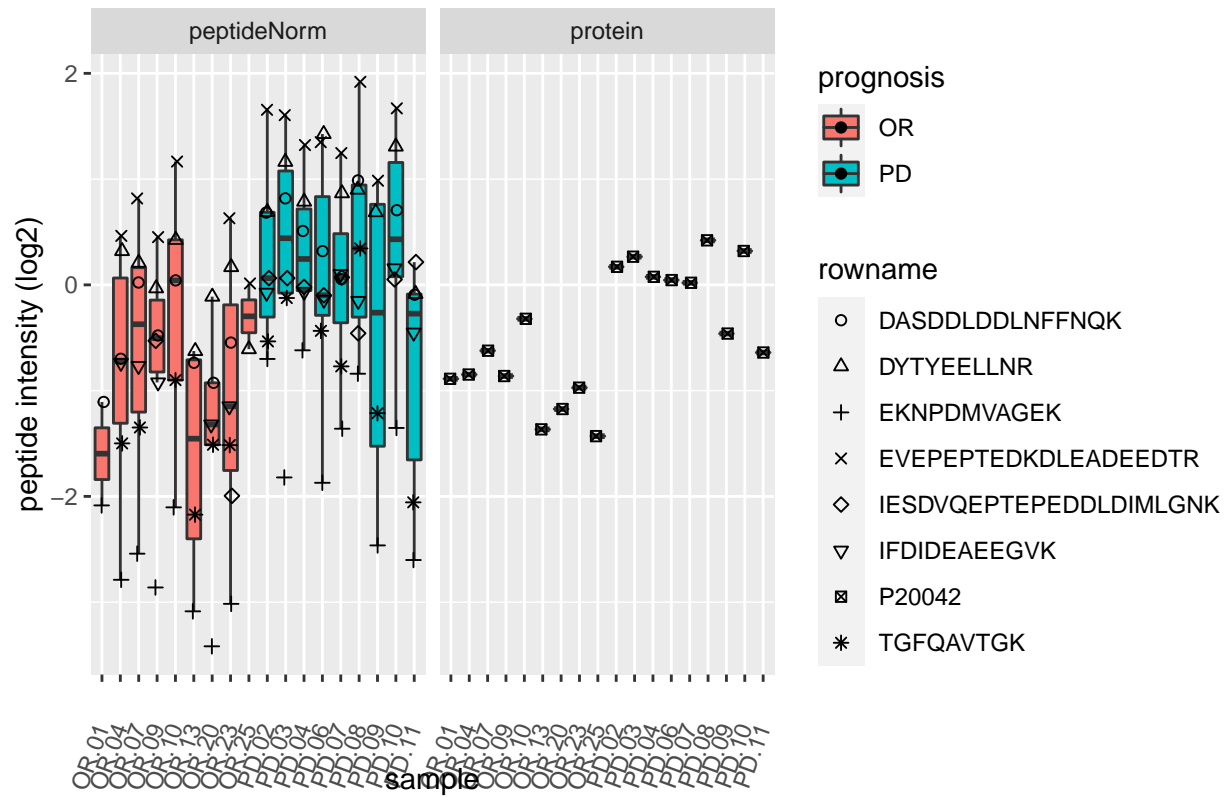
rowname

- EAENPEGEEKEAATLEVERPLPMEVEK
- △ GFSEGLWEIENNPTVK
- + GPPQEEEEEEEEEEEEATKEDAEAPGIR
- × GPPQEEEEEEEEEEEEATKEDAEAPGIRDHESL
- ◇ IDEMPEAAVK
- ▽ KGFSEGLWEIENNPTVK
- ⊠ NSTPSEPGSGR
- * P51858
- ⬠ RAGDLLEDSPK
- ⊕ SCVEEPEPEPEAAEGDGDKK
- ⊗ YQVFFFGTHETAFLGPK

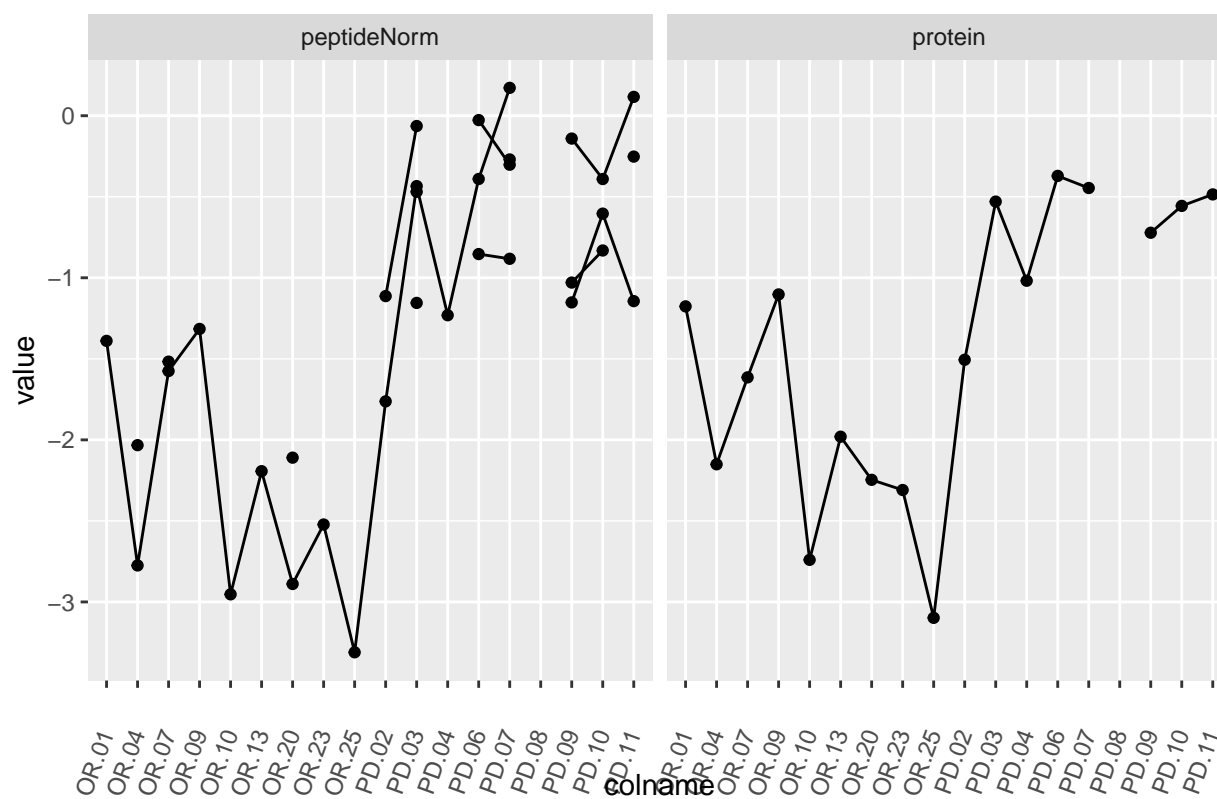
P20042



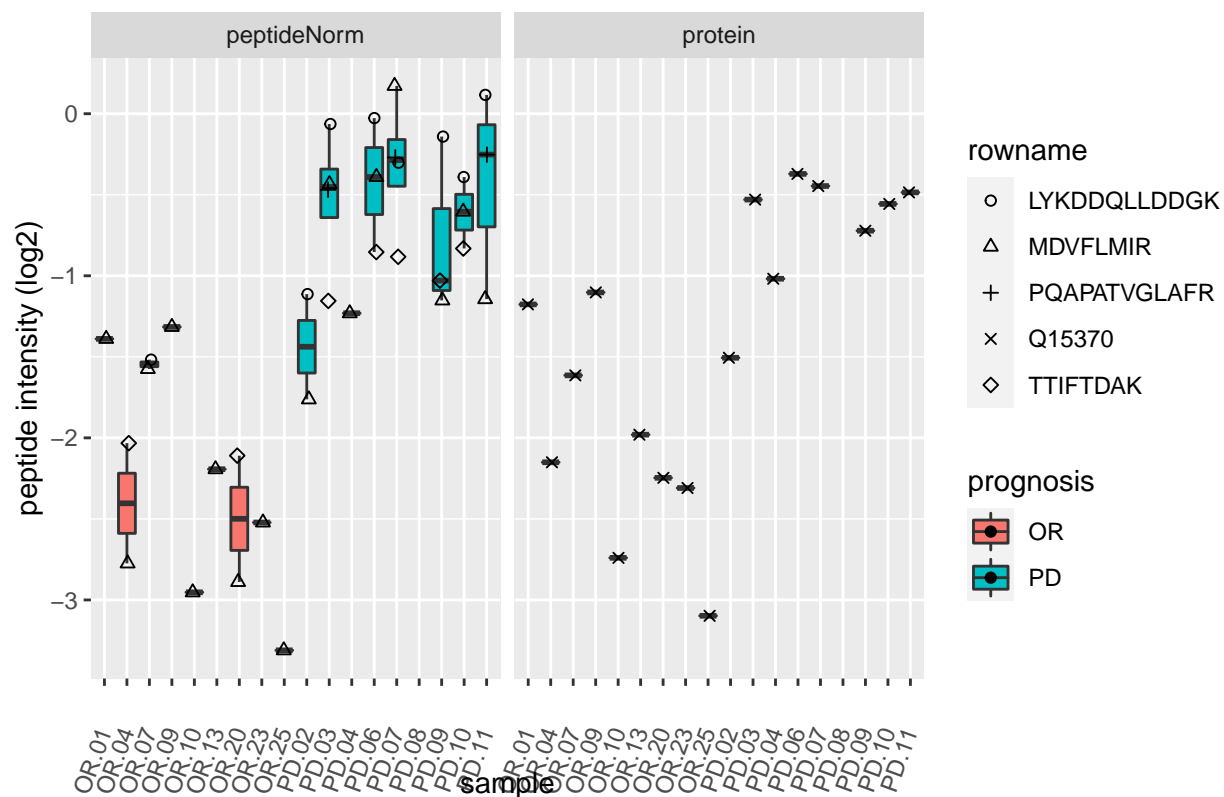
P20042



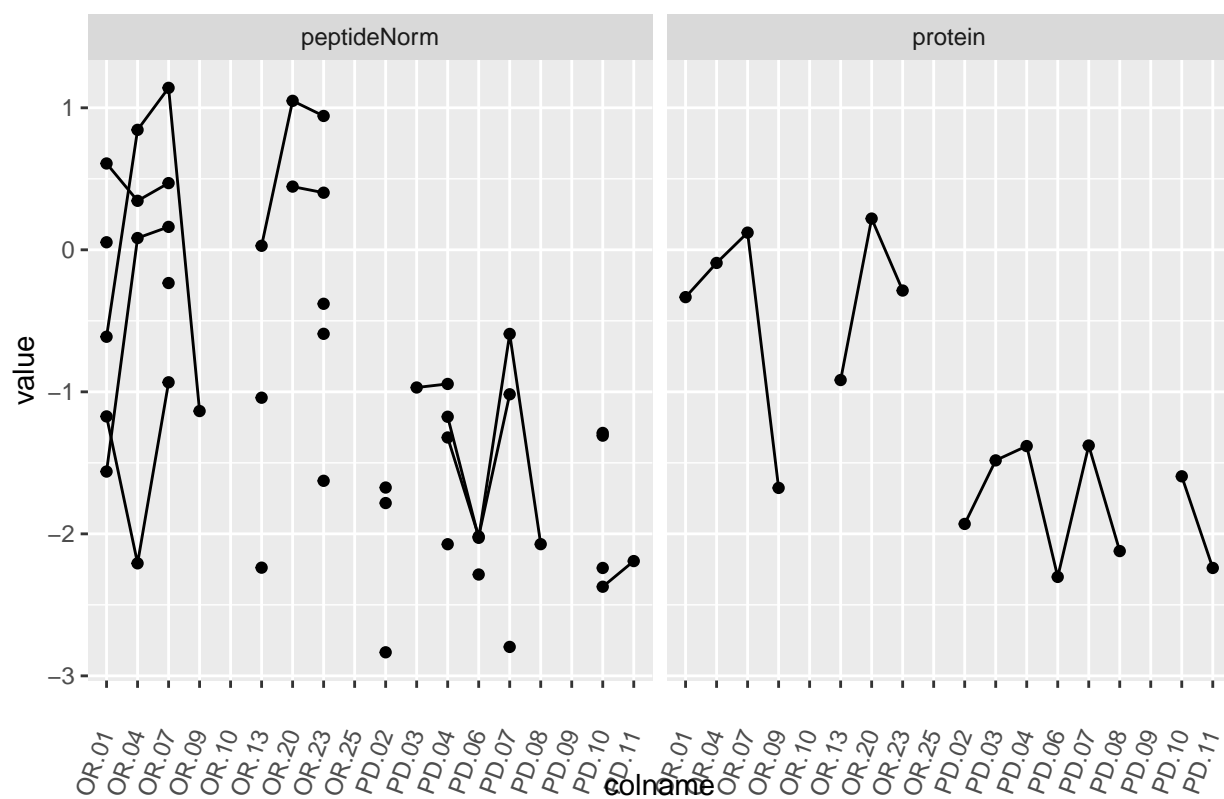
Q15370



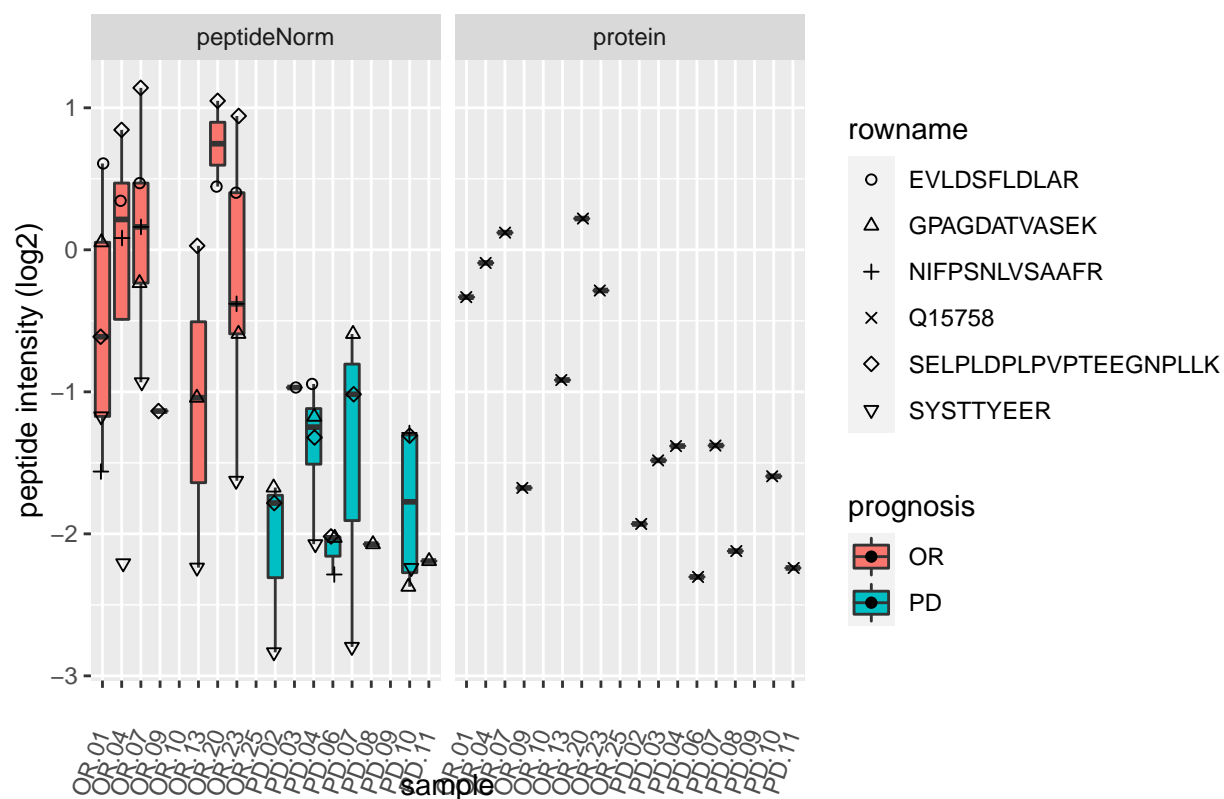
Q15370



Q15758



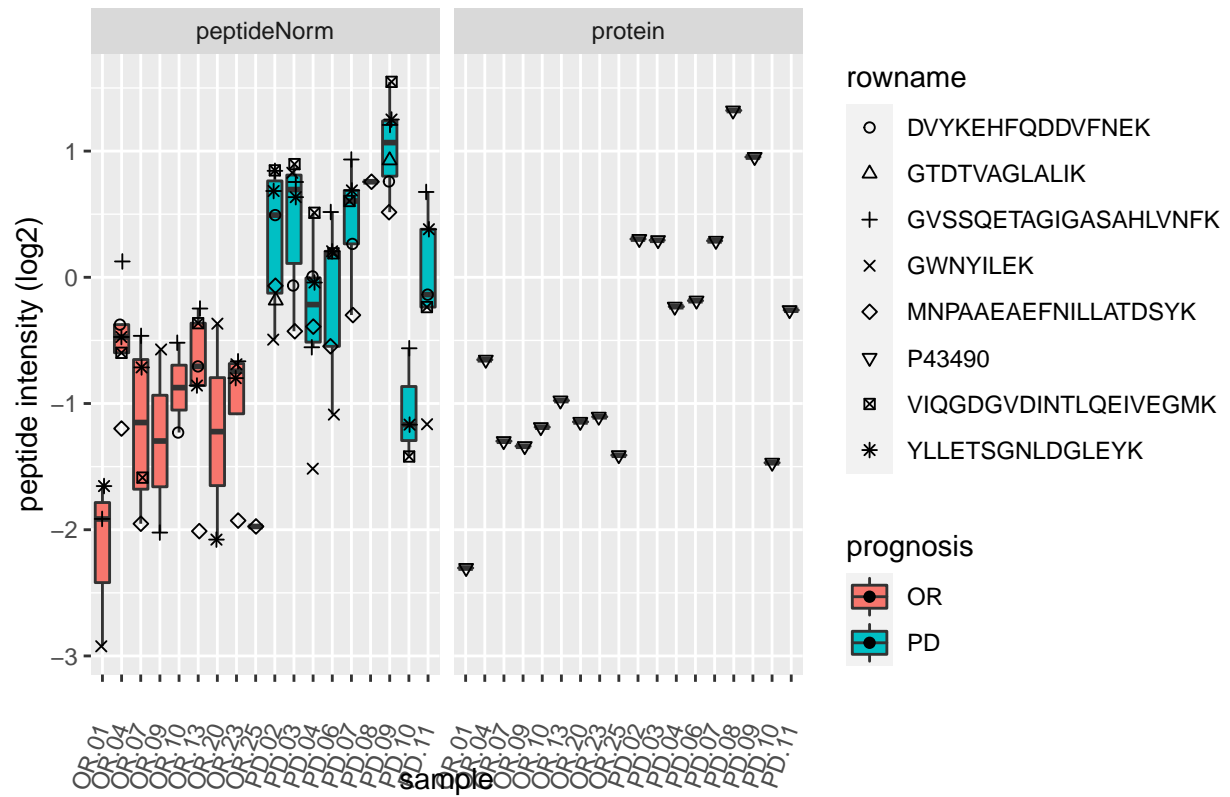
Q15758



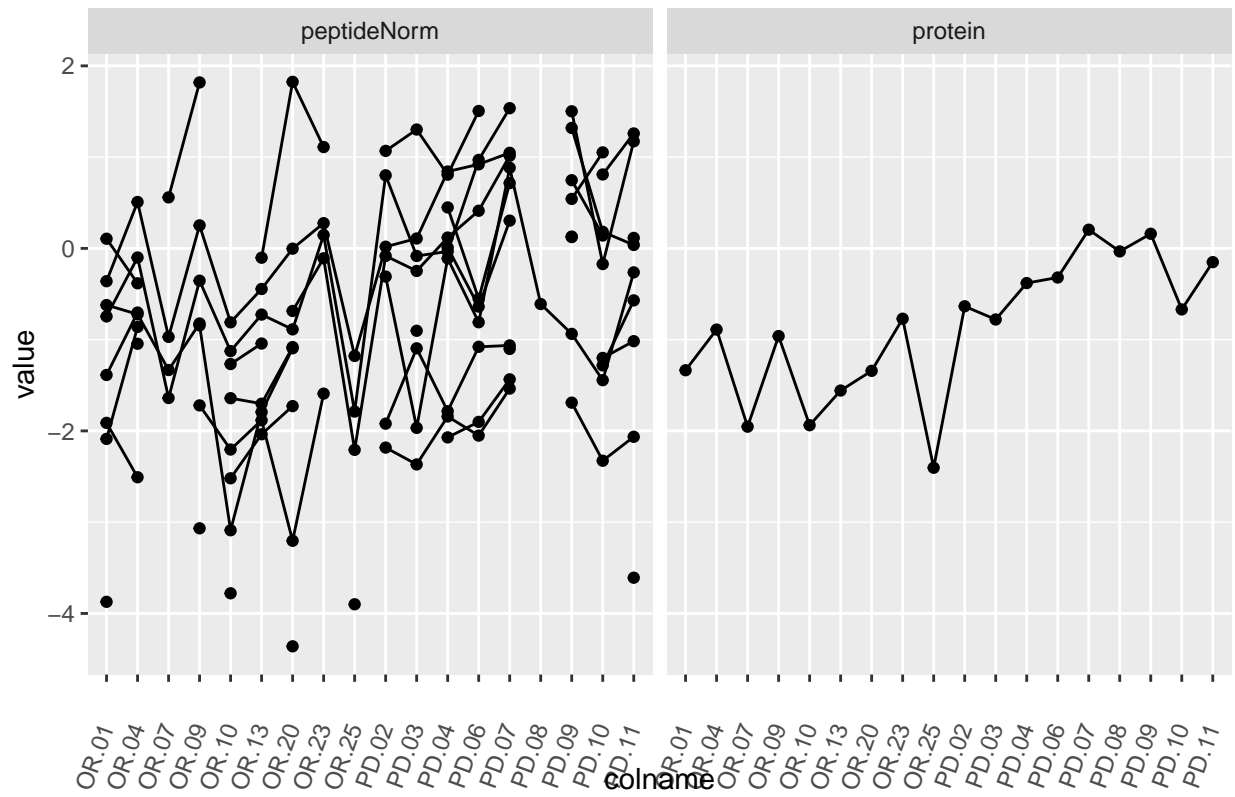
P43490

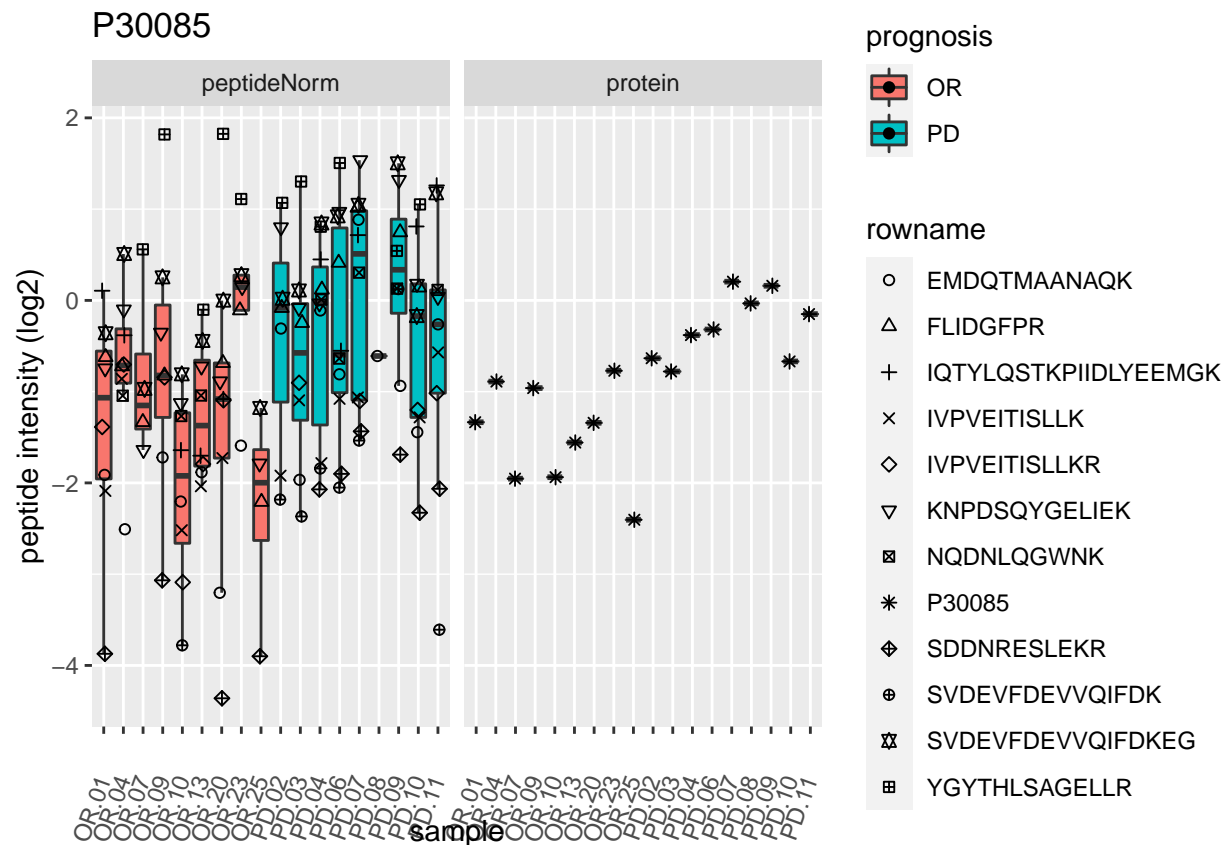


P43490



P30085

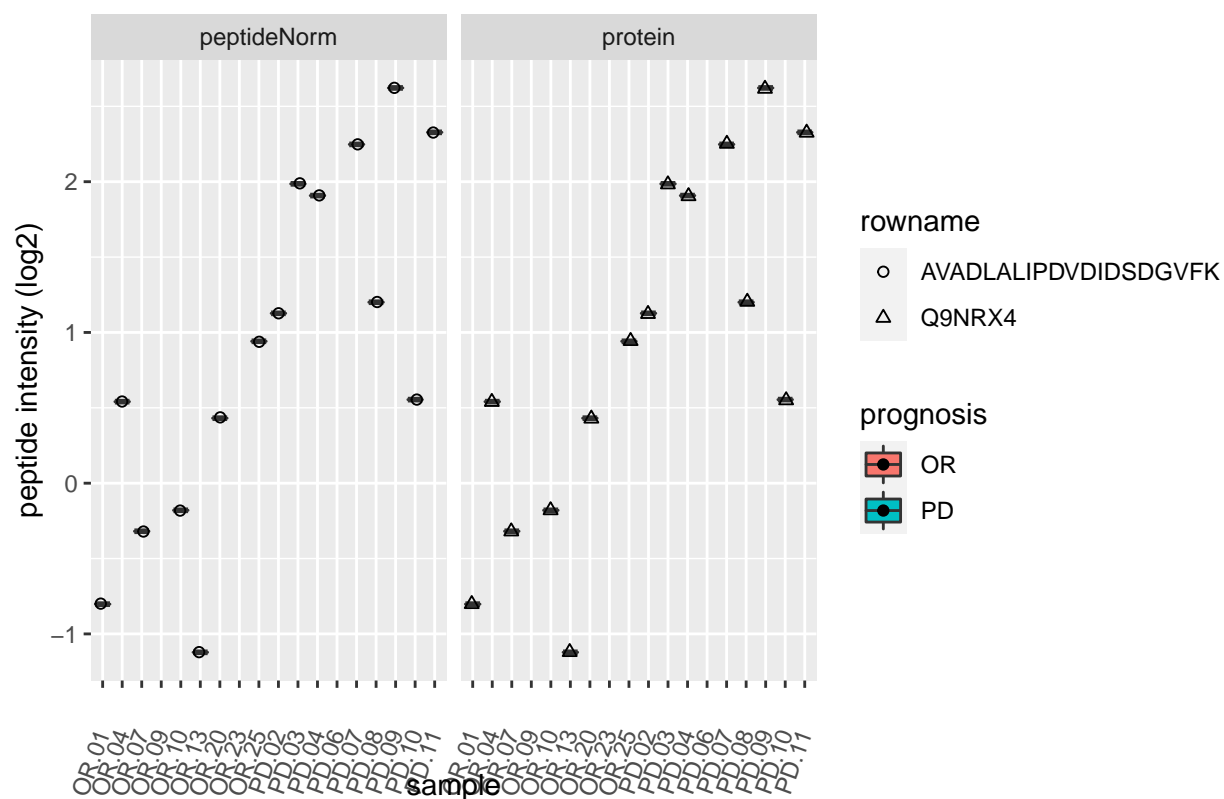




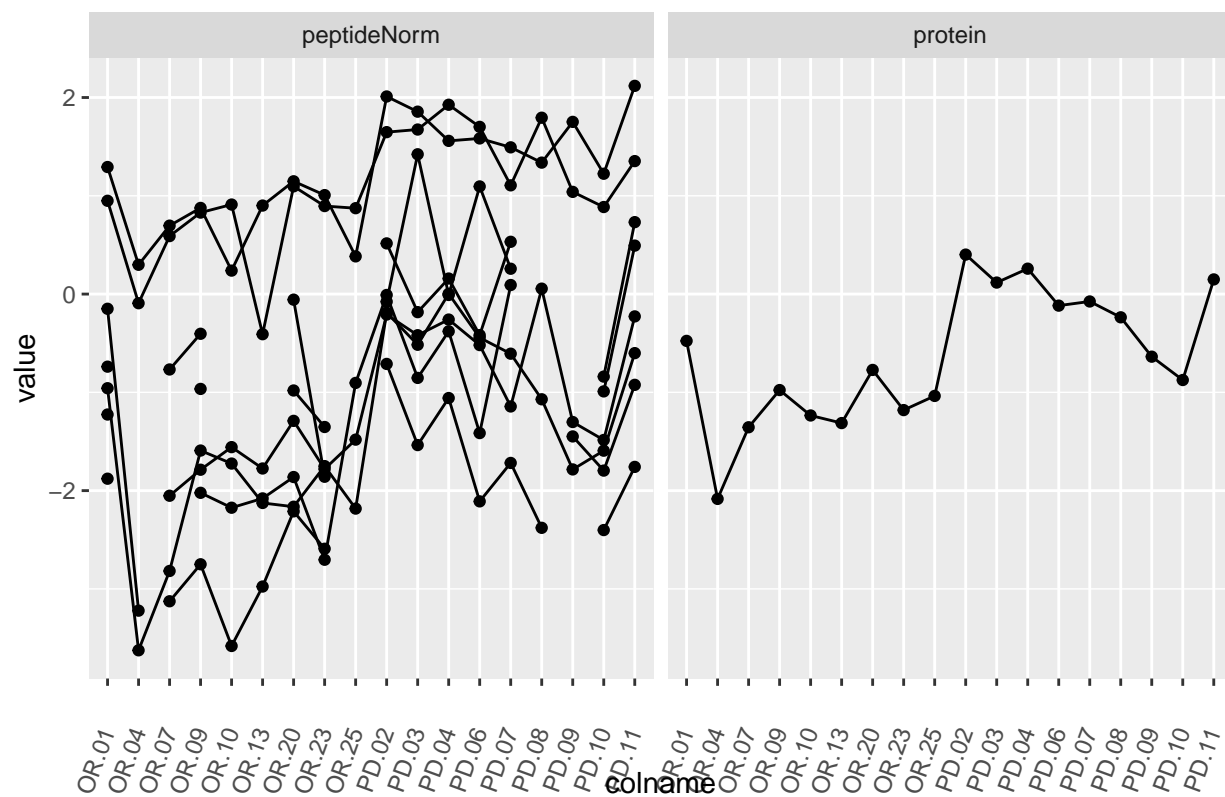
Q9NRX4

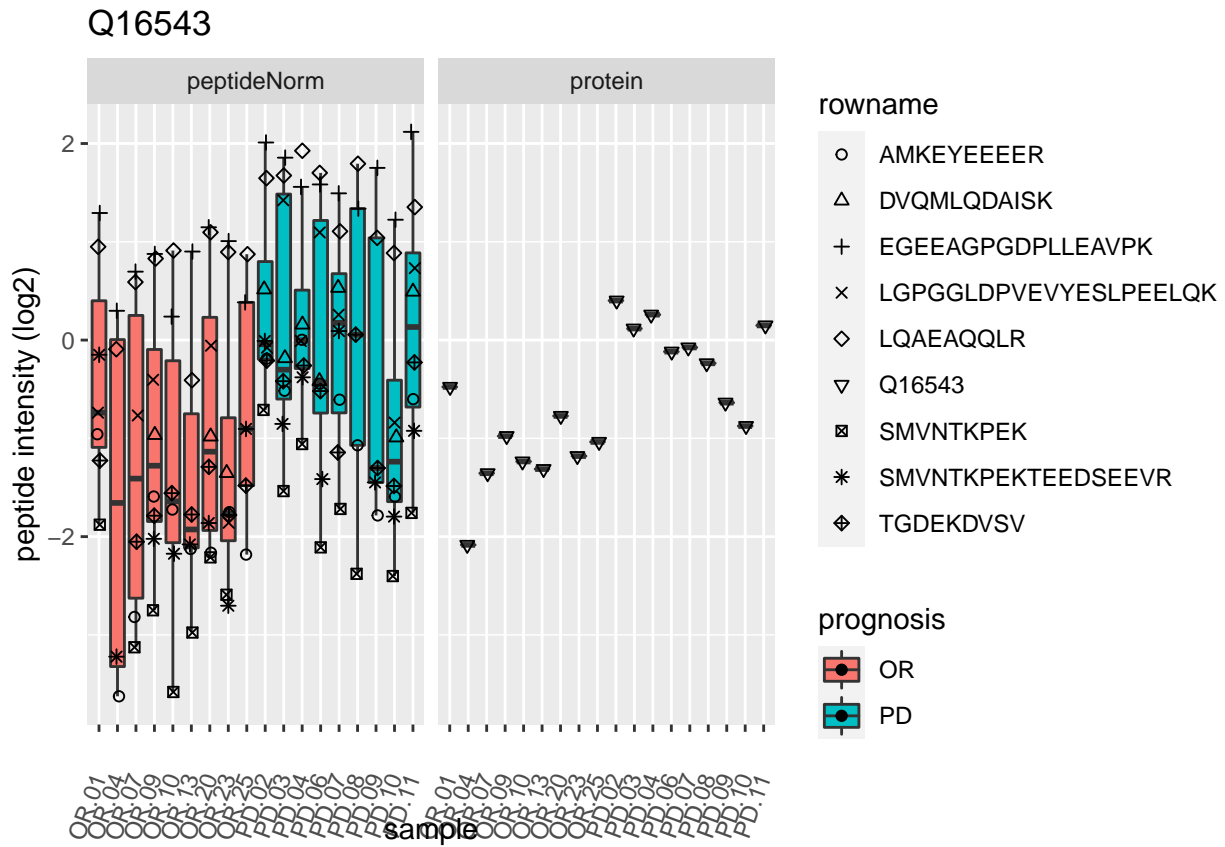


Q9NRX4



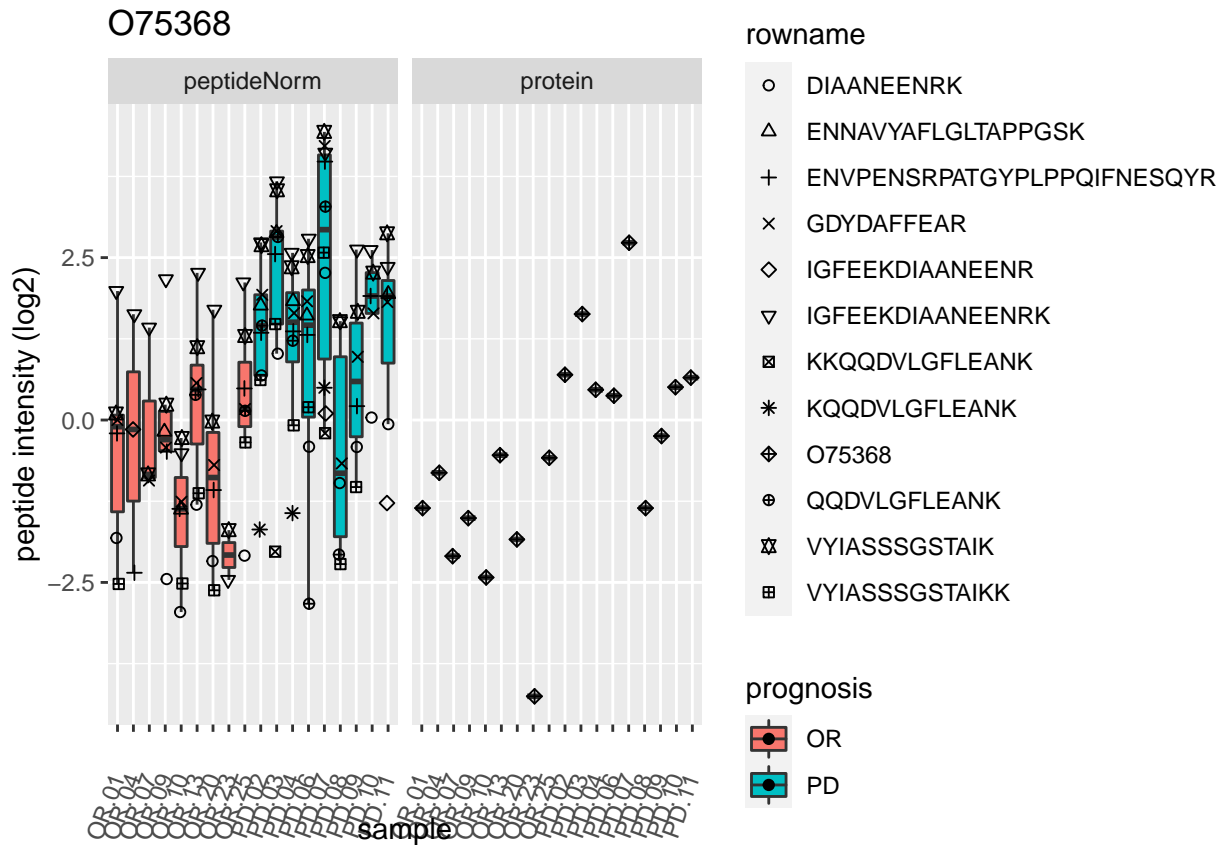
Q16543





O75368

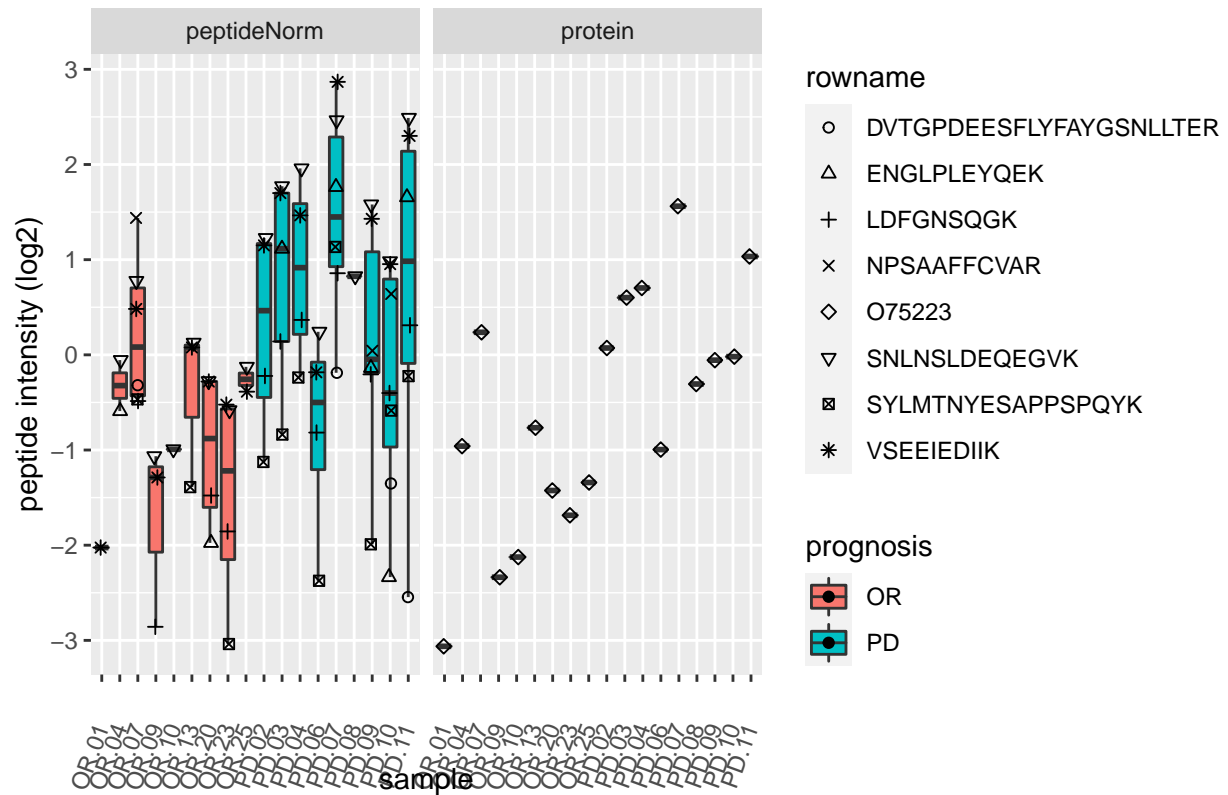




O75223



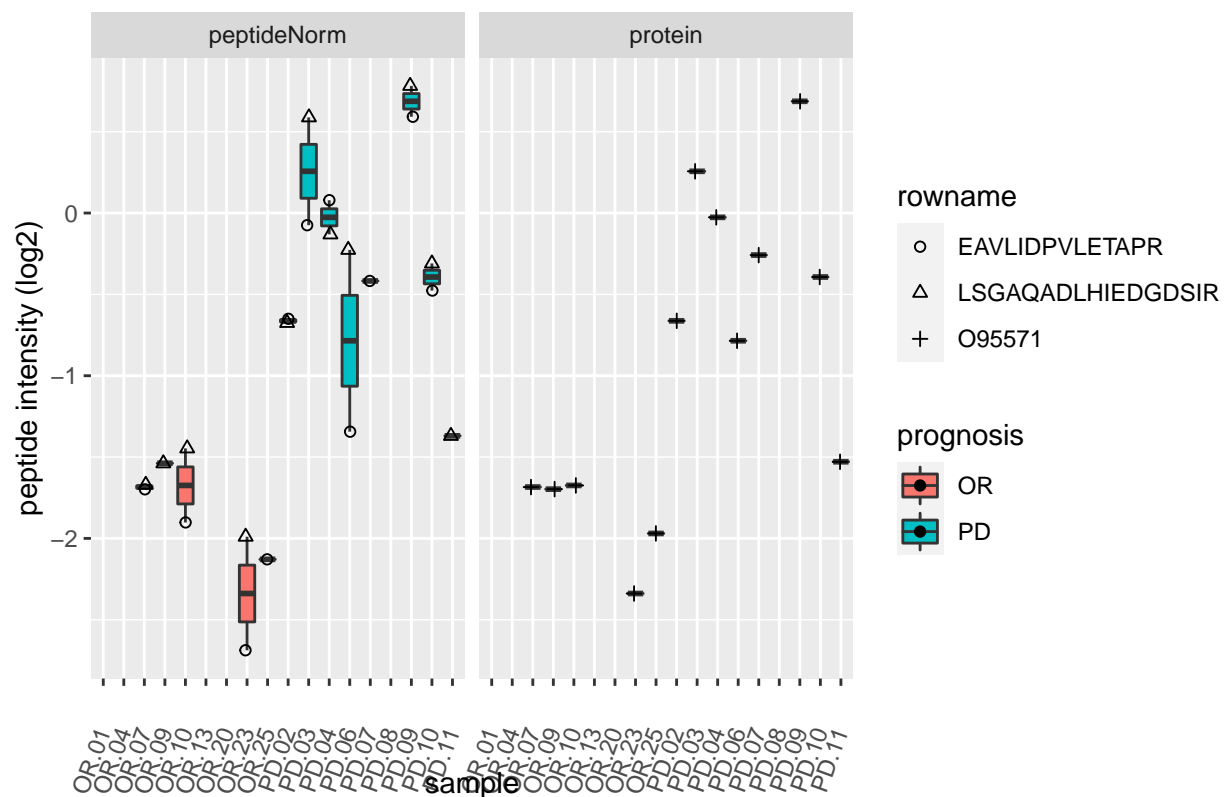
O75223



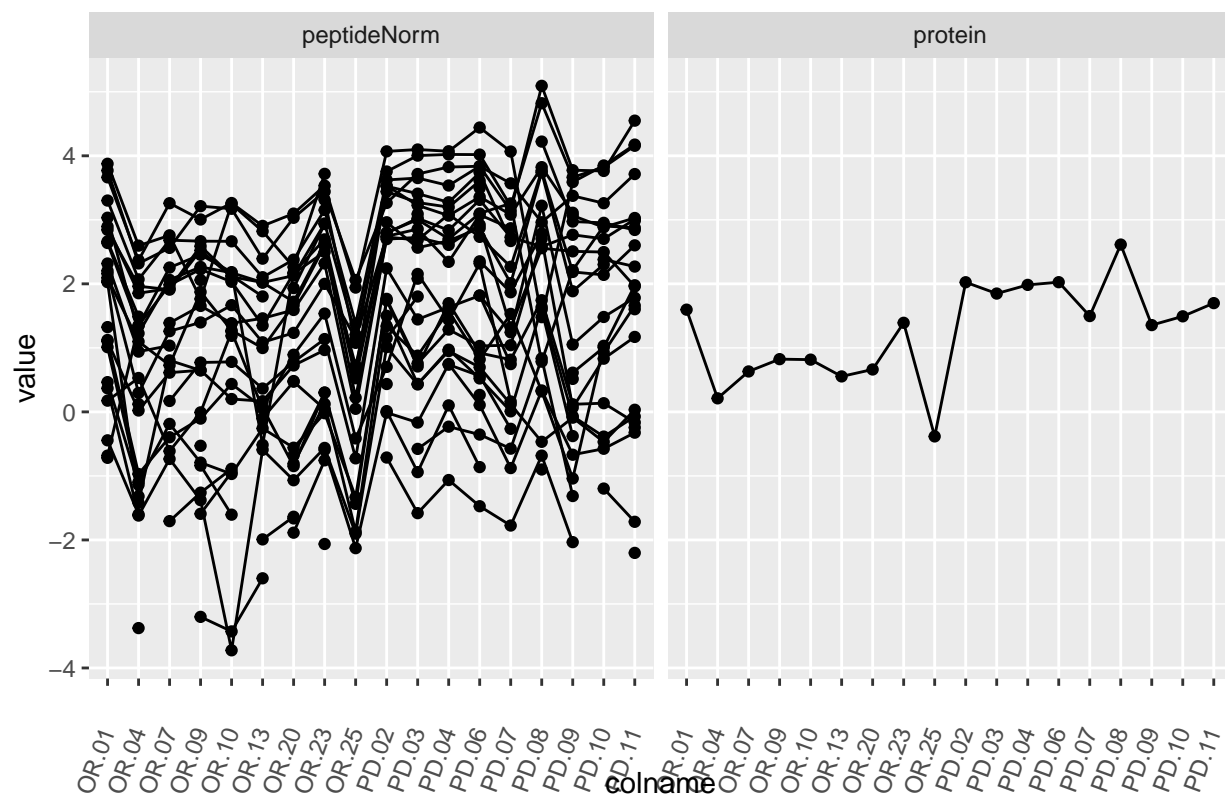
O95571

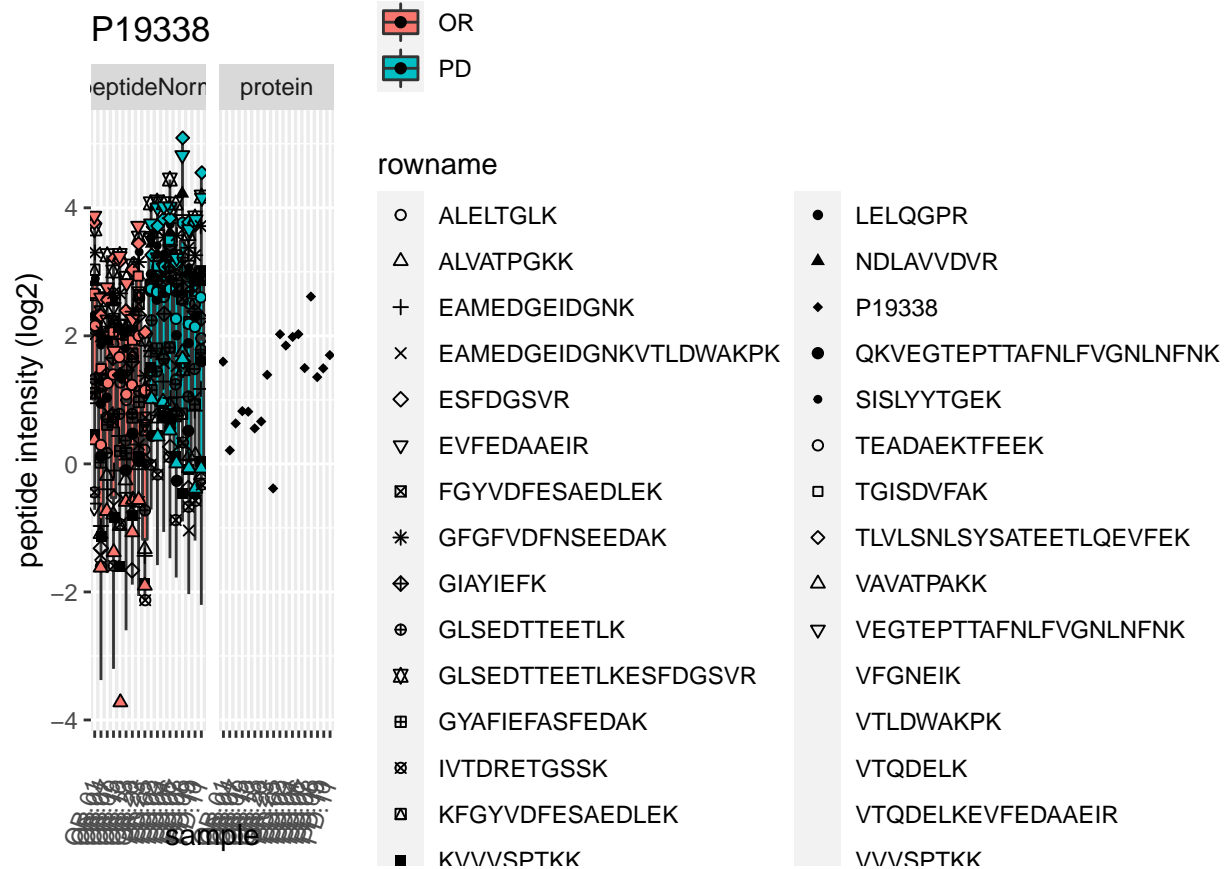


O95571



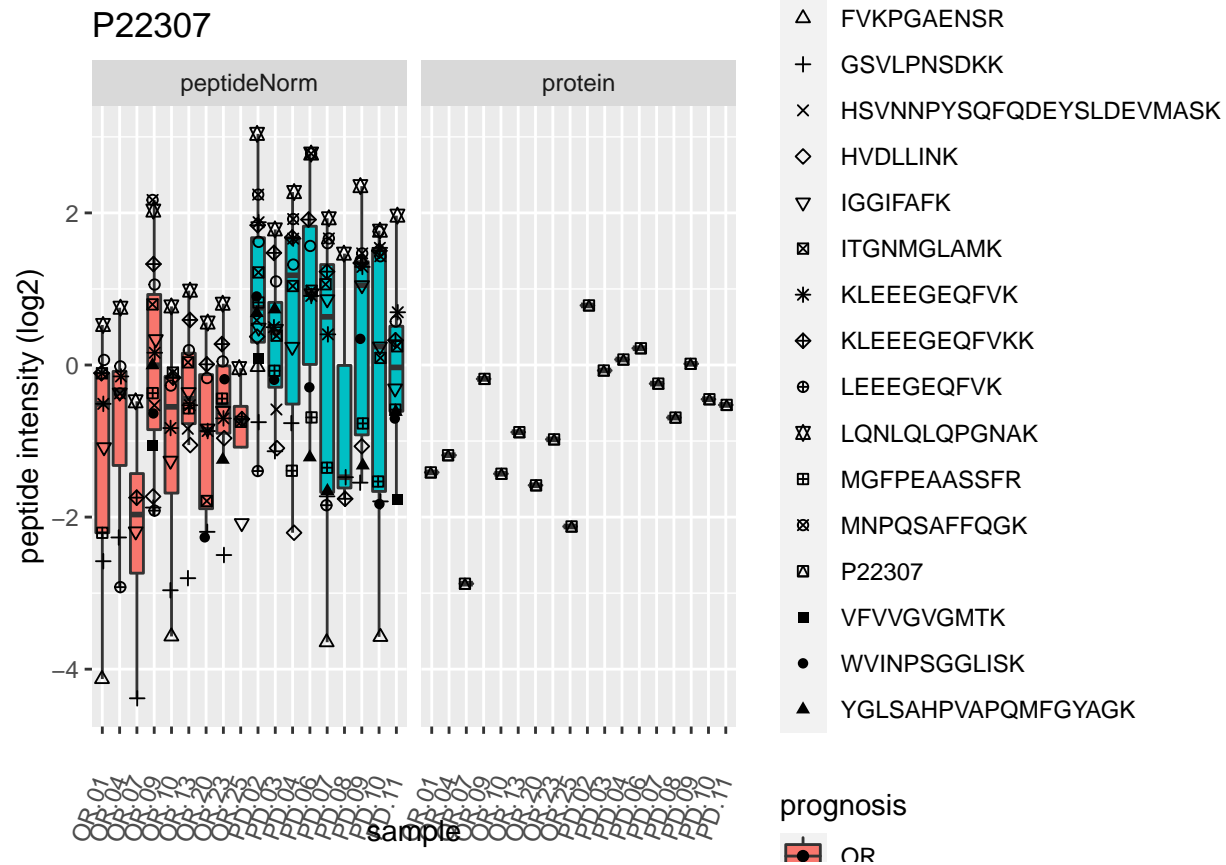
P19338



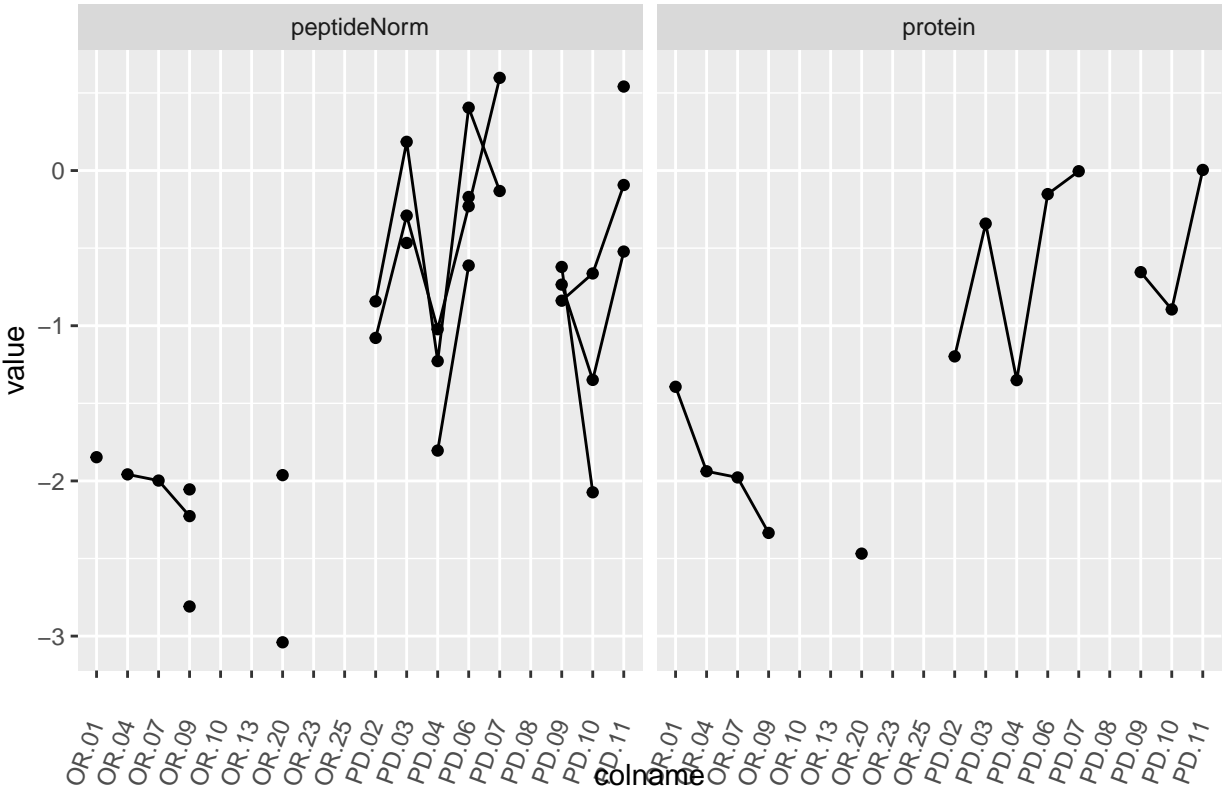


P22307

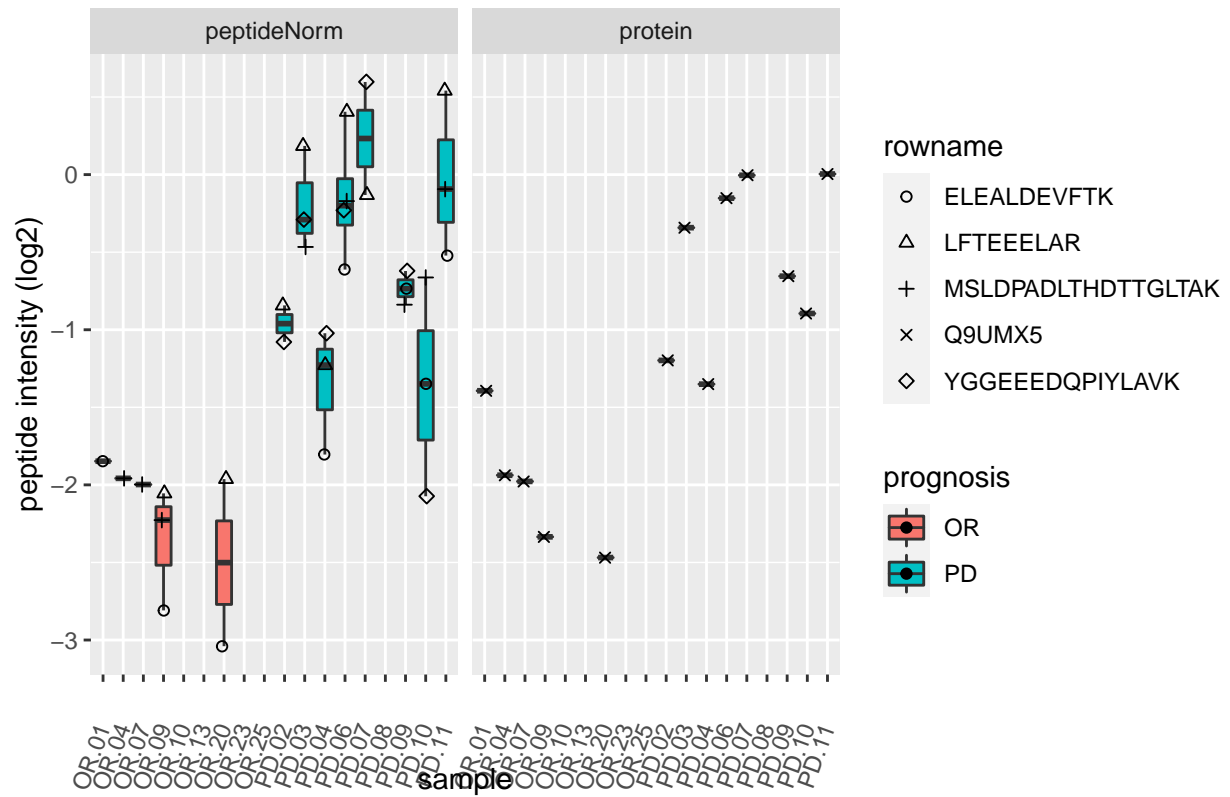




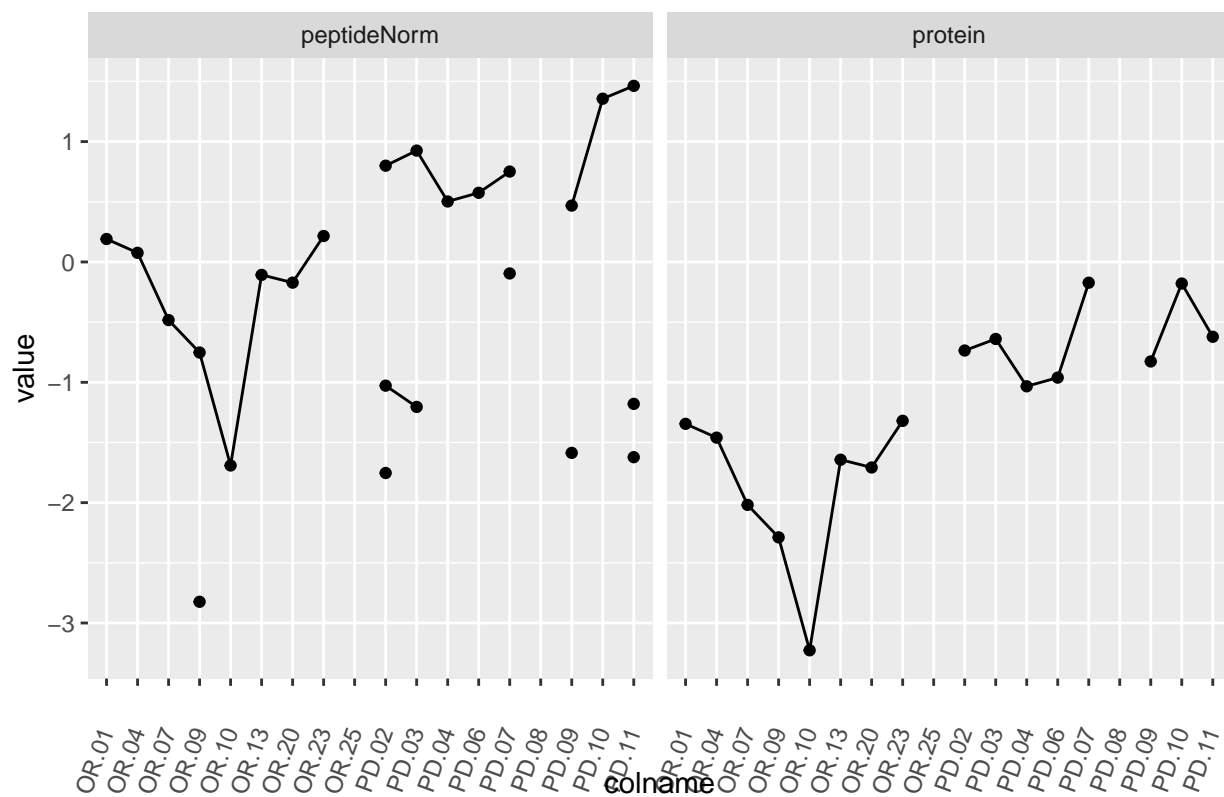
Q9UMX5



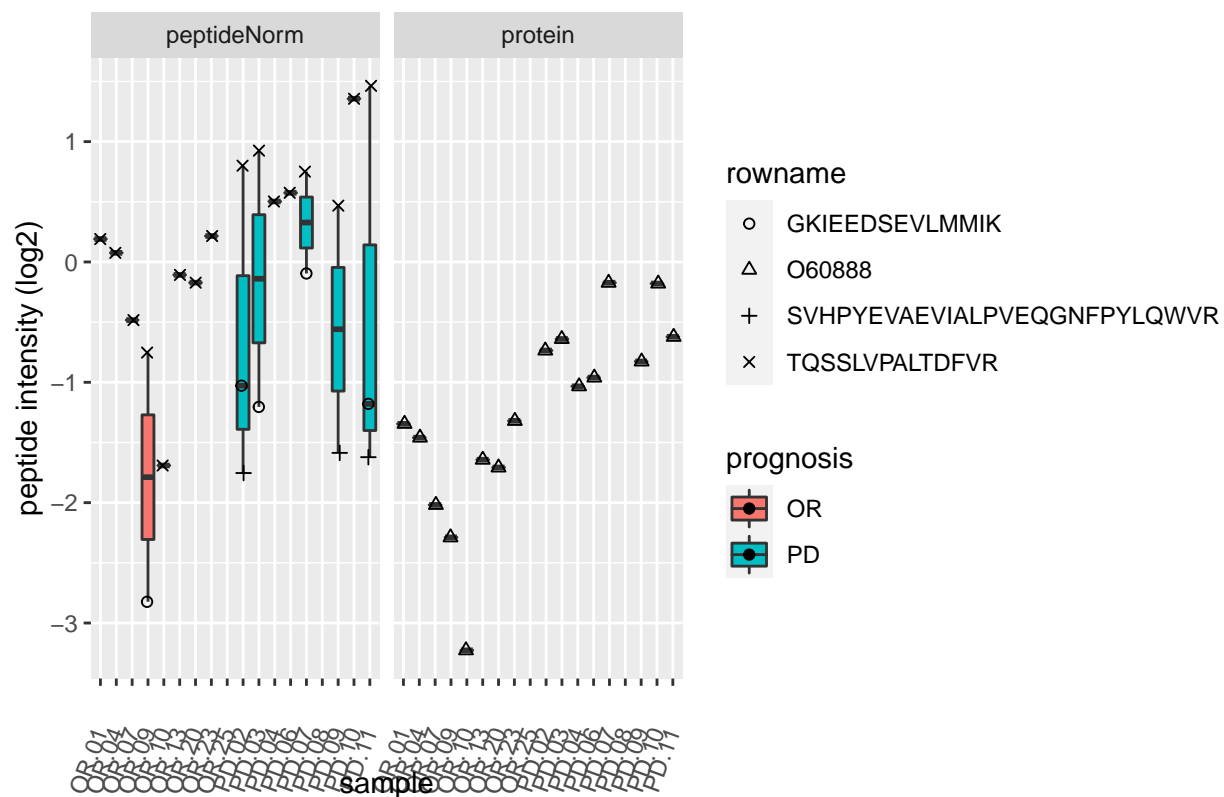
Q9UMX5



O60888



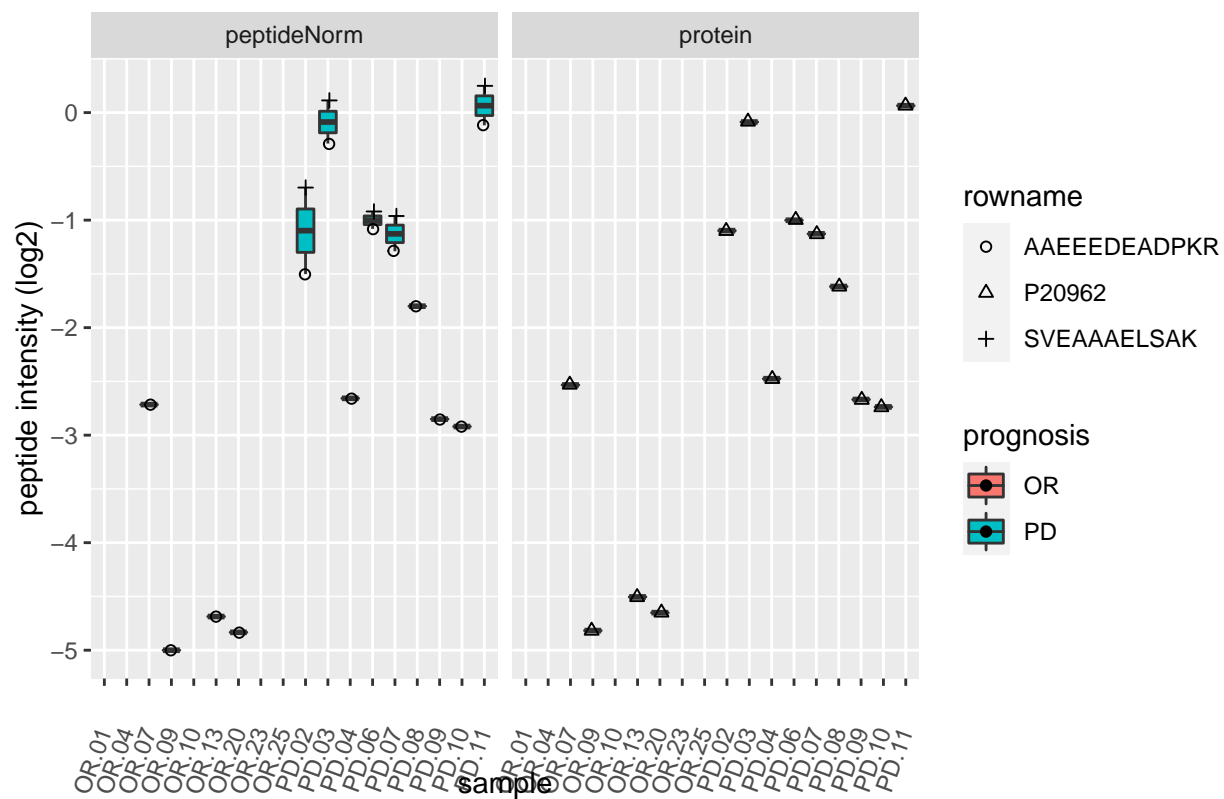
O60888



P20962



P20962



Q14980

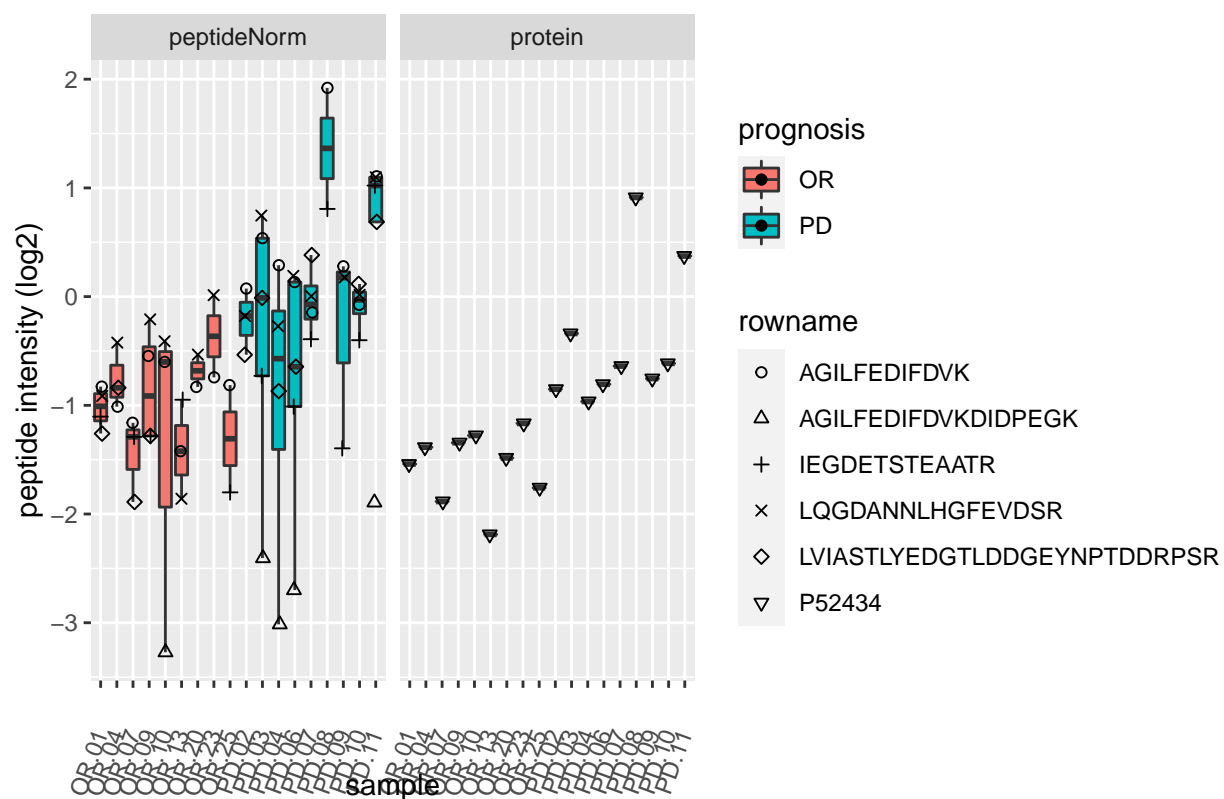


Z	%	HLTAQVR	7	LGSPDYGNSALLSLPGYRPTTR	I	QELTSQ
	&	HQVEQLSSSLK	8	LLQAETASNSAR	J	QEQHE/
	'	HREELEQSK	9	LPPKVESLESLYFTPIPAR	K	QFCSTC
	(IATTASAATAAAIGATPR	:	LQAQLNELQAQLSQK	L	QFLEVE
\R)	IHGTEEGQQILK	:	LQNALNEQR	M	QLEALE
	*	INQLSEENGDLFSK	<	LQQLGEAHQAETEVLR	N	QPEWLE
\AGR	+	IQAELAVILK	=	LQQLGEAHQAETEVLR	O	QQEQAI
SEAAGR	,	KHPSSPECLVSAQK	>	LSQLEEHLSQLQDNPPQEK	P	QQLSSL
IQEQASQGLR	-	KINQLSEENGDLFSK	?	LTAQVASLTSELTTLNATIQQDQELAGLK	Q	QQNELA
ESECEQLVK	·	KLDVEEPDSANSSFYSTR	@	LTAQVEQLEVFQR	R	QQNQEI
fMR	/	KNSLISSLEEEVSILNR	A	LVMAESEK	S	RSQAG\
	0	KQQNQELQEQLR	B	MTMLLLYHSTMSSK	T	SAPASQ
	1	KVEELQACVETAR	C	NSLISSLEEEVSILNR	U	SLEAQV
STQALVSELLPAK	2	LADDLSTLQEK	D	PSLSLGTITDEEMK	V	SLVEQH
	3	LALLNEK	E	Q14980	W	SNRDEL
EDLENFLQK	4	LDFVCSFLQK	F	QAQLAQTLLQQEQASQGLR	X	SNRDEL

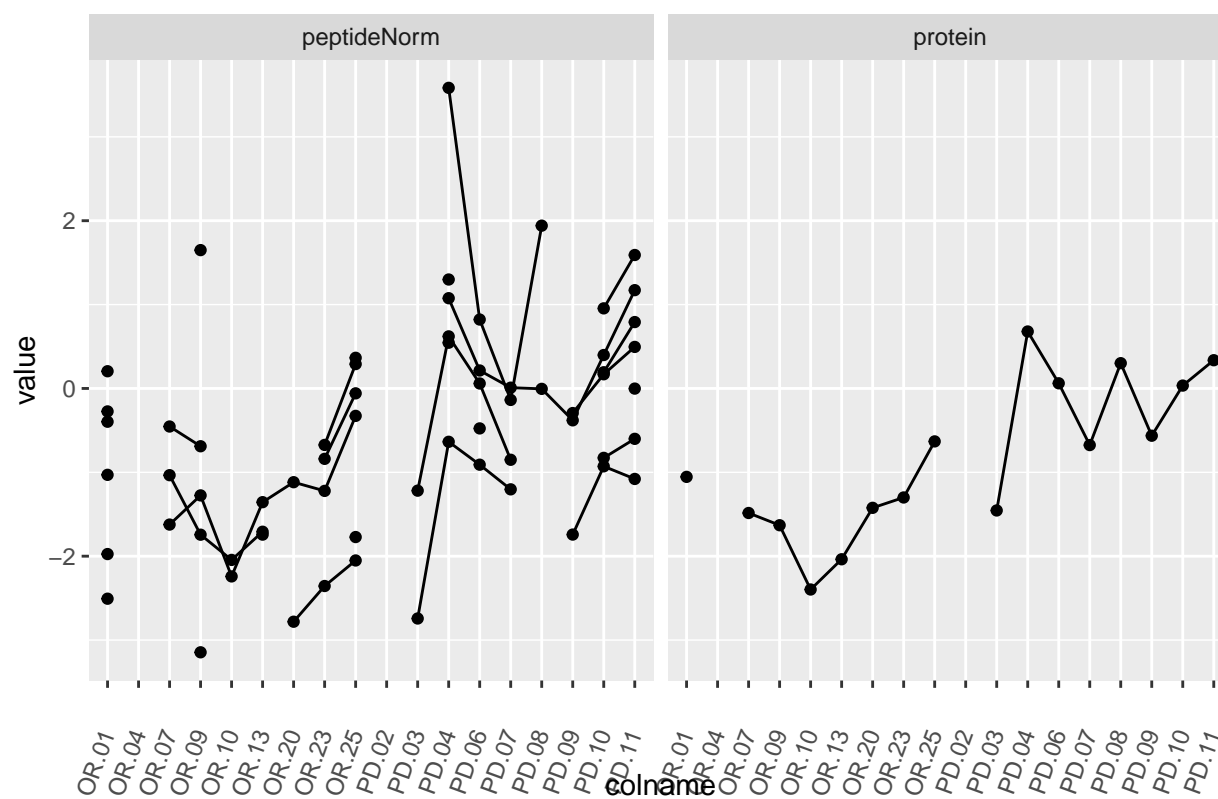
P52434



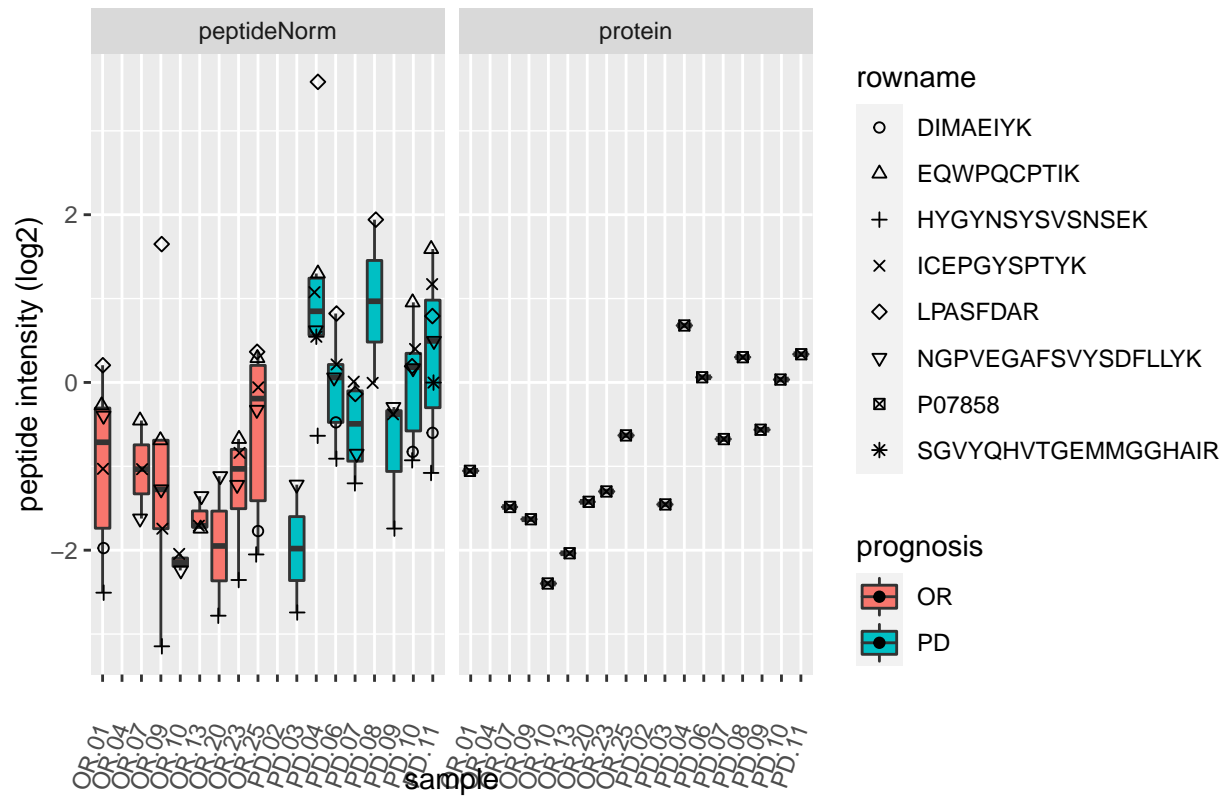
P52434



P07858



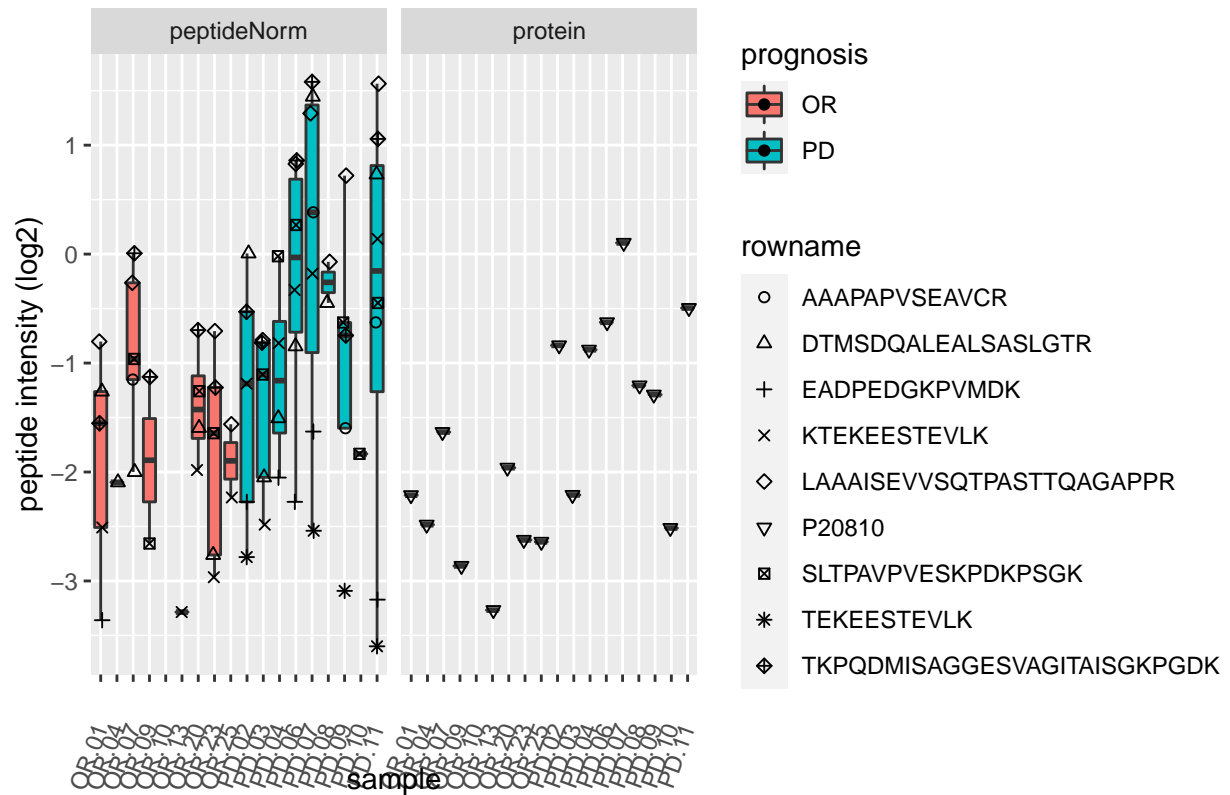
P07858



P20810



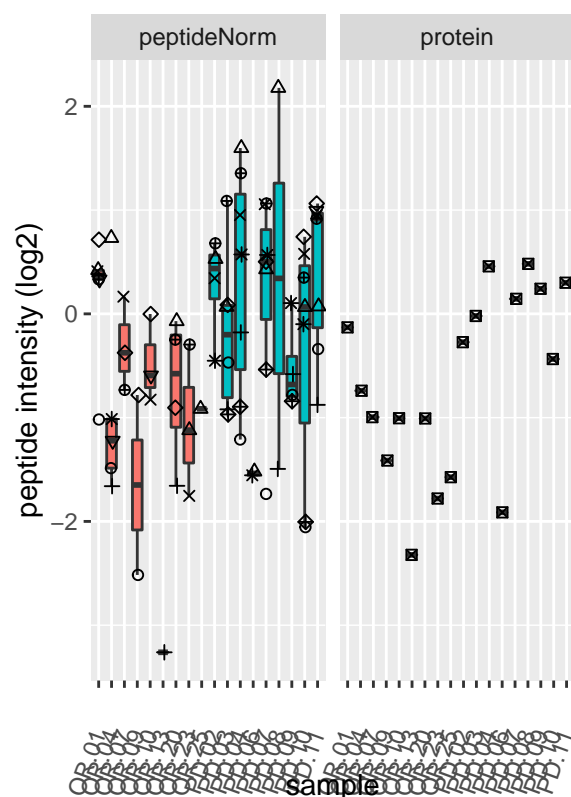
P20810



P22061



P22061

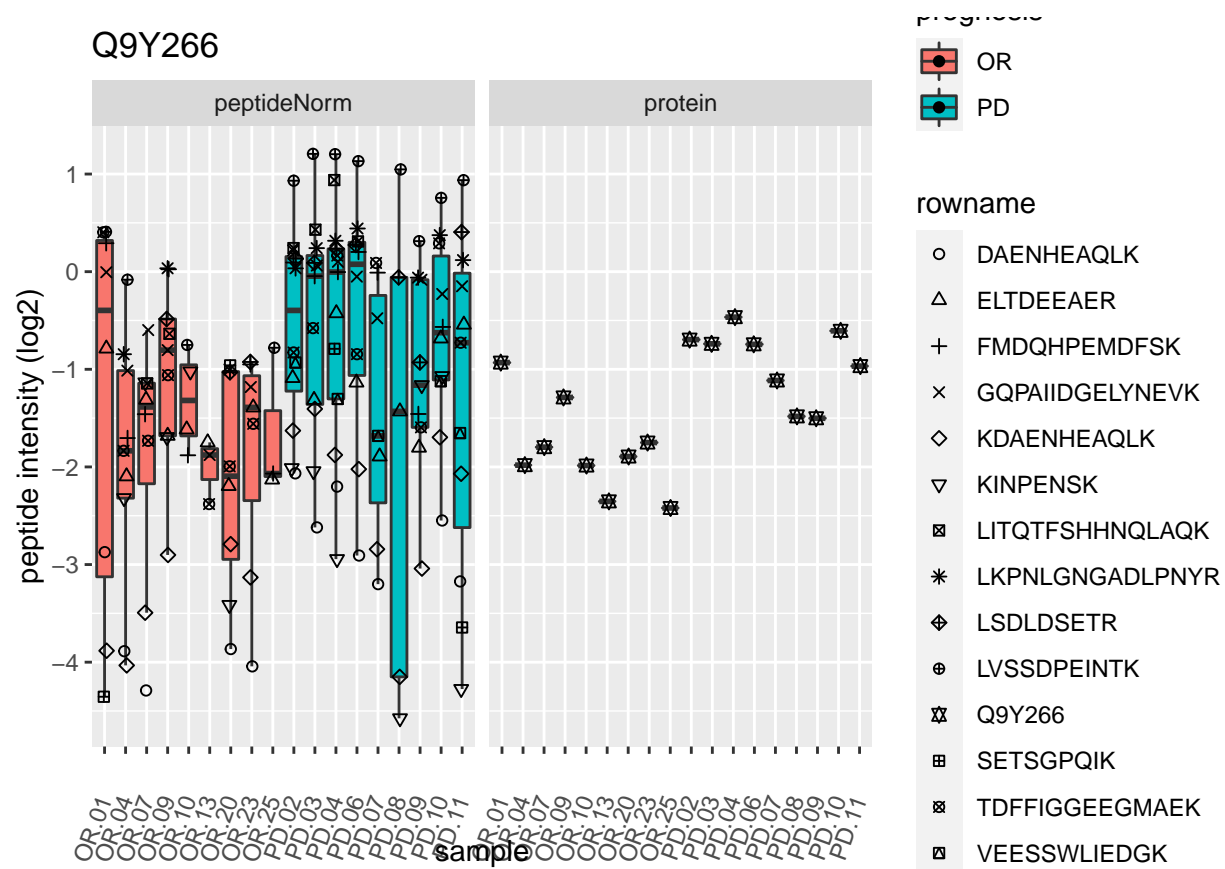


rowname

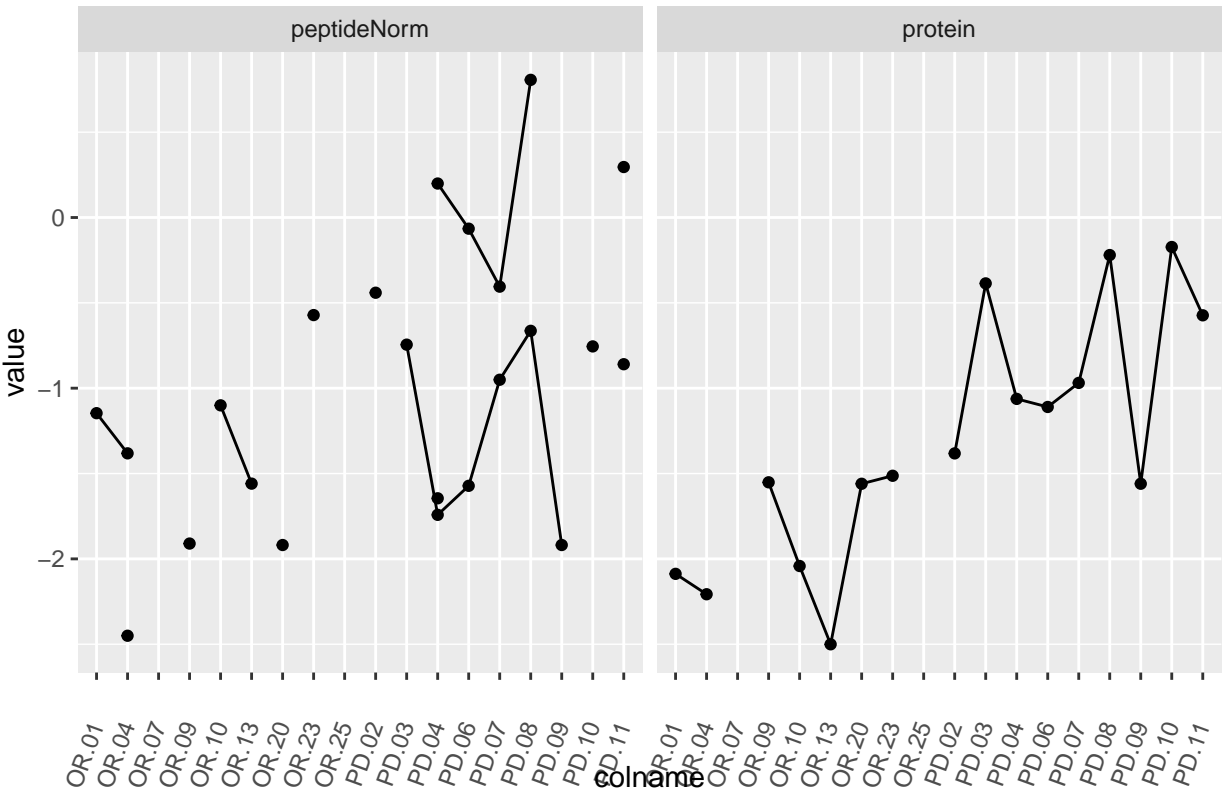
- ALDVGSGSGILTACFAR
- △ ELVDDSVNNVR
- + KDDPTLLSSGR
- × LILPVGPAAGNQMLEQYDK
- ◇ LILPVGPAAGNQMLEQYDKLQDGSIK
- ▽ MGYAEEAPYDAIHVGAAAPVVPQALIDQLKPGGR
- ⊠ P22061
- * SGGASHSELIHNLR
- ⬠ VFEVMLATDR
- ⊕ VQLVVG DGR

Q9Y266

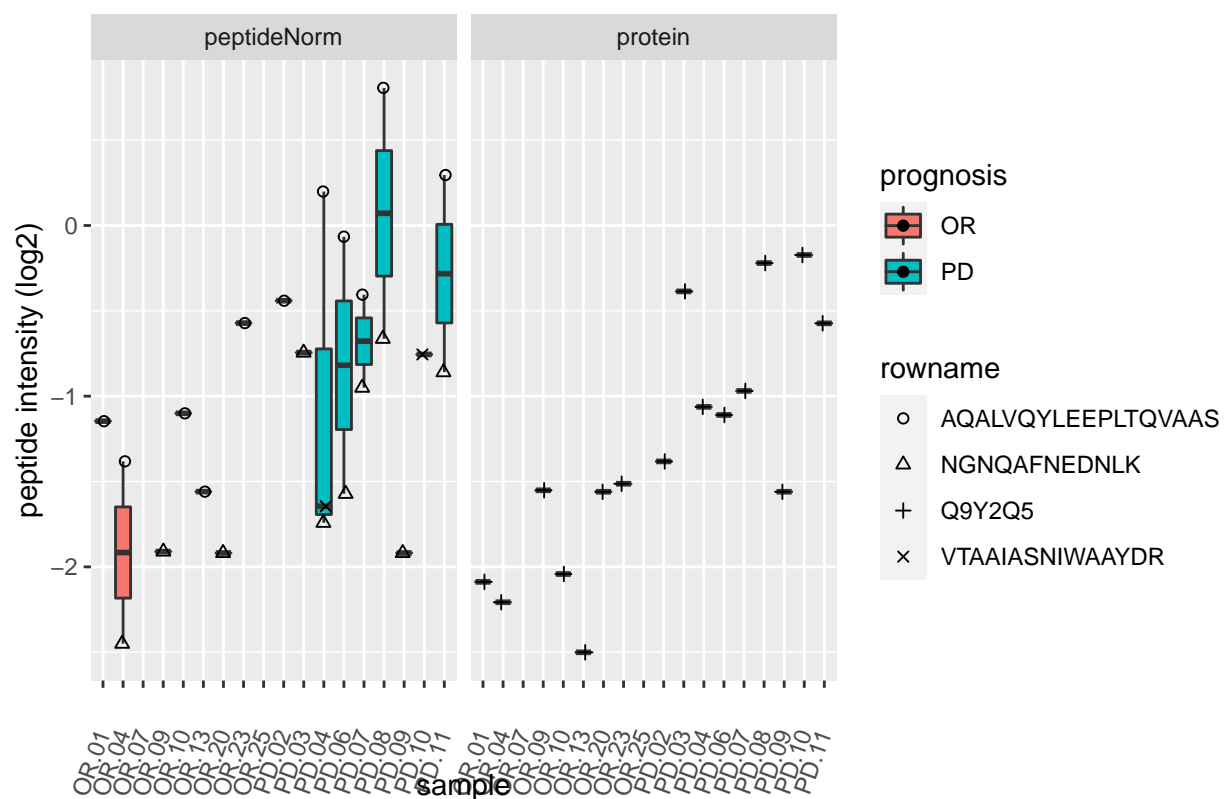




Q9Y2Q5

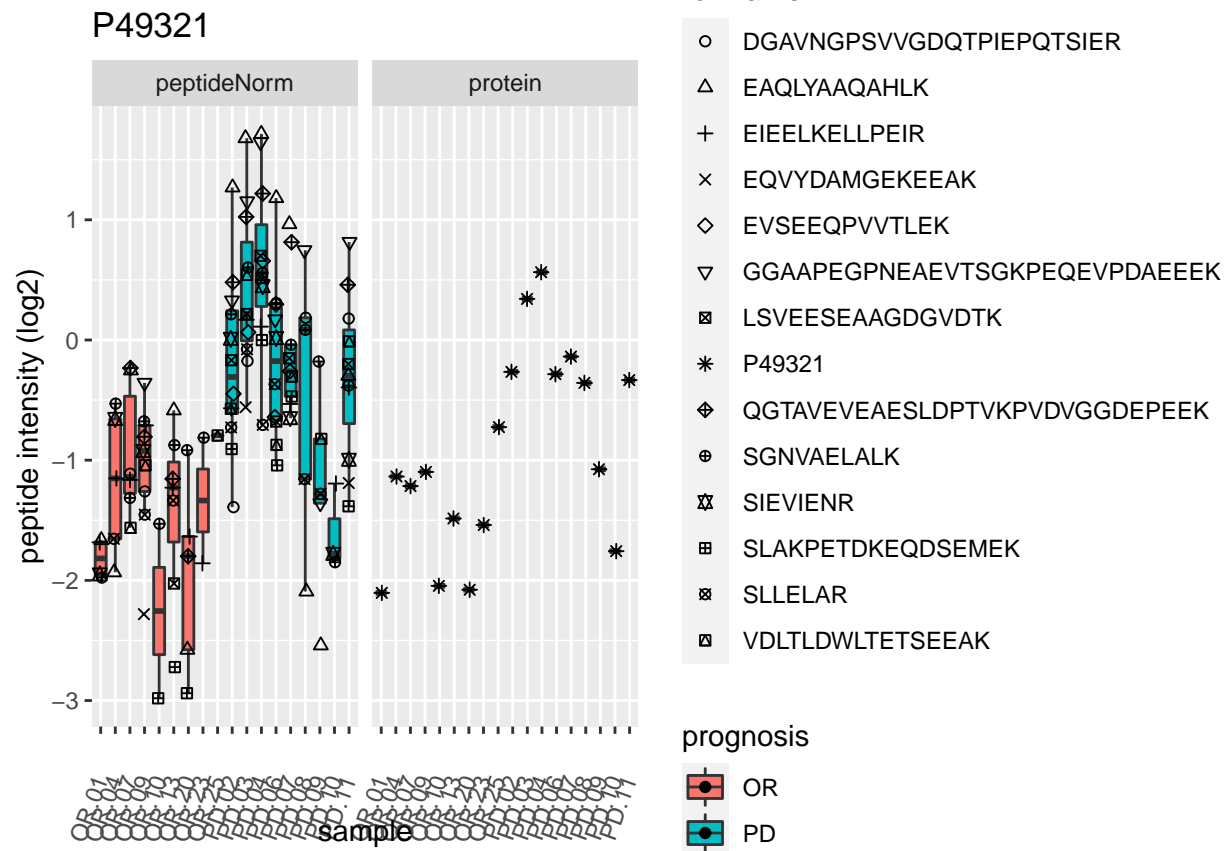


Q9Y2Q5



P49321

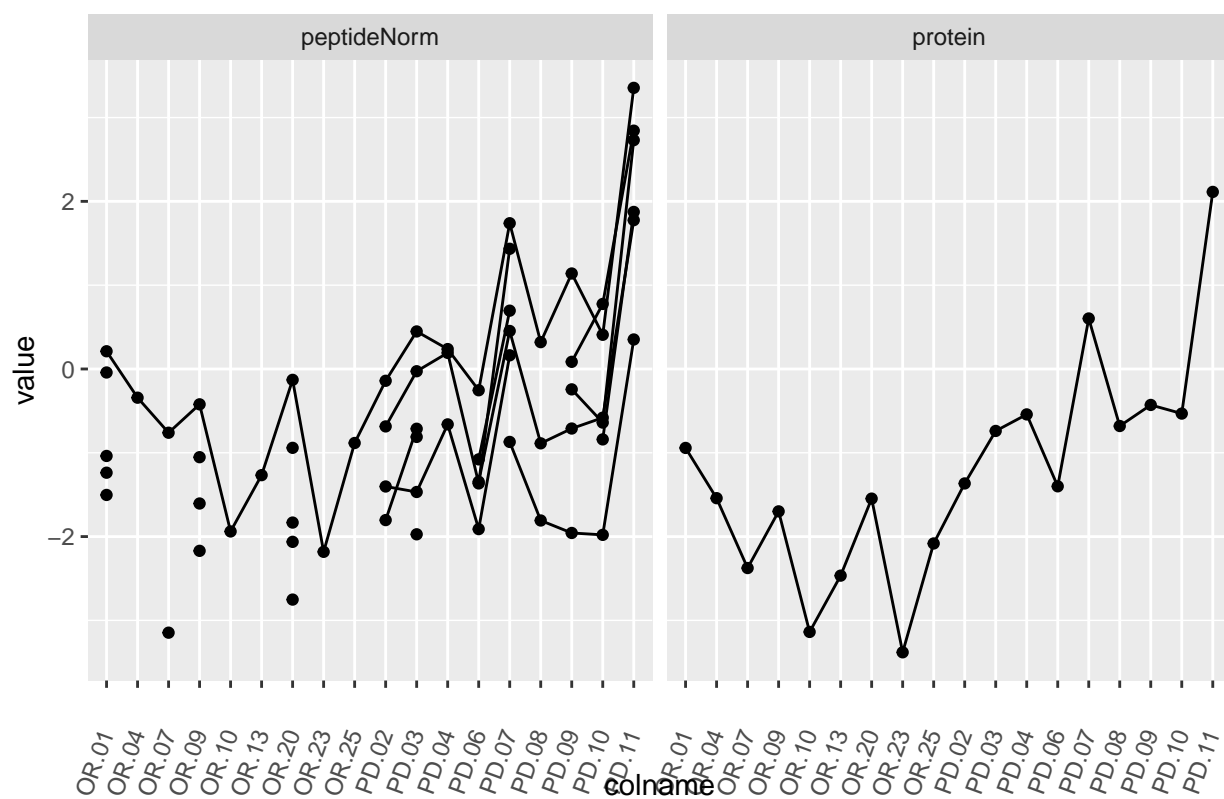




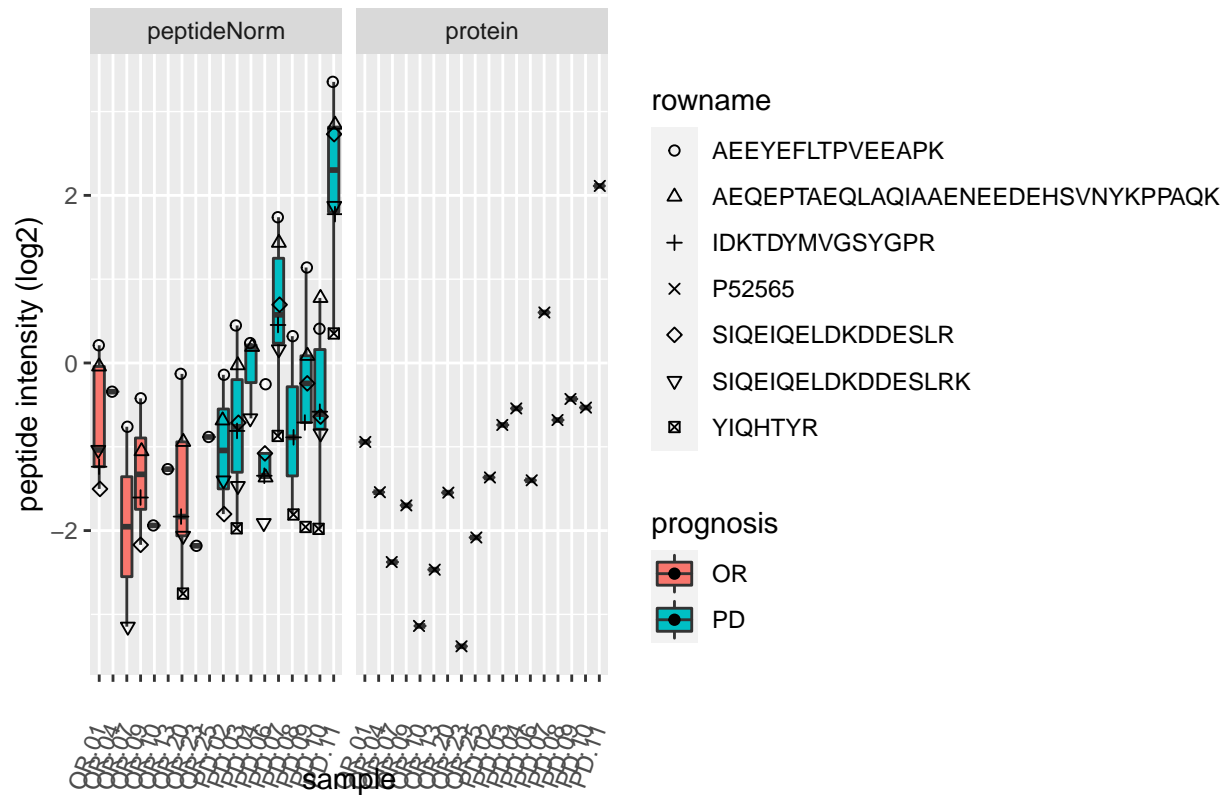
Q99497



P52565



P52565



P02787



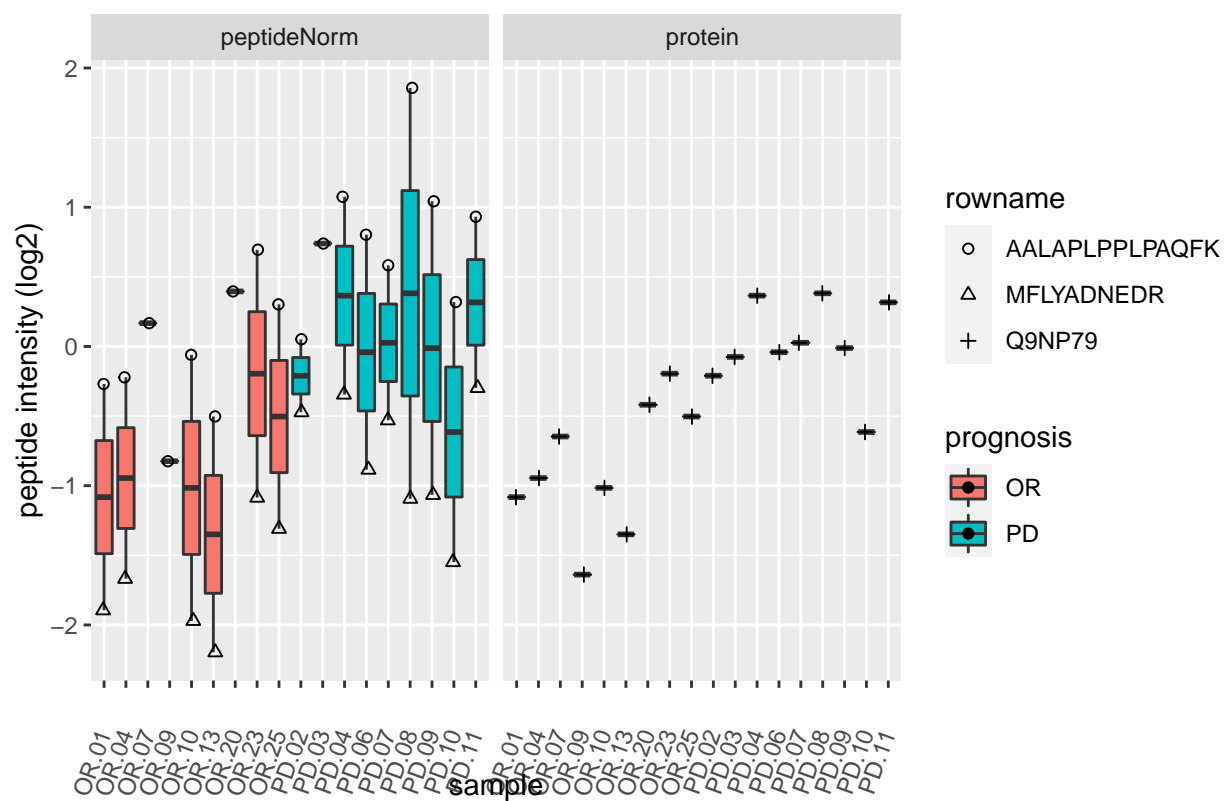


▽	IMINGLEADAMOLEDCSTVTAQR
△	KASYLDCIR
▽	KPVDEYKDCHLAQVPSHTVVAR
	KPVEEYANCHLAR
	LCMGSGNLNCEPNNK
	LKCDEWSVNSVGK
	MYLGYEYVTAIR
	NLNEKDYELLCLDGTR
	NPDPWAK
	P02787
!	SAGWNIPIGLLYCDLPEPR
"	SASDLTWDNLK
#	SKEFQLFSSPHGK
\$	SVIPSDGPSVACVK
%	TAGWNIPMGLLYNK
&	WCALSHHER
'	WCAVSEHEATK
(YLGEELYVK

Q9NP79



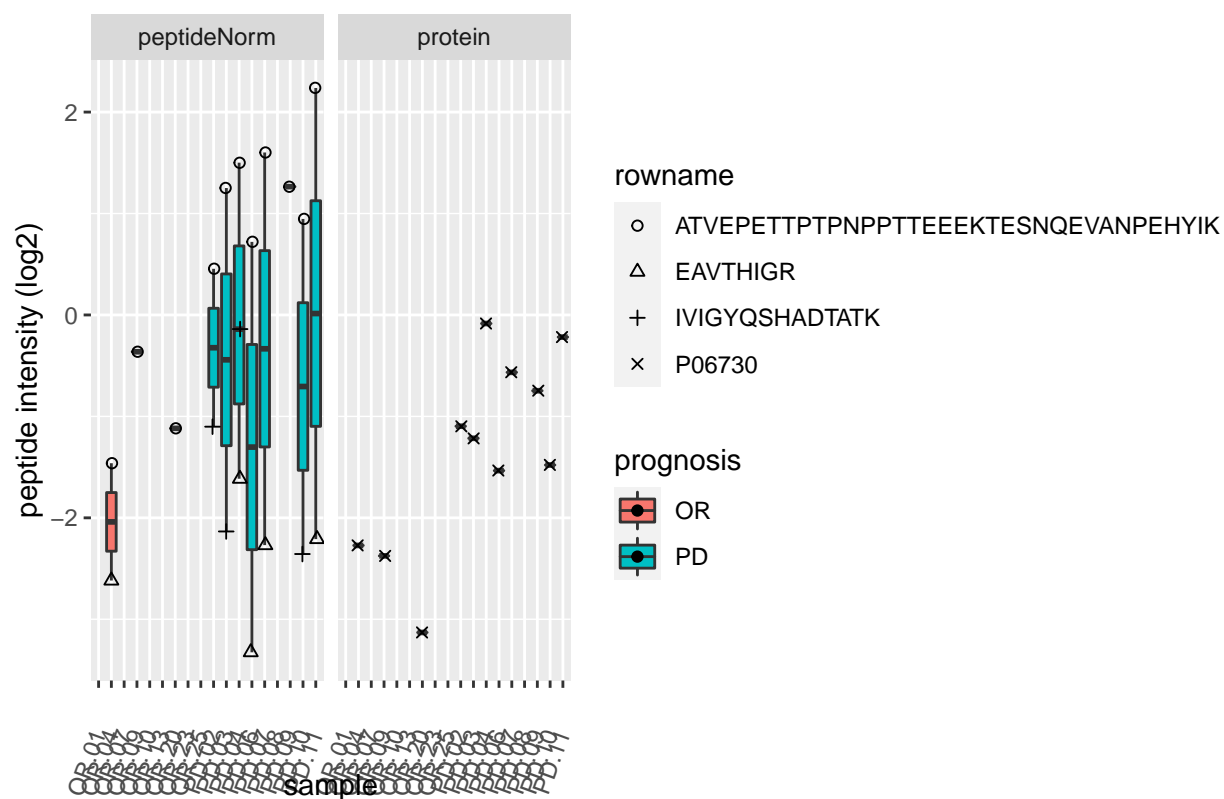
Q9NP79



P06730



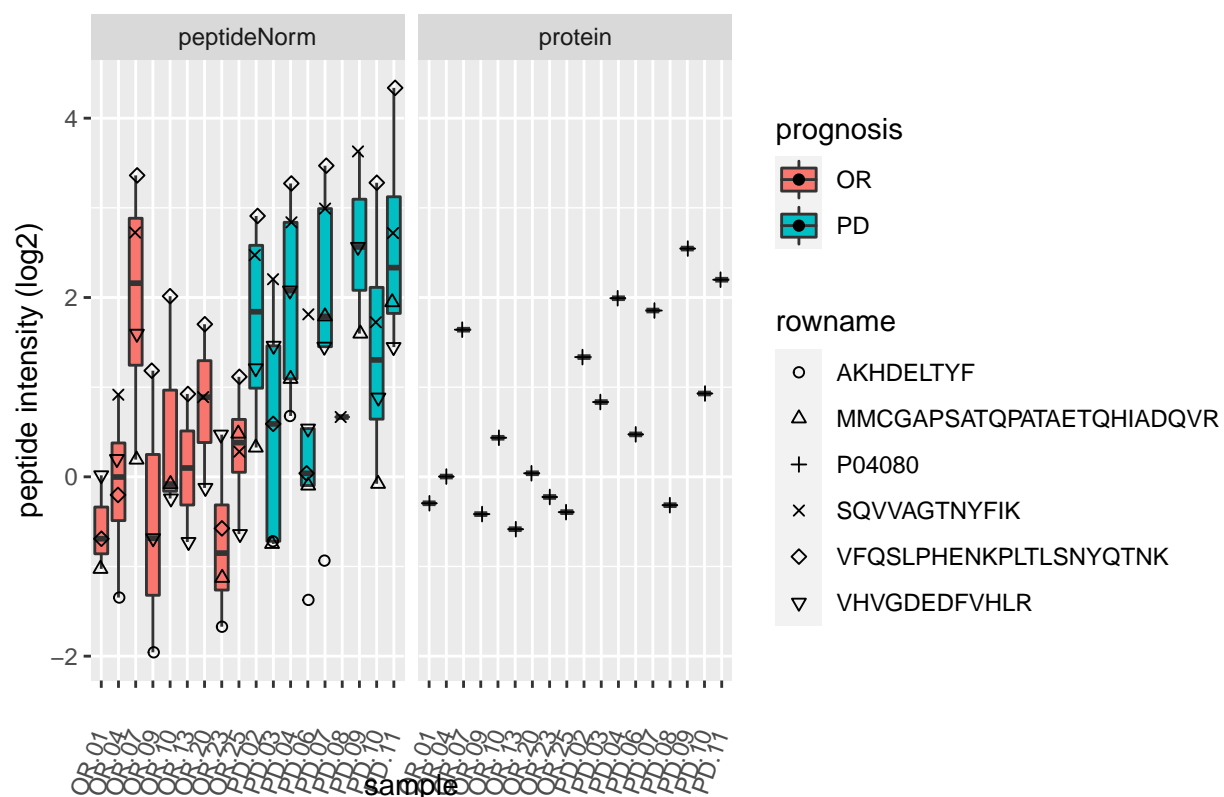
P06730



P04080



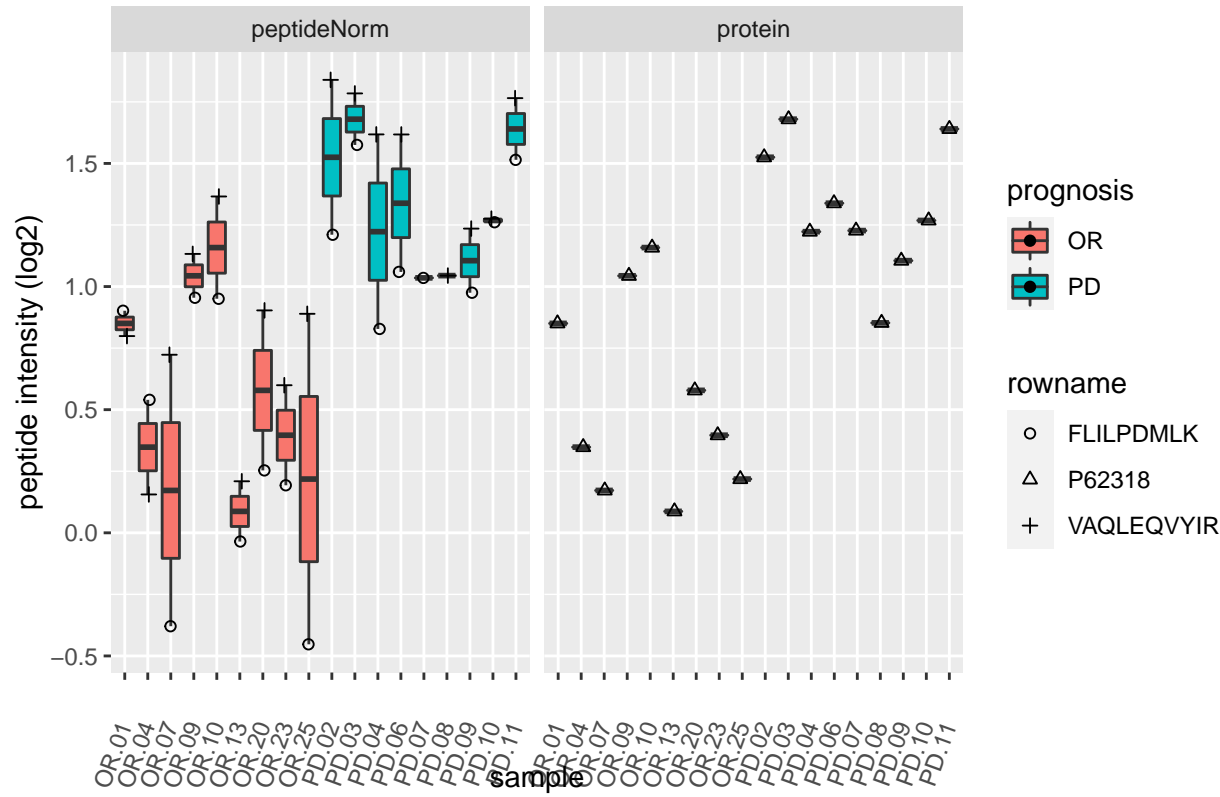
P04080



P62318

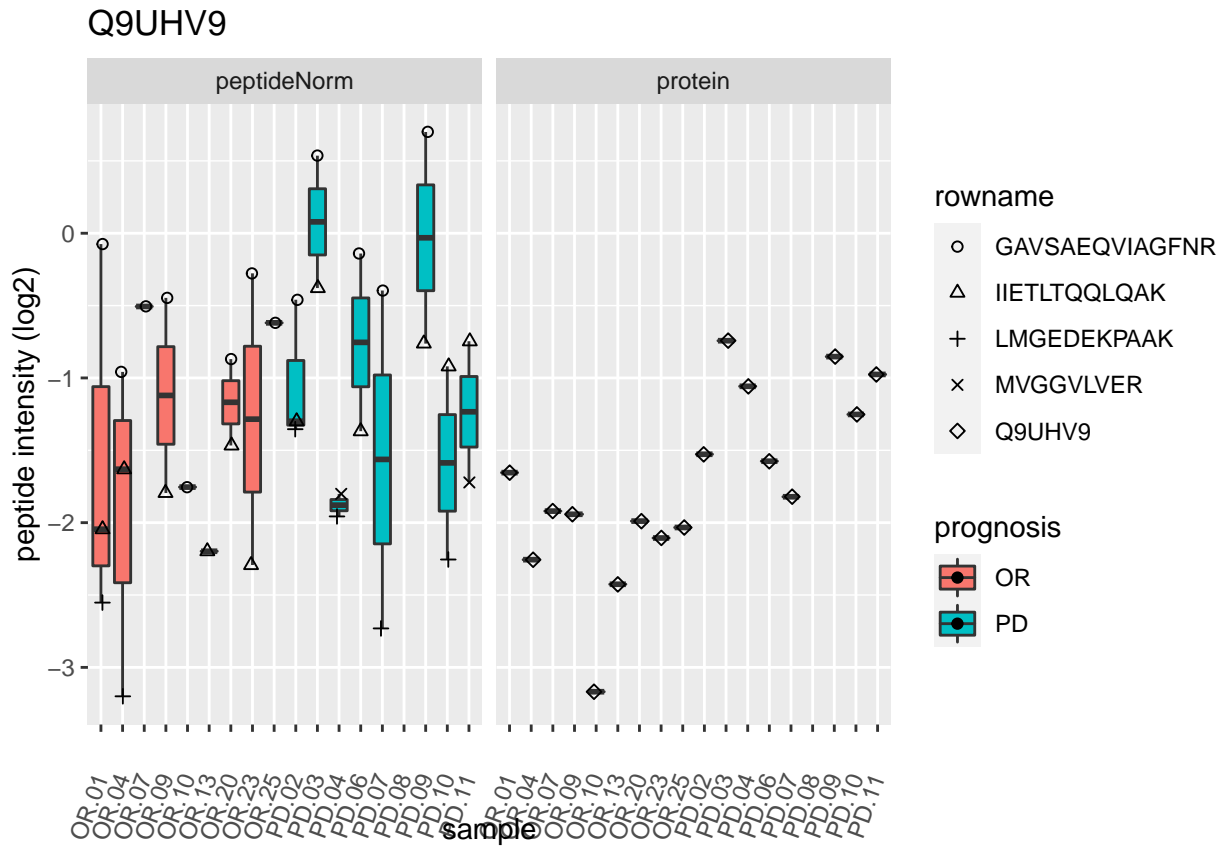


P62318



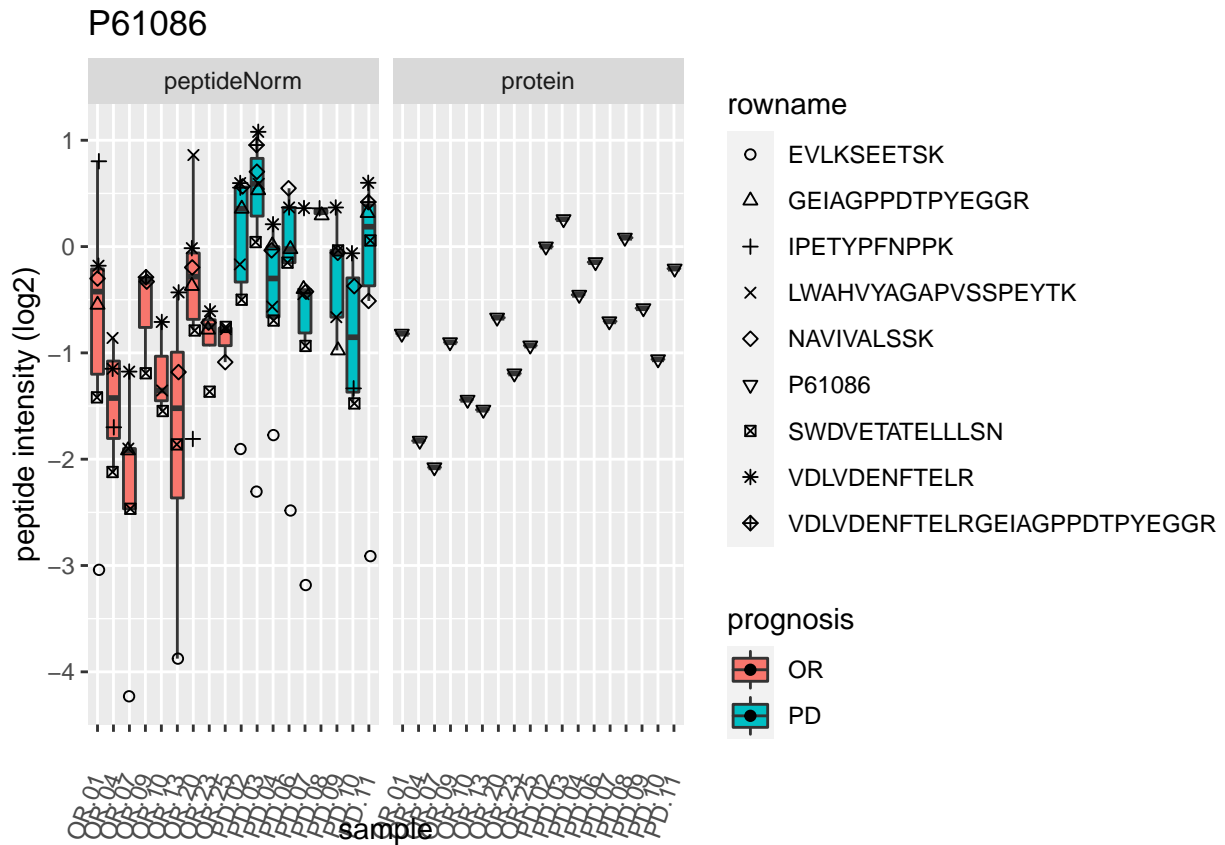
Q9UHV9





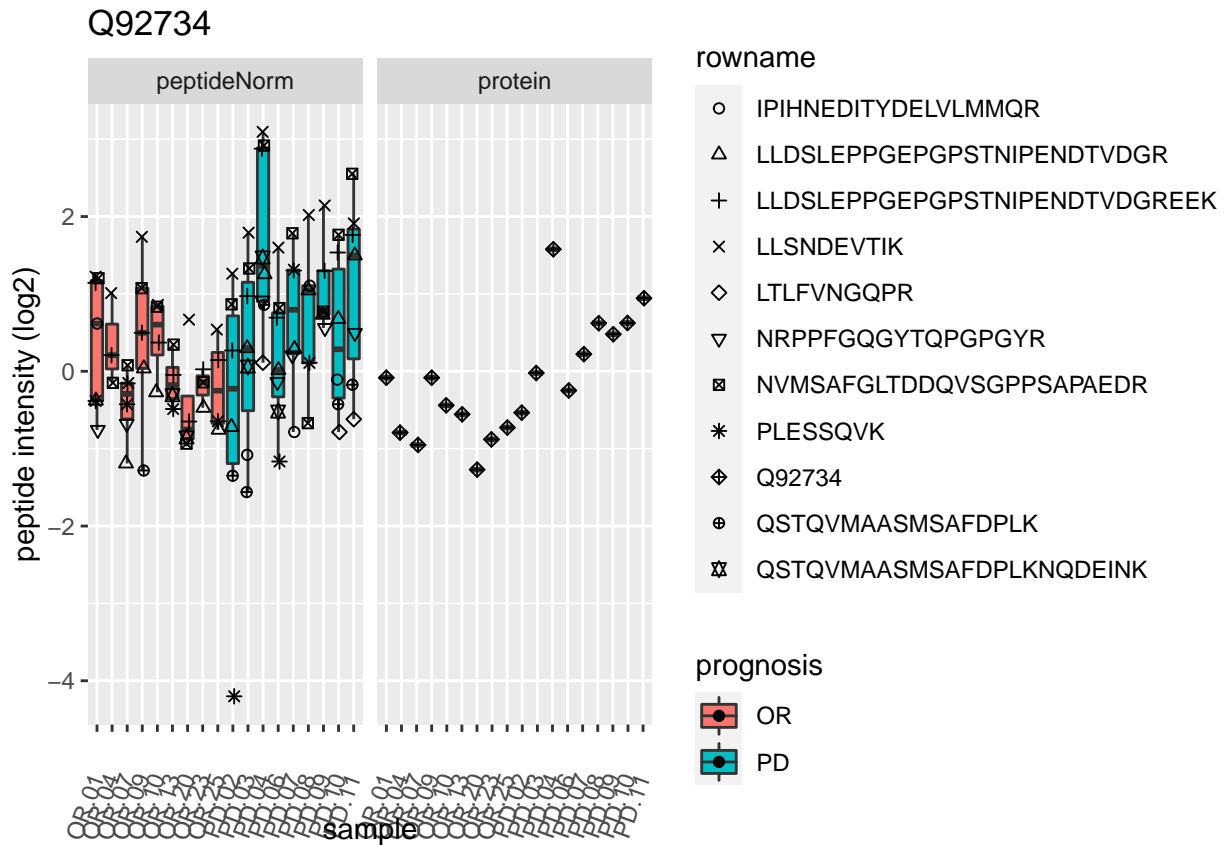
P61086



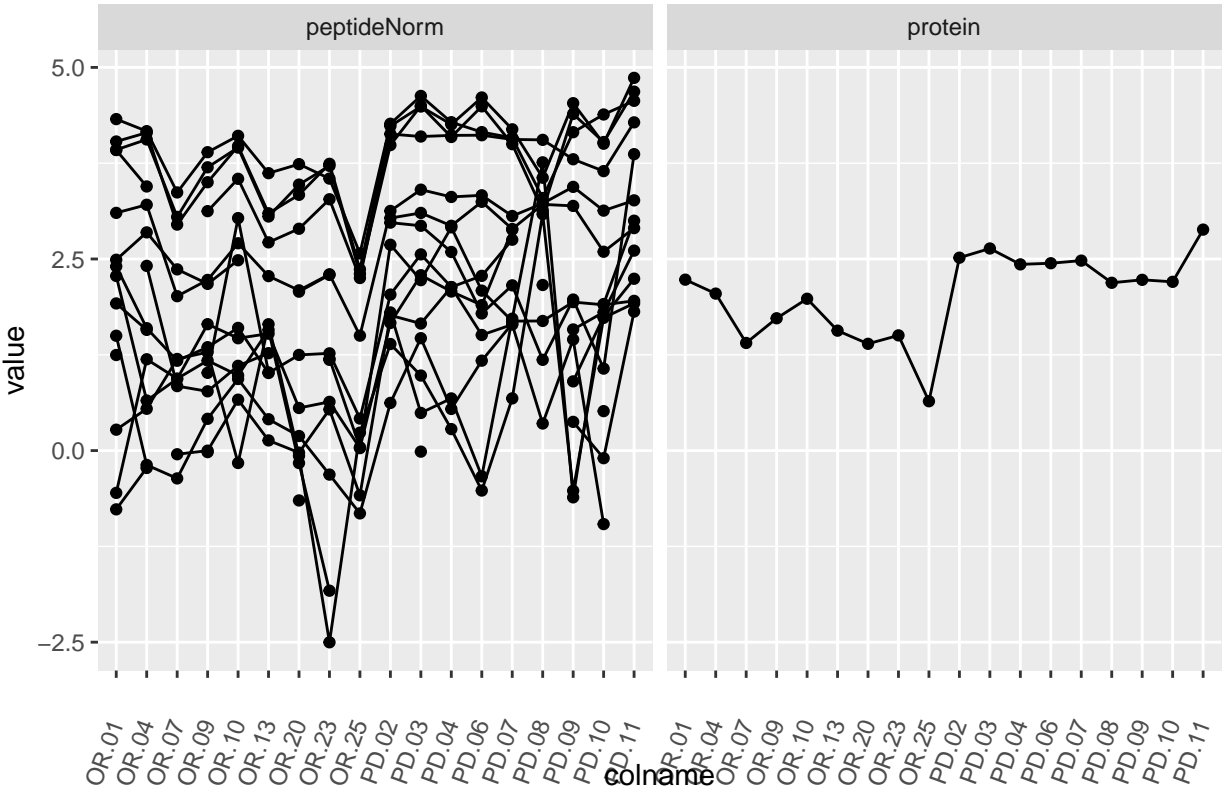


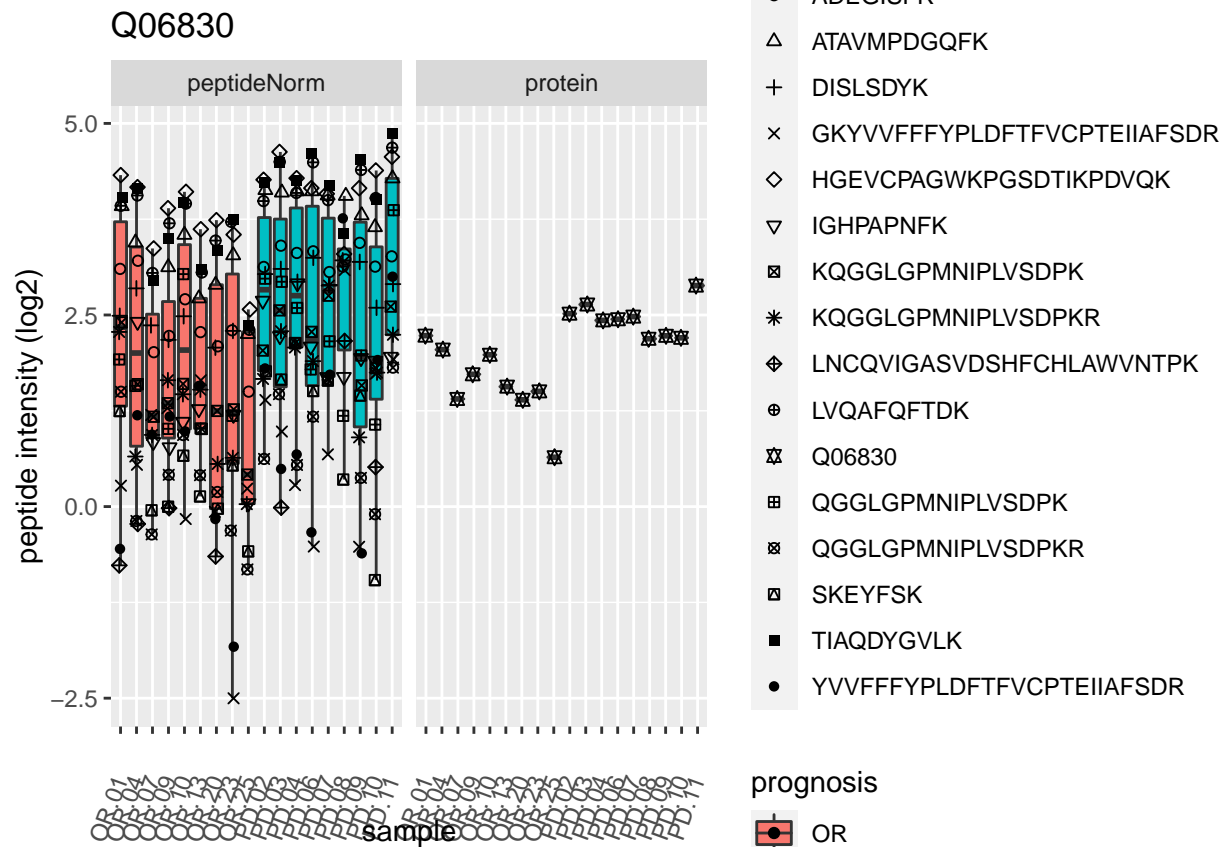
Q92734





Q06830

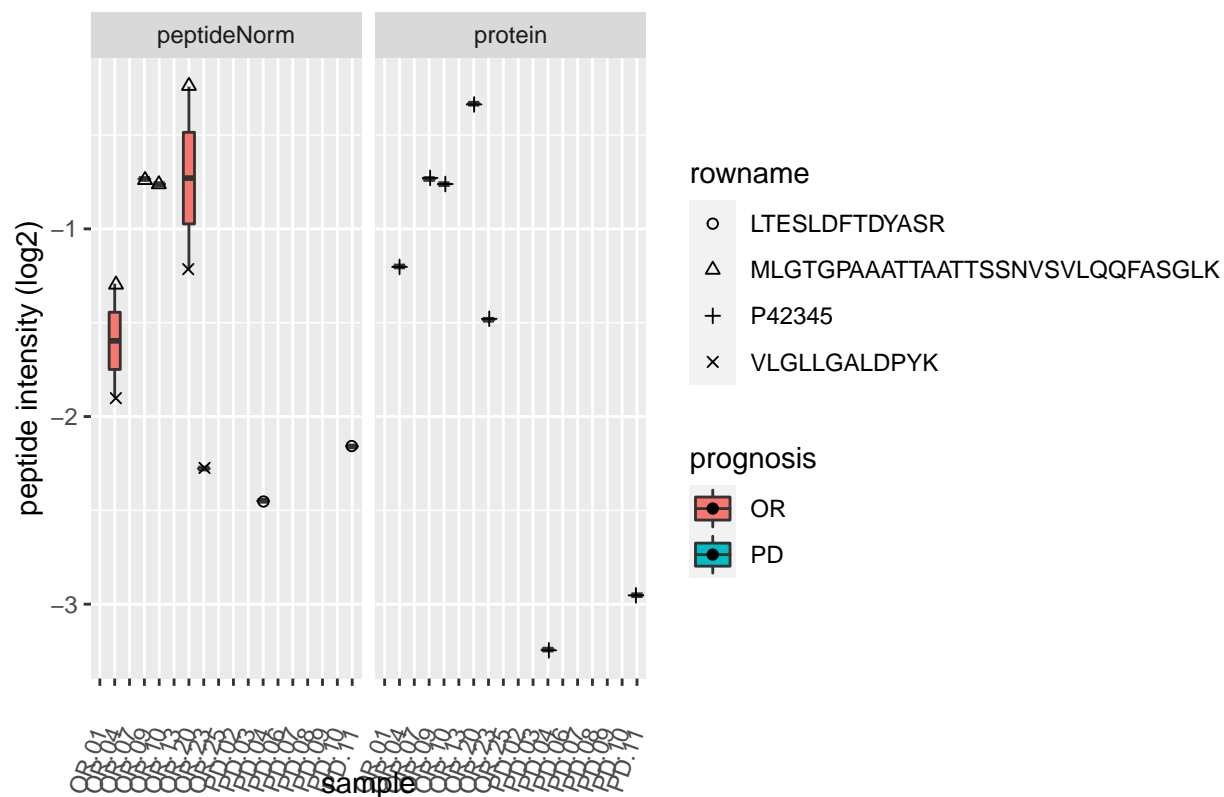




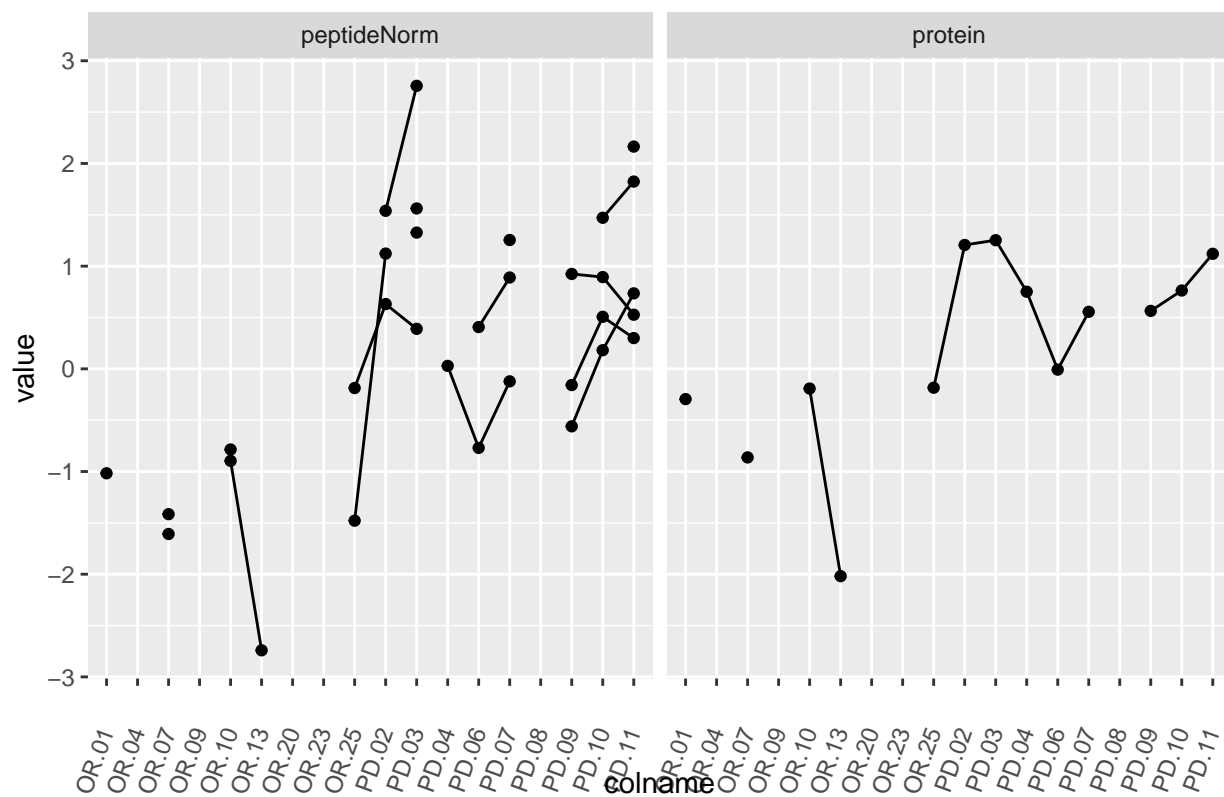
P42345



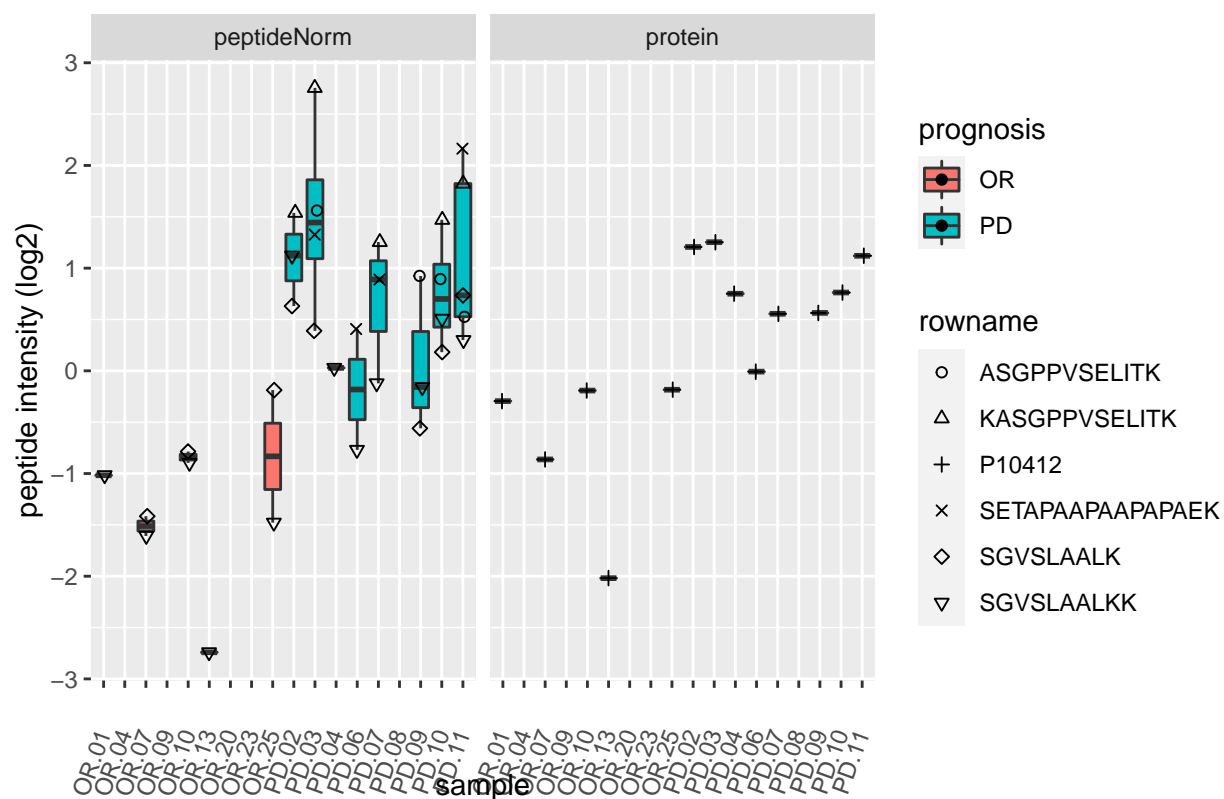
P42345



P10412

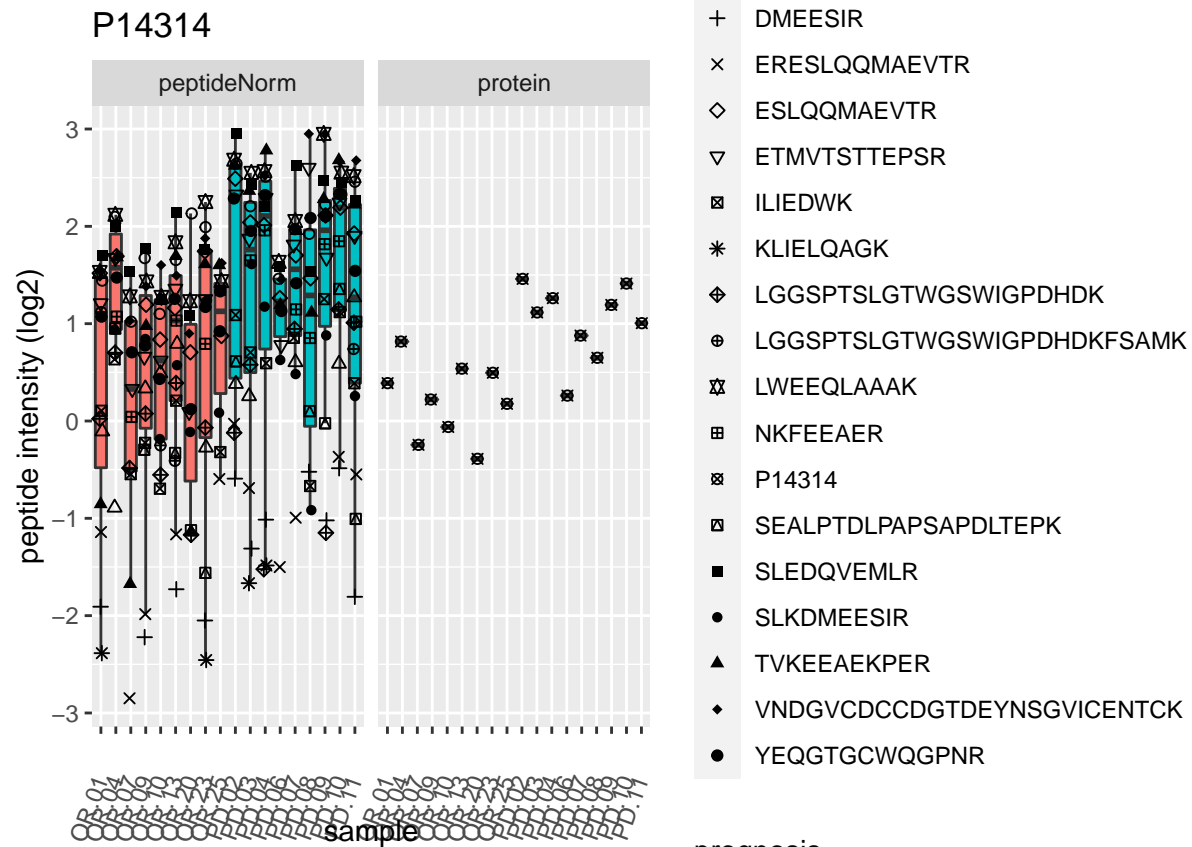


P10412



P14314



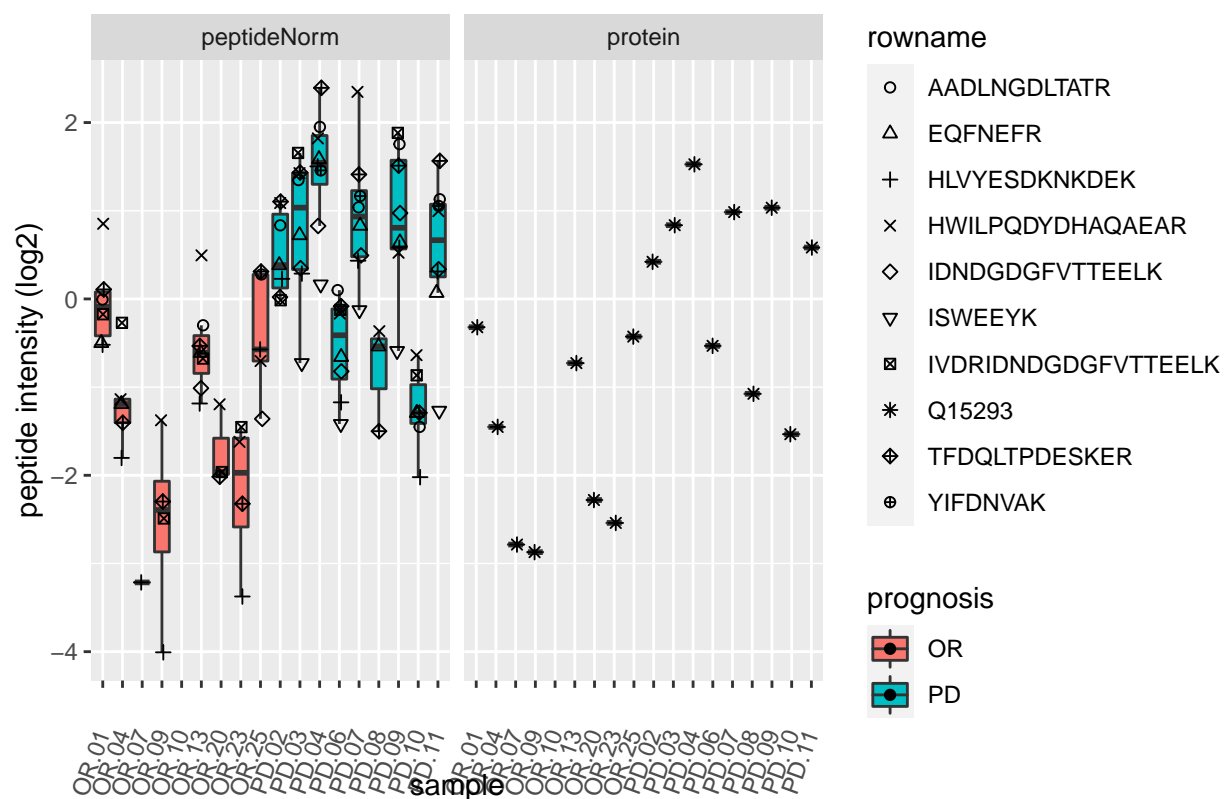


prognosis

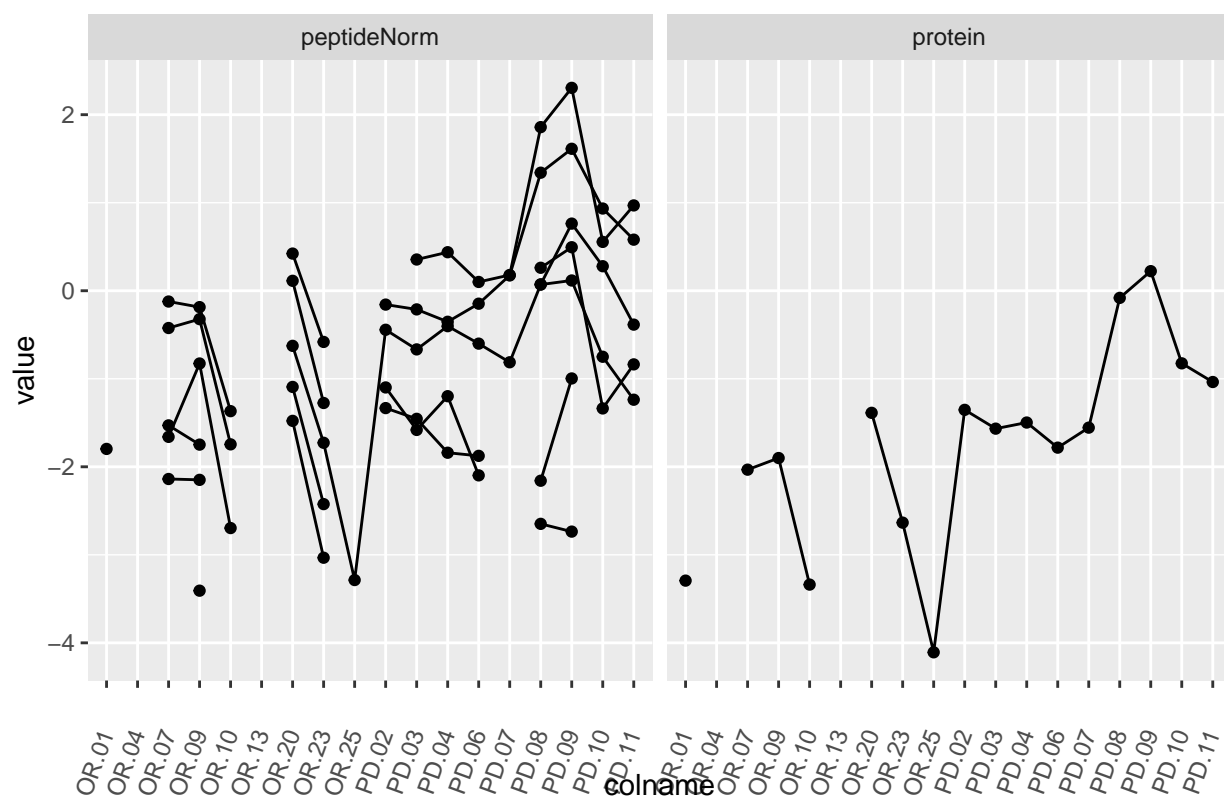
Q15293



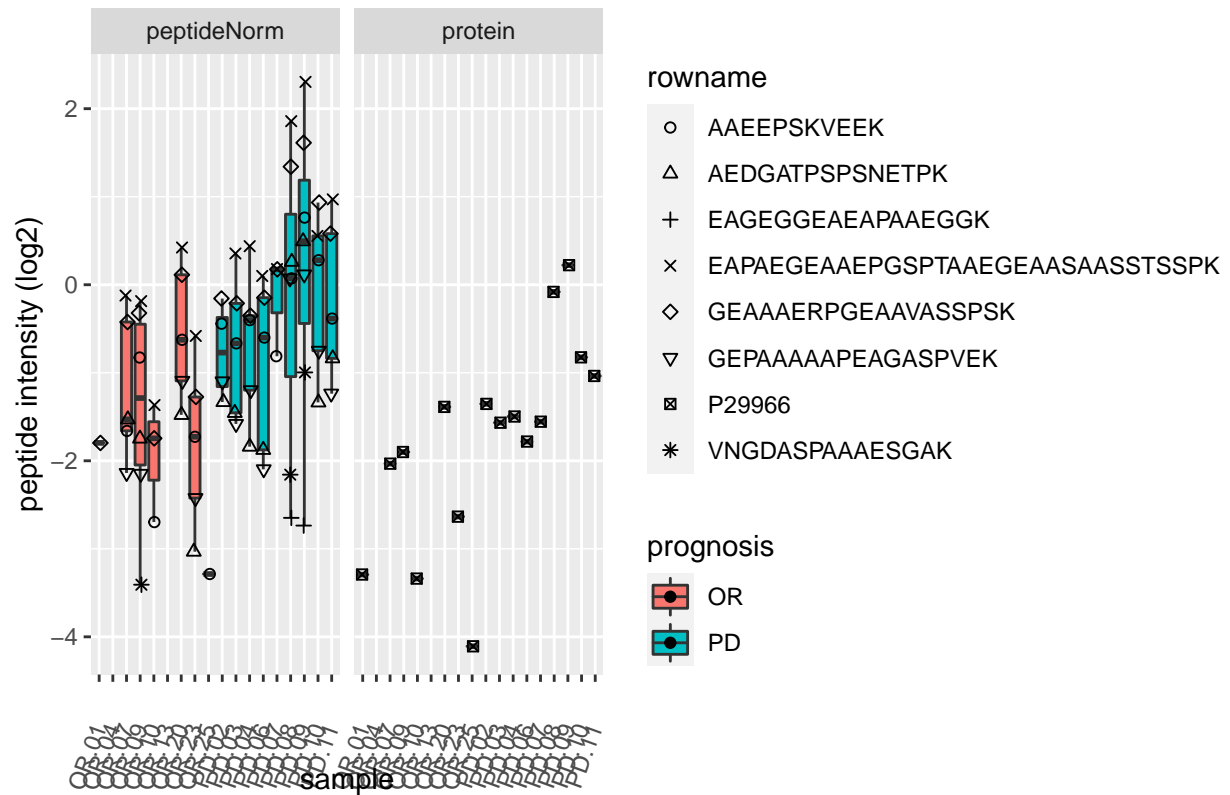
Q15293



P29966

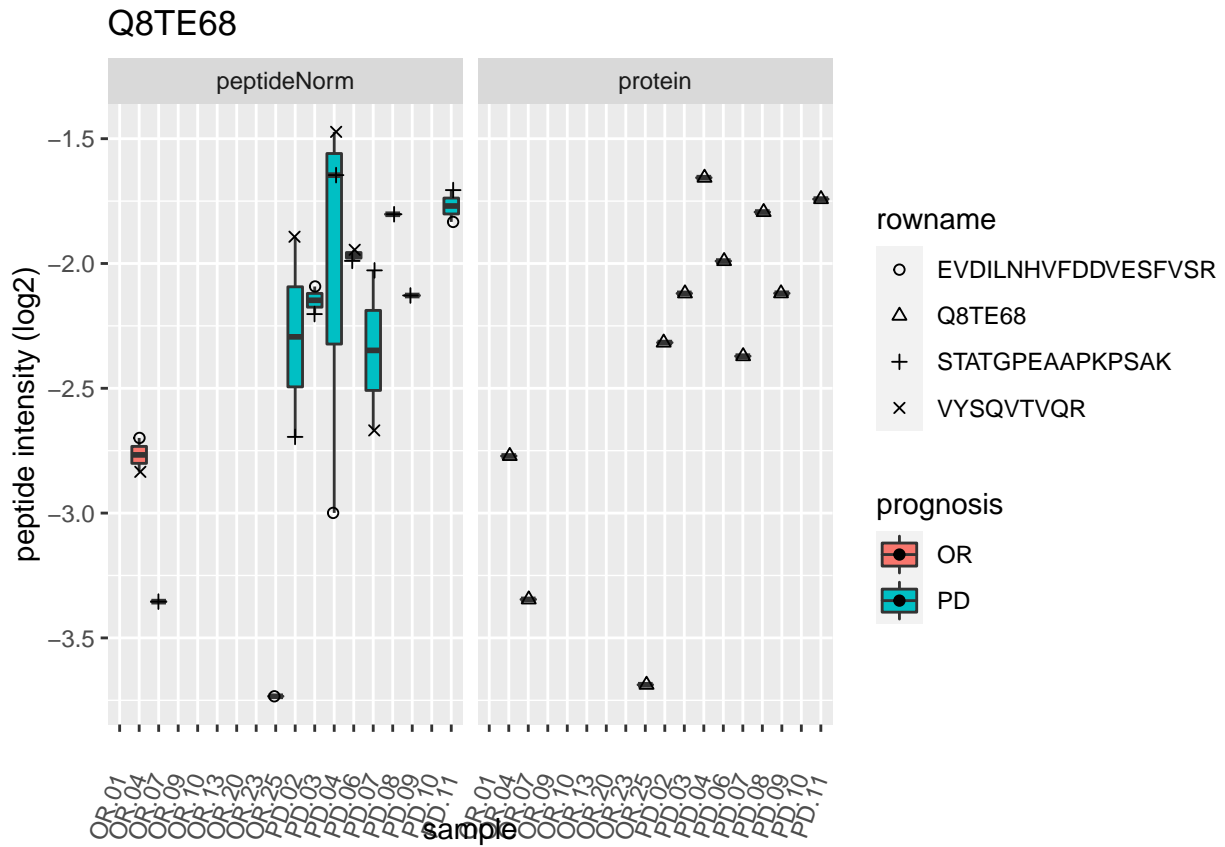


P29966



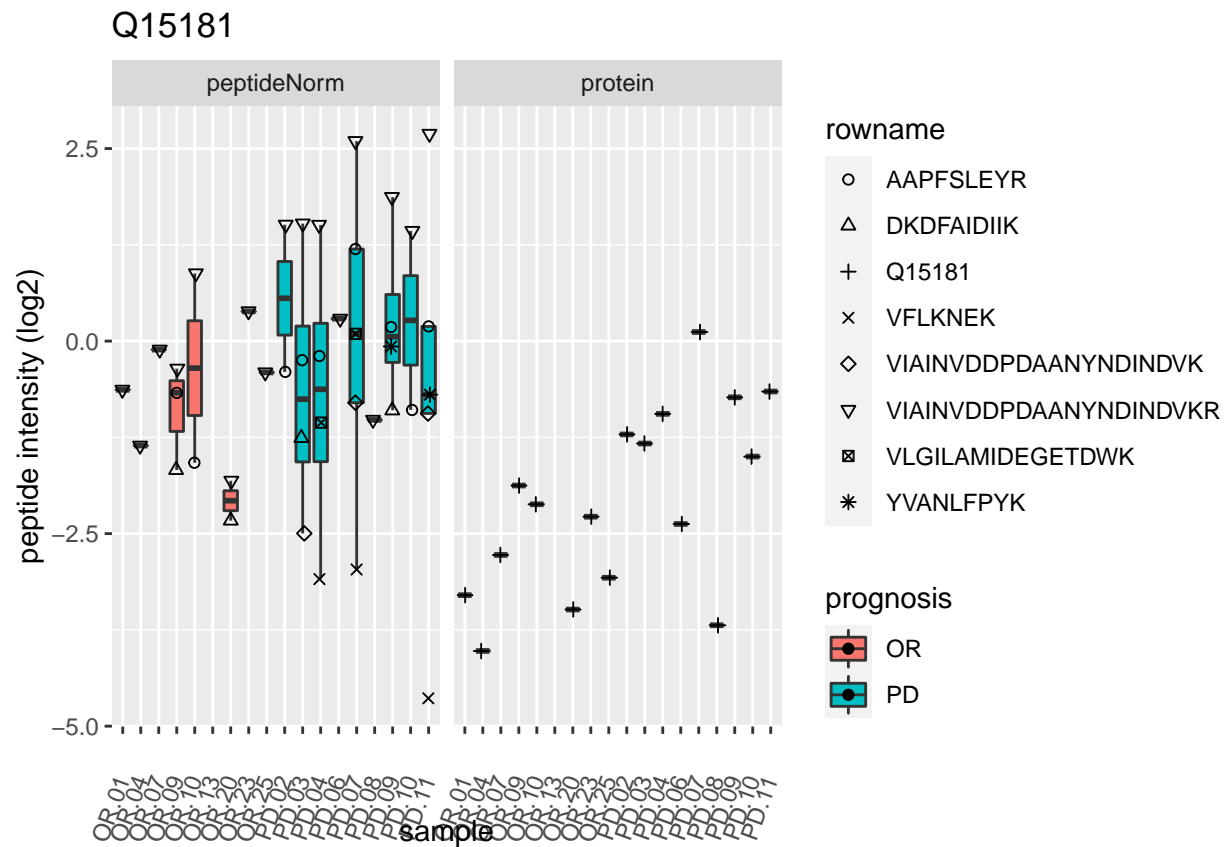
Q8TE68





Q15181

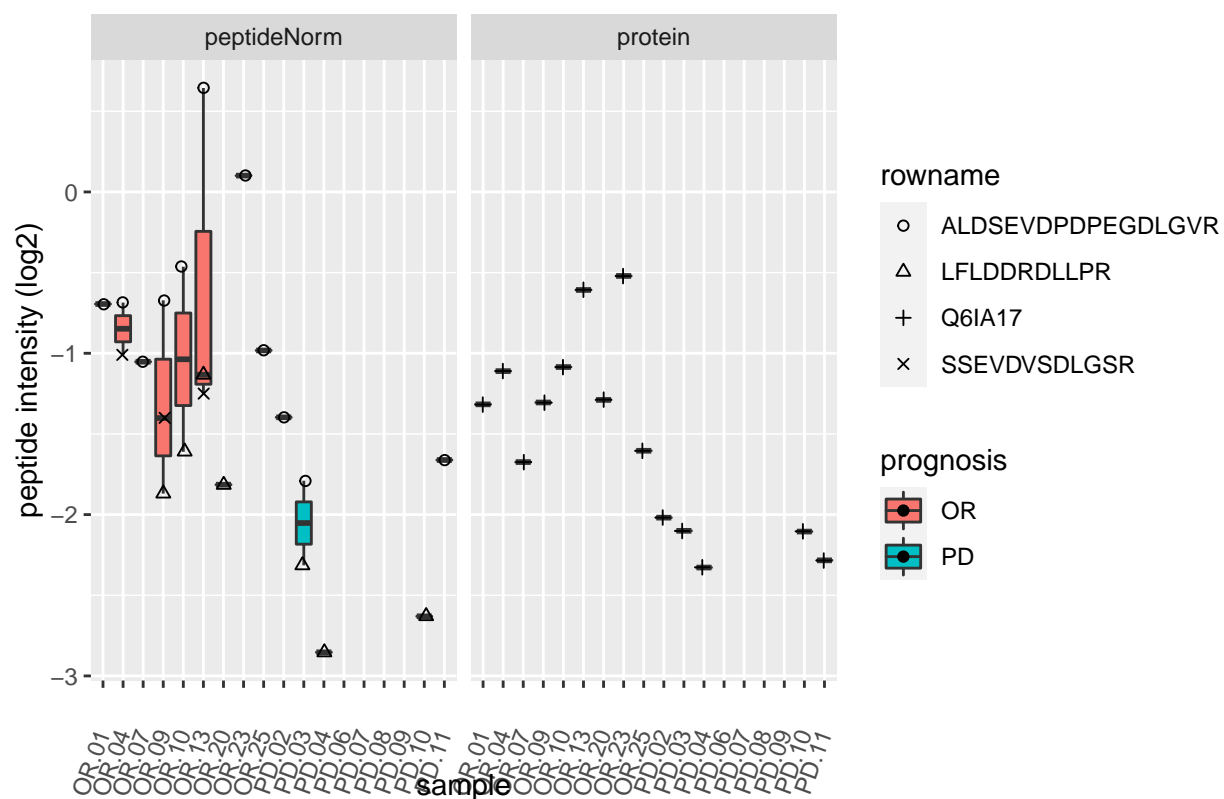




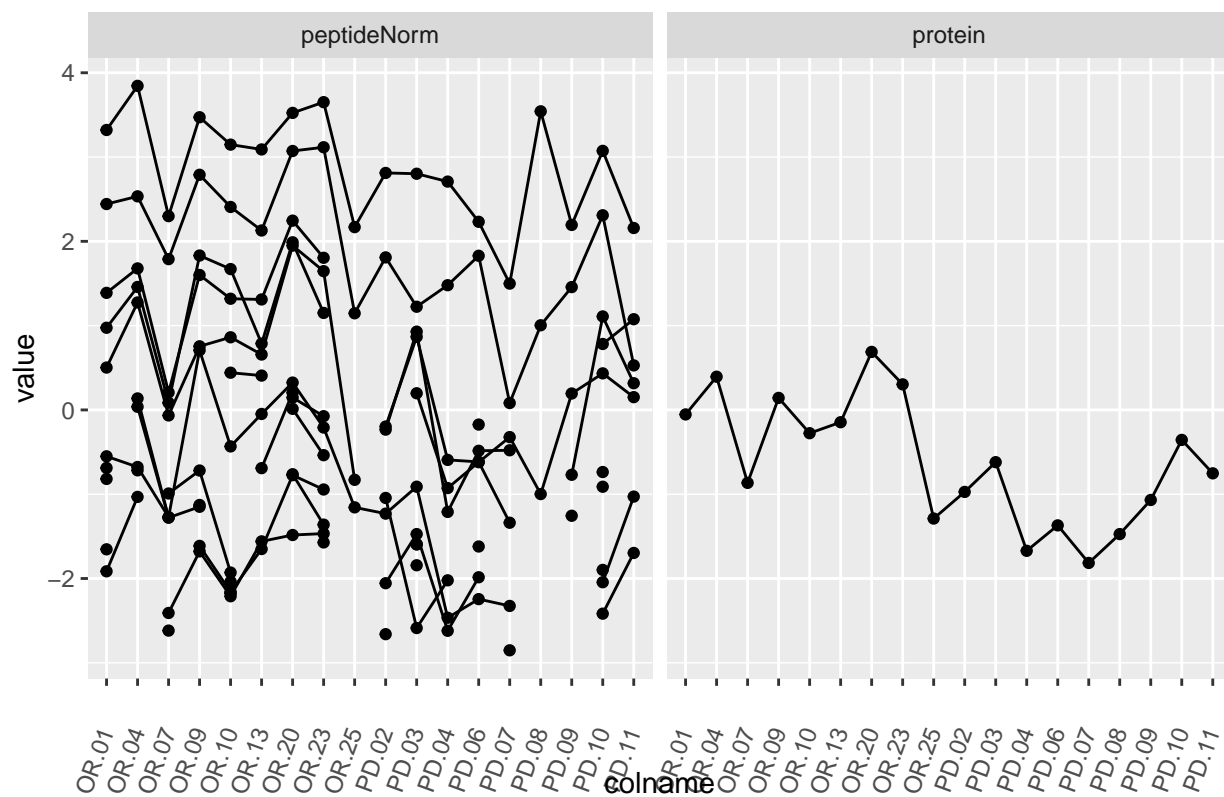
Q6IA17

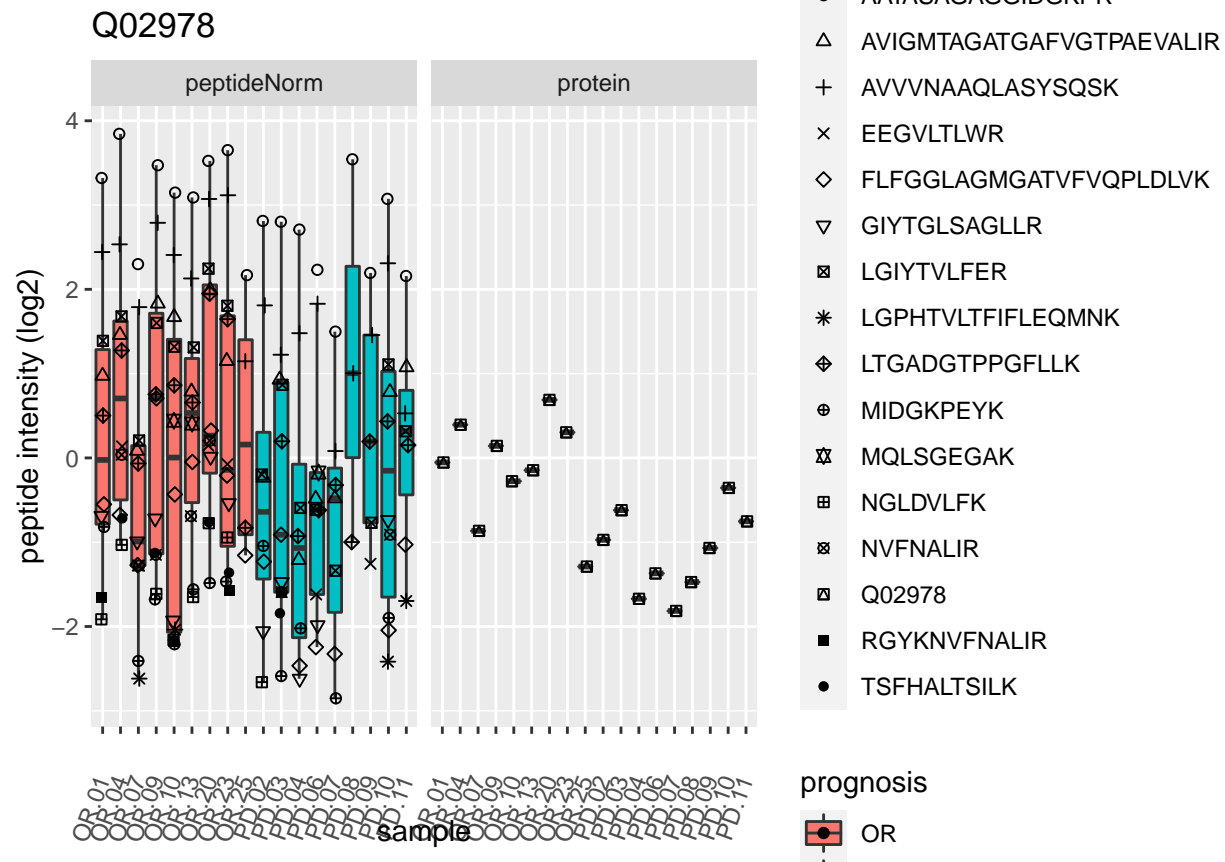


Q6IA17



Q02978

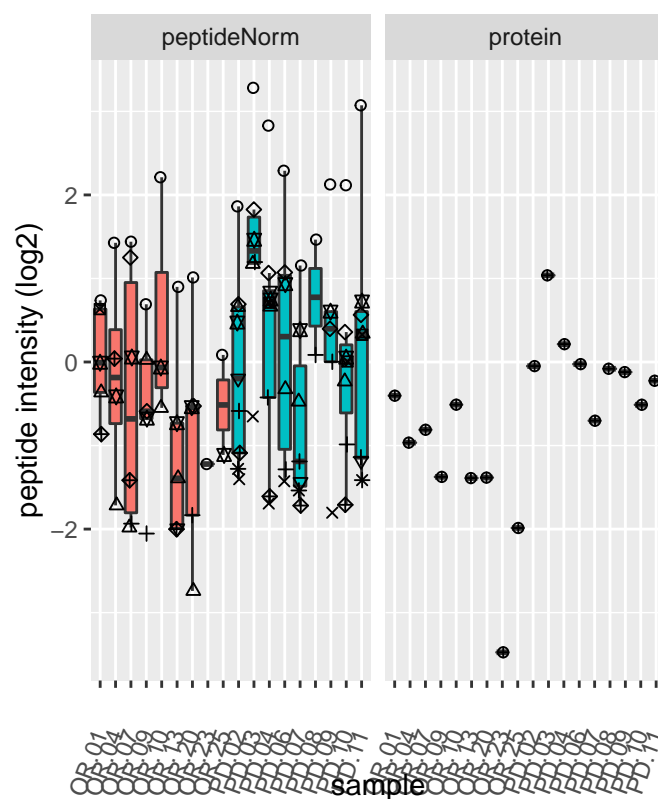




P12004



P12004



rowname

- AEDNADTLALVFEAPNQEK
- △ ATPLSSTVTLSMSADVPLVVEYK
- + CAGNEDIITLR
- × DLSHIGDAVVISCAK
- ◇ FSASGELGNGNIK
- ▽ IADMGHLK
- ⊠ LSQTSNVDKEEEAVTIEMNEPVQLTFALR
- * MPSGEFAR
- ⬠ NLAGGVNLTSMK
- ⊕ P12004
- ⊗ YLNFFTK

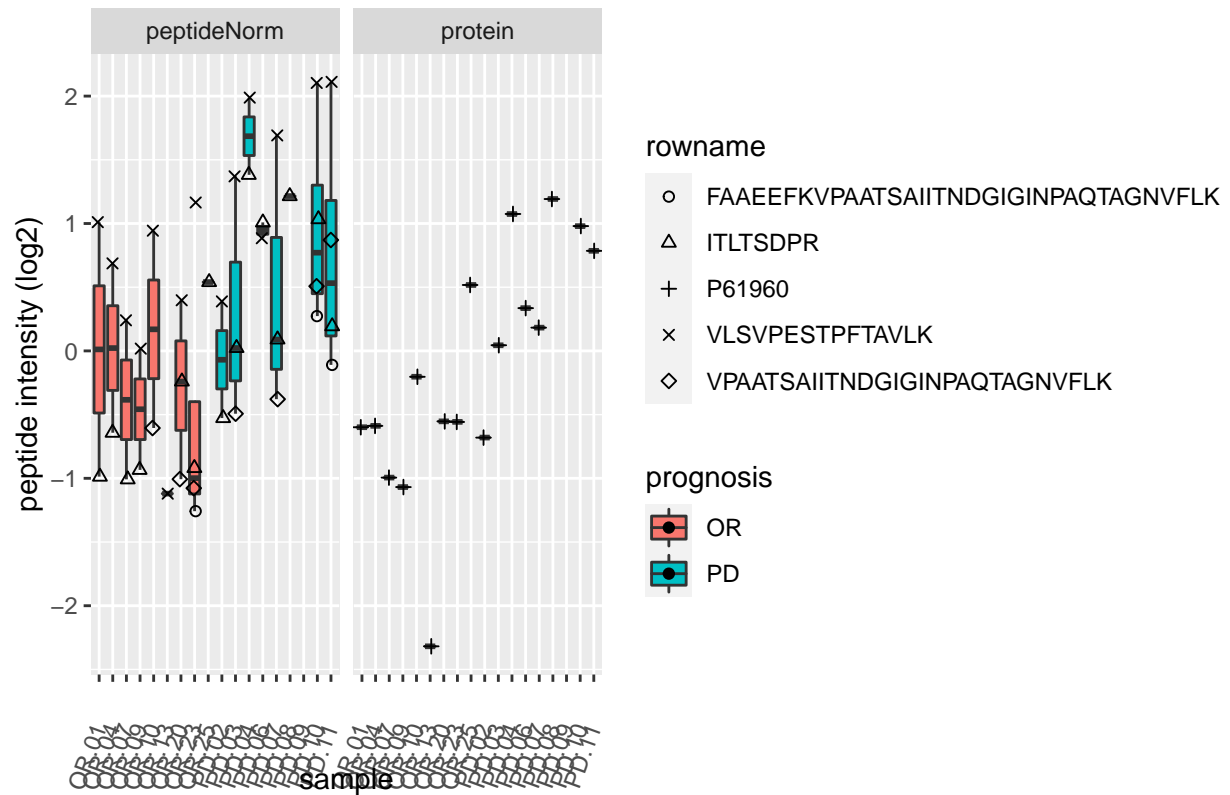
prognosis

- OR
- PD

P61960

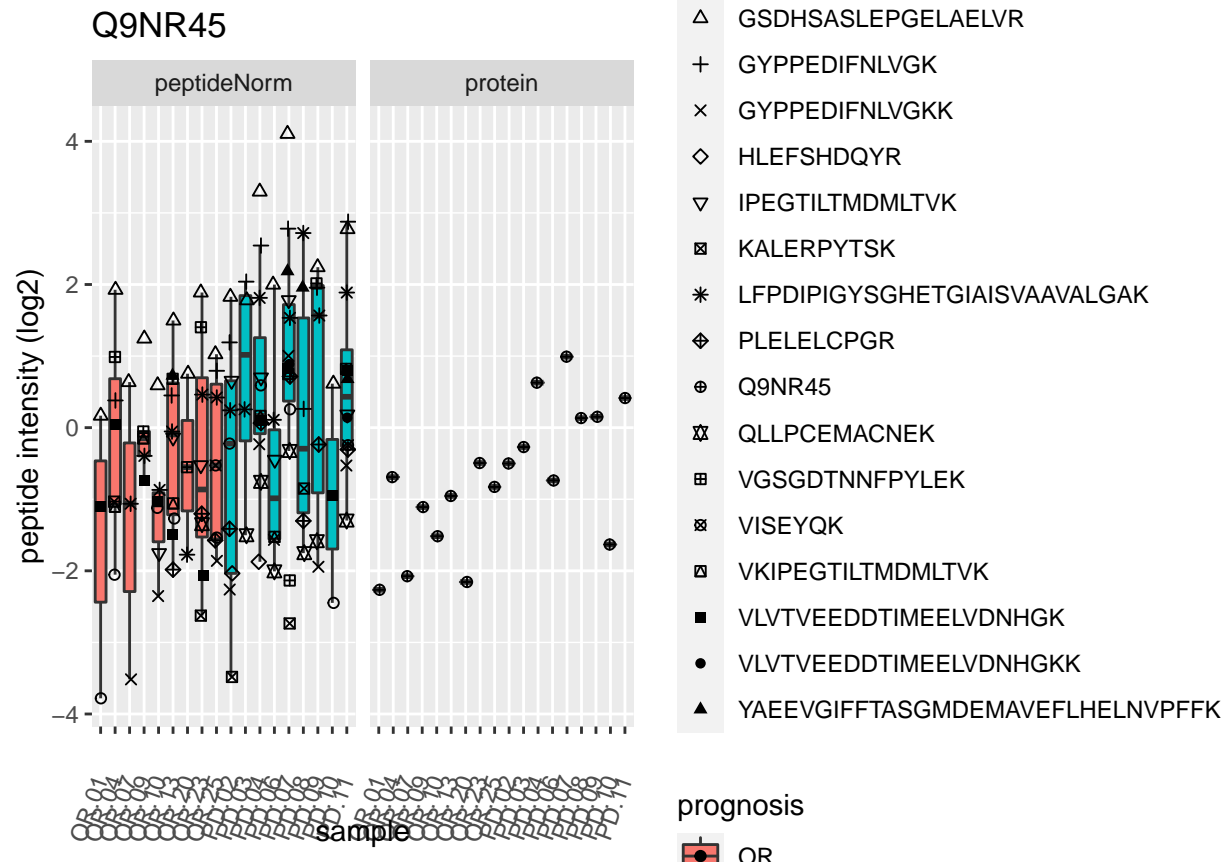


P61960



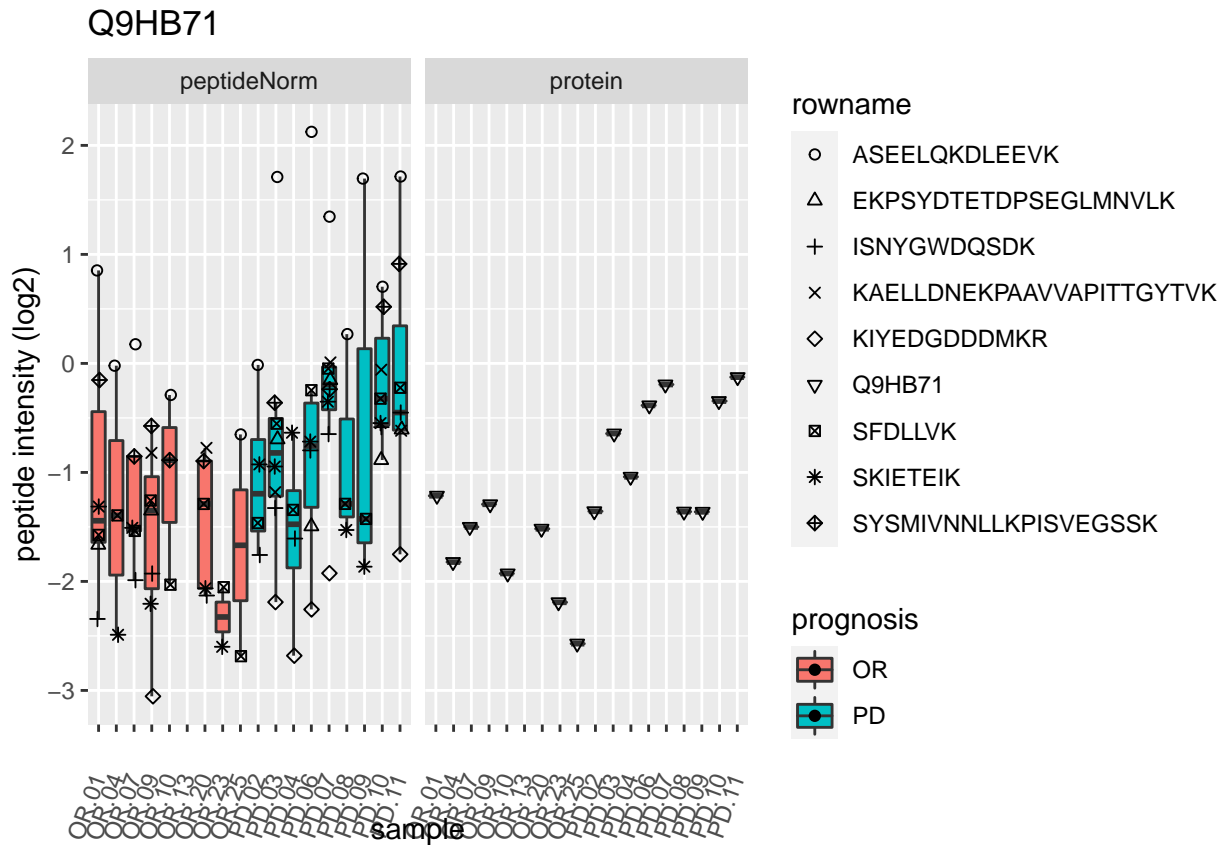
Q9NR45



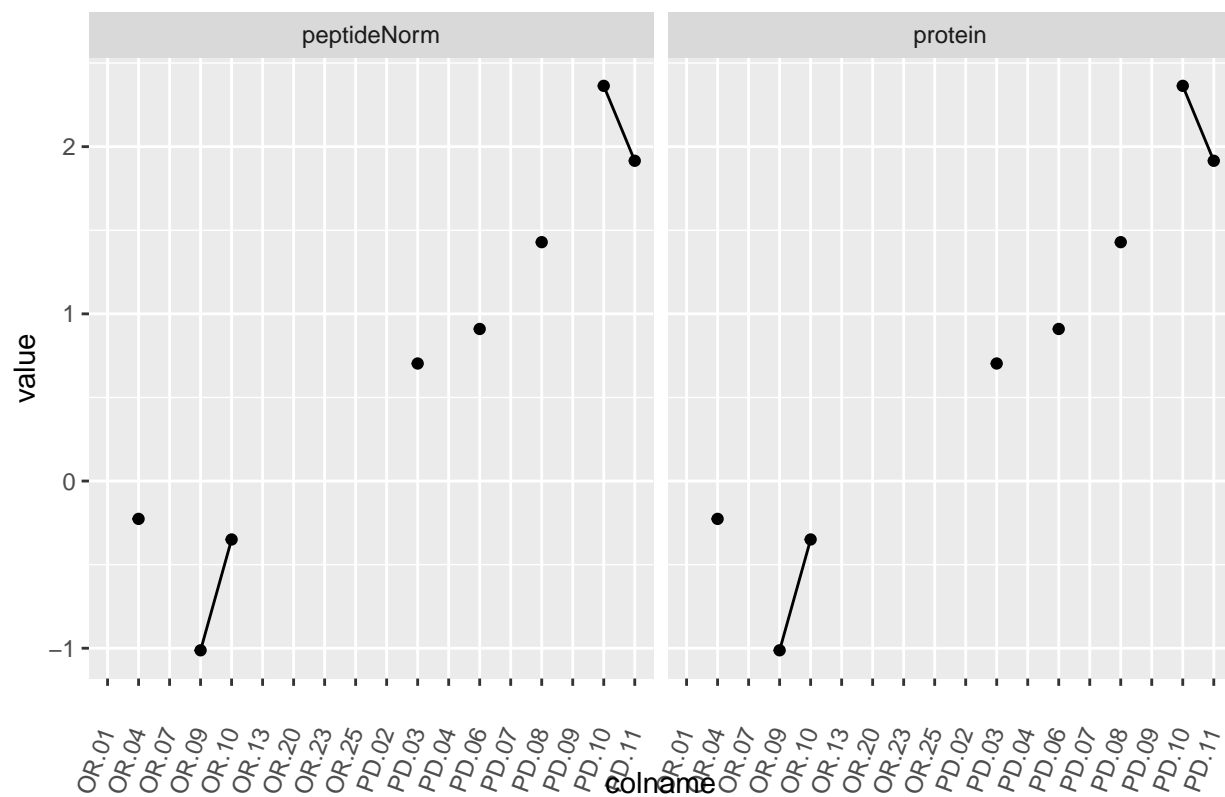


Q9HB71

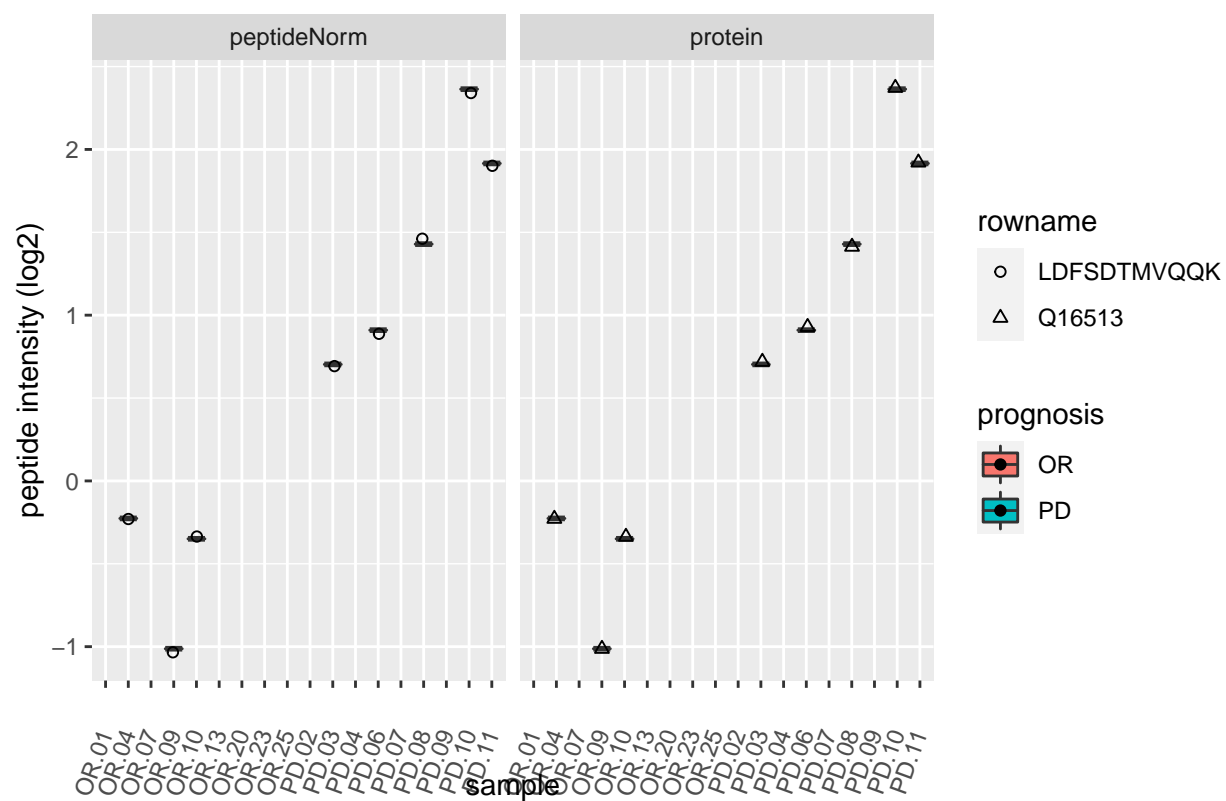




Q16513



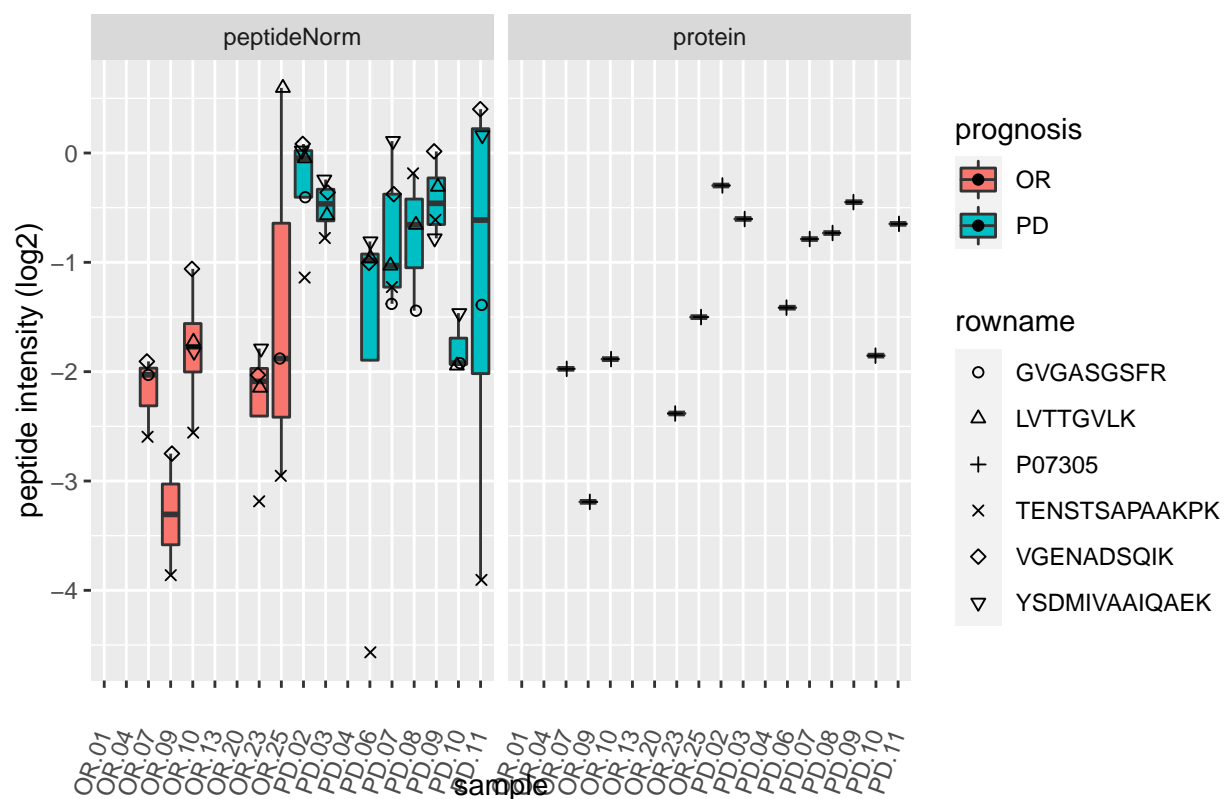
Q16513



P07305

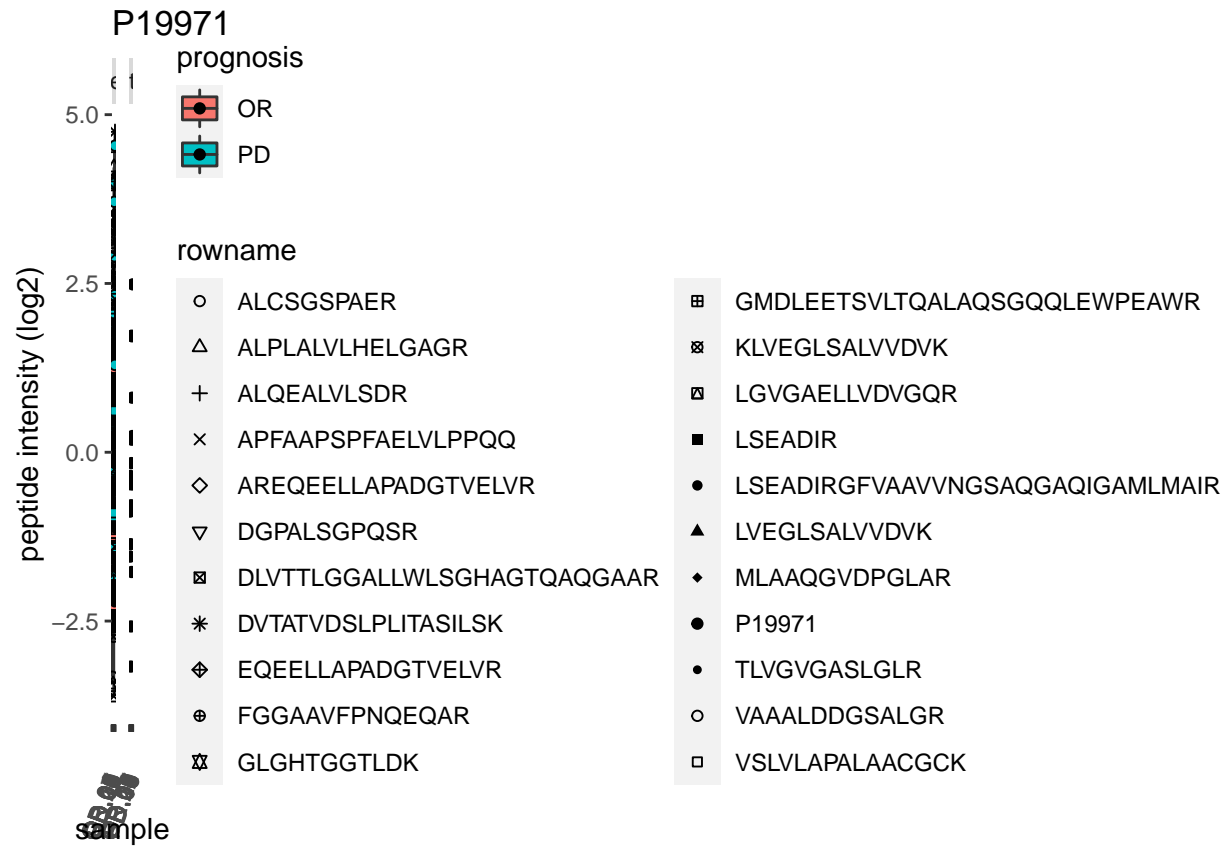


P07305



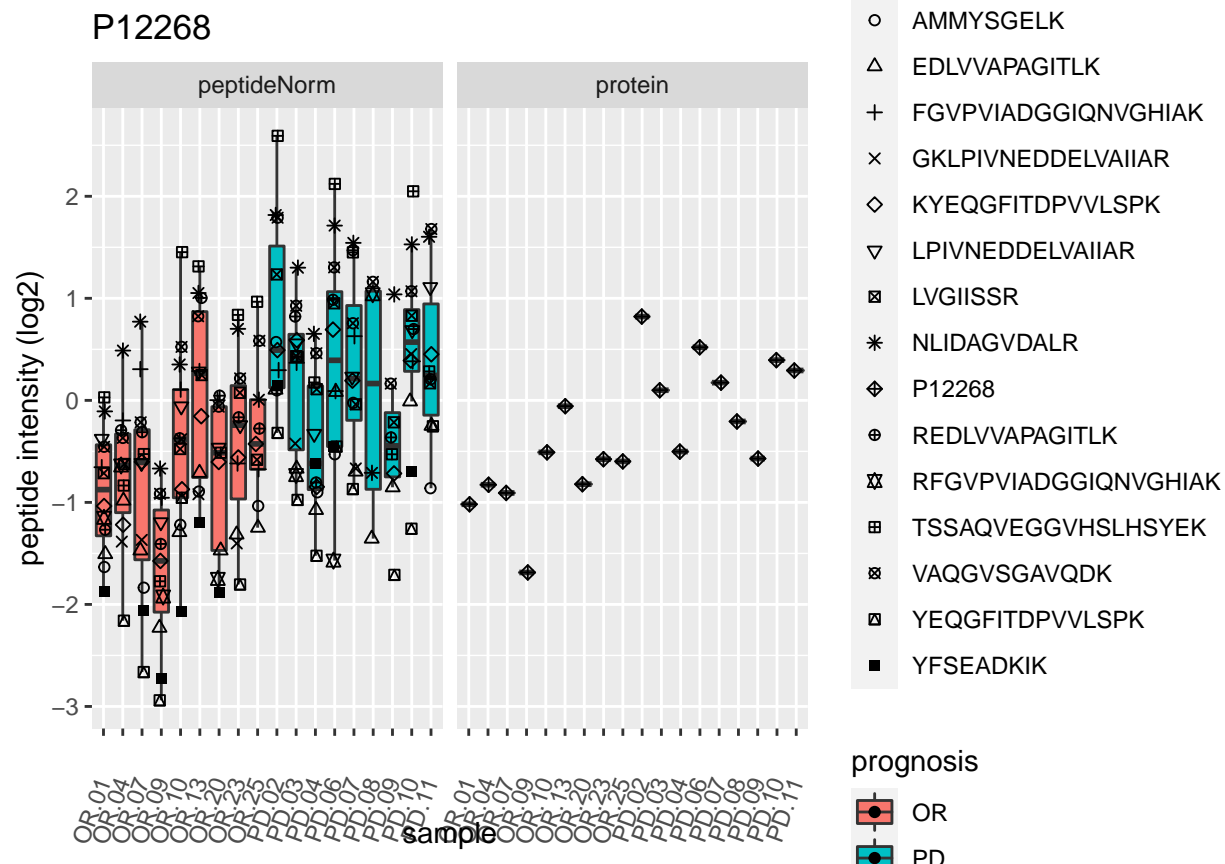
P19971





P12268

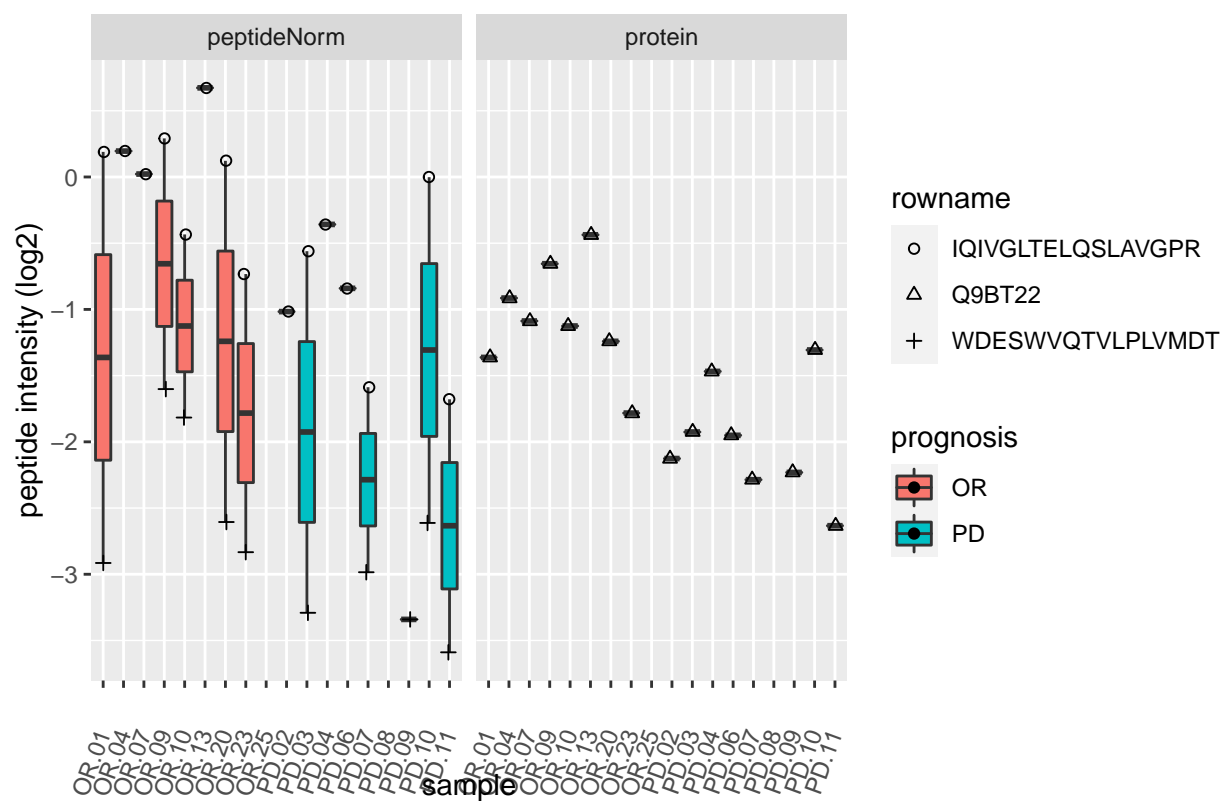




Q9BT22

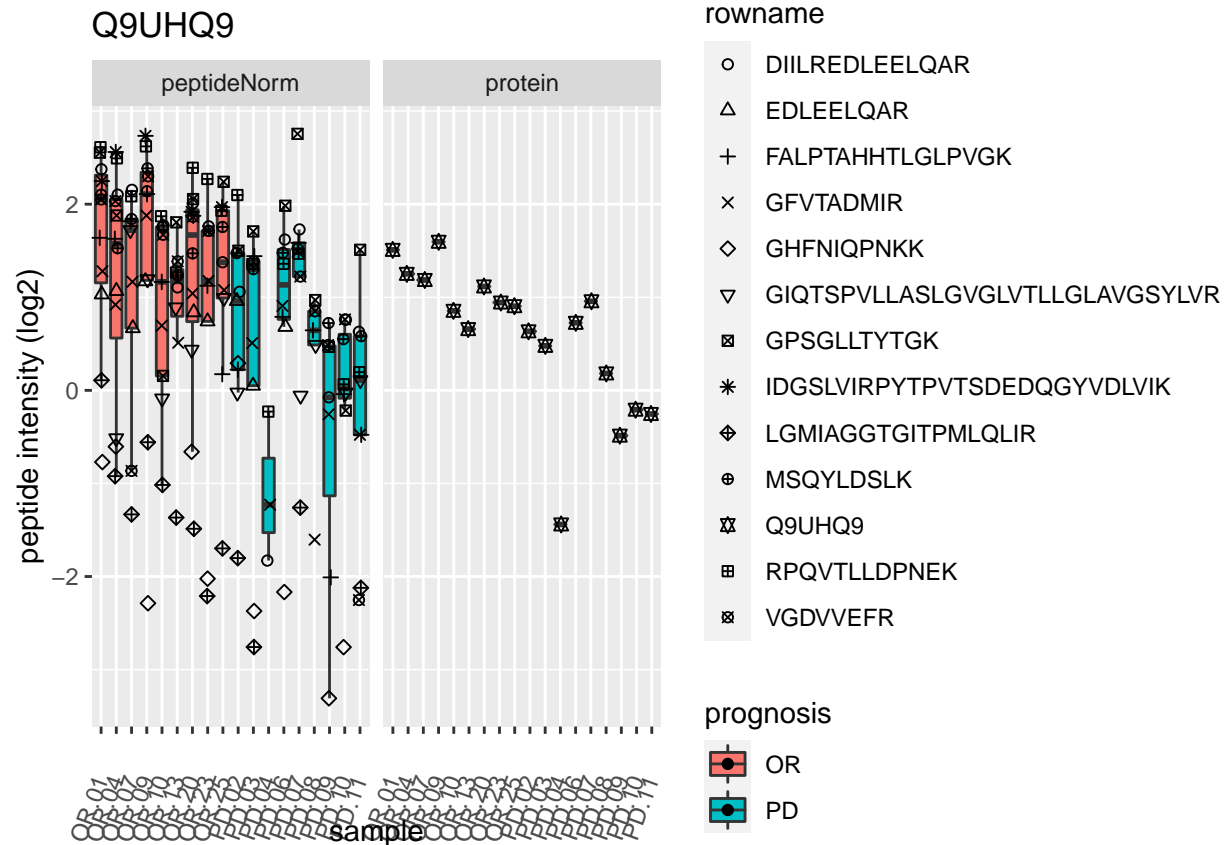


Q9BT22



Q9UHQ9

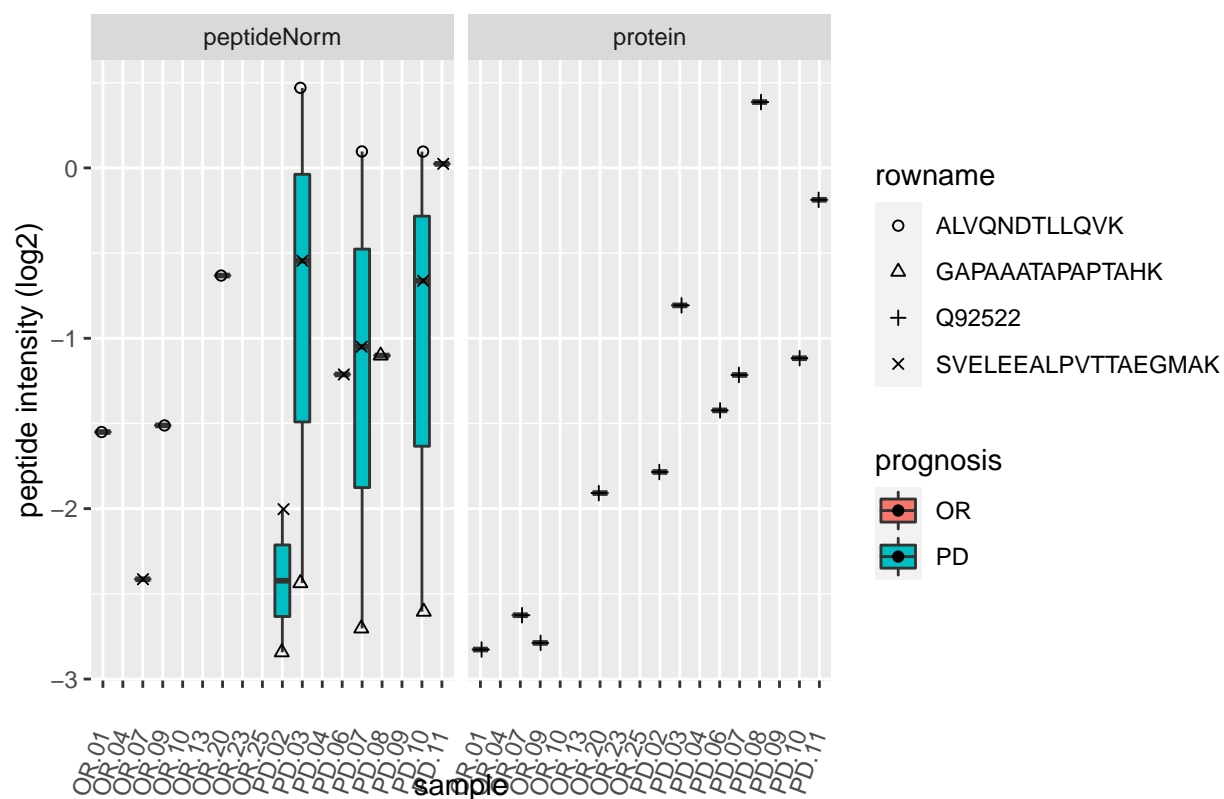




Q92522



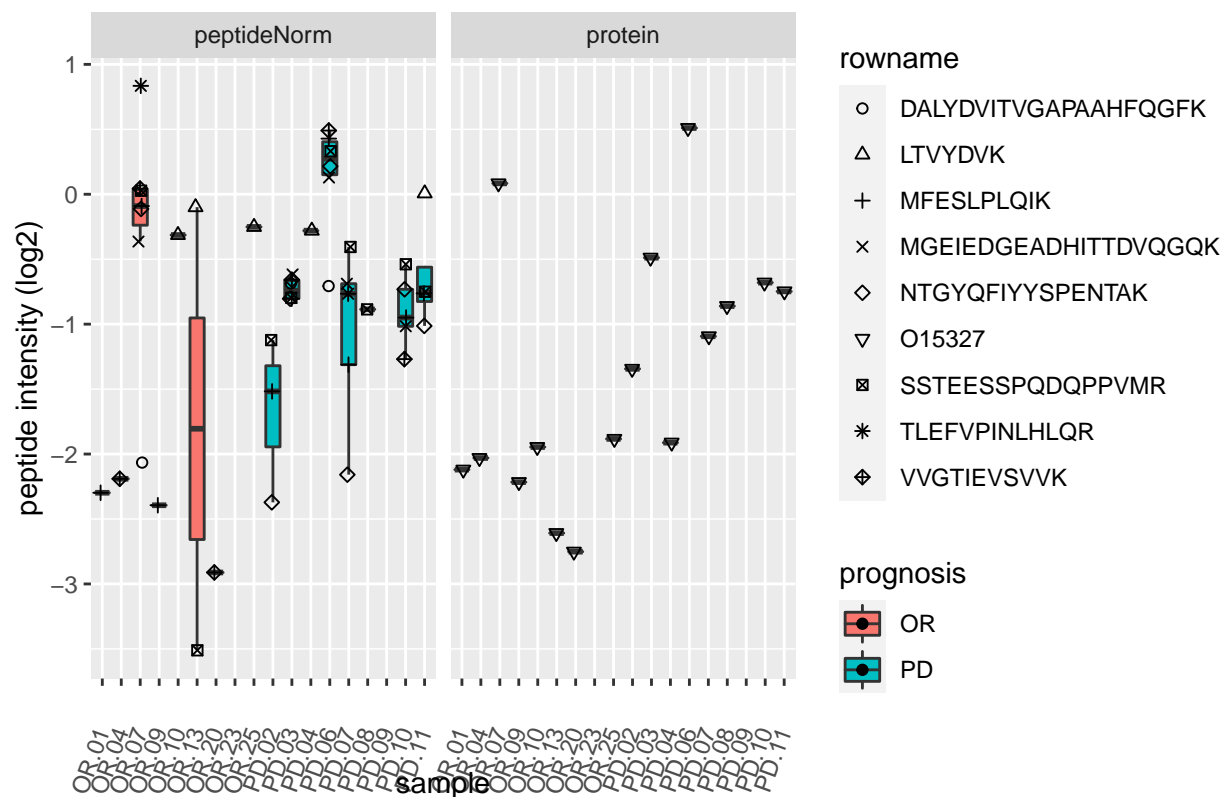
Q92522



O15327



O15327



P21333



/K

TYGGHQVPGSPFK

IVTITWGGQNIGR

IVDPNVDEHSVMTYLSQFPK

PFPLEAVAPTKPSK

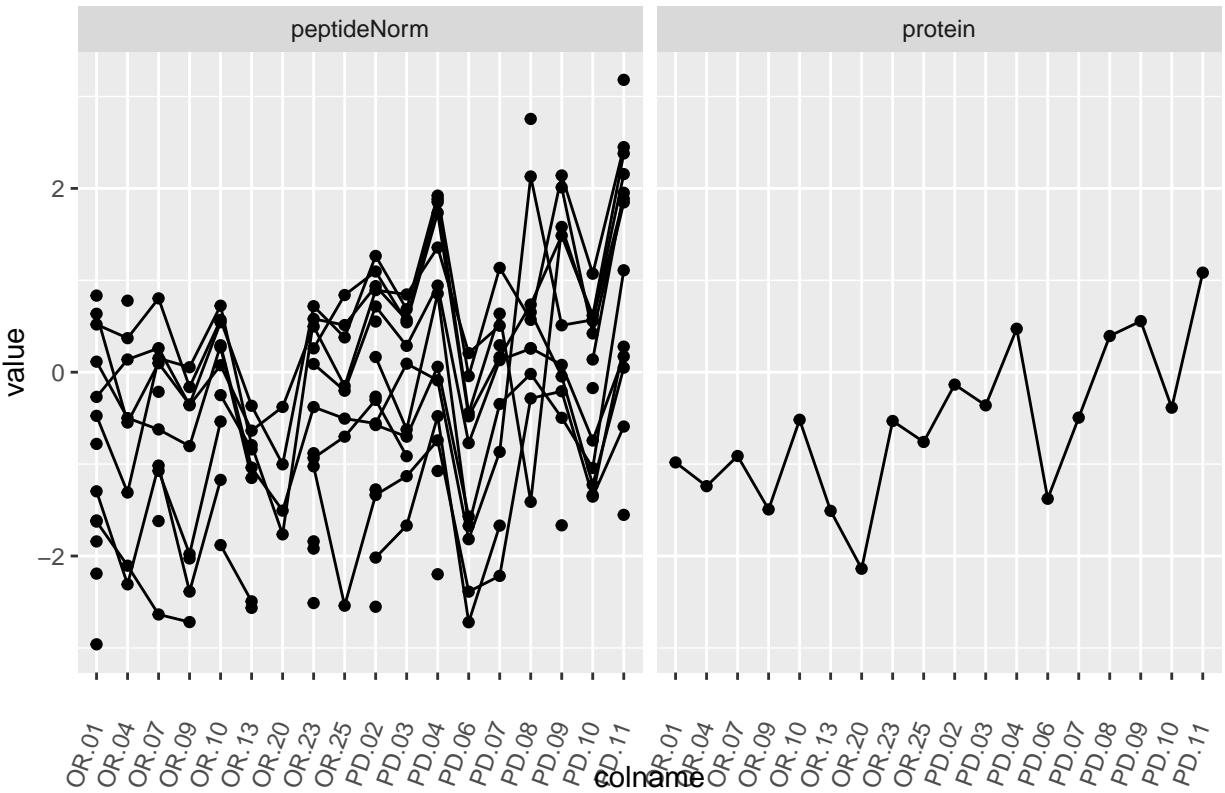
PSVQPPLR

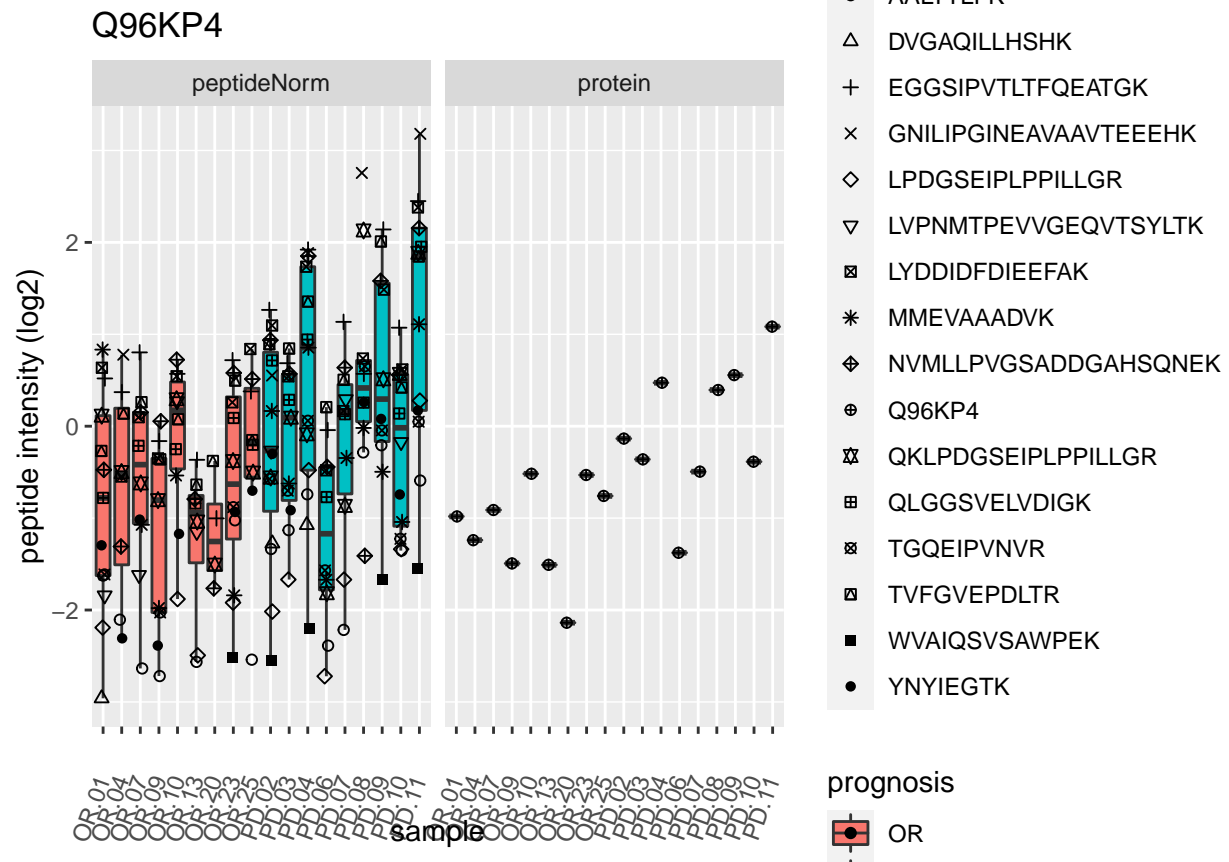
DAR

) GAGSYTIMVLFADQATPTSPIR
 * GAGTGGLGLAVEGPSEAK
 + GKLDVQFSGLTK
 ' GLVEPVDVVDNADGTQTVNYVPSR
 - GQHVPGPSPFQFTVGPLGEGGAHK
 • GTVEPQLEAR
 / HTAMVSWGGVSIPNSPFR
 0 IANLQTDLSGDLR
 1 IECDDKGDGSCDVR
 2 IPEISIQDMTAQVTSPSGK
 3 IVGPSGAAPVCK
 4 KGEITGEVR
 5 KTHIQDNHDGTYTVAYVPDVTGR
 6 LDVQFSGLTK
 7 LIALLEVLSQKK
 8 LLGWIQNKLPQLPITNFSR
 9 LQVEPAVDTSQVQCYGPGIEGQGVFR

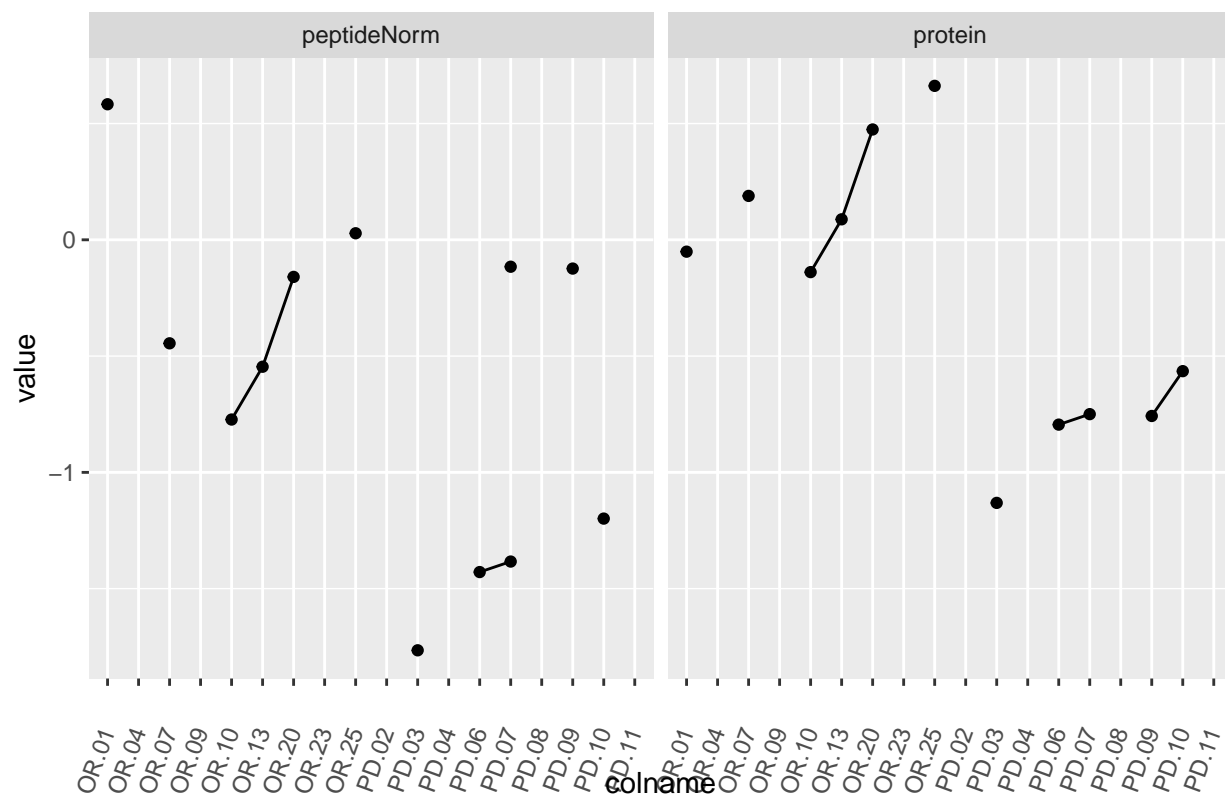
< LVSNHSLHETSSVFVDSLTK
 = LYSVSYLLK
 > MDCQECPEGYR
 ? NDNDTFTVK
 @ NGHVGISFVPK
 A NGQHVASSPIPVVISQSEIGDASI
 B P21333
 C PGAPLRPK
 D RAEFTVETR
 E RAPSVANVGSHCDLSLK
 F RLTVSSLQESGLK
 G SADFFVEAIGDDVGTLGFSVEGF
 H SAGQGEVLVYVEDPAGHQEEAK
 I SPFEVYVDK
 J SPFSVAVSPSLDLSK
 K SPYTVTVGQACNPSACR
 L TFSVWYVPEVTGTHK

Q96KP4

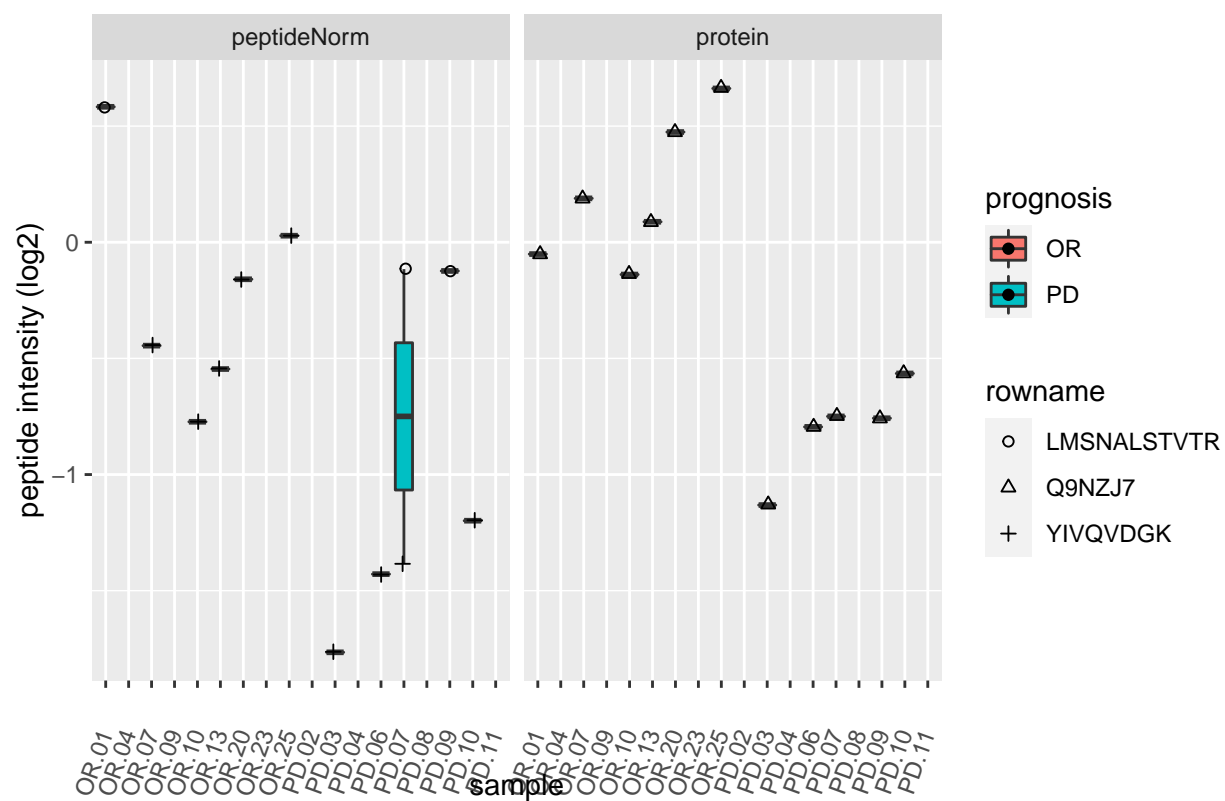




Q9NZJ7

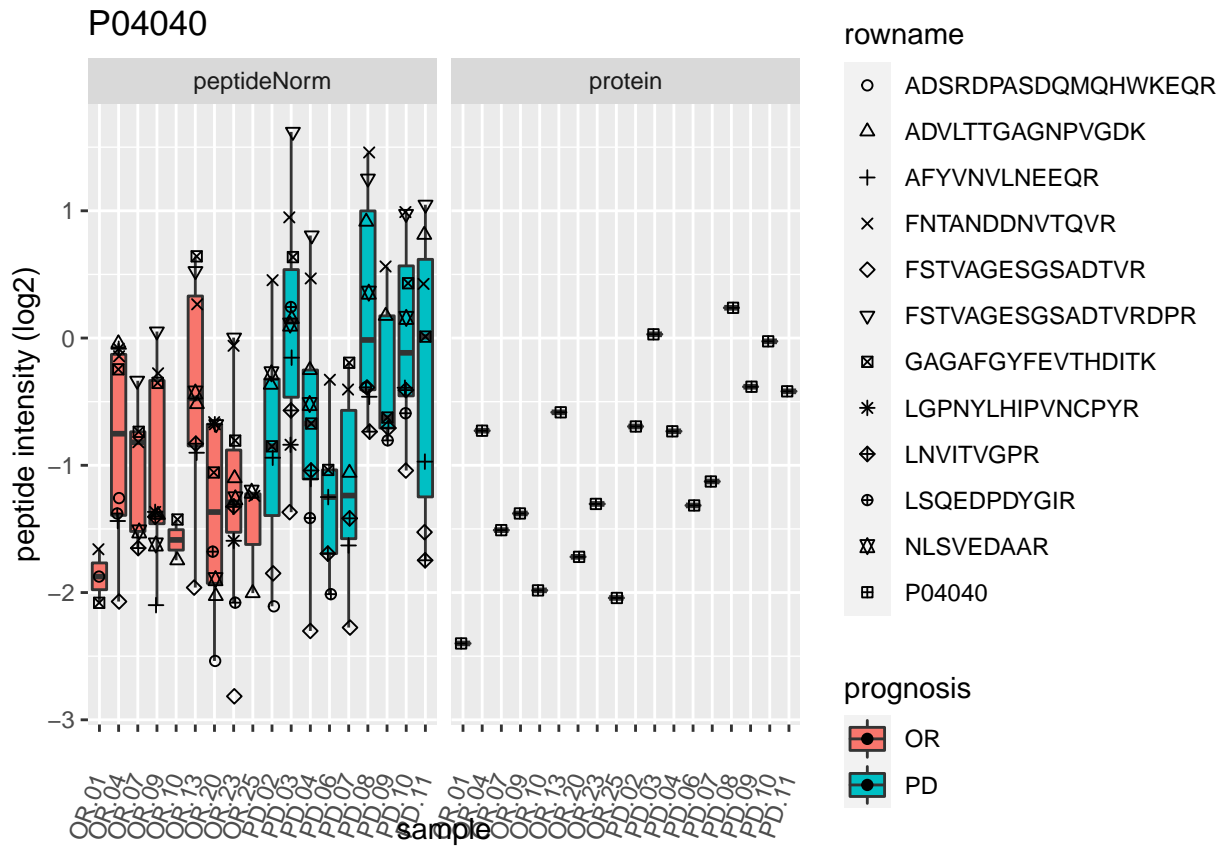


Q9NZJ7



P04040

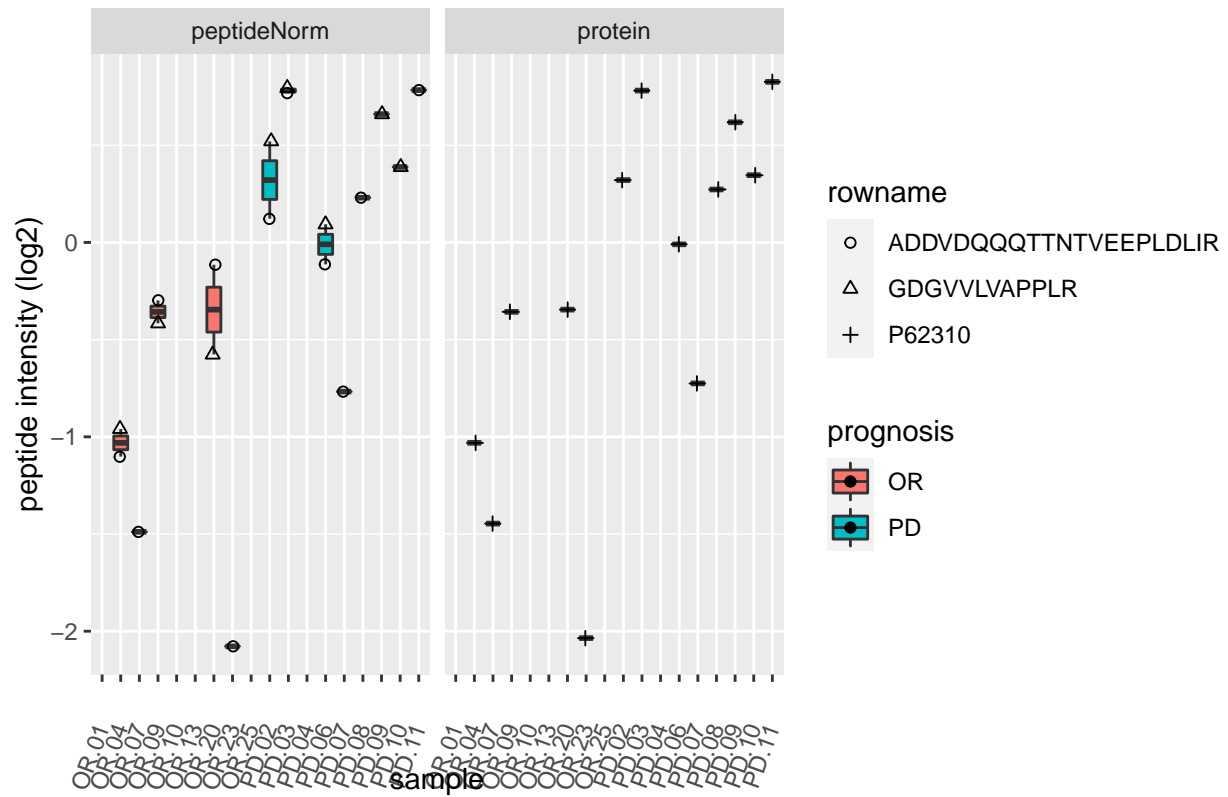




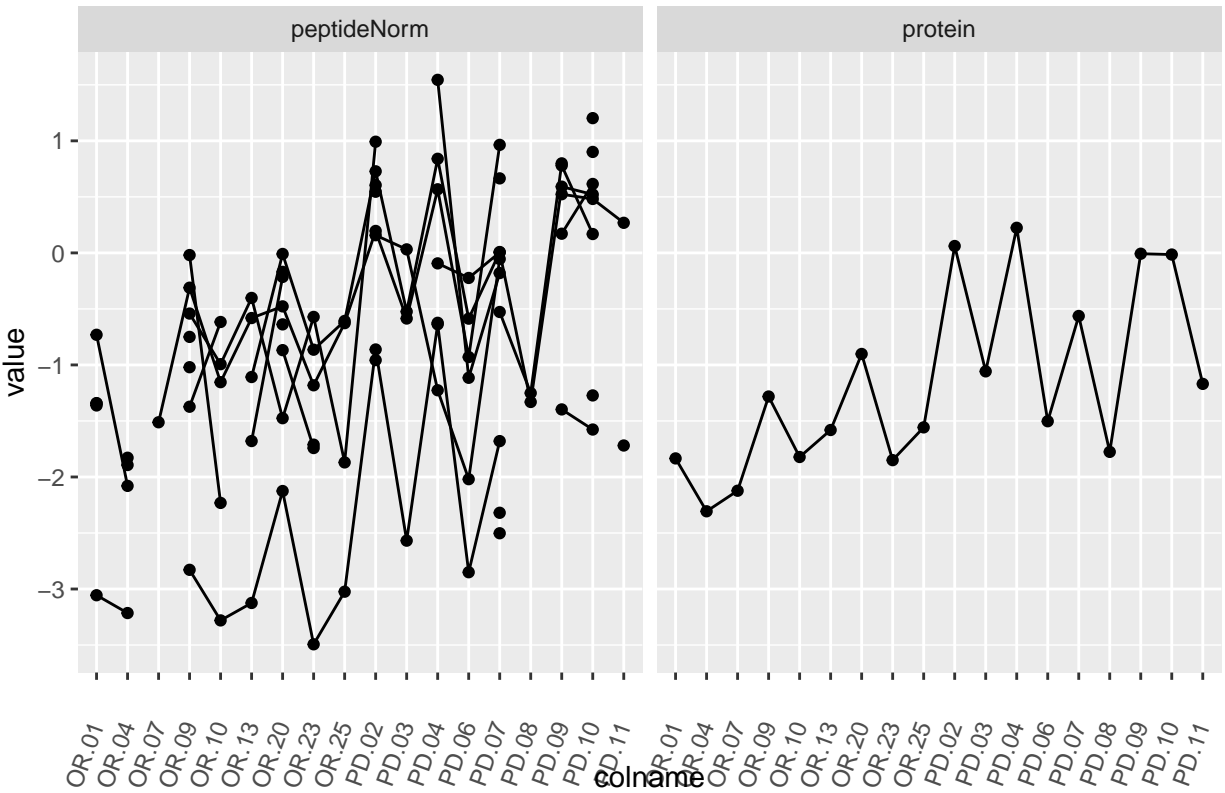
P62310

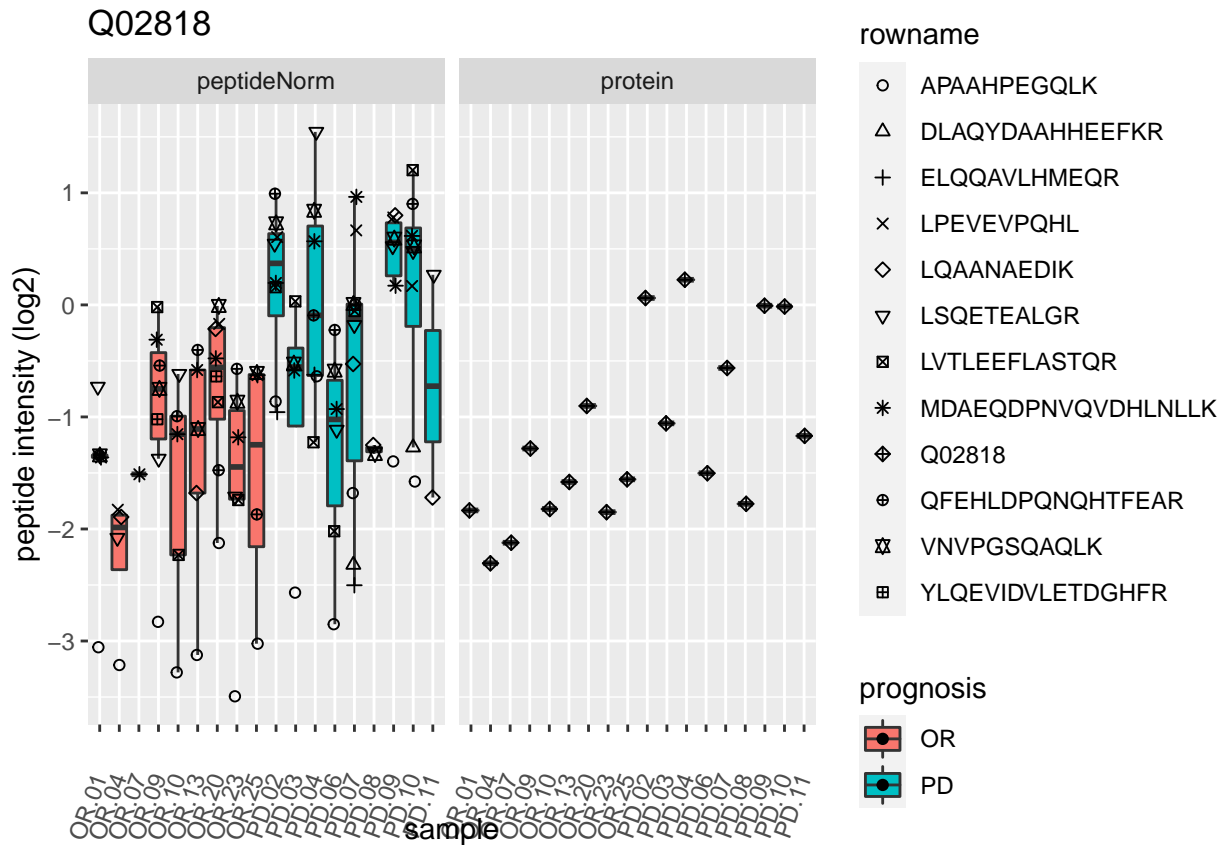


P62310



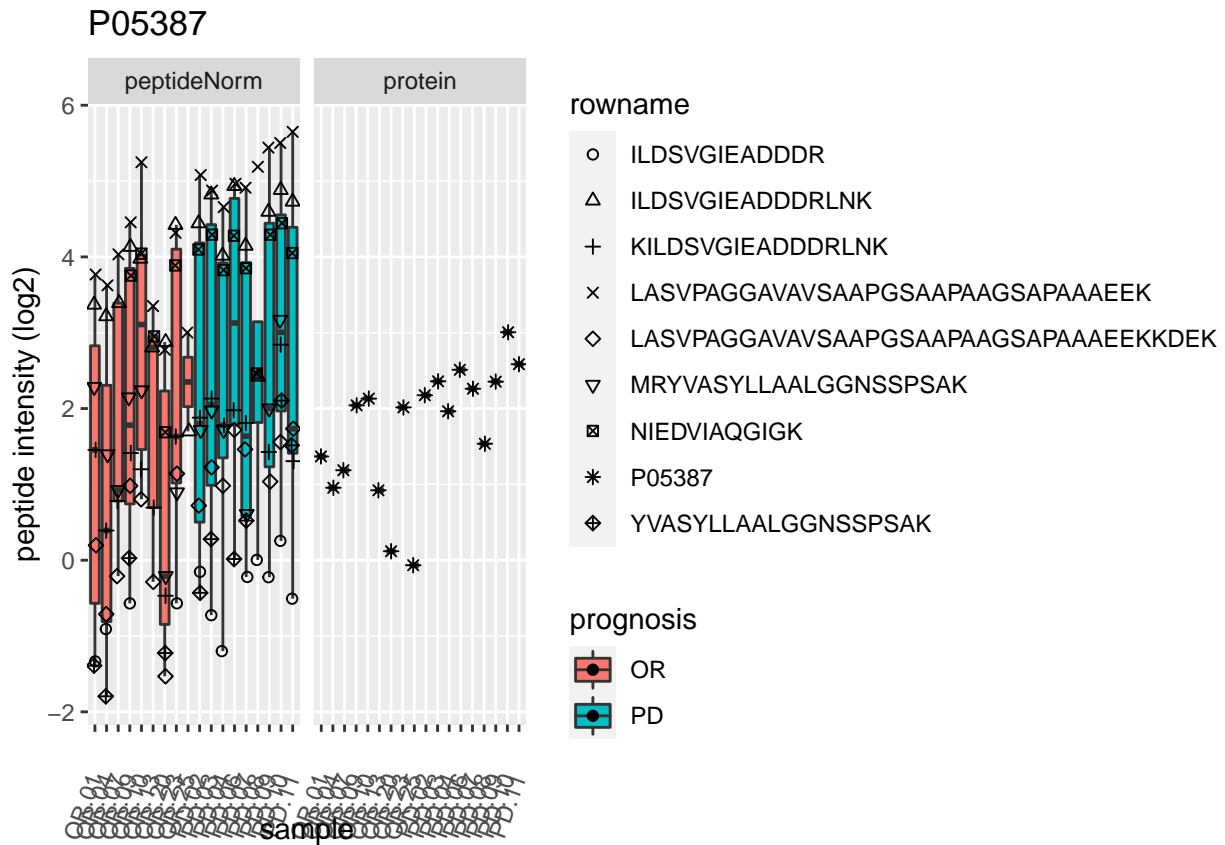
Q02818



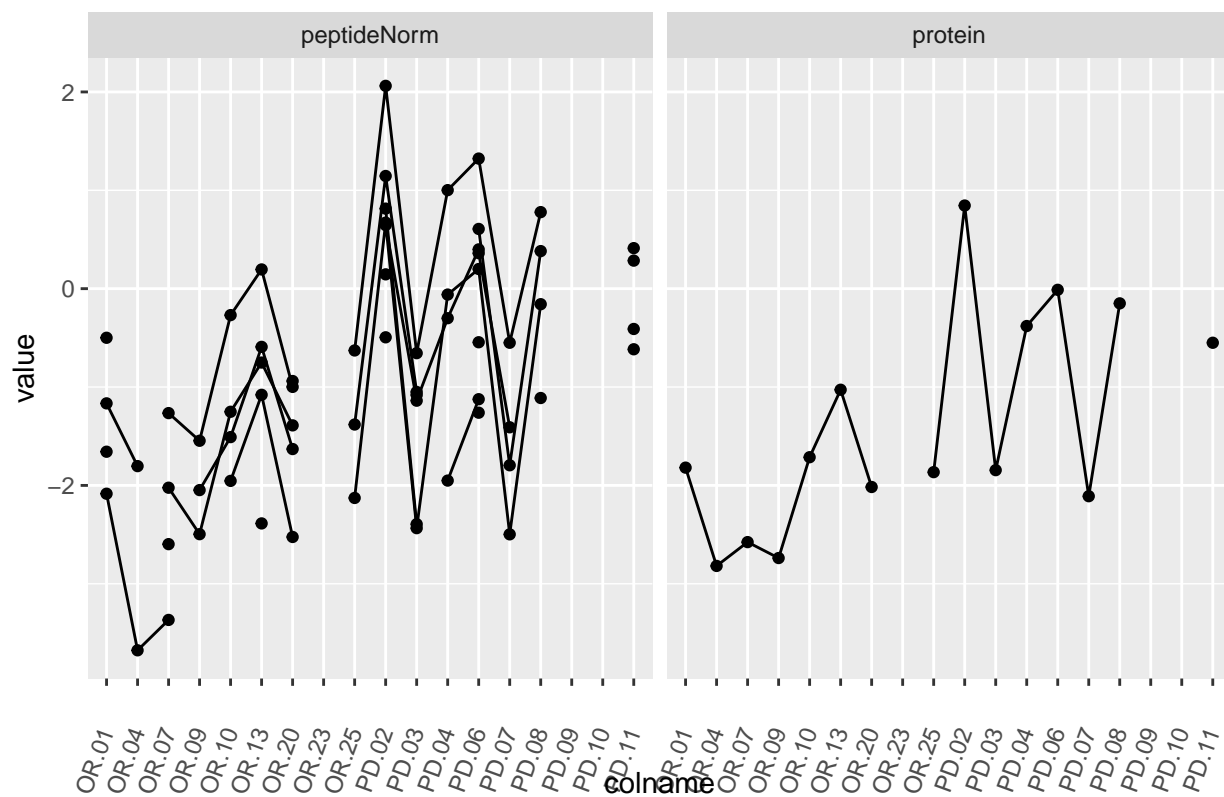


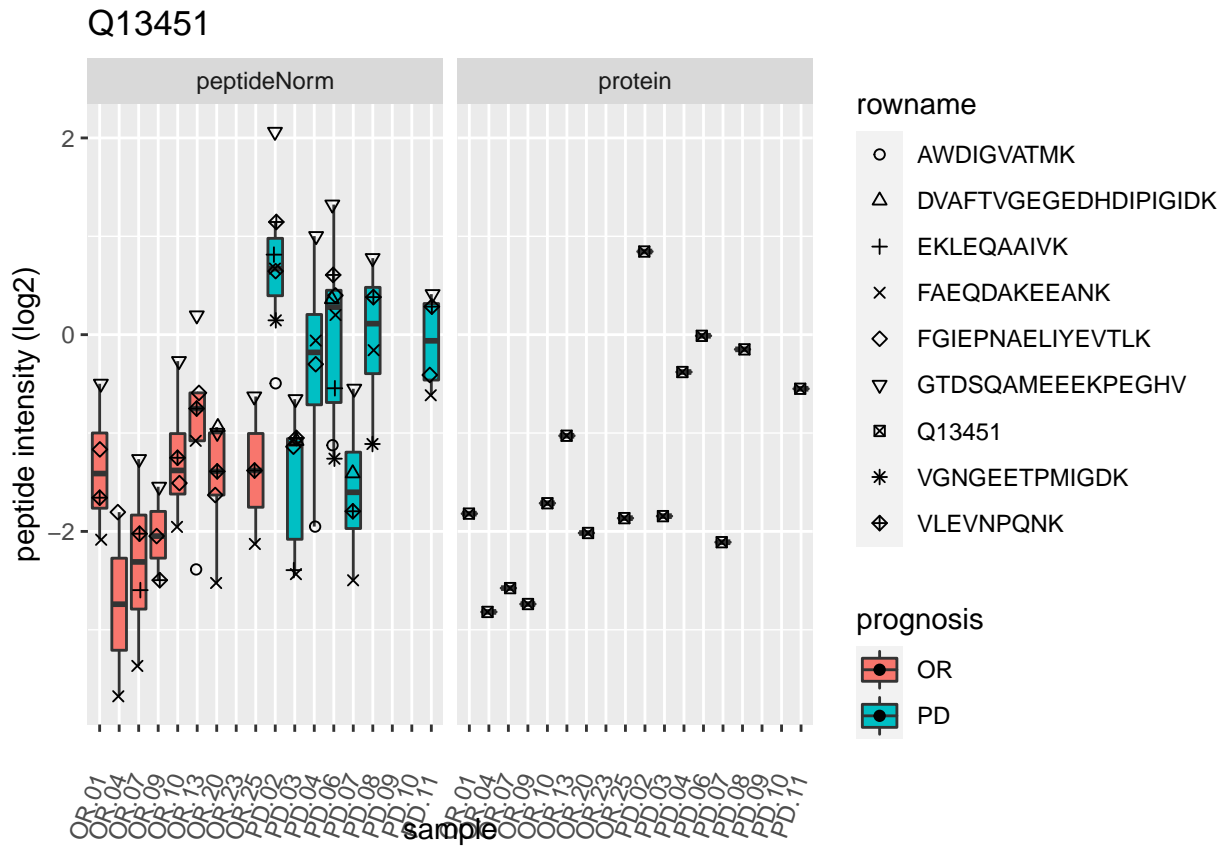
P05387





Q13451

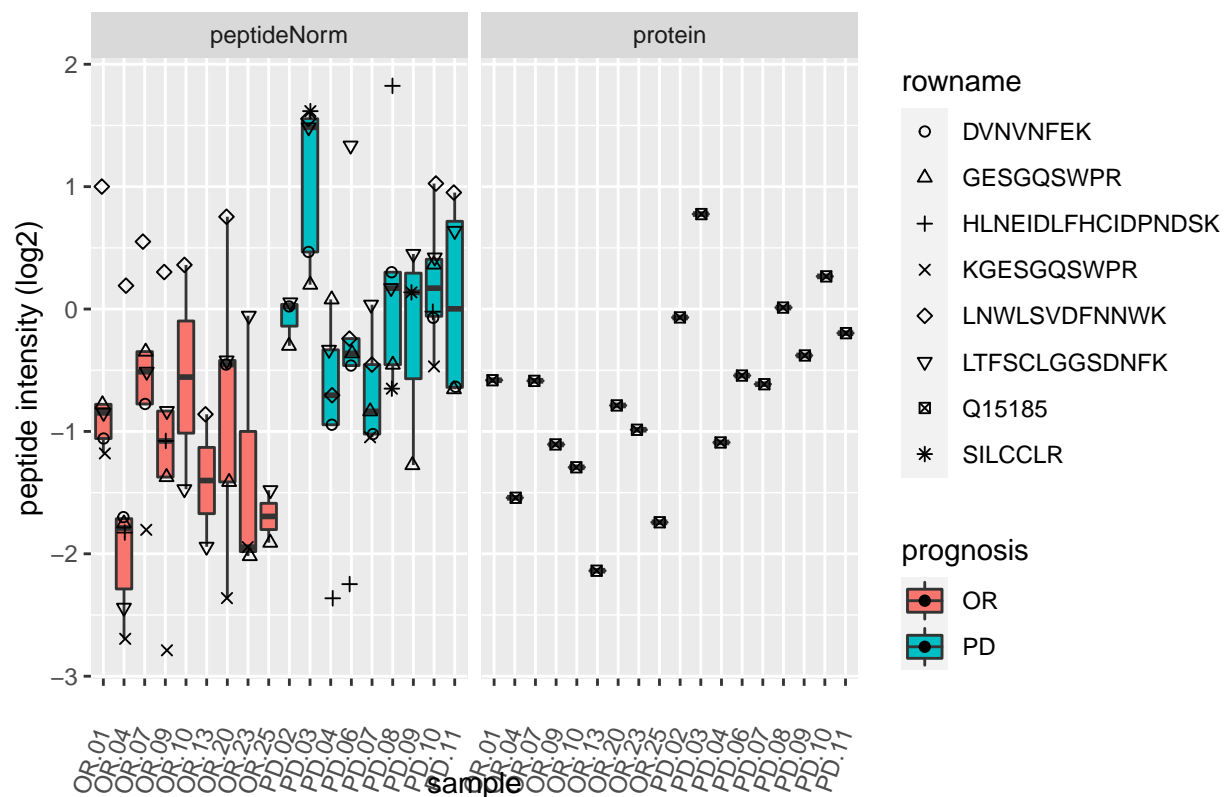




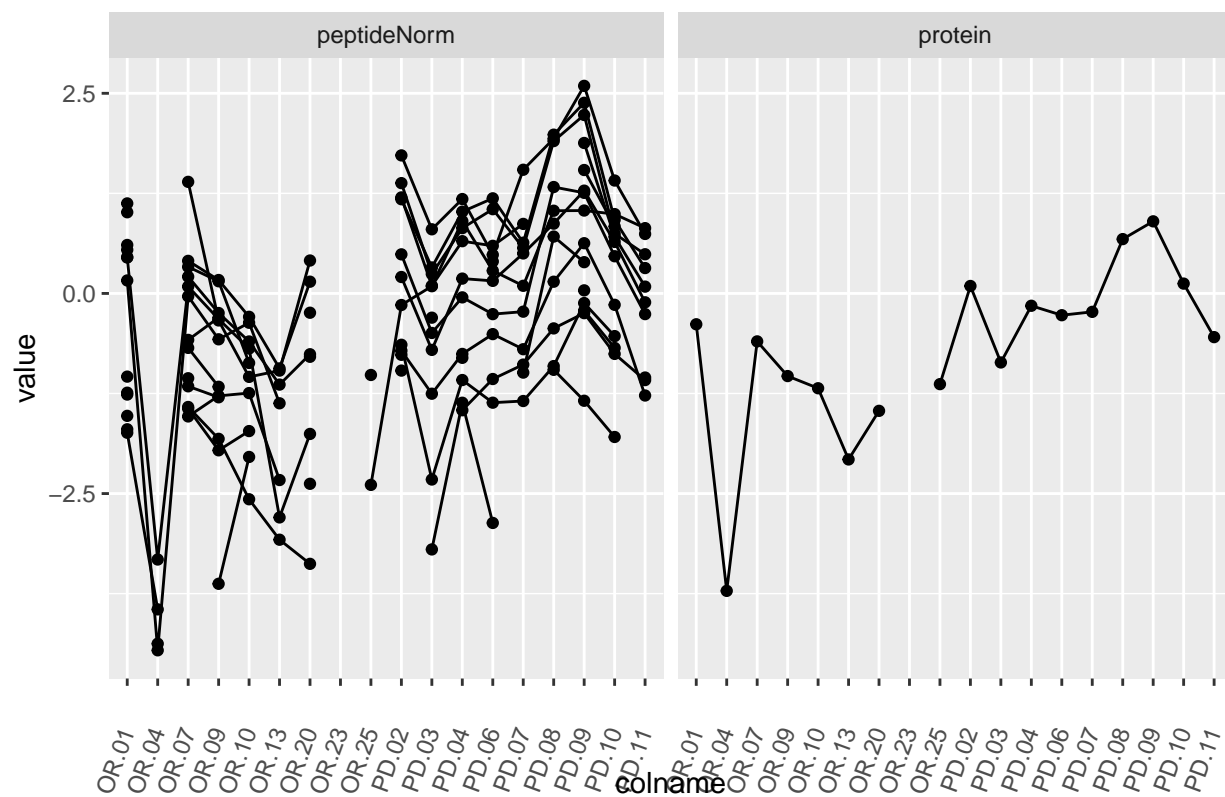
Q15185

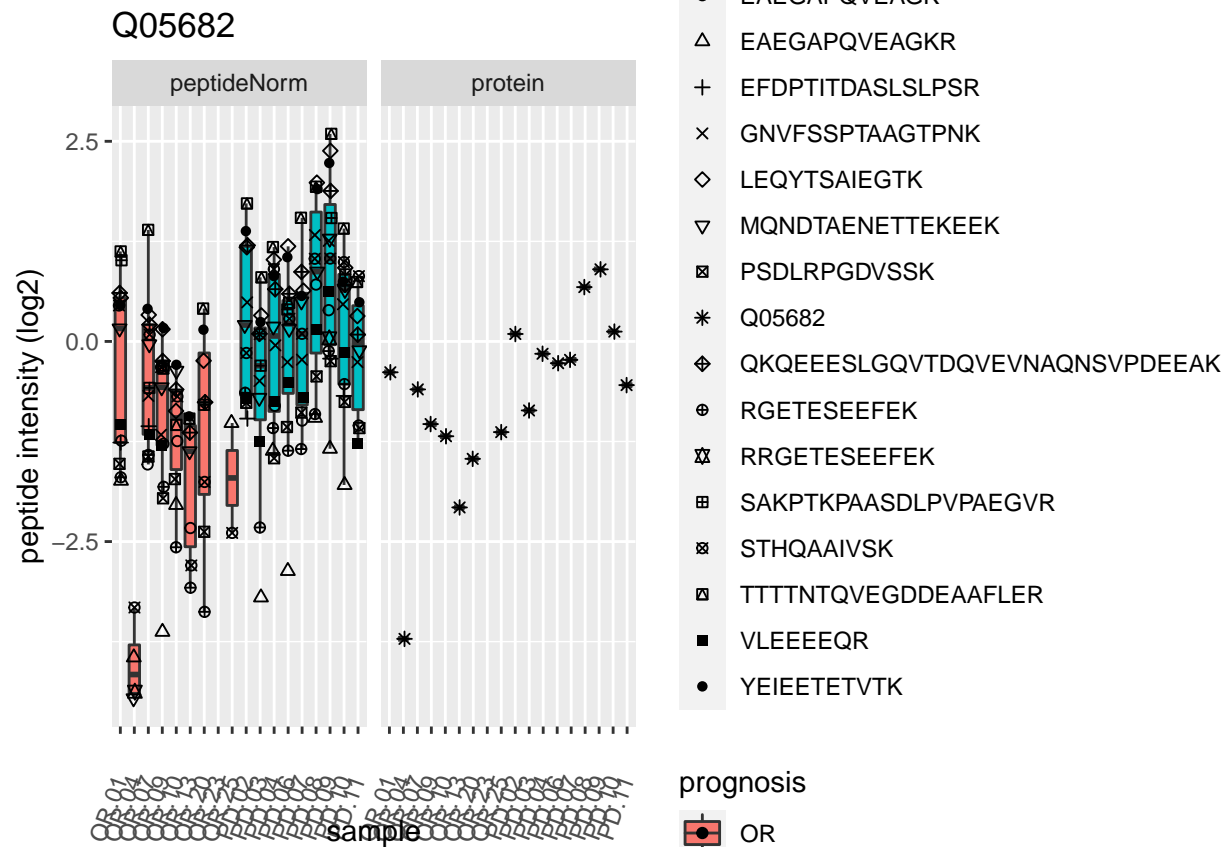


Q15185

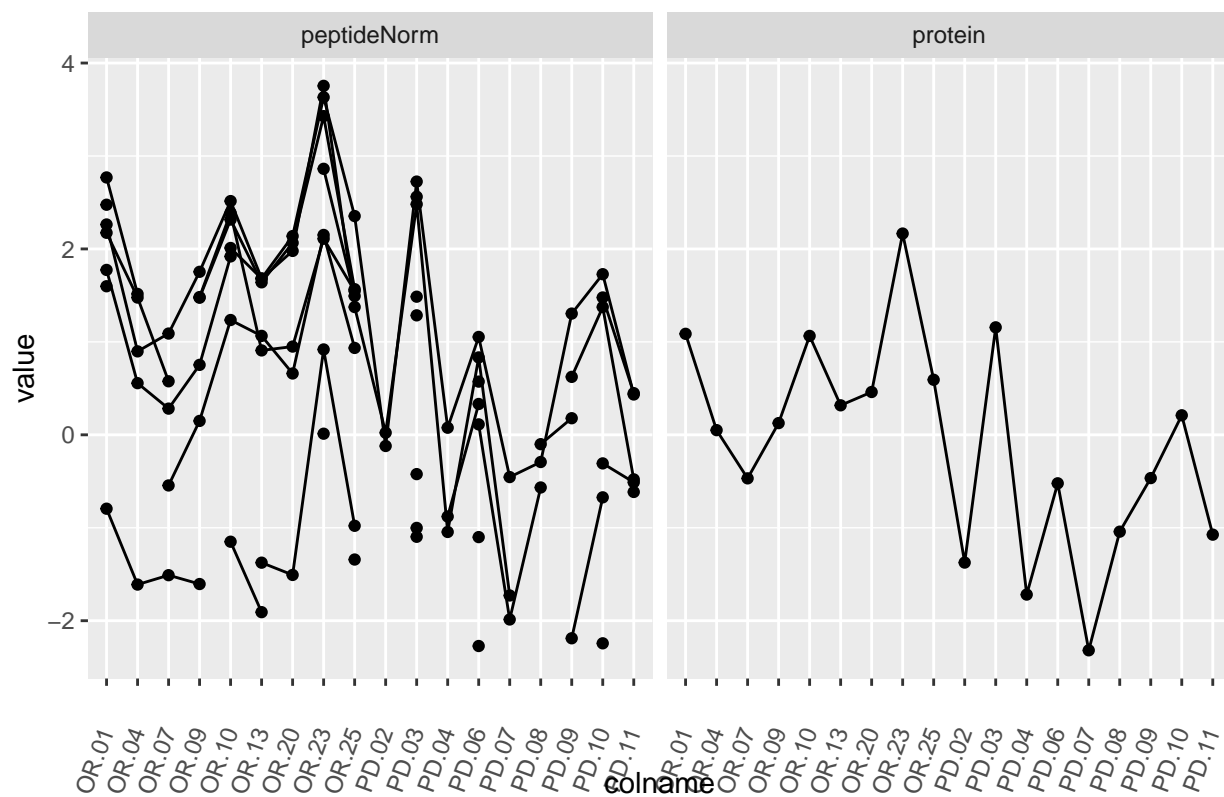


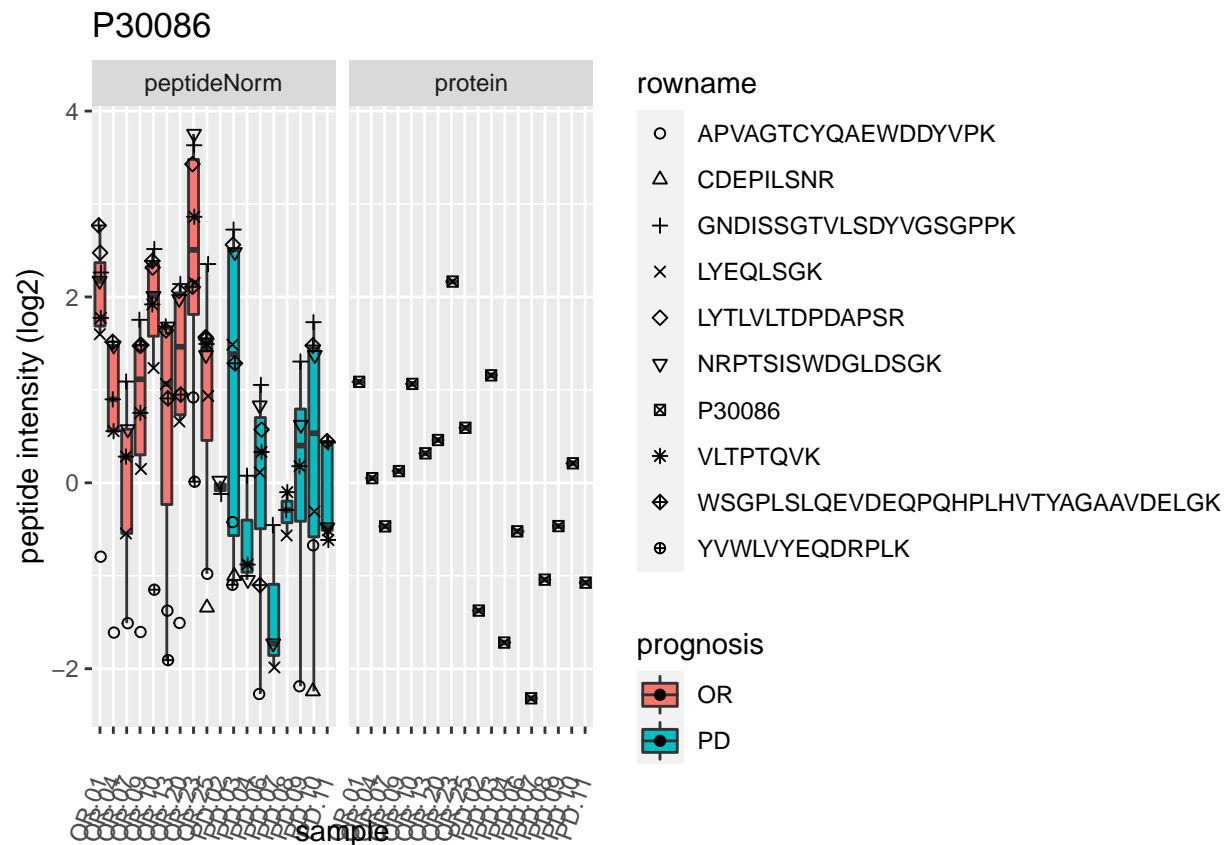
Q05682





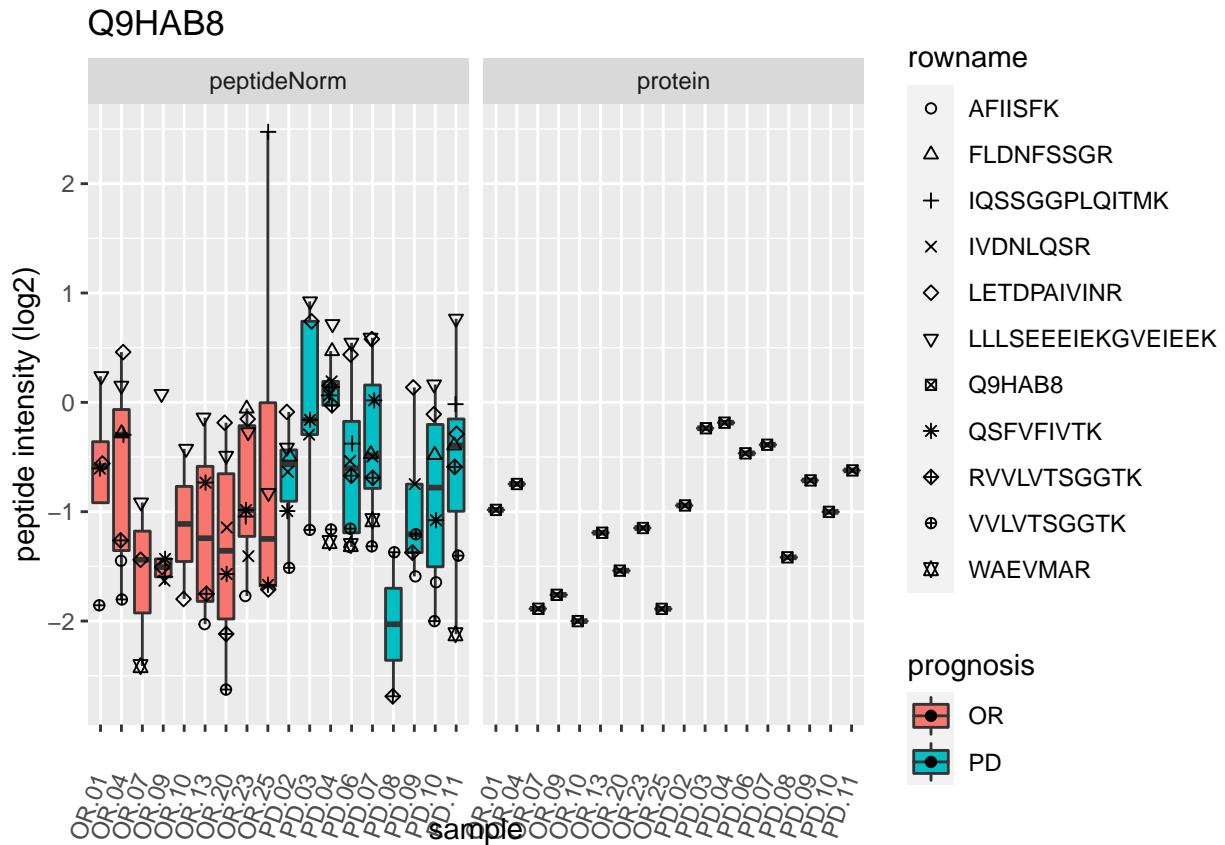
P30086





Q9HAB8

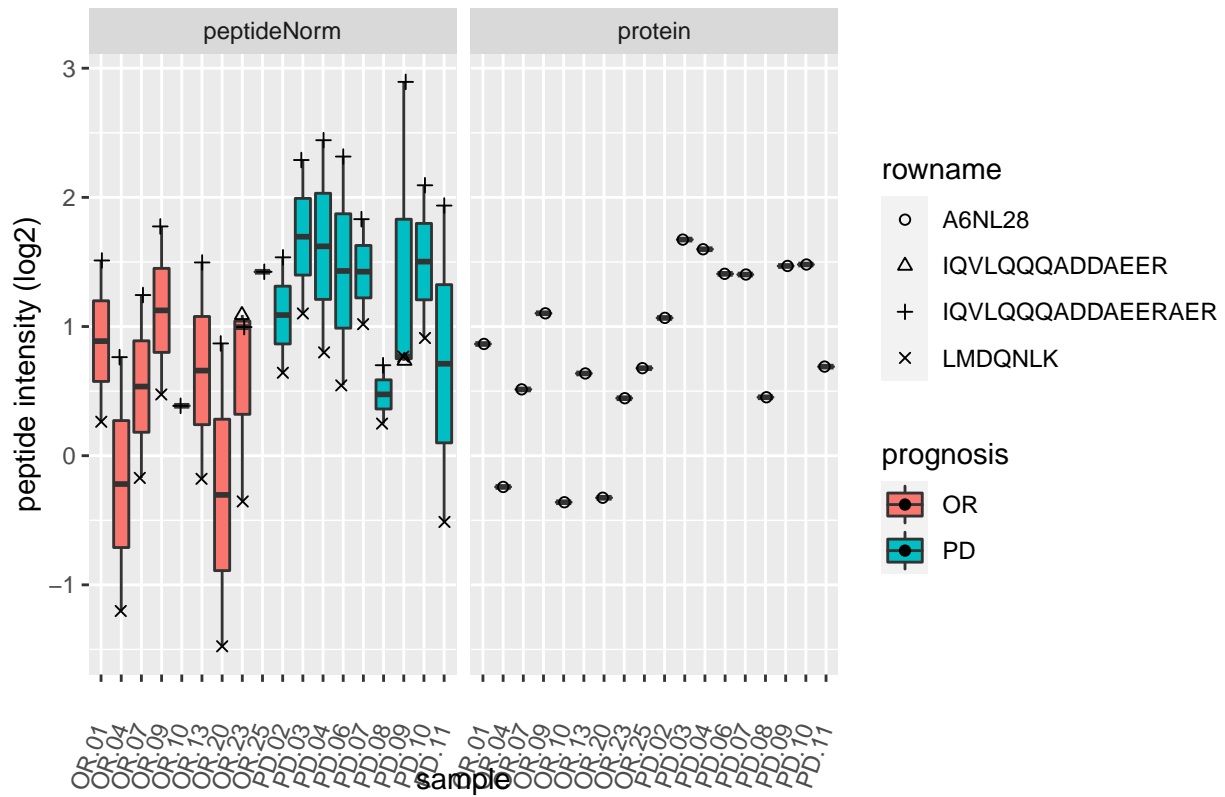




A6NL28



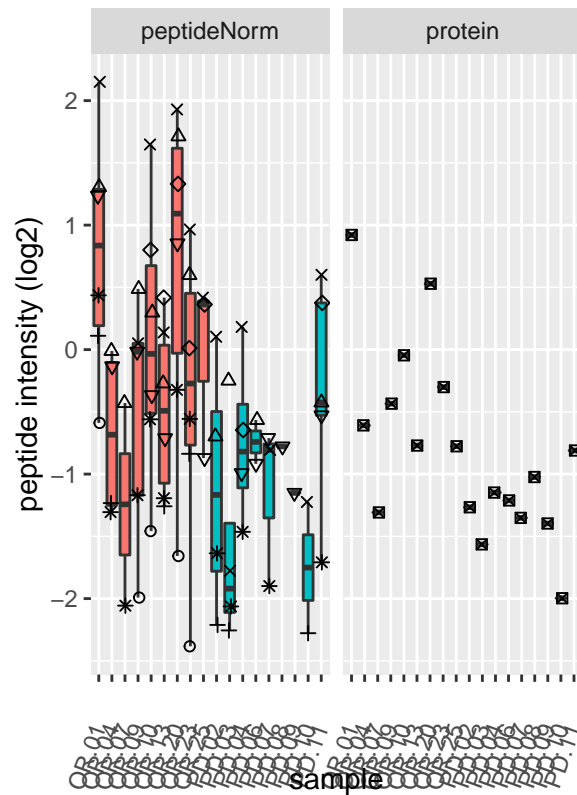
A6NL28



Q9H936



Q9H936



rowname

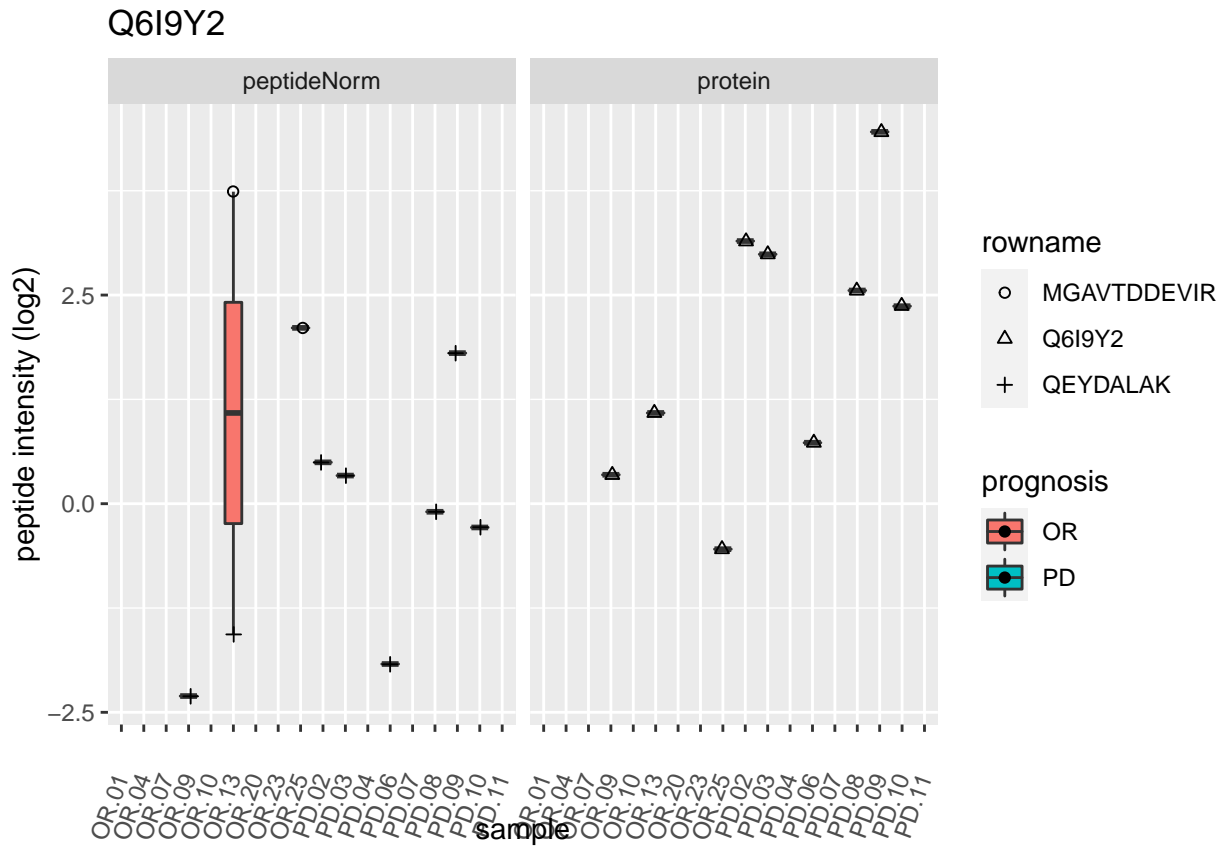
- DVPFSVVYFPLFANLNQLGRPASEEK
- △ GAAVNLTTLVTPEK
- + GLGATLLR
- × ILAAQGQLSAQGGAQPSVEAPAAPRPTATQLTR
- ◇ KILAAQGQLSAQGGAQPSVEAPAAPRPTATQLTR
- ▽ LAANDFFR
- ⊠ Q9H936
- * SEGYFGMYR

prognosis

- OR
- PD

Q6I9Y2

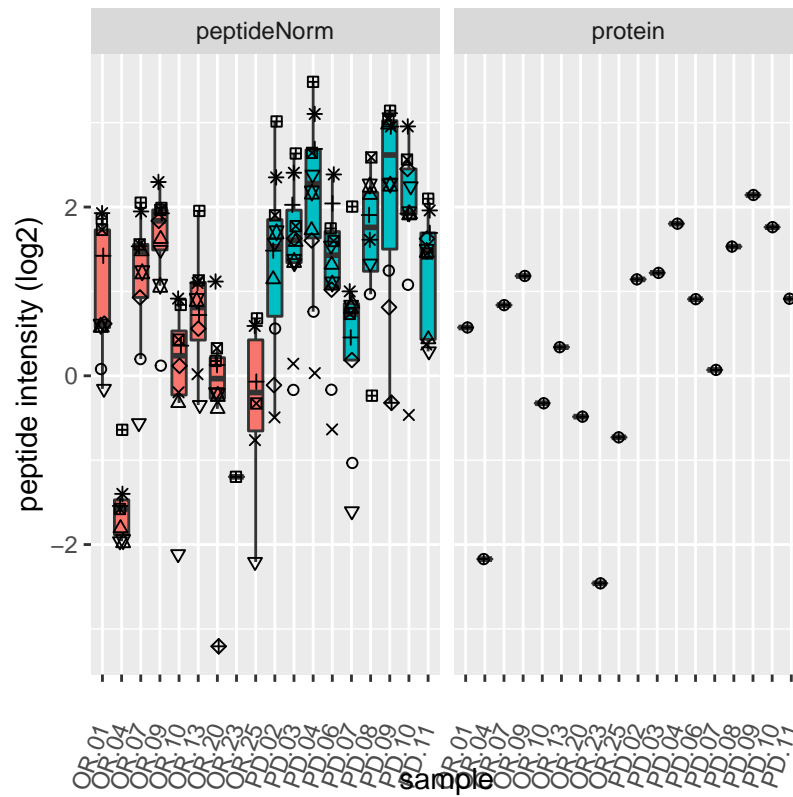




P67936



P67936



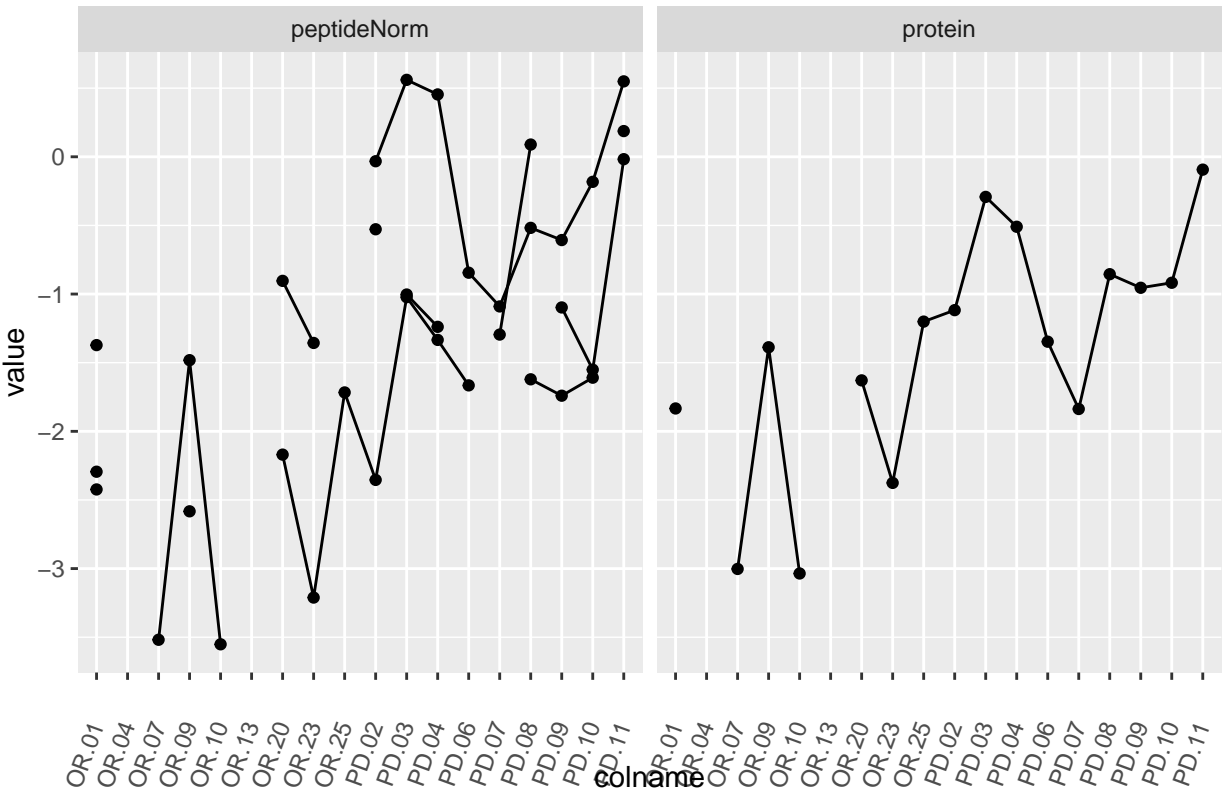
rowname

- AEGDVAALNR
- △ AGLNSLEAVK
- + AGLNSLEAVKR
- × CGDLEELKKNVTNNLK
- ◇ EENVGLHQTLDQTLNELNCI
- ▽ EKAEGDVAALNR
- ⊠ IQALQQQADEAEDR
- * KIQUALQQQADEAEDR
- ⊕ KLVILEGELERAEEER
- ⊗ P67936
- ⊠ TIDDLLEEK
- ⊠ YSEKEDKYEEEEIK

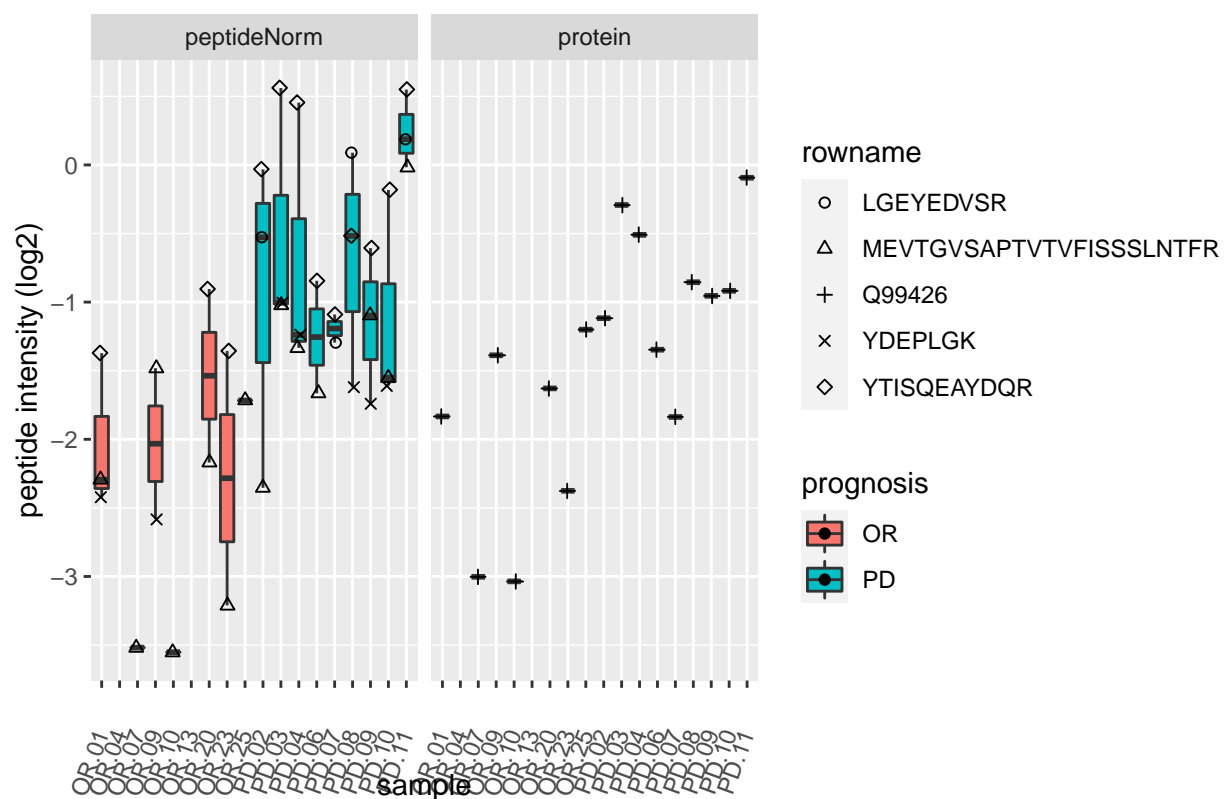
prognosis

- OR
- PD

Q99426

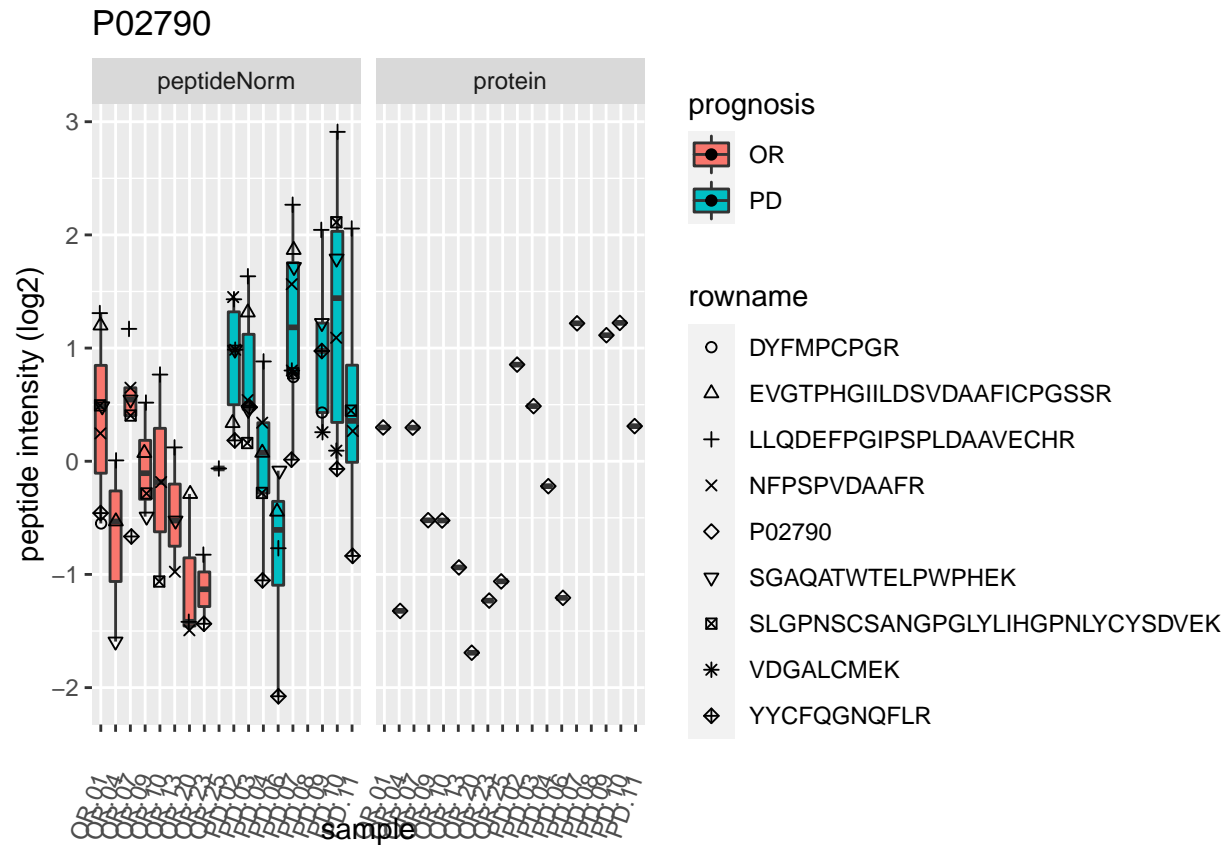


Q99426

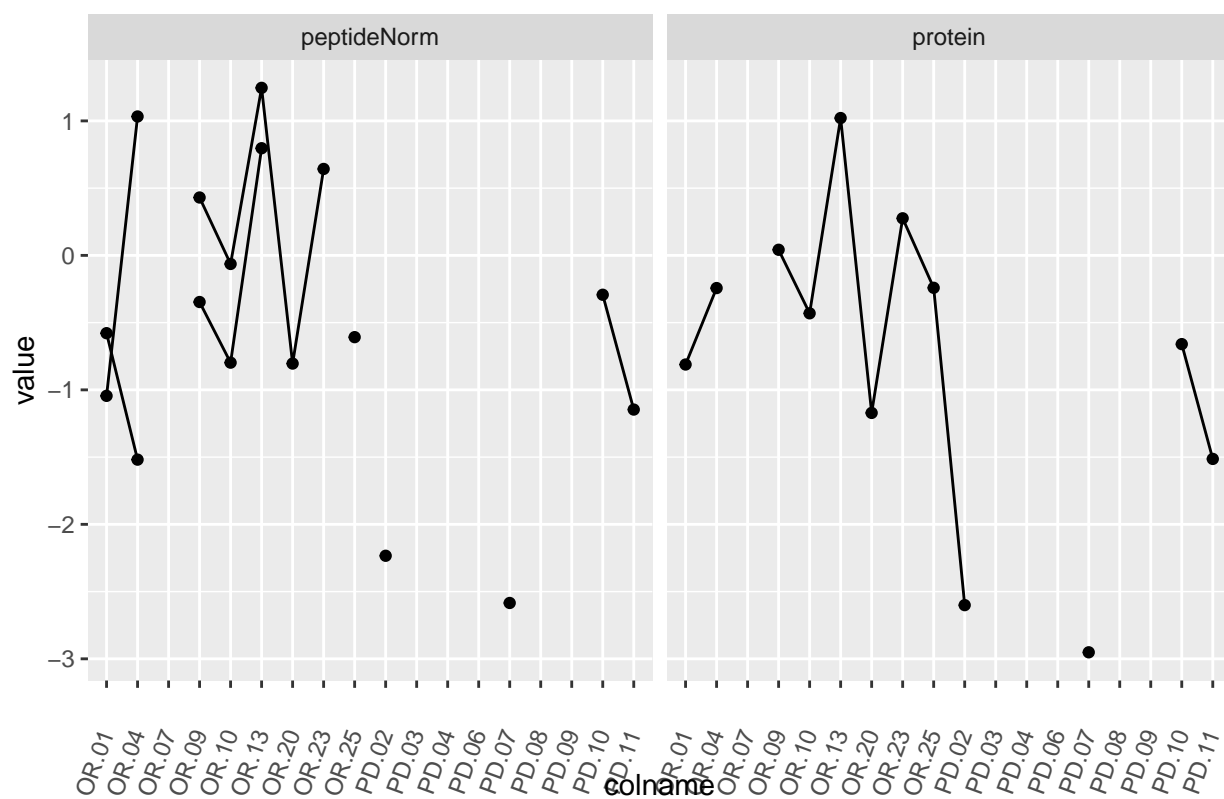


P02790

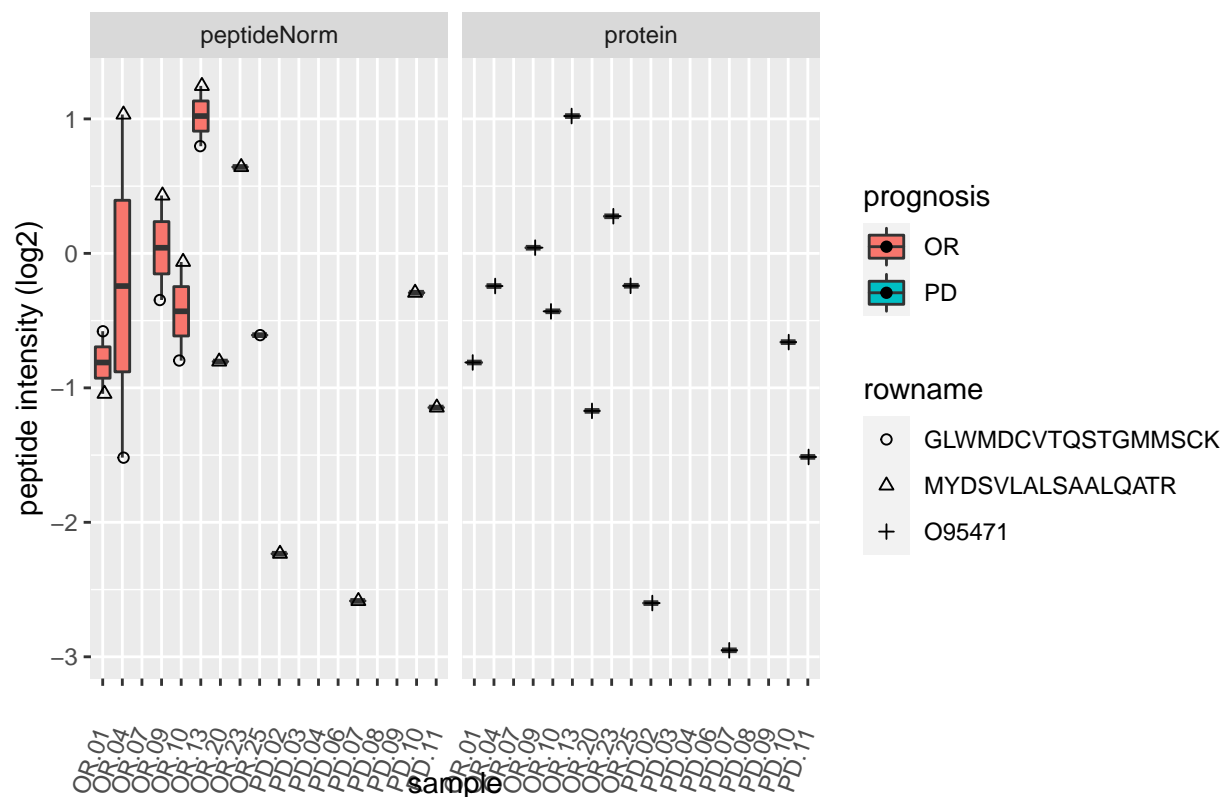




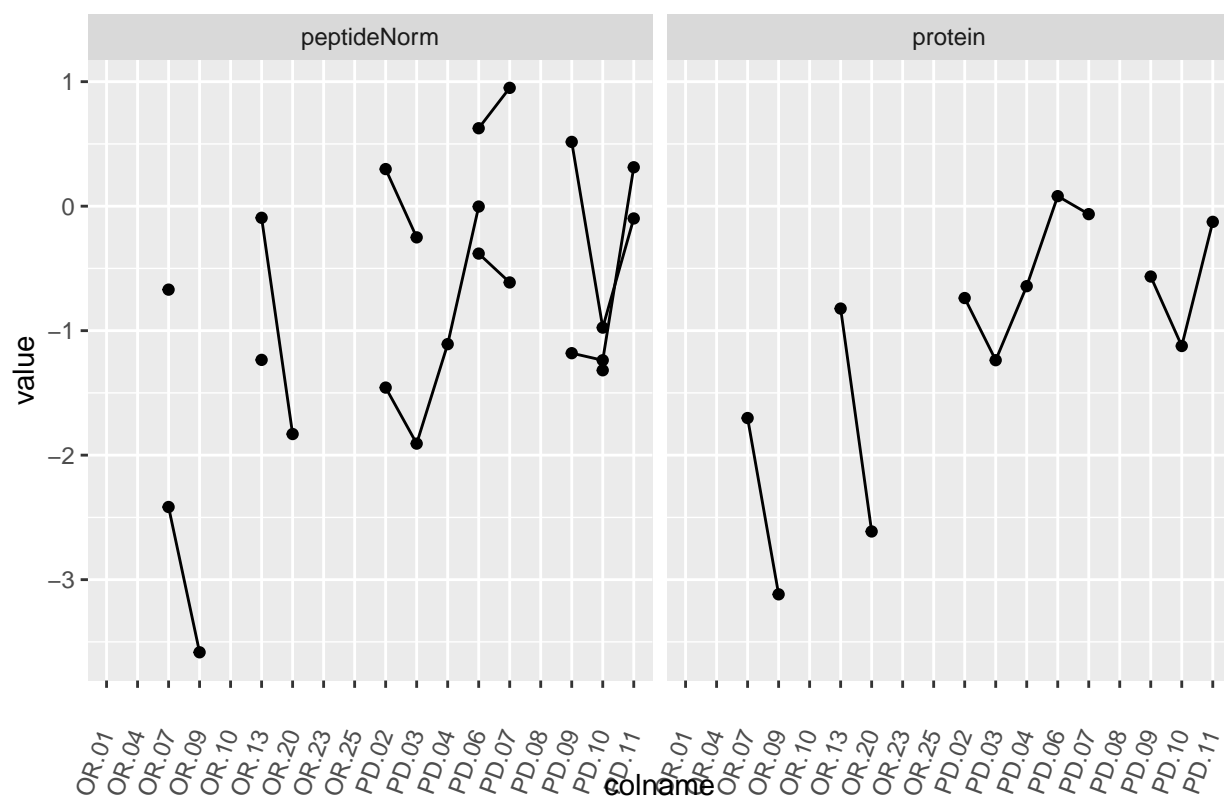
O95471

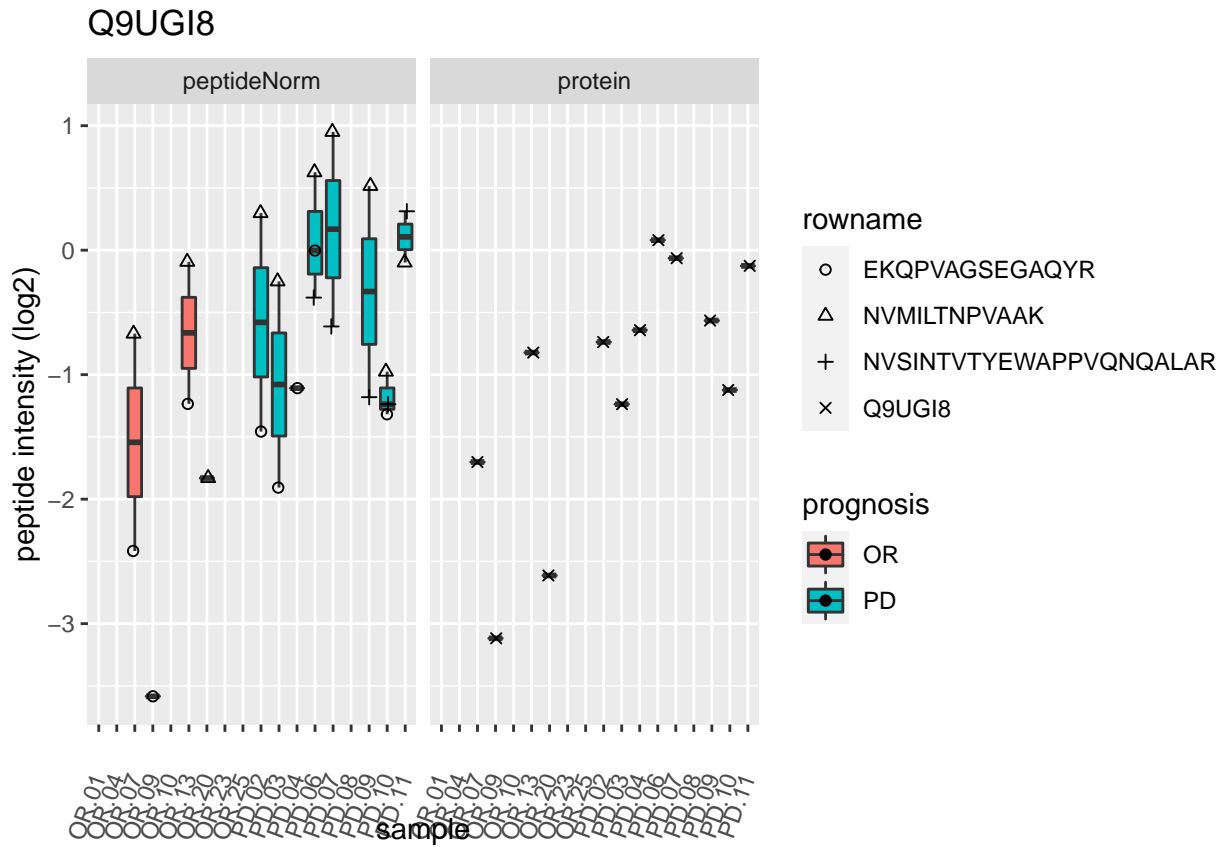


O95471



Q9UGI8

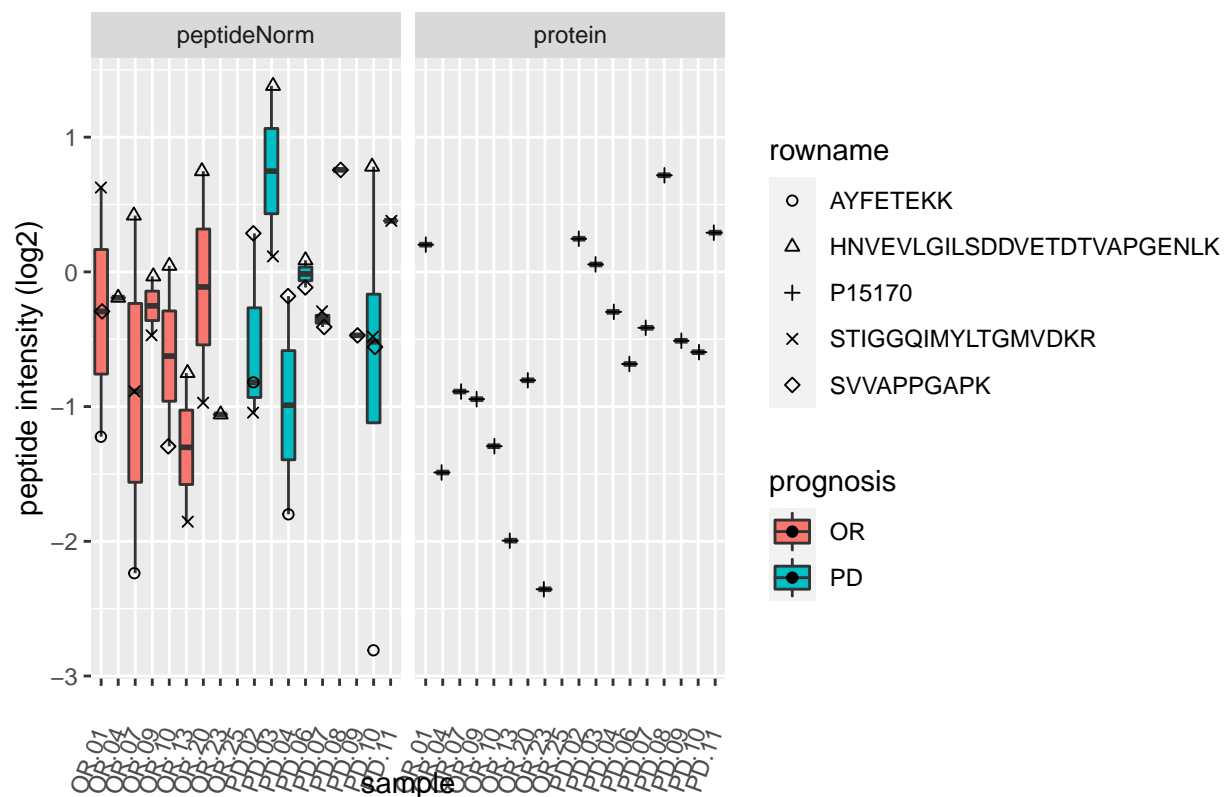




P15170

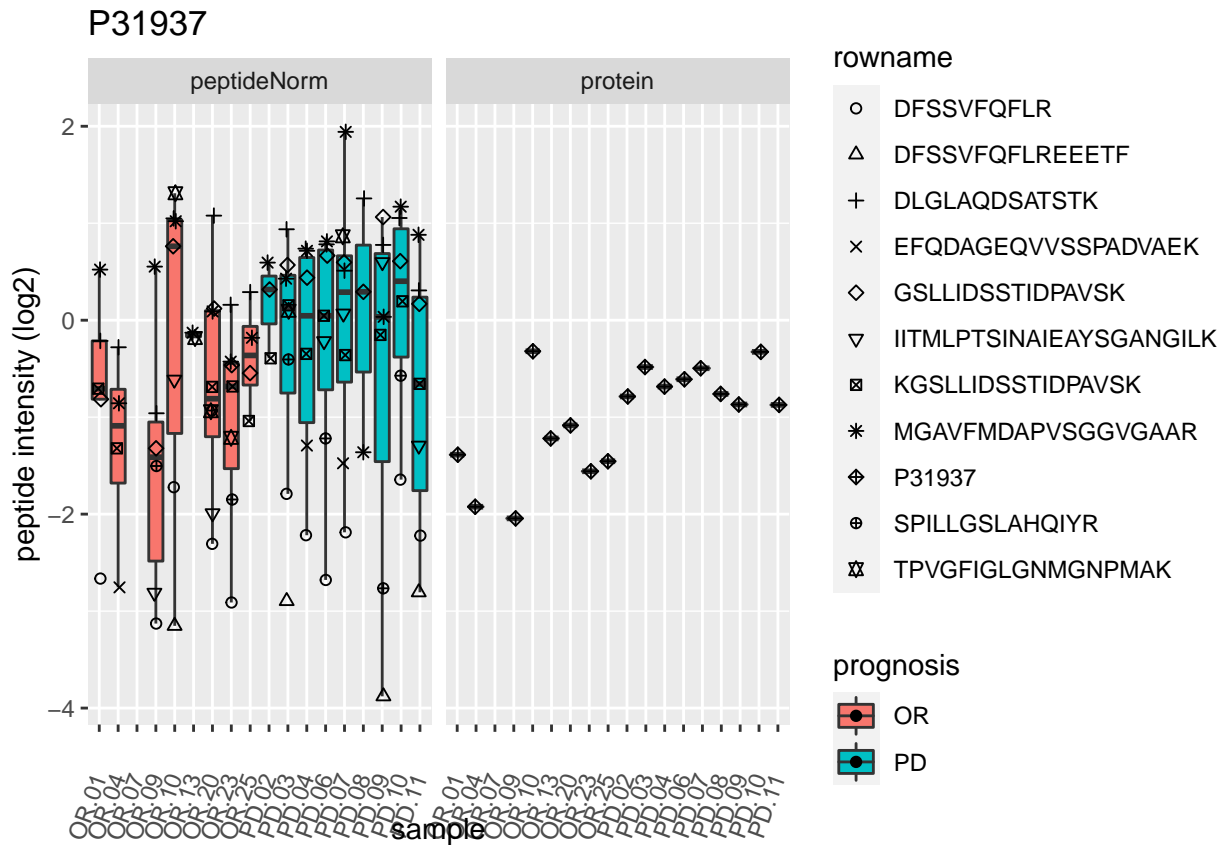


P15170

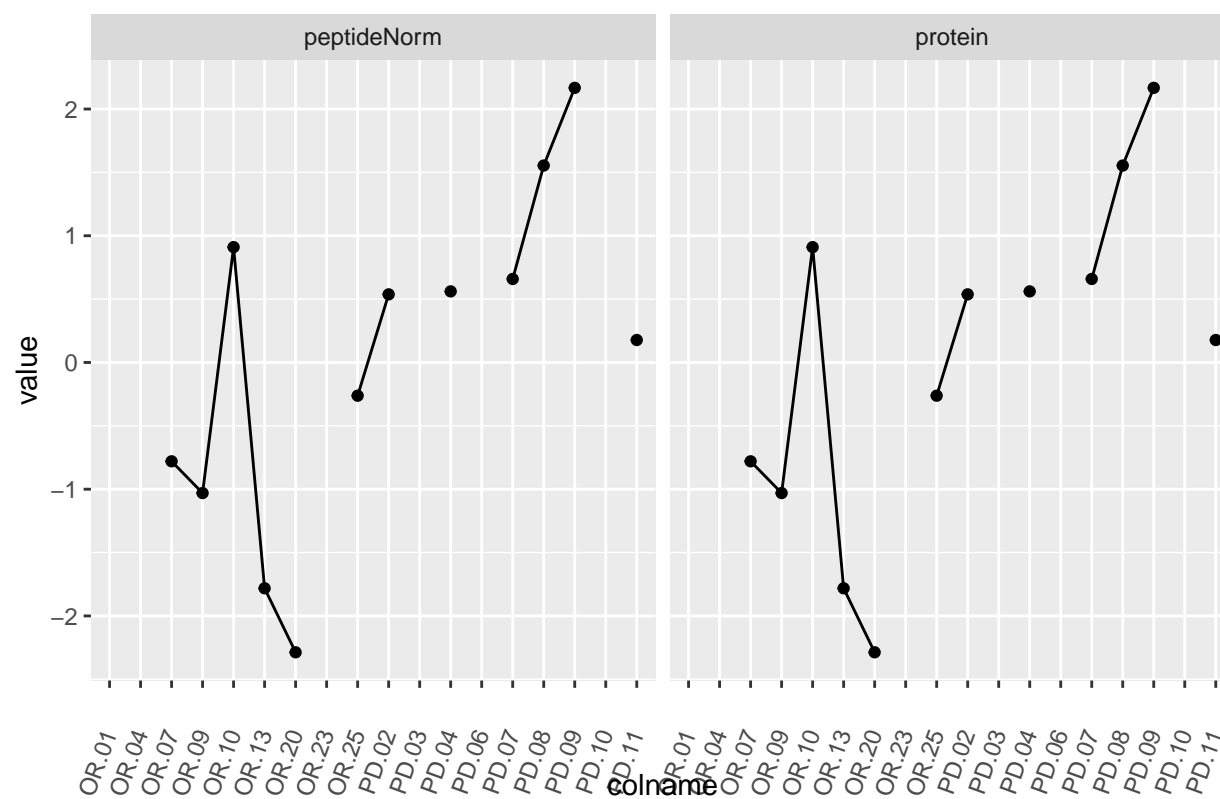


P31937

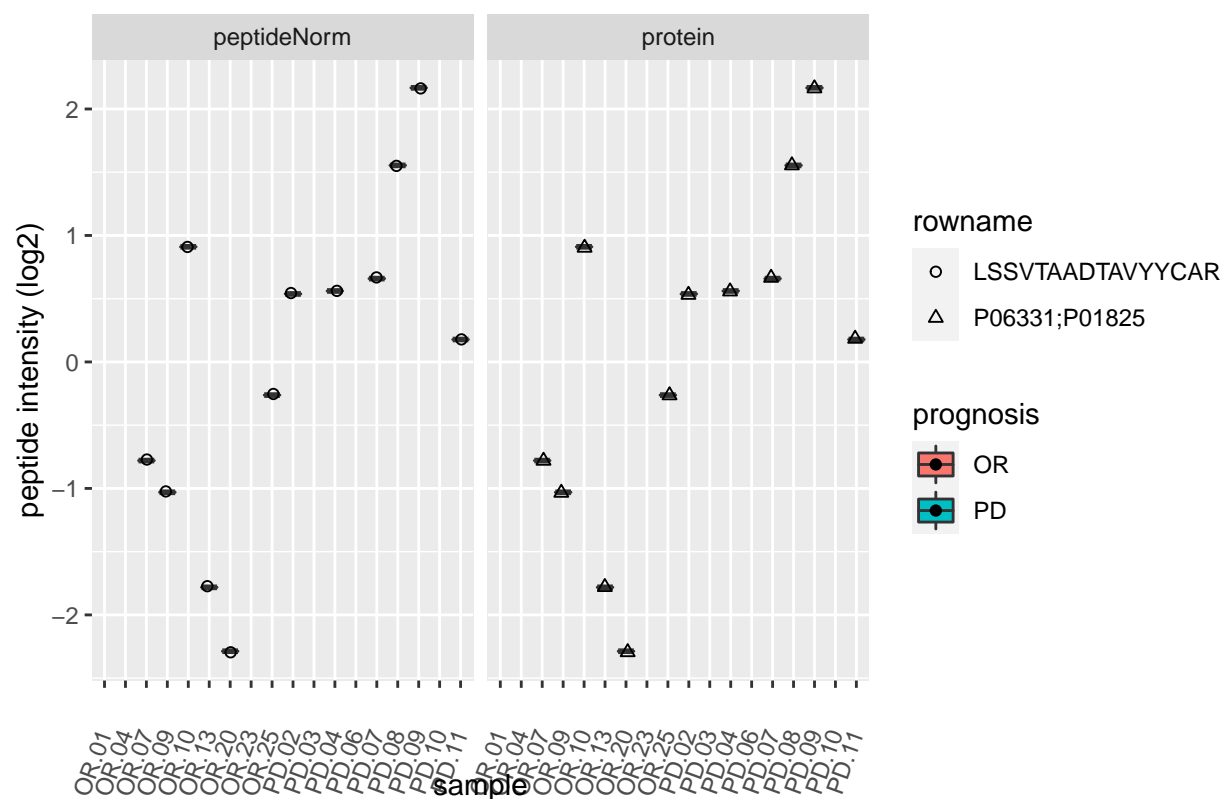




P06331;P01825



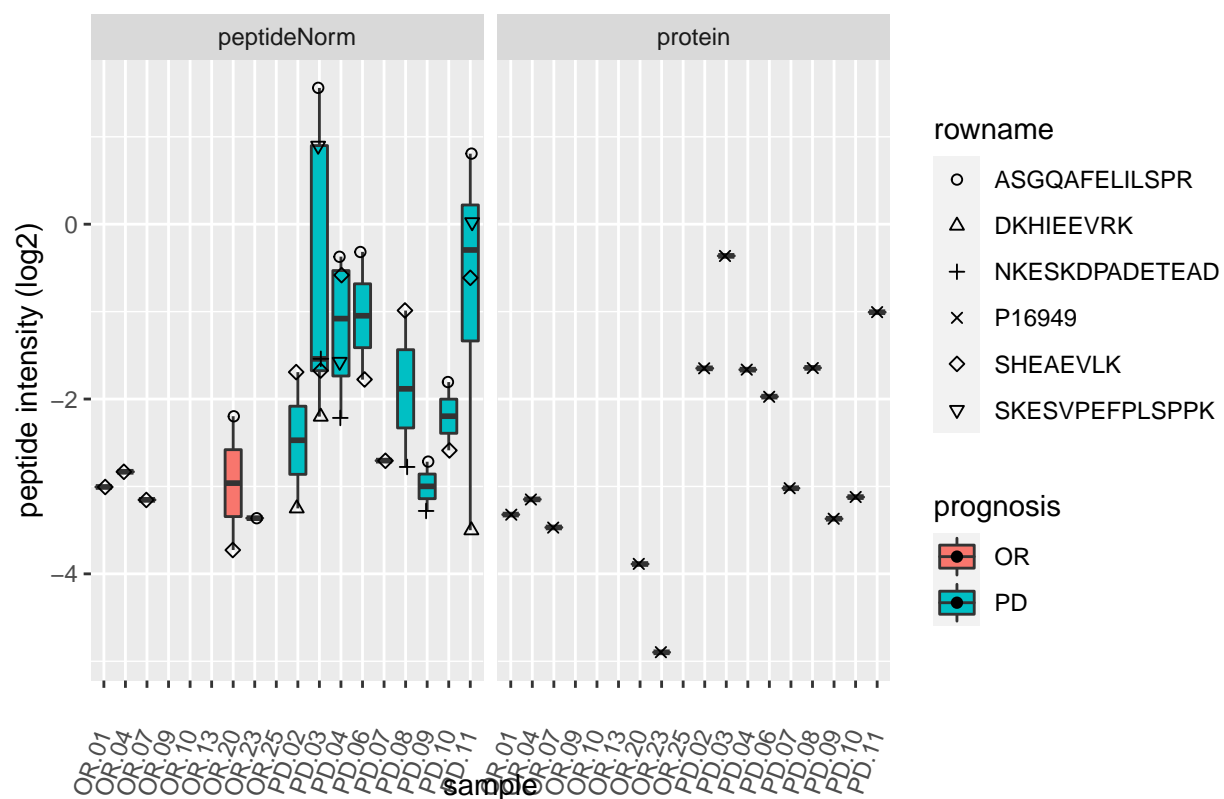
P06331;P01825



P16949



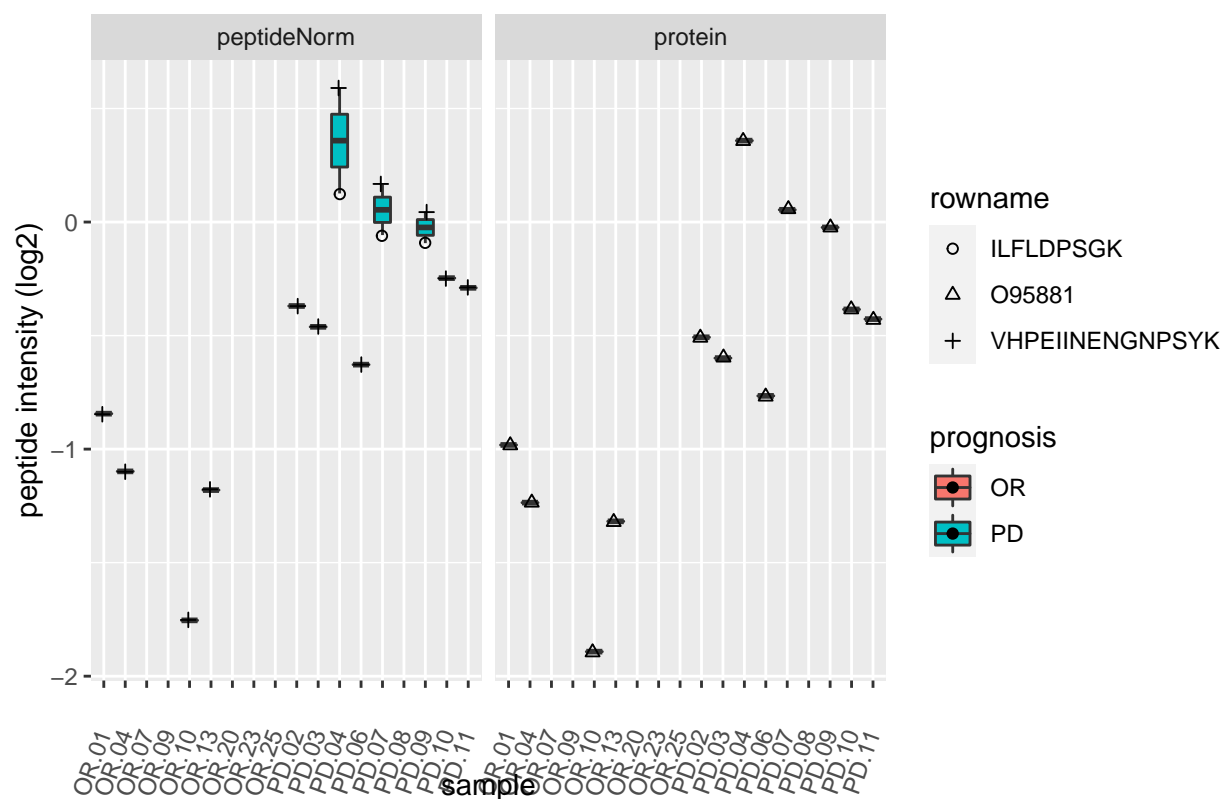
P16949



O95881



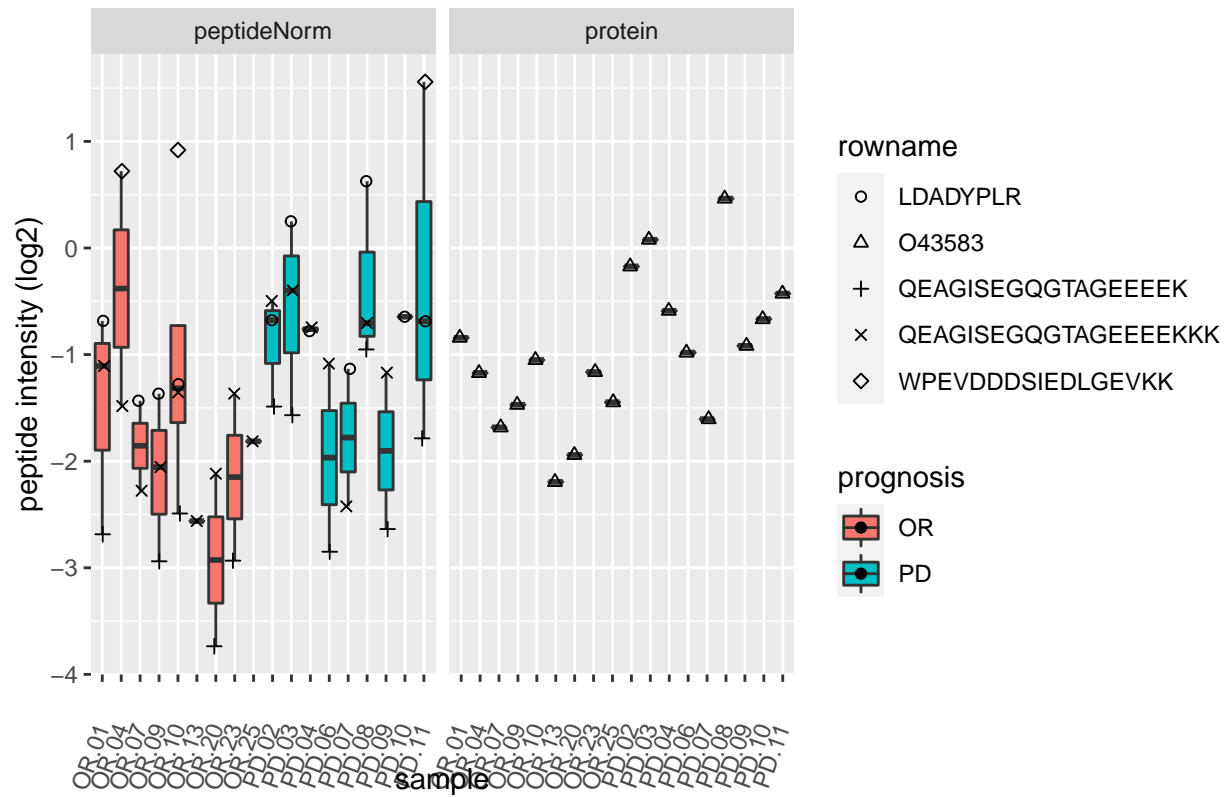
O95881



O43583



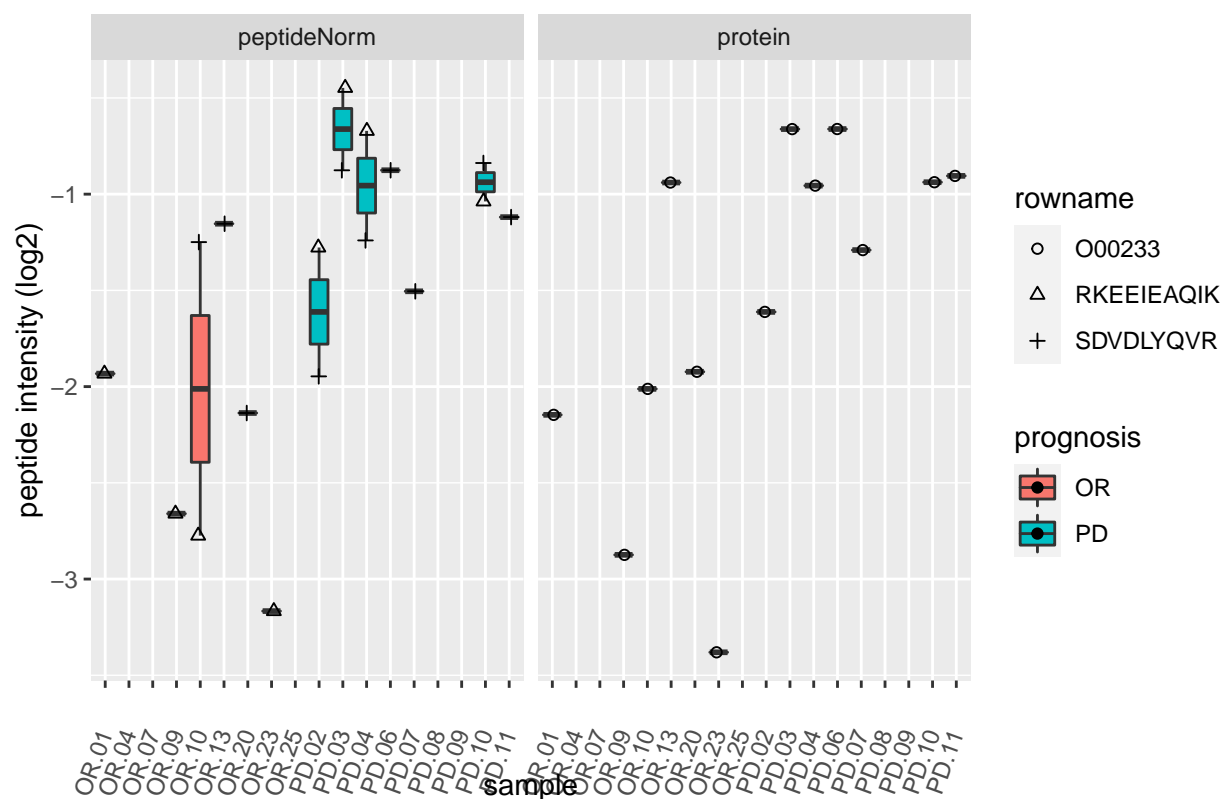
O43583



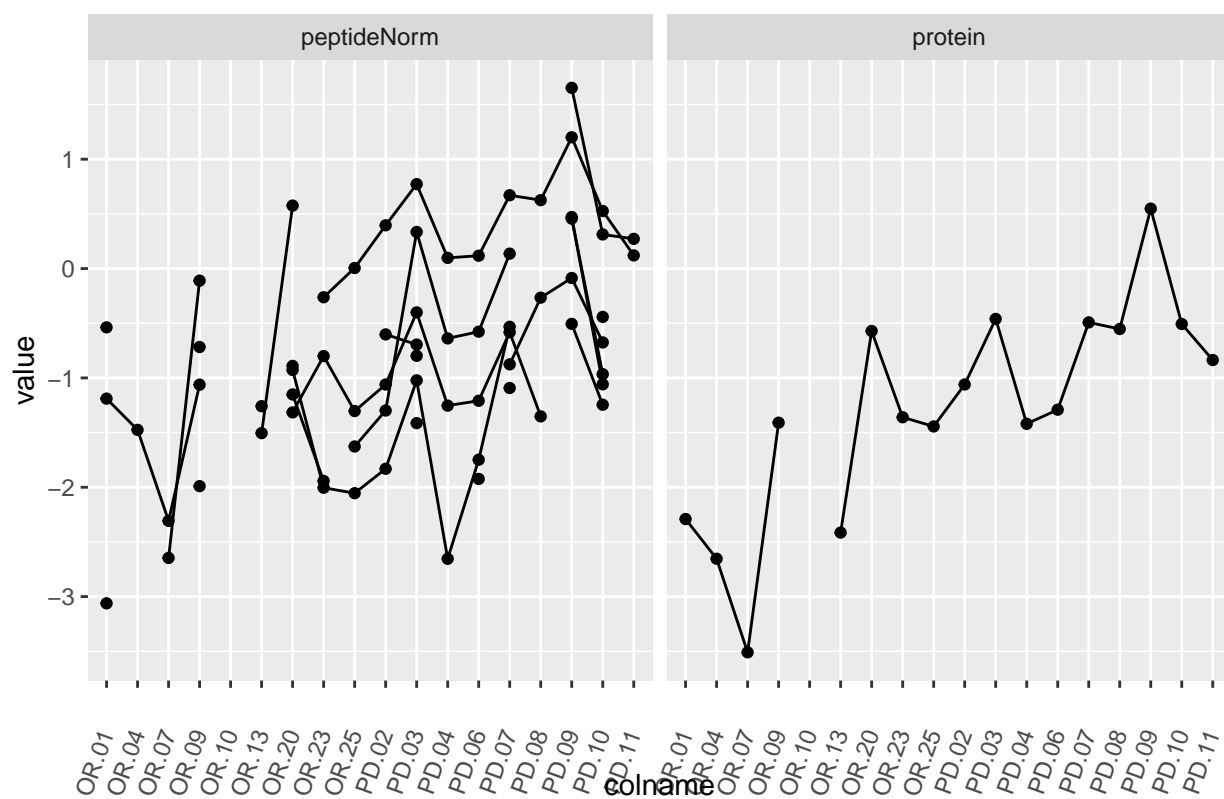
O00233



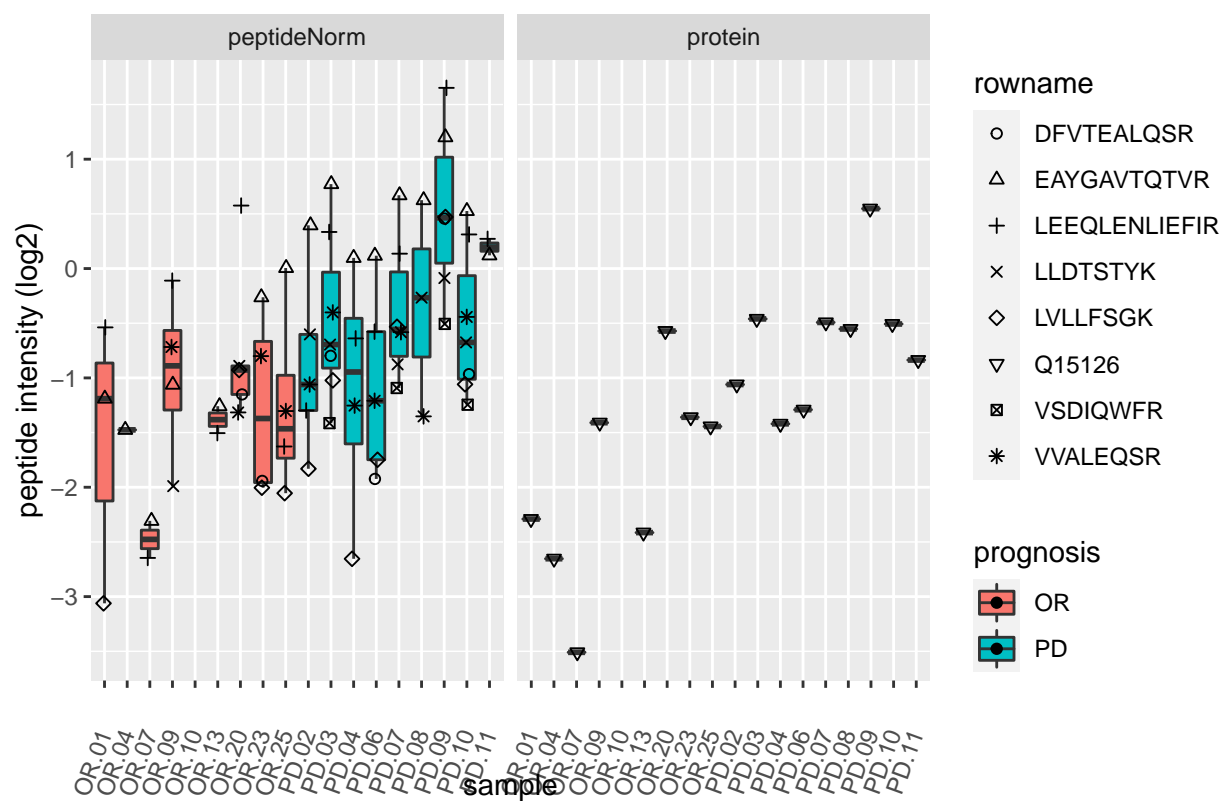
O00233



Q15126



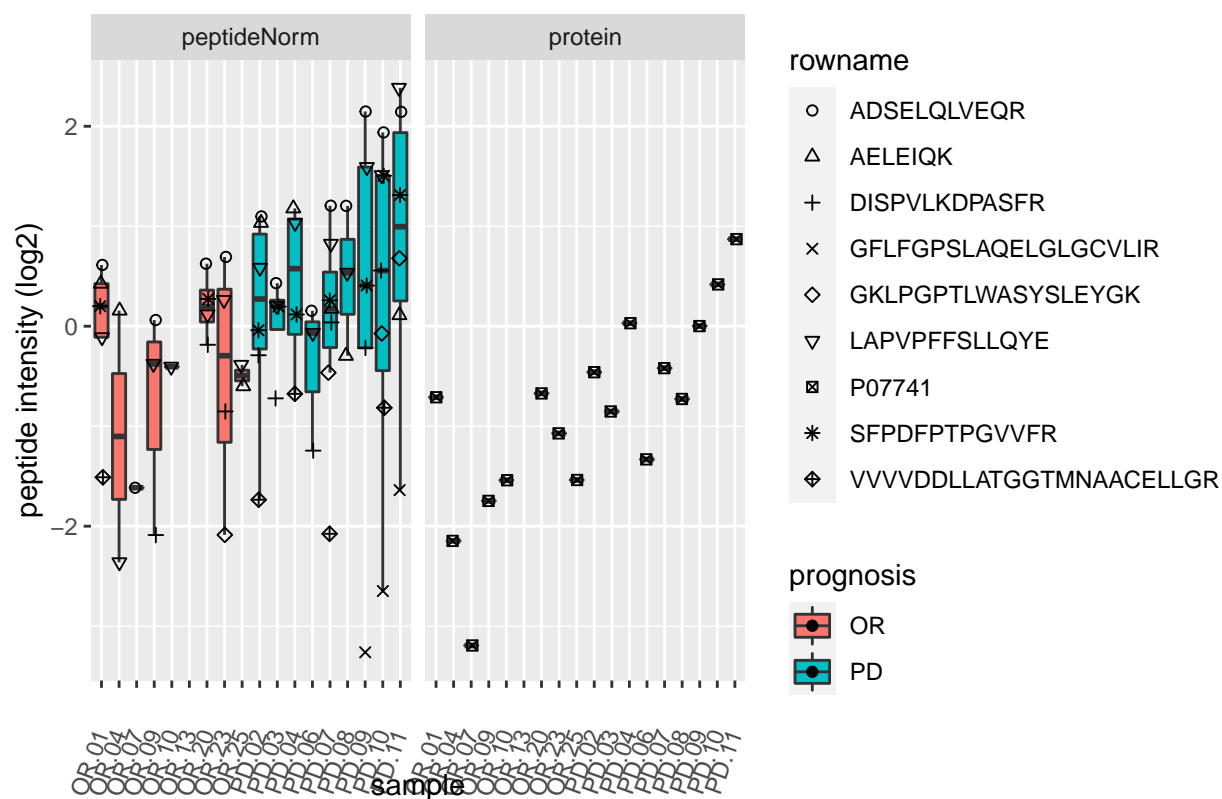
Q15126



P07741

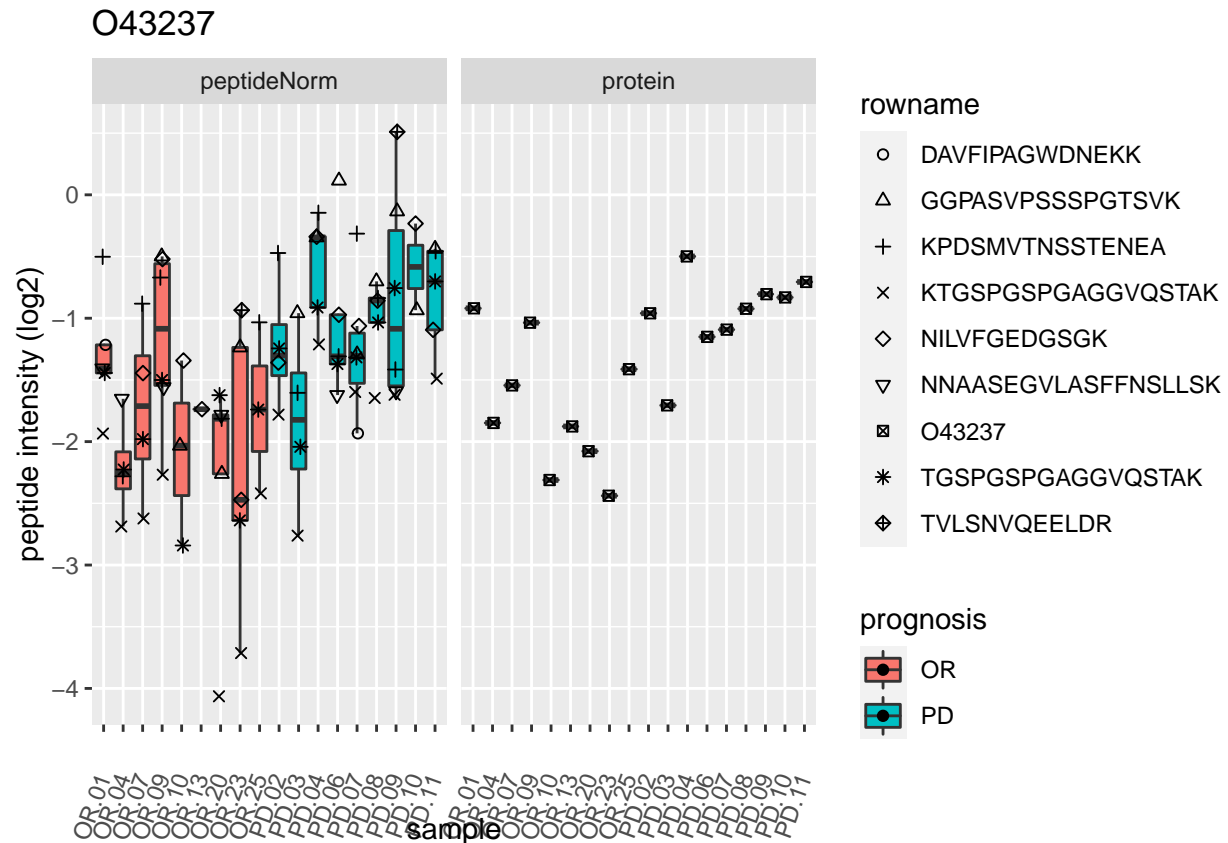


P07741



O43237





5 Session Info

With respect to reproducibility, it is highly recommended to include a session info in your script so that readers of your output can see your particular setup of R.

```
sessionInfo()
```

```
## R version 4.2.3 (2023-03-15)
## Platform: x86_64-pc-linux-gnu (64-bit)
## Running under: Ubuntu 22.04.3 LTS
##
## Matrix products: default
## BLAS: /usr/lib/x86_64-linux-gnu/openblas-pthread/libblas.so.3
## LAPACK: /usr/lib/x86_64-linux-gnu/openblas-pthread/libopenblas-p-r0.3.20.so
##
## locale:
##  [1] LC_CTYPE=C.UTF-8      LC_NUMERIC=C           LC_TIME=C.UTF-8
##  [4] LC_COLLATE=C.UTF-8    LC_MONETARY=C.UTF-8    LC_MESSAGES=C.UTF-8
##  [7] LC_PAPER=C.UTF-8      LC_NAME=C              LC_ADDRESS=C
## [10] LC_TELEPHONE=C        LC_MEASUREMENT=C.UTF-8 LC_IDENTIFICATION=C
##
## attached base packages:
## [1] stats4      stats      graphics  grDevices datasets  utils      methods
## [8] base
```

```

##
## other attached packages:
## [1] ExploreModelMatrix_1.8.0    plotly_4.10.0
## [3] msqrob2_1.4.0               QFeatures_1.6.0
## [5] MultiAssayExperiment_1.22.0 SummarizedExperiment_1.26.1
## [7] Biobase_2.56.0              GenomicRanges_1.48.0
## [9] GenomeInfoDb_1.32.2        IRanges_2.30.0
## [11] S4Vectors_0.34.0           BiocGenerics_0.42.0
## [13] MatrixGenerics_1.8.0       matrixStats_0.62.0
## [15] limma_3.52.1               forcats_0.5.1
## [17] stringr_1.4.1              dplyr_1.0.9
## [19] purrr_0.3.4                readr_2.1.2
## [21] tidyr_1.2.0                tibble_3.1.7
## [23] ggplot2_3.3.6              tidyverse_1.3.2
##
## loaded via a namespace (and not attached):
## [1] googledrive_2.0.0          minqa_1.2.4                colorspace_2.0-3
## [4] ellipsis_0.3.2            XVector_0.36.0            fs_1.5.2
## [7] clue_0.3-61               farver_2.1.0              DT_0.23
## [10] fansi_1.0.3               lubridate_1.8.0           xml2_1.3.3
## [13] codetools_0.2-18         splines_4.2.3             knitr_1.40.1
## [16] jsonlite_1.8.0           nloptr_2.0.3              broom_0.8.0
## [19] cluster_2.1.3            dbplyr_2.1.1              shinydashboard_0.7.2
## [22] shiny_1.7.1              BiocManager_1.30.18       compiler_4.2.3
## [25] httr_1.4.3               backports_1.4.1           assertthat_0.2.1
## [28] Matrix_1.4-1             fastmap_1.1.0             lazyeval_0.2.2
## [31] gargle_1.2.0             cli_3.3.0                 later_1.3.0
## [34] htmltools_0.5.2          tools_4.2.3               igraph_1.3.2
## [37] gtable_0.3.0             glue_1.6.2                GenomeInfoDbData_1.2.8
## [40] Rcpp_1.0.8.3             cellranger_1.1.0          jquerylib_0.1.4
## [43] vctrs_0.4.1              nlme_3.1-157              rintrojs_0.3.0
## [46] xfun_0.33                lme4_1.1-29               rvest_1.0.2
## [49] mime_0.12                lifecycle_1.0.1           renv_0.15.4
## [52] googlesheets4_1.0.0      zlibbioc_1.42.0           MASS_7.3-57
## [55] scales_1.2.0             promises_1.2.0.1          hms_1.1.1
## [58] ProtGenerics_1.28.0      parallel_4.2.3            AnnotationFilter_1.20.0
## [61] yaml_2.3.5               sass_0.4.1                stringi_1.7.8
## [64] highr_0.9                boot_1.3-28               BiocParallel_1.30.2
## [67] rlang_1.0.2              pkgconfig_2.0.3           bitops_1.0-7
## [70] evaluate_0.16            lattice_0.20-45           htmlwidgets_1.5.4
## [73] labeling_0.4.2           cowplot_1.1.1             tidyselect_1.1.2
## [76] magrittr_2.0.3           R6_2.5.1                  generics_0.1.2
## [79] DelayedArray_0.22.0      DBI_1.1.2                 pillar_1.7.0
## [82] haven_2.5.0              withr_2.5.0               MsCoreUtils_1.8.0
## [85] RCurl_1.98-1.6           modelr_0.1.8              crayon_1.5.1
## [88] utf8_1.2.2               tzdb_0.3.0                rmarkdown_2.14
## [91] grid_4.2.3              readxl_1.4.0              data.table_1.14.2
## [94] reprex_2.0.1            digest_0.6.29             xtable_1.8-4
## [97] httpuv_1.6.5            munsell_0.5.0             viridisLite_0.4.0
## [100] bslib_0.3.1             shinyjs_2.1.0

```