Analisis de datos omicos, PEC1

Anaixis del Valle

Contents

0.1 Selección del DataSet y explicación de los resultados:

0.1.1 Descripción del estudio seleccionado

Para la realizacion de la PEC se seleccionó el dataset de caquexia. Se descargaron del repositorio github code/download zip A continuación se realizó una busqueda y estudio de la publiacion original Eisner et al. (2011), y se revisó información adicional de la emfermedad Evans et al. (2008).

0.1.1.1 Definición y síntomas clínicos: La caquexia es un síndrome metabólico complejo asociado a una enfermedad subyacente y caracterizado por pérdida de masa muscular, con o sin pérdida de masa grasa. Los síntomas clínicos se caracterizan por la pérdida de peso, la pérdida de masa muscular, la debilidad y fatiga, la anorexia, una bioquímica anormal (aumento de los marcadores inflamatorios, anemia e hipoalbuminemia Cabe destacar que la caquexia debe distinguirse de la inanición, la malabsorción, el hipertiroidismo, la deshidratación o la sarcopenia (disminución de la masa muscular esquelética asociada a la edad).

0.1.1.2 Descripción del estudio Eisner et al. (2011): La investigación se centra en el uso de la metabolómica para diagnosticar la pérdida de masa muscular asociada a la caquexia en pacientes con cáncer, con el objetivo de establecer un método no invasivo, de diagnóstico y de caracterización de la enfermedad en el individuo.

0.1.1.3 Diseño experimental y limitaciones: El estudio analizó 93 muestras de orina aleatorias de pacientes con cáncer de colon o pulmón en estadio avanzado (localmente recurrente o metastásico). Se excluyeron pacientes con radiación previa en los riñones, malignidad de los riñones o del tracto urinario. Se utilizó una sola muestra de orina por paciente, tomada en un momento aleatorio del día y sin control de la ingesta de alimentos. Esta forma de colectar las muestras introduce variabilidad en las concentraciones de metabolitos, dificultando la identificación de patrones. En el caso de la pérdida muscular, se cuantificó a partir de dos tomografías computarizadas (TC) realizadas durante la atención clínica rutinaria, con un intervalo aproximado de 100 días entre ellas. Cabe mencionar que esta medición tiene una precisión limitada y solo refleja la pérdida muscular en un periodo específico. Los autores realizaron un estudio observacional, sin intervenir, de todos estos pacientes.

0.1.1.4 Colección de los datos crudos y preprocesamiento de los mismos:

La investigación se centró en el empleo de la espectroscopia de resonancia magnética nuclear de protones (1H-RMN), esta técnica permite identificar y cuantificar un amplio rango de metabolitos en una muestra biológica (se cuantificaron 63 metabolitos). Sin embargo, tiene una sensibilidad limitada, por lo que solo detecta metabolitos con concentraciones superiores a 1 M. Aspecto que implica una pérdida de la información debido a que algunos metabolitos relevantes para la pérdida muscular podrían no haberse detectado. En el caso de la selección del área para la TC, se seleccionó el área del músculo esquelético lumbar a nivel de la tercera vértebra lumbar. La elección de esta región específica podría influir en los resultados, ya que la pérdida muscular puede no ser uniforme en todo el cuerpo.

El estudio identifica la variabilidad en la concentración de metabolitos en la orina como un desafío para el análisis. Esta variabilidad puede ser causada por factores como la ingesta de agua, la dieta y la hora del día. Para abordar este desafío, se utilizaron tres métodos de normalización de los datos: normalización por concentración de creatinina, normalización por área total de pico y normalización por cociente de probabilidad. Además, se aplicó una transformación logarítmica a los datos para corregir la distribución no normal de las concentraciones de metabolitos. Sin embargo, ninguno de estos métodos de normalización mejoró la precisión de los clasificadores. La transformación logarítmica fue el único preprocesamiento que resultó beneficioso.

0.1.1.5 Resultados principales e implicaciones:

El estudio demuestra que es posible predecir la pérdida de masa muscular asociada a la caquexia en pacientes con cáncer utilizando perfiles de metabolitos urinarios. El estudio seleccionó una herramienta de aprendizaje automatizado para determinar patrones dentro de los datos, asignando pesos diferentes a cada metabolito, con el objetivo de predecir la presencia o no de la enfermedad. Se evaluaron ocho algoritmos de aprendizaje automático diferentes a los datos y se seleccionó específicamente un clasificador basado en máquinas de vectores de soporte (SVM) que logró una precisión del 82,2% en la predicción de la pérdida muscular. Los metabolitos urinarios relacionados con la pérdida muscular incluyeron creatina, creatinina y varios aminoácidos (valina, leucina, isoleucina, alanina, treonina, tirosina, glutamina y serina), lo que sugiere un aumento en el catabolismo muscular. Se observaron niveles elevados de glucosa en la orina de pacientes con pérdida muscular, lo que podría indicar resistencia a la insulina como un factor contribuyente a la caquexia. De maneta más amplia el estudio implica el desarrollo de un test de orina no invasivo para diagnosticar la pérdida muscular podría permitir la detección temprana y el manejo oportuno de la caquexia en pacientes con cáncer. La identificación de metabolitos específicos asociados a la pérdida muscular proporciona información sobre los mecanismos subyacentes a la caquexia, lo que podría guiar el desarrollo de nuevas terapias. Es importante tener en cuenta que este estudio se basa en una muestra limitada de pacientes y que se necesitan más investigaciones para validar estos hallazgos y explorar su aplicabilidad en otros contextos clínicos.

0.1.2 Herramientas para el desarrollo de la PEC.

Para el desarrollo de la PEC se estudió el material de la asignatura, y se incluyó el contenido de la asignatura Machine Learning, para desarrollar el informe dinámico, Bioconductor (2024), Wickham (2016), Allaire, Xie, and McPherson (2019), y se estudio el material extra del SummarizedExperiment del paquete Bioconductor Morgan et al. (2023)

SummarizedExperiment es una clase de Bioconductor. Se utiliza para almacenar matrices rectangulares de resultados experimentales, que son producidos comúnmente por experimentos de secuenciación y microarrays, en este caso metabolómica. Cabe destacar que SummarizedExperiment puede gestionar simultáneamente varios resultados experimentales o ensayos, siempre y cuando tengan las *mismas dimensiones*. Cada objeto almacena observaciones de una o más muestras, junto con metadatos adicionales que describen tanto las observaciones (características) como las muestras (fenotipos). Un aspecto clave de la clase SummarizedExperiment es la coordinación de los metadatos y los ensayos al hacer submuestras. Por ejemplo, si se desea excluir una muestra determinada, se puede hacer para ambos, los metadatos y el ensayo, en una sola operación, lo que garantiza que los metadatos y los datos observados se mantendrán sincronizados. La falta de una gestión adecuada entre los metadatos y los datos observacionales ha dado lugar a numerosos resultados

incorrectos y retractaciones, por lo que esta es una propiedad muy deseable. SummarizedExperiment es, en muchos aspectos, similar a ExpressionSet, siendo la principal distinción que SummarizedExperiment es más flexible en la información de sus filas, permitiendo tanto el uso de GRanges como la descripción mediante DataFrames arbitrarios. Esto lo hace ideal para una variedad de experimentos, en particular los basados en secuenciación, como RNA-Seq y ChIP-Seq. Bioconductor (n.d.) Bioconductor (n.d.)

0.2 Creación del contenedor SummarizedExperiment y análisis de los datos:

0.2.1 Instalación de los paquetes necesarios:

```
if (!require("BiocManager", quietly = TRUE))
    install.packages("BiocManager")

BiocManager::install("SummarizedExperiment")
```

```
## Bioconductor version 3.20 (BiocManager 1.30.25), R 4.4.2 (2024-10-31 ucrt)
```

```
## Warning: package(s) not installed when version(s) same as or greater than current; use
##   `force = TRUE` to re-install: 'SummarizedExperiment'
```

```
## Old packages: 'rmarkdown'
```

```
if (!requireNamespace("tinytex", quietly = TRUE)) {
    install.packages("tinytex")
    tinytex::install_tinytex()
}
```

0.2.2 Cargarlas librerías:

```
# Cargar las librerías necesarias
library(SummarizedExperiment)
```

```
## Cargando paquete requerido: MatrixGenerics
```

```
## Cargando paquete requerido: matrixStats
```

```
##
## Adjuntando el paquete: 'MatrixGenerics'
```

```
## The following objects are masked from 'package:matrixStats':
##
##     colAlls, colAnyNAs, colAnys, colAvgsPerRowSet, colCollapse,
##     colCounts, colCummaxs, colCummins, colCumprods, colCumsums,
##     colDiffs, colIQRDiffs, colIQRs, colLogSumExps, colMadDiffs,
##     colMads, colMaxs, colMeans2, colMedians, colMins, colOrderStats,
##     colProds, colQuantiles, colRanges, colRanks, colSdDiffs, colSds,
##     colSums2, colTabulates, colVarDiffs, colVars, colWeightedMads,
```

```
##     colWeightedMeans, colWeightedMedians, colWeightedSds,
##     colWeightedVars, rowAlls, rowAnyNAs, rowAnys, rowAvgsPerColSet,
##     rowCollapse, rowCounts, rowCummaxs, rowCummins, rowCumprods,
##     rowCumsums, rowDiffs, rowIQRDiffs, rowIQRs, rowLogSumExps,
##     rowMadDiffs, rowMads, rowMaxs, rowMeans2, rowMedians, rowMins,
##     rowOrderStats, rowProds, rowQuantiles, rowRanges, rowRanks,
##     rowSdDiffs, rowSds, rowSums2, rowTabulates, rowVarDiffs, rowVars,
##     rowWeightedMads, rowWeightedMeans, rowWeightedMedians,
##     rowWeightedSds, rowWeightedVars

## Cargando paquete requerido: GenomicRanges

## Cargando paquete requerido: stats4

## Cargando paquete requerido: BiocGenerics

##
## Adjuntando el paquete: 'BiocGenerics'

## The following objects are masked from 'package:stats':
##
##     IQR, mad, sd, var, xtabs

## The following objects are masked from 'package:base':
##
##     anyDuplicated, aperm, append, as.data.frame, basename, cbind,
##     colnames, dirname, do.call, duplicated, eval, evalq, Filter, Find,
##     get, grep, grepl, intersect, is.unsorted, lapply, Map, mapply,
##     match, mget, order, paste, pmax, pmax.int, pmin, pmin.int,
##     Position, rank, rbind, Reduce, rownames, sapply, saveRDS, setdiff,
##     table, tapply, union, unique, unsplit, which.max, which.min

## Cargando paquete requerido: S4Vectors

##
## Adjuntando el paquete: 'S4Vectors'

## The following object is masked from 'package:utils':
##
##     findMatches

## The following objects are masked from 'package:base':
##
##     expand.grid, I, unname

## Cargando paquete requerido: IRanges

##
## Adjuntando el paquete: 'IRanges'
```

```
## The following object is masked from 'package:grDevices':
##
##     windows

## Cargando paquete requerido: GenomeInfoDb

## Cargando paquete requerido: Biobase

## Welcome to Bioconductor
##
##     Vignettes contain introductory material; view with
##     'browseVignettes()'. To cite Bioconductor, see
##     'citation("Biobase")', and for packages 'citation("pkgname")'.

##
## Adjuntando el paquete: 'Biobase'

## The following object is masked from 'package:MatrixGenerics':
##
##     rowMedians

## The following objects are masked from 'package:matrixStats':
##
##     anyMissing, rowMedians
```

0.2.3 Importar los datos desde el sitio de descarga:

En primer lugar, para la imortacion del archivo en estudio, se crea una variable que almacena unicamente la ruta del archivo, esto permite que si es necesario cambiar la ruta se actualiza en todo el archivo, pues es solo redefinir una variable una sola vez.

A continuación se crea un datarame cachexia_data, para almacenar la informacion en formato CSV, se incluye la especificacion de que la primera columa se ID como etiqueta de la datA, es decir el ID del paciente

```
file_ruta <- "C:/Users/Hp/OneDrive/Documentos/Máster en Bioinformática/Asignaturas/III Semestre/Análisis
cachexia_data <- read.csv(file_ruta, row.names = 1)
write.csv(cachexia_data, file = "datos_originales.csv", row.names = TRUE)
```

0.2.4 Observación de las primeras filas del row Data, para tener una vision global del Dataframe:

```
head (cachexia_data)
```

```
##             Muscle.loss X1.6.Anhydro.beta.D.glucose X1.Methylnicotinamide
## PIF_178        cachexic                       40.85                 65.37
## PIF_087        cachexic                       62.18                340.36
## PIF_090        cachexic                      270.43                 64.72
## NETL_005_V1    cachexic                      154.47                 52.98
## PIF_115        cachexic                       22.20                 73.70
## PIF_110        cachexic                      212.72                 31.82
```

```
##             X2.Aminobutyrate X2.Hydroxyisobutyrate X2.Oxoglutarate
## PIF_178                18.73                 26.05           71.52
## PIF_087                24.29                 41.68           67.36
## PIF_090                12.18                 65.37           23.81
## NETL_005_V1           172.43                 74.44         1199.91
## PIF_115                15.64                 83.93           33.12
## PIF_110                18.36                 80.64           47.94
##             X3.Aminoisobutyrate X3.Hydroxybutyrate X3.Hydroxyisovalerate
## PIF_178                1480.30              56.83                 10.07
## PIF_087                 116.75              43.82                 79.84
## PIF_090                  14.30               5.64                 23.34
## NETL_005_V1             555.57             175.91                 25.03
## PIF_115                  29.67              76.71                 69.41
## PIF_110                  17.46              31.82                 35.16
##             X3.Indoxylsulfate X4.Hydroxyphenylacetate Acetate Acetone Adipate
## PIF_178                566.80                  120.30  126.47    9.49   38.09
## PIF_087                368.71                  432.68  212.72   11.82  327.01
## PIF_090                665.14                  292.95  314.19    4.44  131.63
## NETL_005_V1            411.58                  214.86   37.34  206.44  144.03
## PIF_115                165.67                   97.51  407.48   44.26   15.03
## PIF_110                183.09                  132.95   81.45   14.44   25.28
##             Alanine Asparagine Betaine Carnitine  Citrate Creatine Creatinine
## PIF_178      314.19     159.17  109.95    265.07  3714.50   196.37   16481.60
## PIF_087      871.31     157.59  244.69    120.30  2617.57   212.72   15835.35
## PIF_090      464.05      89.12  116.75     25.03   862.64   221.41   24587.66
## NETL_005_V1  589.93     273.14  278.66    200.34 13629.61    85.63   20952.22
## PIF_115     1118.79      42.52  391.51     84.77   854.06   105.64    6768.26
## PIF_110      237.46     157.59   66.69     40.04  1958.63   200.34   15677.78
##             Dimethylamine Ethanolamine Formate Fucose Fumarate Glucose
## PIF_178            632.70       645.48  441.42 336.97     7.69  395.44
## PIF_087            607.89       487.85  252.14 198.34    18.92 8690.62
## PIF_090            735.10       407.48  249.64 186.79     7.10 1352.89
## NETL_005_V1       1064.22       820.57  468.72 407.48    96.54  862.64
## PIF_115            242.26       365.04  114.43  26.05    19.69 6836.29
## PIF_110            614.00       459.44  314.19 123.97     5.05  512.86
##             Glutamine Glycine Glycolate Guanidoacetate Hippurate Histidine
## PIF_178        871.31 2038.56    685.40         154.47   4582.50    925.19
## PIF_087        601.85 1107.65    651.97         109.95   1737.15    845.56
## PIF_090        301.87  620.17    141.17         183.09   4315.64    284.29
## NETL_005_V1   1685.81 5064.45     70.81         102.51    757.48   1043.15
## PIF_115        432.68  395.44     26.58          52.98   1152.86    327.01
## PIF_110        298.87  482.99    428.38          57.97   3568.85    459.44
##             Hypoxanthine Isoleucine Lactate Leucine Lysine Methylamine
## PIF_178            97.51       5.58  106.70   42.10 146.94       52.46
## PIF_087            82.27       8.17  368.71   77.48 284.29       23.57
## PIF_090           114.43       9.30  749.95   31.50  97.51       18.73
## NETL_005_V1       223.63      37.71  368.71  103.54 290.03       48.91
## PIF_115            66.69      40.04 3640.95  101.49 122.73       27.94
## PIF_110            62.80       8.17  113.30   28.79 120.30       36.97
##             Methylguanidine N.N.Dimethylglycine O.Acetylcarnitine Pantothenate
## PIF_178                9.97               23.34             52.98        25.79
## PIF_087                7.69               87.36             50.40       186.79
## PIF_090                4.66               24.53              5.58       145.47
## NETL_005_V1          141.17               40.04            254.68        42.52
```

```
## PIF_115                5.31              46.06             45.60        74.44
## PIF_110               43.38              24.29             13.46        35.52
##             Pyroglutamate Pyruvate Quinolinate  Serine Succinate Sucrose
## PIF_178            437.03    21.12      165.67  284.29    154.47   45.15
## PIF_087            437.03    36.97       72.97  391.51    244.69  459.44
## PIF_090            713.37    29.37      192.48  295.89    142.59  160.77
## NETL_005_V1        566.80    64.07       86.49 1248.88    144.03  111.05
## PIF_115            184.93    12.30       38.09  206.44     68.72   75.19
## PIF_110            432.68    32.79      112.17  387.61     33.45  336.97
##             Tartrate Taurine Threonine Trigonelline Trimethylamine.N.oxide
## PIF_178        97.51 1919.85    184.93       943.88                2121.76
## PIF_087        32.79 1261.43    198.34       208.51                 639.06
## PIF_090        16.28 4272.69    109.95       192.48                1152.86
## NETL_005_V1   837.15 1525.38    376.15       992.27                1450.99
## PIF_115         4.53  468.72     64.07        86.49                 172.43
## PIF_110        24.05 2059.05    105.64       862.64                 880.07
##             Tryptophan Tyrosine Uracil Valine  Xylose cis.Aconitate
## PIF_178         259.82   290.03 111.05  86.49   72.24        237.46
## PIF_087          83.10   167.34  46.99 109.95  192.48        333.62
## PIF_090          82.27    60.34  31.50  59.15 2164.62        330.30
## NETL_005_V1     235.10   323.76  30.57 102.51  125.21       1863.11
## PIF_115         103.54   142.59  44.26 160.77  186.79        101.49
## PIF_110         239.85   127.74  29.67  36.97   89.12        287.15
##             myo.Inositol trans.Aconitate pi.Methylhistidine tau.Methylhistidine
## PIF_178           135.64           51.94             157.59              160.77
## PIF_087           376.15          217.02             307.97              130.32
## PIF_090            86.49           58.56             145.47               83.93
## NETL_005_V1       247.15           75.94             249.64              254.68
## PIF_115           749.95           98.49              84.77               79.84
## PIF_110           129.02          121.51             399.41               68.72
```

```
str(cachexia_data)
```

```
## 'data.frame':    77 obs. of  64 variables:
##  $ Muscle.loss                : chr  "cachexic" "cachexic" "cachexic" "cachexic" ...
##  $ X1.6.Anhydro.beta.D.glucose: num  40.9 62.2 270.4 154.5 22.2 ...
##  $ X1.Methylnicotinamide      : num  65.4 340.4 64.7 53 73.7 ...
##  $ X2.Aminobutyrate           : num  18.7 24.3 12.2 172.4 15.6 ...
##  $ X2.Hydroxyisobutyrate      : num  26.1 41.7 65.4 74.4 83.9 ...
##  $ X2.Oxoglutarate            : num  71.5 67.4 23.8 1199.9 33.1 ...
##  $ X3.Aminoisobutyrate        : num  1480.3 116.8 14.3 555.6 29.7 ...
##  $ X3.Hydroxybutyrate         : num  56.83 43.82 5.64 175.91 76.71 ...
##  $ X3.Hydroxyisovalerate      : num  10.1 79.8 23.3 25 69.4 ...
##  $ X3.Indoxylsulfate          : num  567 369 665 412 166 ...
##  $ X4.Hydroxyphenylacetate    : num  120.3 432.7 292.9 214.9 97.5 ...
##  $ Acetate                    : num  126.5 212.7 314.2 37.3 407.5 ...
##  $ Acetone                    : num  9.49 11.82 4.44 206.44 44.26 ...
##  $ Adipate                    : num  38.1 327 131.6 144 15 ...
##  $ Alanine                    : num  314 871 464 590 1119 ...
##  $ Asparagine                 : num  159.2 157.6 89.1 273.1 42.5 ...
##  $ Betaine                    : num  110 245 117 279 392 ...
##  $ Carnitine                  : num  265.1 120.3 25 200.3 84.8 ...
##  $ Citrate                    : num  3714 2618 863 13630 854 ...
##  $ Creatine                   : num  196.4 212.7 221.4 85.6 105.6 ...
```

```
##  $ Creatinine                : num  16482 15835 24588 20952 6768 ...
##  $ Dimethylamine             : num  633 608 735 1064 242 ...
##  $ Ethanolamine              : num  645 488 407 821 365 ...
##  $ Formate                   : num  441 252 250 469 114 ...
##  $ Fucose                    : num  337 198.3 186.8 407.5 26.1 ...
##  $ Fumarate                  : num  7.69 18.92 7.1 96.54 19.69 ...
##  $ Glucose                   : num  395 8691 1353 863 6836 ...
##  $ Glutamine                 : num  871 602 302 1686 433 ...
##  $ Glycine                   : num  2039 1108 620 5064 395 ...
##  $ Glycolate                 : num  685.4 652 141.2 70.8 26.6 ...
##  $ Guanidoacetate            : num  154 110 183 103 53 ...
##  $ Hippurate                 : num  4582 1737 4316 757 1153 ...
##  $ Histidine                 : num  925 846 284 1043 327 ...
##  $ Hypoxanthine              : num  97.5 82.3 114.4 223.6 66.7 ...
##  $ Isoleucine                : num  5.58 8.17 9.3 37.71 40.04 ...
##  $ Lactate                   : num  107 369 750 369 3641 ...
##  $ Leucine                   : num  42.1 77.5 31.5 103.5 101.5 ...
##  $ Lysine                    : num  146.9 284.3 97.5 290 122.7 ...
##  $ Methylamine               : num  52.5 23.6 18.7 48.9 27.9 ...
##  $ Methylguanidine           : num  9.97 7.69 4.66 141.17 5.31 ...
##  $ N.N.Dimethylglycine       : num  23.3 87.4 24.5 40 46.1 ...
##  $ O.Acetylcarnitine         : num  52.98 50.4 5.58 254.68 45.6 ...
##  $ Pantothenate              : num  25.8 186.8 145.5 42.5 74.4 ...
##  $ Pyroglutamate             : num  437 437 713 567 185 ...
##  $ Pyruvate                  : num  21.1 37 29.4 64.1 12.3 ...
##  $ Quinolinate               : num  165.7 73 192.5 86.5 38.1 ...
##  $ Serine                    : num  284 392 296 1249 206 ...
##  $ Succinate                 : num  154.5 244.7 142.6 144 68.7 ...
##  $ Sucrose                   : num  45.1 459.4 160.8 111 75.2 ...
##  $ Tartrate                  : num  97.51 32.79 16.28 837.15 4.53 ...
##  $ Taurine                   : num  1920 1261 4273 1525 469 ...
##  $ Threonine                 : num  184.9 198.3 110 376.1 64.1 ...
##  $ Trigonelline              : num  943.9 208.5 192.5 992.3 86.5 ...
##  $ Trimethylamine.N.oxide    : num  2122 639 1153 1451 172 ...
##  $ Tryptophan                : num  259.8 83.1 82.3 235.1 103.5 ...
##  $ Tyrosine                  : num  290 167.3 60.3 323.8 142.6 ...
##  $ Uracil                    : num  111 47 31.5 30.6 44.3 ...
##  $ Valine                    : num  86.5 110 59.1 102.5 160.8 ...
##  $ Xylose                    : num  72.2 192.5 2164.6 125.2 186.8 ...
##  $ cis.Aconitate             : num  237 334 330 1863 101 ...
##  $ myo.Inositol              : num  135.6 376.1 86.5 247.2 750 ...
##  $ trans.Aconitate           : num  51.9 217 58.6 75.9 98.5 ...
##  $ pi.Methylhistidine        : num  157.6 308 145.5 249.6 84.8 ...
##  $ tau.Methylhistidine       : num  160.8 130.3 83.9 254.7 79.8 ...
```

```
colnames(cachexia_data)
```

```
##  [1] "Muscle.loss"                "X1.6.Anhydro.beta.D.glucose"
##  [3] "X1.Methylnicotinamide"      "X2.Aminobutyrate"
##  [5] "X2.Hydroxyisobutyrate"      "X2.Oxoglutarate"
##  [7] "X3.Aminoisobutyrate"        "X3.Hydroxybutyrate"
##  [9] "X3.Hydroxyisovalerate"      "X3.Indoxylsulfate"
## [11] "X4.Hydroxyphenylacetate"    "Acetate"
## [13] "Acetone"                    "Adipate"
```

```
## [15] "Alanine"                    "Asparagine"
## [17] "Betaine"                    "Carnitine"
## [19] "Citrate"                    "Creatine"
## [21] "Creatinine"                 "Dimethylamine"
## [23] "Ethanolamine"               "Formate"
## [25] "Fucose"                     "Fumarate"
## [27] "Glucose"                    "Glutamine"
## [29] "Glycine"                    "Glycolate"
## [31] "Guanidoacetate"             "Hippurate"
## [33] "Histidine"                  "Hypoxanthine"
## [35] "Isoleucine"                 "Lactate"
## [37] "Leucine"                    "Lysine"
## [39] "Methylamine"                "Methylguanidine"
## [41] "N.N.Dimethylglycine"        "O.Acetylcarnitine"
## [43] "Pantothenate"               "Pyroglutamate"
## [45] "Pyruvate"                   "Quinolinate"
## [47] "Serine"                     "Succinate"
## [49] "Sucrose"                    "Tartrate"
## [51] "Taurine"                    "Threonine"
## [53] "Trigonelline"               "Trimethylamine.N.oxide"
## [55] "Tryptophan"                 "Tyrosine"
## [57] "Uracil"                     "Valine"
## [59] "Xylose"                     "cis.Aconitate"
## [61] "myo.Inositol"               "trans.Aconitate"
## [63] "pi.Methylhistidine"         "tau.Methylhistidine"
```

```
#Se puede apreciar que la primera columna se corresponde con los diagnosticos
#de perdida de masa muscular o no (clasificacion de la data), mientras que las restantes
#63 son los metabolitos cuantificados en las muestras de los pacientes,

#Por otro lado tambien se aprecia que las filas son los pacientes y
#las columnas los metabolitos analizados
```

0.2.5 Modificación de la disposicion de los datos para realizar el contenedor:

El paquete *SummarizedExperiment* contiene dos clases: *SummarizedExperiment* y *RangedSummarizedExperiment*. *SummarizedExperiment* es un contenedor de tipo matriz donde las **filas** representan características de interés (por ejemplo, genes, transcripciones, exones, en nuestro caso deberían ser los metabolitos.) y las columnas representan muestras (que en este caso deben ser los pacientes). Los objetos contienen uno o más ensayos, cada uno representado por un objeto de tipo matriz de modo numérico u otro. Las filas de un *SummarizedExperiment* objeto representan características de interés. La información sobre estas características se almacena en un *DataFrame* objeto, accesible mediante la función *rowData()*. Cada fila de DataFrame proporciona información sobre la característica en la fila correspondiente del SummarizedExperiment objeto. Traducido y adaptado de Bioconductor (n.d.). Por lo tanto el primer paso es separa los datos de las clasificaciones de caquexia en la clasificacion de muscle loss, y a continuacion transponer filas y columnas para que coincida con el formato necesario de filas para metabolitos y columnas para pacientes:

```
metabolite_data <- cachexia_data[, -1]  # Crea una matriz de datos bidimensional
#a la vez que excluye la primera columna "Muscle.loss"
```

```
muscle_info <- data.frame(MuscleLoss = cachexia_data$Muscle.loss) #Crea un dataFrame de los metadatos,
#clasificacion de los datos,

# Transponer metabolite_data para que los pacientes estén en columnas y los metabolitos en filas

metabolite_data <- t(metabolite_data)
```

0.2.5.1 Separacion de datos y transposicion:

0.2.5.2 Chequear que las dimensiones dde la matriz de datos y el dataFrame de los metadatos sean las mismas: Teniendo en cuenta que SummarizedExperiment puede gestionar simultáneamente varios resultados experimentales o ensayos, siempre y cuando tengan las *mismas dimensiones*

```
# Verificar que las dimensiones coincidan después de la transposición

dim(metabolite_data)   # Deben ser 63 x 77 (63 metabolitos x 77 pacientess)
```

```
## [1] 63 77
```

```
dim(muscle_info)       # Deben ser 77 x 1 (77 muestras con una variable de clasificación)
```

```
## [1] 77  1
```

```
#Visualizarlo:
metabolite_data
```

```
##                              PIF_178  PIF_087  PIF_090 NETL_005_V1 PIF_115
## X1.6.Anhydro.beta.D.glucose    40.85    62.18   270.43      154.47   22.20
## X1.Methylnicotinamide          65.37   340.36    64.72       52.98   73.70
## X2.Aminobutyrate               18.73    24.29    12.18      172.43   15.64
## X2.Hydroxyisobutyrate          26.05    41.68    65.37       74.44   83.93
## X2.Oxoglutarate                71.52    67.36    23.81     1199.91   33.12
## X3.Aminoisobutyrate          1480.30   116.75    14.30      555.57   29.67
## X3.Hydroxybutyrate             56.83    43.82     5.64      175.91   76.71
## X3.Hydroxyisovalerate          10.07    79.84    23.34       25.03   69.41
## X3.Indoxylsulfate             566.80   368.71   665.14      411.58  165.67
## X4.Hydroxyphenylacetate       120.30   432.68   292.95      214.86   97.51
## Acetate                       126.47   212.72   314.19       37.34  407.48
## Acetone                         9.49    11.82     4.44      206.44   44.26
## Adipate                        38.09   327.01   131.63      144.03   15.03
## Alanine                       314.19   871.31   464.05      589.93 1118.79
## Asparagine                    159.17   157.59    89.12      273.14   42.52
## Betaine                       109.95   244.69   116.75      278.66  391.51
## Carnitine                     265.07   120.30    25.03      200.34   84.77
## Citrate                      3714.50  2617.57   862.64    13629.61  854.06
## Creatine                      196.37   212.72   221.41       85.63  105.64
## Creatinine                  16481.60 15835.35 24587.66    20952.22 6768.26
## Dimethylamine                 632.70   607.89   735.10     1064.22  242.26
## Ethanolamine                  645.48   487.85   407.48      820.57  365.04
## Formate                       441.42   252.14   249.64      468.72  114.43
```

```
## Fucose                          336.97   198.34   186.79      407.48   26.05
## Fumarate                          7.69    18.92     7.10       96.54   19.69
## Glucose                         395.44  8690.62  1352.89      862.64 6836.29
## Glutamine                       871.31   601.85   301.87     1685.81  432.68
## Glycine                        2038.56  1107.65   620.17     5064.45  395.44
## Glycolate                       685.40   651.97   141.17       70.81   26.58
## Guanidoacetate                  154.47   109.95   183.09      102.51   52.98
## Hippurate                      4582.50  1737.15  4315.64      757.48 1152.86
## Histidine                       925.19   845.56   284.29     1043.15  327.01
## Hypoxanthine                     97.51    82.27   114.43      223.63   66.69
## Isoleucine                        5.58     8.17     9.30       37.71   40.04
## Lactate                         106.70   368.71   749.95      368.71 3640.95
## Leucine                          42.10    77.48    31.50      103.54  101.49
## Lysine                          146.94   284.29    97.51      290.03  122.73
## Methylamine                      52.46    23.57    18.73       48.91   27.94
## Methylguanidine                   9.97     7.69     4.66      141.17    5.31
## N.N.Dimethylglycine              23.34    87.36    24.53       40.04   46.06
## O.Acetylcarnitine                52.98    50.40     5.58      254.68   45.60
## Pantothenate                     25.79   186.79   145.47       42.52   74.44
## Pyroglutamate                   437.03   437.03   713.37      566.80  184.93
## Pyruvate                         21.12    36.97    29.37       64.07   12.30
## Quinolinate                     165.67    72.97   192.48       86.49   38.09
## Serine                          284.29   391.51   295.89     1248.88  206.44
## Succinate                       154.47   244.69   142.59      144.03   68.72
## Sucrose                          45.15   459.44   160.77      111.05   75.19
## Tartrate                         97.51    32.79    16.28      837.15    4.53
## Taurine                        1919.85  1261.43  4272.69     1525.38  468.72
## Threonine                       184.93   198.34   109.95      376.15   64.07
## Trigonelline                    943.88   208.51   192.48      992.27   86.49
## Trimethylamine.N.oxide         2121.76   639.06  1152.86     1450.99  172.43
## Tryptophan                      259.82    83.10    82.27      235.10  103.54
## Tyrosine                        290.03   167.34    60.34      323.76  142.59
## Uracil                          111.05    46.99    31.50       30.57   44.26
## Valine                           86.49   109.95    59.15      102.51  160.77
## Xylose                           72.24   192.48  2164.62      125.21  186.79
## cis.Aconitate                   237.46   333.62   330.30     1863.11  101.49
## myo.Inositol                    135.64   376.15    86.49      247.15  749.95
## trans.Aconitate                  51.94   217.02    58.56       75.94   98.49
## pi.Methylhistidine              157.59   307.97   145.47      249.64   84.77
## tau.Methylhistidine             160.77   130.32    83.93      254.68   79.84
##                                PIF_110 NETL_019_V1 NETCR_014_V1 NETCR_014_V2
## X1.6.Anhydro.beta.D.glucose     212.72      151.41        31.50        51.42
## X1.Methylnicotinamide            31.82       36.60         6.82        30.27
## X2.Aminobutyrate                 18.36        8.67         4.18         7.54
## X2.Hydroxyisobutyrate            80.64       42.52        12.94        34.81
## X2.Oxoglutarate                  47.94      223.63        25.03        80.64
## X3.Aminoisobutyrate              17.46       56.26         8.67        17.99
## X3.Hydroxybutyrate               31.82       11.59         1.73         9.03
## X3.Hydroxyisovalerate            35.16       25.79         8.76         3.25
## X3.Indoxylsulfate               183.09      223.63       111.05       391.51
## X4.Hydroxyphenylacetate         132.95       59.15        33.78       145.47
## Acetate                          81.45       51.42         7.46         9.97
## Acetone                          14.44        3.25         2.80         8.67
## Adipate                          25.28        8.41         3.53         8.25
```

```
## Alanine                        237.46      336.97       69.41       102.51
## Asparagine                     157.59       71.52       13.87        32.79
## Betaine                         66.69      149.90       15.33        31.19
## Carnitine                       40.04      127.74        9.87         7.32
## Citrate                       1958.63     3944.19      788.40      1669.03
## Creatine                       200.34      383.75        5.81        35.16
## Creatinine                   15677.78     8022.46     2208.35      6634.24
## Dimethylamine                  614.00      333.62       73.70       214.86
## Ethanolamine                   459.44      217.02       55.70       183.09
## Formate                        314.19       67.36       49.90        68.03
## Fucose                         123.97       55.70       18.17        72.97
## Fumarate                         5.05        4.71        1.86         3.56
## Glucose                        512.86      237.46       80.64       177.68
## Glutamine                      298.87      561.16       71.52       145.47
## Glycine                        482.99     3428.92      196.37       292.95
## Glycolate                      428.38      290.03       70.11        33.12
## Guanidoacetate                  57.97      101.49       42.52        56.26
## Hippurate                     3568.85     2368.47      254.68       365.04
## Histidine                      459.44      327.01      130.32       183.09
## Hypoxanthine                    62.80       25.79       20.70        80.64
## Isoleucine                       8.17        2.10        2.18         7.10
## Lactate                        113.30      130.32       22.65        39.65
## Leucine                         28.79       39.25       11.47        16.61
## Lysine                         120.30      127.74       65.37        63.43
## Methylamine                     36.97       24.78        3.60        12.30
## Methylguanidine                 43.38       28.79        4.31        13.46
## N.N.Dimethylglycine             24.29       42.10        8.17        11.70
## O.Acetylcarnitine               13.46        9.68        2.41         2.41
## Pantothenate                    35.52       22.65        3.63        11.02
## Pyroglutamate                  432.68      183.09       30.88        84.77
## Pyruvate                        32.79       16.61        2.41         7.46
## Quinolinate                    112.17       46.53       14.15        38.09
## Serine                         387.61      275.89       48.42        47.94
## Succinate                       33.45       21.33        5.31        18.54
## Sucrose                        336.97       25.79       22.20       162.39
## Tartrate                        24.05      175.91        2.44         8.67
## Taurine                       2059.05      387.61       73.70       247.15
## Threonine                      105.64      135.64       19.49        60.34
## Trigonelline                   862.64      188.67       17.81        62.80
## Trimethylamine.N.oxide         880.07      614.00      190.57       403.43
## Tryptophan                     239.85      100.48       23.34        15.80
## Tyrosine                       127.74       97.51       35.16        54.60
## Uracil                          29.67       27.66        4.31        24.53
## Valine                          36.97       39.25        9.97        20.09
## Xylose                          89.12       91.84       29.67        33.12
## cis.Aconitate                  287.15      129.02       32.14        79.84
## myo.Inositol                   129.02       32.14       12.55        58.56
## trans.Aconitate                121.51       24.78        8.25        27.39
## pi.Methylhistidine             399.41      232.76       55.15       169.02
## tau.Methylhistidine             68.72       21.98       17.29       101.49
##                              PIF_154 NETL_022_V1 NETL_022_V2 NETL_008_V1
## X1.6.Anhydro.beta.D.glucose   117.92       20.70      127.74       59.74
## X1.Methylnicotinamide          52.46      221.41      177.68       50.91
## X2.Aminobutyrate               19.49       15.18       12.68        6.82
```

```
## X2.Hydroxyisobutyrate         72.24       28.79       15.03       46.06
## X2.Oxoglutarate               73.70      357.81       68.03      111.05
## X3.Aminoisobutyrate           57.97       93.69      105.64        8.08
## X3.Hydroxybutyrate            26.84       13.07       29.08       17.12
## X3.Hydroxyisovalerate         28.50        4.26       53.52       16.78
## X3.Indoxylsulfate            116.75      361.41      376.15      379.93
## X4.Hydroxyphenylacetate       50.40       59.74      160.77      174.16
## Acetate                      100.48       27.94       30.88       55.15
## Acetone                        9.12        6.49        7.92        9.21
## Adipate                       14.59       18.54      259.82       11.02
## Alanine                      962.95      164.02      502.70      217.02
## Asparagine                   221.41       32.14       64.72       32.14
## Betaine                      149.90      219.20      137.00      167.34
## Carnitine                    487.85      230.44       35.87       14.88
## Citrate                     4675.07     3533.34      854.06     1772.24
## Creatine                     126.47     1450.99     1863.11      125.21
## Creatinine                  8690.62     8433.78     6904.99    15677.78
## Dimethylamine                350.72      361.41      273.14      678.58
## Ethanolamine                 437.03      184.93      175.91      354.25
## Formate                      320.54       83.93      165.67       46.06
## Fucose                        57.40      138.38       94.63      210.61
## Fumarate                      12.06       10.91       11.47        6.05
## Glucose                      972.63      170.72      473.43      419.89
## Glutamine                   1022.49      179.47      445.86      237.46
## Glycine                     3294.47      492.75      607.89      880.07
## Glycolate                    589.93      132.95      149.90      228.15
## Guanidoacetate               188.67      137.00      154.47       83.93
## Hippurate                    632.70     2697.28    19341.34     4272.69
## Histidine                    706.27      247.15      497.70      154.47
## Hypoxanthine                  43.82       40.85       33.78      162.39
## Isoleucine                    14.44        8.76       12.30        6.69
## Lactate                      196.37       66.02      192.48      149.90
## Leucine                       23.10       19.89       23.10       30.57
## Lysine                       265.07      119.10      181.27       44.70
## Methylamine                   14.73       46.99       47.94       27.94
## Methylguanidine               43.82       70.81       19.89       16.95
## N.N.Dimethylglycine           33.78       39.25       30.88       27.66
## O.Acetylcarnitine            157.59       40.04        7.17        9.58
## Pantothenate                  19.89      126.47       49.40       90.92
## Pyroglutamate                399.41      162.39      419.89      327.01
## Pyruvate                      20.91       26.05       52.46       45.15
## Quinolinate                  151.41       39.25      196.37      177.68
## Serine                       706.27      160.77      292.95      219.20
## Succinate                    121.51       74.44       26.31       40.45
## Sucrose                      196.37       24.53     2079.74       53.52
## Tartrate                       9.58       55.70       13.07       11.94
## Taurine                      812.41      221.41      544.57       57.40
## Threonine                    450.34       99.48      170.72       70.11
## Trigonelline                 478.19       79.04      225.88      507.76
## Trimethylamine.N.oxide       411.58      626.41      295.89      584.06
## Tryptophan                    82.27       90.92       82.27       96.54
## Tyrosine                     137.00       29.08       90.92      111.05
## Uracil                        23.34       58.56      108.85       53.52
## Valine                        38.09       31.82       52.98       50.40
```

```
## Xylose                          95.58       59.15       60.34      129.02
## cis.Aconitate                  179.47      232.76      270.43      450.34
## myo.Inositol                    64.72      154.47       41.68       84.77
## trans.Aconitate                117.92       24.53       24.53       70.81
## pi.Methylhistidine              88.23      146.94     1074.92      242.26
## tau.Methylhistidine             81.45       47.94       95.58       60.95
##                                PIF_146 PIF_119 PIF_099 PIF_162  PIF_160 PIF_113
## X1.6.Anhydro.beta.D.glucose      89.12   23.57   41.26  589.93   112.17  167.34
## X1.Methylnicotinamide            32.79    6.89    8.67   21.98    25.28   19.89
## X2.Aminobutyrate                 10.38    2.12    2.56   15.18    15.49   13.46
## X2.Hydroxyisobutyrate            32.14    7.85    7.85   46.06    47.94   31.19
## X2.Oxoglutarate                  32.46    8.33    6.89   32.79    28.79   47.94
## X3.Aminoisobutyrate              43.38    2.97    6.36   31.82    16.12   79.04
## X3.Hydroxybutyrate                8.08    1.70    3.42   25.03    30.27   11.70
## X3.Hydroxyisovalerate            20.49    5.58    6.23    7.69    21.33   12.55
## X3.Indoxylsulfate               317.35   82.27   90.02  109.95   347.23  184.93
## X4.Hydroxyphenylacetate          86.49   17.64   25.03  148.41    73.70   74.44
## Acetate                          95.58   69.41   79.84   91.84    70.81   42.52
## Acetone                           8.67    6.23    3.16   17.64     4.22    9.39
## Adipate                           9.03    3.16    4.81   22.87    15.80   12.43
## Alanine                         167.34   34.47   26.84  441.42   188.67  237.46
## Asparagine                       47.94   13.33   14.30   79.04    54.05   35.87
## Betaine                          56.83   41.68    4.06  157.59    78.26   60.34
## Carnitine                        16.95   24.53   18.36   62.80    24.05   12.06
## Citrate                         323.76  265.07   80.64  897.85  2489.91 4447.07
## Creatine                        102.51   11.70   18.54  419.89   170.72   97.51
## Creatinine                    12209.87 1480.30 1635.98 9701.15 10198.54 6974.39
## Dimethylamine                   437.03   46.99   56.26  395.44  1422.26  275.89
## Ethanolamine                    144.03   37.34   29.96  200.34   244.69  290.03
## Formate                          91.84   79.84   57.40   53.52    89.12  160.77
## Fucose                          101.49   24.05   31.19   64.07    26.84   61.56
## Fumarate                          3.49    1.48    2.23   10.49     3.39    5.21
## Glucose                         183.09   43.82   57.97  105.64   387.61  221.41
## Glutamine                       121.51   36.60   26.84  512.86   214.86  225.88
## Glycine                         330.30  104.58   74.44  160.77  1141.39 2298.47
## Glycolate                       249.64   12.06   36.23  181.27   190.57  141.17
## Guanidoacetate                   99.48   18.17   25.28  112.17    51.42   18.54
## Hippurate                      2643.87  113.30   92.76  934.49  4023.87 2807.36
## Histidine                       190.57   24.05   22.87  160.77   190.57  343.78
## Hypoxanthine                     36.60    4.22    5.05   29.37    92.76   42.52
## Isoleucine                       11.25    2.32    3.35   14.88     6.82   10.91
## Lactate                         107.77   17.46  194.42   18.17   132.95   90.02
## Leucine                          24.05    3.46    4.81   14.01    21.76   14.30
## Lysine                           47.94   85.63   15.18  123.97    80.64   67.36
## Methylamine                      21.98    8.08    2.53   15.49    20.70   19.11
## Methylguanidine                   8.00    2.56    6.75    3.29     4.26    8.50
## N.N.Dimethylglycine               7.24    4.57    3.42   14.73    26.84   44.70
## O.Acetylcarnitine                 7.32    4.76    3.60   33.45    14.44    6.96
## Pantothenate                     20.09    2.86    2.61    7.17    11.13   14.73
## Pyroglutamate                   239.85   42.95   37.71  252.14   301.87  343.78
## Pyruvate                          4.62    4.01    4.85    5.64    18.17    2.92
## Quinolinate                      56.26   16.12   24.53   62.80    79.84   90.02
## Serine                          151.41   33.12   32.46  217.02   225.88  142.59
## Succinate                        44.70   15.96    6.69   13.74   117.92   81.45
```

```
## Sucrose                          56.83   10.49   24.29  175.91    95.58   72.24
## Tartrate                        127.74    4.39    3.67    5.37    14.73    5.70
## Taurine                         544.57  108.85  126.47   91.84   219.20  301.87
## Threonine                        58.56   20.70   26.84    8.25    68.72  106.70
## Trigonelline                    131.63   40.45   62.18   10.28   320.54  330.30
## Trimethylamine.N.oxide          897.85   90.92   66.69 1465.57  1900.74  343.78
## Tryptophan                       71.52   11.25    9.87  169.02    46.99  115.58
## Tyrosine                         62.80   14.01   15.80  144.03    86.49   87.36
## Uracil                           18.92    4.22    5.70   25.79    28.79    8.50
## Valine                           34.47    4.35    8.41   15.03    53.52   24.29
## Xylose                          154.47   40.85   16.61   38.09    79.84   27.66
## cis.Aconitate                    79.04   21.54   15.03  160.77   232.76  159.17
## myo.Inositol                    117.92   23.10   21.98  160.77    72.97   83.10
## trans.Aconitate                  64.07   46.06    7.92   30.88   103.54   77.48
## pi.Methylhistidine              699.24   20.91  175.91  862.64   196.37  275.89
## tau.Methylhistidine             159.17    8.00   36.60   75.94    43.82   41.26
##                                PIF_143 NETCR_007_V1 NETCR_007_V2  PIF_137 PIF_100
## X1.6.Anhydro.beta.D.glucose     183.09       208.51        34.81   333.62   32.46
## X1.Methylnicotinamide            90.92        53.52        95.58    35.87    9.68
## X2.Aminobutyrate                  8.94         5.26        23.57     7.92    3.90
## X2.Hydroxyisobutyrate            64.07        47.94        68.03    54.60   11.02
## X2.Oxoglutarate                  20.49       212.72       287.15    20.49  170.72
## X3.Aminoisobutyrate              18.73        50.40       104.58    63.43    2.97
## X3.Hydroxybutyrate               26.05        30.27        60.34    29.96    6.36
## X3.Hydroxyisovalerate            51.42         6.82        42.95    47.47    2.46
## X3.Indoxylsulfate               204.38       200.34       333.62   247.15   34.81
## X4.Hydroxyphenylacetate         115.58        46.53       117.92   237.46   70.11
## Acetate                          82.27        25.03        82.27    50.40   77.48
## Acetone                           3.82         5.05         5.26     4.35    2.29
## Adipate                          20.49        18.54        28.79    23.10    3.60
## Alanine                         333.62       254.68       555.57   399.41   78.26
## Asparagine                       61.56        96.54        94.63   102.51   16.61
## Betaine                          68.72       131.63       170.72    66.02   50.91
## Carnitine                        15.18        29.37        19.30    20.91    4.44
## Citrate                        2643.87      2835.57      5377.61  1958.63  223.63
## Creatine                         55.70        44.26        48.91    71.52    9.58
## Creatinine                   11158.98      9798.65     14328.42 13359.73 1261.43
## Dimethylamine                   379.93       361.41       665.14   539.15  102.51
## Ethanolamine                    407.48       450.34       713.37   350.72   16.12
## Formate                         314.19       130.32       198.34   154.47   58.56
## Fucose                          117.92        82.27       156.02    93.69   13.60
## Fumarate                          3.10         4.85         7.85    19.11   17.46
## Glucose                         473.43       267.74       528.48   845.56 5943.18
## Glutamine                       399.41       487.85       888.91   445.86   38.09
## Glycine                        1096.63       992.27      1261.43  1958.63   52.46
## Glycolate                       595.86       437.03       478.19    23.81   10.91
## Guanidoacetate                  132.95        57.40        98.49    49.40   19.69
## Hippurate                      4230.18      4675.07      6438.17  6568.23  217.02
## Histidine                       419.89       347.23       437.03   720.54   14.15
## Hypoxanthine                     23.81        45.60       165.67    44.26    6.49
## Isoleucine                       10.49        11.13        18.36    15.33    2.92
## Lactate                          90.92        80.64       177.68   149.90   55.15
## Leucine                          16.78        21.33        40.04    62.18    8.76
## Lysine                          117.92       121.51       119.10   237.46   25.28
```

```
## Methylamine                    43.82        11.94        26.58    30.27    1.77
## Methylguanidine                11.13         6.30        34.47    31.82    2.53
## N.N.Dimethylglycine            28.79        52.46       114.43    49.40    5.42
## O.Acetylcarnitine              12.68        16.95        14.15    42.95    1.55
## Pantothenate                  137.00        27.39        23.34    24.29    2.59
## Pyroglutamate                 278.66       149.90       290.03   379.93   44.70
## Pyruvate                       35.52        26.05        48.42    23.57    9.21
## Quinolinate                    74.44        53.52        85.63   127.74   17.81
## Serine                        407.48       114.43       407.48   115.58   38.86
## Succinate                      51.42        28.22        82.27    57.97   48.91
## Sucrose                       502.70        64.72        42.10   528.48   70.11
## Tartrate                       85.63        27.11        26.84    20.49    8.33
## Taurine                      1495.18      1187.97      1164.45    79.84  212.72
## Threonine                     141.17        91.84        98.49   188.67    8.94
## Trigonelline                   80.64       196.37       387.61  1096.63   83.10
## Trimethylamine.N.oxide        658.52       671.83      1571.84  1107.65  152.93
## Tryptophan                     56.83        82.27        98.49   162.39   15.49
## Tyrosine                       49.90        61.56        83.93   102.51   21.54
## Uracil                         38.47        62.80        72.24    12.94    9.03
## Valine                         40.04        42.95        46.99    75.94   10.59
## Xylose                        112.17        42.95        54.05    64.72   36.97
## cis.Aconitate                 252.14       262.43       445.86   287.15   16.61
## myo.Inositol                  179.47       206.44       267.74   174.16  114.43
## trans.Aconitate                62.18        14.30        38.86    74.44   19.89
## pi.Methylhistidine             79.84      2697.28       671.83    84.77   49.40
## tau.Methylhistidine            78.26       151.41       172.43    55.15   18.73
##                           NETL_004_V1 PIF_094  PIF_132  PIF_163 NETCR_003_V1
## X1.6.Anhydro.beta.D.glucose        4.71   68.72   214.86   304.90         37.71
## X1.Methylnicotinamide             11.13   13.87   127.74    25.79         10.80
## X2.Aminobutyrate                  43.38   12.18    31.50    27.11          5.00
## X2.Hydroxyisobutyrate             30.88   25.03    33.78    40.45          8.25
## X2.Oxoglutarate                  104.58   28.22    88.23    70.81         11.70
## X3.Aminoisobutyrate               54.05   72.97    64.07   126.47          8.41
## X3.Hydroxybutyrate                 7.61   11.47    54.05    16.95          6.75
## X3.Hydroxyisovalerate              7.92   25.03   164.02    51.42          5.26
## X3.Indoxylsulfate                210.61  119.10   692.29   144.03         44.26
## X4.Hydroxyphenylacetate           31.19  134.29   278.66    89.12         29.37
## Acetate                           13.07  103.54   411.58   108.85         22.20
## Acetone                            7.61   12.06    14.73     8.67          4.90
## Adipate                            6.11   32.14    68.72    14.15          5.81
## Alanine                          170.72  454.86  1312.91   357.81         29.08
## Asparagine                        27.66   98.49   132.95    37.34         15.64
## Betaine                           94.63   88.23   156.02   107.77          4.53
## Carnitine                         28.79   42.52    33.78   117.92          2.18
## Citrate                         1422.26 3677.54  9045.29  2230.54        415.72
## Creatine                          38.86   43.82   105.64    62.18          4.26
## Creatinine                      4865.87 8349.86 33860.35 11271.13       1737.15
## Dimethylamine                    214.86  350.72  1556.20   336.97         71.52
## Ethanolamine                      86.49  252.14  1436.55   468.72         32.79
## Formate                           36.23  202.35  1480.30   368.71         21.98
## Fucose                            24.29   86.49   181.27   109.95         12.55
## Fumarate                           8.17    7.17     7.54     5.70          0.90
## Glucose                          109.95  403.43  1032.77   632.70         69.41
## Glutamine                        116.75  415.72   539.15   772.78         32.14
```

```
## Glycine                          518.01 1422.26  2751.77  3428.92        68.72
## Glycolate                        107.77  204.38   428.38    90.02        42.95
## Guanidoacetate                   108.85   95.58   265.07   145.47        15.18
## Hippurate                        645.48 1919.85  8022.46  1339.43       533.79
## Histidine                        146.94  383.75  1863.11  1164.45        53.52
## Hypoxanthine                      14.30   24.05   265.07    24.05        29.37
## Isoleucine                         8.17    9.30    11.70    18.92         3.82
## Lactate                           41.26  138.38   424.11    87.36        15.18
## Leucine                           20.91   15.80    58.56    27.39         5.05
## Lysine                            17.81   69.41   239.85   177.68        26.05
## Methylamine                       15.80   21.98    19.30    10.80         6.49
## Methylguanidine                    7.46   10.80     6.42     2.41         2.34
## N.N.Dimethylglycine               29.96   34.81   120.30    40.45         0.79
## O.Acetylcarnitine                 15.33   19.89    46.06    33.78         1.57
## Pantothenate                      12.30   17.29    36.97    27.39        32.46
## Pyroglutamate                    109.95  162.39   788.40   343.78        46.06
## Pyruvate                          21.54    4.57    58.56    27.94         2.41
## Quinolinate                       83.93   61.56    54.05   102.51        20.09
## Serine                           132.95  141.17   391.51   441.42        25.28
## Succinate                         16.95   65.37   589.93    97.51        16.61
## Sucrose                           21.98   75.94    71.52    28.22        16.95
## Tartrate                          18.92   12.81   196.37    23.34        14.15
## Taurine                          518.01  290.03   323.76  1737.15        24.29
## Threonine                         81.45   68.03   295.89   267.74        10.18
## Trigonelline                      21.54  149.90  2252.96   880.07        24.78
## Trimethylamine.N.oxide           175.91  372.41  1326.10   323.76       148.41
## Tryptophan                        79.04  107.77    83.10    96.54         8.67
## Tyrosine                          53.52  162.39   539.15   159.17        11.59
## Uracil                            12.81   11.94   179.47    14.44         6.36
## Valine                            33.12   38.47   120.30    90.92         5.42
## Xylose                            24.29   54.60    70.11    70.11        19.30
## cis.Aconitate                     29.96  242.26  1236.45   254.68        15.03
## myo.Inositol                     561.16   70.11   230.44    79.84        13.87
## trans.Aconitate                   11.70   26.84    93.69    44.26         6.69
## pi.Methylhistidine                16.61  275.89  1248.88  2670.44        18.36
## tau.Methylhistidine               64.72  170.72   130.32   265.07        15.18
##                           NETL_028_V1 NETL_028_V2 NETCR_013_V1 NETL_020_V1
## X1.6.Anhydro.beta.D.glucose       45.60       34.12        107.77       13.33
## X1.Methylnicotinamide            473.43       92.76         16.61       50.91
## X2.Aminobutyrate                  16.28        8.25         26.84        2.92
## X2.Hydroxyisobutyrate             63.43       16.61         32.46       40.85
## X2.Oxoglutarate                  221.41       55.15         62.80       46.99
## X3.Aminoisobutyrate               15.49        3.39         29.67       22.42
## X3.Hydroxybutyrate                41.68        9.03         44.26       10.07
## X3.Hydroxyisovalerate             52.46       16.61         20.91        4.06
## X3.Indoxylsulfate               1043.15      278.66        459.44       97.51
## X4.Hydroxyphenylacetate          149.90       30.57        162.39       75.19
## Acetate                           31.82       10.38         70.81       29.37
## Acetone                           14.01        6.05          5.31        8.58
## Adipate                           21.33        8.94          8.50       11.36
## Alanine                          473.43      212.72        330.30       95.58
## Asparagine                       125.21       35.52         45.15       19.69
## Betaine                          114.43       56.26         64.72      127.74
## Carnitine                         91.84       54.60         70.81       61.56
```

```
## Citrate                          3714.50      915.99      3071.74     2186.37
## Creatine                          424.11      270.43        40.85        7.92
## Creatinine                      21590.31     4188.09     11731.12     5431.66
## Dimethylamine                     665.14      142.59       424.11      230.44
## Ethanolamine                      212.72      208.51       336.97      135.64
## Formate                           115.58      102.51       196.37      130.32
## Fucose                            167.34       38.09       159.17       60.95
## Fumarate                           10.07        1.82         2.69        2.32
## Glucose                           333.62       62.80       267.74      126.47
## Glutamine                         333.62      114.43       492.75      157.59
## Glycine                           720.54      415.72       671.83      336.97
## Glycolate                         148.41      172.43       267.74       94.63
## Guanidoacetate                     62.80       62.80        96.54       18.92
## Hippurate                        9045.29     2864.07       550.04     1790.05
## Histidine                         473.43      148.41       347.23      108.85
## Hypoxanthine                       97.51       13.20        55.15       33.12
## Isoleucine                         10.38        5.10         8.17        3.90
## Lactate                           125.21       35.52        73.70       42.10
## Leucine                            46.53       10.70        46.53       14.01
## Lysine                            137.00       16.95        62.18      115.58
## Methylamine                        27.11       12.06        24.05       10.38
## Methylguanidine                    34.12       18.54        11.82        3.97
## N.N.Dimethylglycine                73.70       21.98        24.05       21.98
## O.Acetylcarnitine                  25.03        9.30         8.94       29.37
## Pantothenate                       41.26       13.46        31.19       10.07
## Pyroglutamate                     340.36       76.71       270.43       99.48
## Pyruvate                           56.26       18.73        21.33        6.23
## Quinolinate                       107.77       57.40        75.94       37.34
## Serine                            278.66      138.38       290.03       64.72
## Succinate                          34.47        7.39        75.94       27.39
## Sucrose                            55.70       56.26       116.75       23.10
## Tartrate                           24.78        6.55        17.81        5.93
## Taurine                           428.38      123.97        82.27      555.57
## Threonine                         137.00       48.91        81.45       31.82
## Trigonelline                     1352.89      459.44        53.52       49.90
## Trimethylamine.N.oxide            502.70      175.91       812.41      424.11
## Tryptophan                         76.71       31.19        42.95       36.60
## Tyrosine                           98.49       15.03        62.80       26.58
## Uracil                             19.89        7.61        17.12       13.60
## Valine                             56.26       14.59        35.87       17.46
## Xylose                            194.42       45.15        47.47       36.97
## cis.Aconitate                     459.44       87.36       395.44       41.68
## myo.Inositol                      139.77       51.42        78.26      632.70
## trans.Aconitate                    68.03        8.25        37.71       15.64
## pi.Methylhistidine                368.71      265.07       267.74      347.23
## tau.Methylhistidine               119.10       84.77       287.15       46.06
##                              NETL_020_V2 PIF_192 NETCR_012_V1 NETCR_012_V2
## X1.6.Anhydro.beta.D.glucose        27.94  141.17        14.01       244.69
## X1.Methylnicotinamide              80.64   68.03        46.06       116.75
## X2.Aminobutyrate                   15.80   40.85        29.08        40.04
## X2.Hydroxyisobutyrate              64.72   12.81        24.53        61.56
## X2.Oxoglutarate                    88.23   26.05        64.07       174.16
## X3.Aminoisobutyrate                11.70   21.76        13.07        53.52
## X3.Hydroxybutyrate                 19.49   45.60        11.82        45.15
```

X3.Hydroxyisovalerate	5.26	20.70	21.12	44.70
X3.Indoxylsulfate	125.21	123.97	48.91	62.80
X4.Hydroxyphenylacetate	183.09	56.83	21.33	43.38
Acetate	42.52	24.29	9.58	16.44
Acetone	28.50	18.36	8.33	11.13
Adipate	11.02	39.65	6.49	10.18
Alanine	145.47	87.36	89.12	273.14
Asparagine	66.69	47.47	24.05	117.92
Betaine	208.51	22.87	45.15	347.23
Carnitine	151.41	11.13	6.62	23.10
Citrate	2298.47	2392.27	1790.05	4188.09
Creatine	34.81	27.66	11.47	192.48
Creatinine	8349.86	5014.05	4315.64	13359.73
Dimethylamine	327.01	190.57	142.59	411.58
Ethanolamine	202.35	125.21	102.51	407.48
Formate	142.59	120.30	62.18	148.41
Fucose	57.40	42.52	18.17	101.49
Fumarate	4.14	2.86	2.01	6.05
Glucose	156.02	99.48	79.84	445.86
Glutamine	214.86	145.47	145.47	368.71
Glycine	424.11	454.86	262.43	749.95
Glycolate	257.24	66.69	20.91	307.97
Guanidoacetate	51.42	19.11	25.03	198.34
Hippurate	3640.95	407.48	437.03	2724.39
Histidine	61.56	101.49	135.64	507.76
Hypoxanthine	40.04	29.08	32.14	101.49
Isoleucine	14.01	3.67	5.64	5.53
Lactate	61.56	19.89	19.69	63.43
Leucine	18.54	11.13	11.25	41.26
Lysine	170.72	75.94	22.20	32.79
Methylamine	9.30	4.26	6.49	18.54
Methylguanidine	3.19	2.08	6.30	33.12
N.N.Dimethylglycine	31.50	15.64	19.89	61.56
O.Acetylcarnitine	40.04	14.15	2.41	11.82
Pantothenate	24.05	57.97	6.49	21.33
Pyroglutamate	142.59	244.69	50.91	198.34
Pyruvate	13.46	3.94	19.11	62.80
Quinolinate	75.94	56.83	46.06	131.63
Serine	129.02	186.79	114.43	225.88
Succinate	41.68	45.15	6.05	18.17
Sucrose	40.85	336.97	14.59	58.56
Tartrate	16.28	25.79	12.81	26.05
Taurine	336.97	55.15	64.72	99.48
Threonine	46.06	45.60	47.94	127.74
Trigonelline	83.10	278.66	116.75	340.36
Trimethylamine.N.oxide	403.43	135.64	219.20	735.10
Tryptophan	44.26	24.29	34.12	103.54
Tyrosine	68.03	15.18	33.45	113.30
Uracil	29.67	11.94	20.09	29.67
Valine	33.45	9.68	19.11	52.98
Xylose	68.03	20.49	20.49	51.42
cis.Aconitate	101.49	51.94	103.54	347.23
myo.Inositol	854.06	60.34	14.30	138.38
trans.Aconitate	28.79	50.91	6.96	48.42

```
## pi.Methylhistidine               160.77  135.64       162.39      1844.57
## tau.Methylhistidine               26.31   36.60        62.18       317.35
##                                 PIF_089 NETCR_002_V1 PIF_179  PIF_114 NETCR_006_V1
## X1.6.Anhydro.beta.D.glucose      123.97       141.17   35.16   685.40       278.66
## X1.Methylnicotinamide             81.45        28.50   26.58    36.23        40.45
## X2.Aminobutyrate                  55.15        20.29    5.21    32.46        55.15
## X2.Hydroxyisobutyrate             70.81        14.30   30.27    85.63        51.42
## X2.Oxoglutarate                   92.76        97.51    7.39    25.03        74.44
## X3.Aminoisobutyrate              561.16         8.41    8.41   184.93       354.25
## X3.Hydroxybutyrate                43.38         5.58    5.81    38.09        94.63
## X3.Hydroxyisovalerate             31.82        23.10   21.33    32.79        16.28
## X3.Indoxylsulfate                144.03        48.42  132.95   572.49       595.86
## X4.Hydroxyphenylacetate           76.71        64.72   62.80   228.15       265.07
## Acetate                          152.93        18.54  103.54   188.67        95.58
## Acetone                            4.01        13.74    6.96     8.41         7.92
## Adipate                           30.57        13.20    6.42    16.78        16.44
## Alanine                          478.19       327.01  194.42   304.90       601.85
## Asparagine                       132.95        62.80   42.10    66.02       177.68
## Betaine                          116.75       126.47   75.94   146.94        39.25
## Carnitine                         23.34       120.30   18.54    19.69        90.02
## Citrate                         2951.30      1380.22 1002.25  3604.72       459.44
## Creatine                         232.76        38.09   37.71    76.71       132.95
## Creatinine                     16481.60      7631.20 3197.10 12332.58     19930.37
## Dimethylamine                    632.70       237.46  125.21  1032.77      1141.39
## Ethanolamine                     645.48       144.03   50.91   239.85       539.15
## Formate                          379.93       175.91  146.94   403.43        89.12
## Fucose                           204.38        43.38   48.42    79.04       336.97
## Fumarate                           9.97         3.67    2.18    10.28         7.32
## Glucose                          595.86       210.61  445.86   314.19      1450.99
## Glutamine                        482.99       454.86  278.66   533.79       780.55
## Glycine                         2697.28       871.31  528.48   595.86      1881.83
## Glycolate                         72.97       200.34  117.92   164.02       550.04
## Guanidoacetate                    82.27        21.12   24.29   130.32        33.78
## Hippurate                       1826.21       584.06 3533.34   812.41      1326.10
## Histidine                        482.99       487.85  142.59   254.68       148.41
## Hypoxanthine                      82.27        59.74   14.88    83.93        67.36
## Isoleucine                         6.30         5.00   10.38     5.47        13.33
## Lactate                          188.67        87.36  145.47    98.49       200.34
## Leucine                           19.11        37.71   31.19    24.53        97.51
## Lysine                            92.76       464.05   31.50    78.26       340.36
## Methylamine                       44.26        10.91    6.30    24.05        29.67
## Methylguanidine                   22.20        14.01    2.29    17.99        34.81
## N.N.Dimethylglycine               55.70        48.42    6.11    44.26         8.17
## O.Acetylcarnitine                  7.24        20.91    4.57    11.47        10.91
## Pantothenate                      29.96        17.99   13.60    26.84        98.49
## Pyroglutamate                    502.70       138.38   68.72   343.78      1064.22
## Pyruvate                          33.78        41.68    3.82    15.03        48.91
## Quinolinate                      259.82        55.15   34.47    98.49       119.10
## Serine                           159.17       237.46  104.58   198.34       692.29
## Succinate                        208.51         6.36   51.94   164.02       204.38
## Sucrose                          281.46        94.63   94.63    17.12       108.85
## Tartrate                          10.28         8.58   14.88    16.78        90.92
## Taurine                          880.07       665.14   97.51    79.04      1790.05
## Threonine                        275.89       144.03   64.07   162.39       198.34
```

```
## Trigonelline                1754.61        38.09  154.47   387.61       170.72
## Trimethylamine.N.oxide       699.24       301.87  284.29  5486.25      5377.61
## Tryptophan                    66.02        64.07   51.94   132.95        28.50
## Tyrosine                     120.30        98.49   73.70   217.02        42.95
## Uracil                        29.37        42.10   10.49    29.37        55.15
## Valine                        42.95        33.12   52.98    36.23        75.19
## Xylose                       107.77        75.94  111.05    79.84       454.86
## cis.Aconitate                254.68       179.47   65.37   202.35       340.36
## myo.Inositol                 175.91        53.52  257.24   102.51       137.00
## trans.Aconitate               90.92        17.81   17.64    57.40        50.40
## pi.Methylhistidine            89.12       210.61  141.17    60.95       249.64
## tau.Methylhistidine           62.80       137.00   28.22   127.74        76.71
##                           PIF_141 NETCR_025_V1 NETCR_025_V2 NETCR_016_V1
## X1.6.Anhydro.beta.D.glucose   15.80        29.96        16.95       292.95
## X1.Methylnicotinamide         23.57        96.54       114.43        57.97
## X2.Aminobutyrate              17.99         6.55         2.53       167.34
## X2.Hydroxyisobutyrate         37.34        65.37        77.48        82.27
## X2.Oxoglutarate               21.33      1053.63      2465.13       468.72
## X3.Aminoisobutyrate           26.84        14.15        19.49        53.52
## X3.Hydroxybutyrate             7.10        45.15        62.18        14.59
## X3.Hydroxyisovalerate         42.52        41.68        14.01        11.36
## X3.Indoxylsulfate            138.38       117.92        82.27       518.01
## X4.Hydroxyphenylacetate       65.37        51.94       114.43       376.15
## Acetate                       21.98        29.37       125.21        72.24
## Acetone                       10.91         4.01         5.00         6.62
## Adipate                       13.87        27.66        37.34        57.97
## Alanine                      103.54       403.43       632.70       502.70
## Asparagine                    64.07        41.26        89.12       101.49
## Betaine                       34.12       130.32       120.30        54.05
## Carnitine                     65.37        60.95        15.96        23.81
## Citrate                     1366.49      4964.16      7480.09      2697.28
## Creatine                      54.05        71.52       117.92        90.02
## Creatinine                  7115.28     14764.78     22247.84     14328.42
## Dimethylamine                204.38       528.48       812.41       584.06
## Ethanolamine                 237.46       383.75       735.10       614.00
## Formate                      165.67        62.18       119.10        27.66
## Fucose                        37.71       130.32       237.46       196.37
## Fumarate                       2.14        31.19        75.94        23.81
## Glucose                      117.92       407.48       399.41       788.40
## Glutamine                    181.27       403.43       528.48       555.57
## Glycine                      487.85       678.58       699.24       962.95
## Glycolate                    244.69       232.76       464.05       177.68
## Guanidoacetate               561.16       103.54       164.02       127.74
## Hippurate                   2038.56      7259.02      2321.57      1366.49
## Histidine                    330.30       100.48       145.47       492.75
## Hypoxanthine                  31.19       135.64       194.42       165.67
## Isoleucine                     1.95        13.20         9.68         7.17
## Lactate                       48.42       139.77       350.72       507.76
## Leucine                       21.98        34.12        36.60        49.40
## Lysine                        45.60        94.63        96.54       295.89
## Methylamine                   20.49        13.46        20.09        46.99
## Methylguanidine                8.85        14.73         6.30        20.09
## N.N.Dimethylglycine           22.87        54.05        69.41        19.69
## O.Acetylcarnitine             32.14        18.54        10.38        15.64
```

```
## Pantothenate                  20.09        55.70        87.36        30.57
## Pyroglutamate                 59.74       244.69       365.04       249.64
## Pyruvate                       7.46        25.28       184.93        32.46
## Quinolinate                   50.91       102.51       139.77       106.70
## Serine                       130.32       323.76       323.76       333.62
## Succinate                     20.49       135.64       204.38        44.26
## Sucrose                       21.33        29.08        36.97        42.95
## Tartrate                       5.87        15.96        17.64        14.88
## Taurine                      713.37       239.85      1224.15       972.63
## Threonine                     62.80       145.47       179.47       148.41
## Trigonelline                 383.75        89.12       186.79        46.53
## Trimethylamine.N.oxide       151.41       482.99       290.03      1096.63
## Tryptophan                    64.72        40.04       105.64       164.02
## Tyrosine                      85.63        39.65        92.76       181.27
## Uracil                        35.52       107.77       120.30        39.65
## Valine                        26.84        52.46        60.34        66.02
## Xylose                        40.85        87.36       113.30       111.05
## cis.Aconitate                 97.51       482.99       953.37       539.15
## myo.Inositol                  60.34       314.19       275.89       626.41
## trans.Aconitate               17.81        20.49        44.70        59.74
## pi.Methylhistidine          1236.45       387.61       399.41      1002.25
## tau.Methylhistidine          210.61       239.85       249.64       144.03
##                            PIF_116 PIF_191  PIF_164 NETL_013_V1 PIF_188
## X1.6.Anhydro.beta.D.glucose   29.67   18.92   127.74       34.81   65.37
## X1.Methylnicotinamide         70.11   24.53  1032.77       12.30   24.05
## X2.Aminobutyrate               5.58    3.29     8.58        5.87    4.71
## X2.Hydroxyisobutyrate         18.73   10.49    66.02       15.18   15.80
## X2.Oxoglutarate                5.53    9.68    38.09       16.78    7.24
## X3.Aminoisobutyrate            2.61   26.84    66.69       11.25    3.13
## X3.Hydroxybutyrate             2.44    5.37    21.76        2.23   14.59
## X3.Hydroxyisovalerate         14.44   12.94    43.82        2.46    9.12
## X3.Indoxylsulfate            188.67   50.40   376.15      108.85   37.71
## X4.Hydroxyphenylacetate       52.98   26.31   149.90       57.40   48.42
## Acetate                       91.84   13.60   116.75        3.49    9.49
## Acetone                        3.03    4.90     7.61        5.58    3.00
## Adipate                        3.94    3.35    19.11        3.90    6.42
## Alanine                       86.49  104.58   432.68       48.91   41.26
## Asparagine                     8.00   33.12   121.51       12.43   13.07
## Betaine                       28.79   59.15   109.95        5.37   11.25
## Carnitine                      5.53   13.20    59.74       14.44   18.92
## Citrate                     2208.35  502.70  4230.18      177.68   87.36
## Creatine                      41.26    2.75   259.82        6.36    9.03
## Creatinine                 2864.07 1702.75 15063.05     2392.27 2489.91
## Dimethylamine                 90.92   44.70   497.70       83.93  142.59
## Ethanolamine                  82.27   48.91   432.68       66.69   35.87
## Formate                       87.36   34.47   219.20       17.29   15.49
## Fucose                        30.27   17.12   196.37       26.58   47.47
## Fumarate                       1.12    1.99     6.89        1.21    1.60
## Glucose                       87.36   34.81   327.01       75.19   44.26
## Glutamine                     92.76   46.99   290.03       24.29   35.52
## Glycine                      257.24  237.46  2275.60       46.06   89.12
## Glycolate                     16.44   32.14   130.32       46.53   50.91
## Guanidoacetate                66.69   17.99   116.75       16.95  106.70
## Hippurate                   1380.22  478.19  6634.24      665.14  275.89
```

```
## Histidine                     35.16  132.95   265.07       30.57   44.26
## Hypoxanthine                   7.77    3.78    57.97       12.18    5.16
## Isoleucine                     2.97    2.69    17.99        4.01    4.01
## Lactate                       53.52   27.11    81.45       94.63   27.66
## Leucine                        9.12    9.21    25.53        9.03    5.31
## Lysine                        26.05   22.20    52.98       16.12   28.79
## Methylamine                    5.26    5.05    39.65        5.58    5.10
## Methylguanidine                2.48    1.70     7.85        2.80    5.16
## N.N.Dimethylglycine            4.57   11.70    52.46        3.10    1.93
## O.Acetylcarnitine              1.65    1.93    13.74        4.53    3.06
## Pantothenate                  56.83   10.80   692.29       13.74    6.82
## Pyroglutamate                 51.94   54.05   298.87       39.65   71.52
## Pyruvate                       1.80    0.90    22.65        6.69    1.28
## Quinolinate                   38.09   21.54   164.02       12.55   51.42
## Serine                        38.09   70.11   225.88       49.40   32.46
## Succinate                     14.88   19.49   221.41        5.99    1.90
## Sucrose                       10.18   30.57    41.68       14.88   43.82
## Tartrate                       3.03   10.91    47.94        9.12    2.20
## Taurine                      132.95  114.43  1510.20       17.81   28.22
## Threonine                     22.20   39.65   119.10       30.57   12.18
## Trigonelline                  41.26   22.65   566.80       70.11   51.94
## Trimethylamine.N.oxide       159.17   55.70   482.99      167.34  125.21
## Tryptophan                    24.05   13.20   120.30       20.09   20.91
## Tyrosine                      27.39   34.12   156.02       14.15   11.47
## Uracil                        36.60    9.68    27.39       14.01    9.58
## Valine                        13.60    7.32    47.94        7.61   10.49
## Xylose                       174.16   39.25    96.54       26.58   32.79
## cis.Aconitate                 31.82   21.98   221.41       26.58   12.94
## myo.Inositol                  23.34   44.70   314.19       14.73   21.98
## trans.Aconitate                8.17    9.68    96.54        7.77   19.49
## pi.Methylhistidine            25.28   73.70   572.49       63.43   54.05
## tau.Methylhistidine           18.54   12.55   125.21       16.44   11.13
##                             PIF_195 NETCR_015_V1 PIF_102 NETL_010_V1
## X1.6.Anhydro.beta.D.glucose   15.18        70.81   25.28       34.47
## X1.Methylnicotinamide         94.63        75.94  101.49       12.81
## X2.Aminobutyrate              11.36        22.65    8.33        3.78
## X2.Hydroxyisobutyrate          8.17        60.95   59.15        8.33
## X2.Oxoglutarate                5.64       230.44   88.23       14.30
## X3.Aminoisobutyrate            5.99        53.52   22.65       24.29
## X3.Hydroxybutyrate             6.49        17.81   34.12        3.16
## X3.Hydroxyisovalerate          3.60         6.96   46.99        5.99
## X3.Indoxylsulfate             62.80       137.00  441.42       42.52
## X4.Hydroxyphenylacetate       41.68        59.15  432.68       52.98
## Acetate                       86.49        16.28  202.35        9.12
## Acetone                        6.05         7.10    7.10       10.49
## Adipate                        4.81         6.17   18.54        3.46
## Alanine                       78.26       376.15  330.30       28.79
## Asparagine                    19.49       130.32   64.07       14.30
## Betaine                        8.58       311.06   55.15        7.92
## Carnitine                      5.26       206.44  111.05       16.12
## Citrate                      214.86      4105.16 3327.58      259.82
## Creatine                      18.54        46.99   93.69       84.77
## Creatinine                  3604.72      9996.60 7480.09     1480.30
## Dimethylamine                142.59       304.90  340.36      102.51
```

```
## Ethanolamine                   34.12       906.87  320.54       58.56
## Formate                        52.98       292.95  235.10       45.60
## Fucose                         31.82       148.41   64.07       15.33
## Fumarate                        3.71         6.82    9.58        1.36
## Glucose                       114.43       320.54  336.97       42.95
## Glutamine                      29.37       437.03  284.29       43.82
## Glycine                       141.17      1286.91  871.31       86.49
## Glycolate                      38.86       320.54   34.81        7.85
## Guanidoacetate                 87.36       192.48   34.81       83.93
## Hippurate                    4817.45       572.49 1085.72      487.85
## Histidine                      51.42       502.70  129.02       26.58
## Hypoxanthine                   12.68       131.63  162.39        7.77
## Isoleucine                      4.06        12.94    7.24        2.89
## Lactate                        62.80       112.17  196.37       17.46
## Leucine                         4.95        25.53   20.91        3.63
## Lysine                         12.18       106.70   48.91       10.49
## Methylamine                     1.51         9.03   44.70        4.10
## Methylguanidine                 6.75        26.58    8.67        5.26
## N.N.Dimethylglycine             6.62        21.33   17.12        3.16
## O.Acetylcarnitine               1.77        29.96   43.82        1.95
## Pantothenate                   24.53        27.66  223.63        9.21
## Pyroglutamate                  82.27       156.02  169.02       35.87
## Pyruvate                        2.23        15.96    8.08        2.89
## Quinolinate                    21.98        32.14  101.49       10.80
## Serine                        127.74       270.43  122.73       30.88
## Succinate                      30.88        24.78   88.23        5.47
## Sucrose                        29.96        19.30  601.85       18.36
## Tartrate                        8.41        12.94   96.54        3.90
## Taurine                        85.63       492.75  228.15      208.51
## Threonine                      23.57       156.02  123.97        9.12
## Trigonelline                   17.12        93.69  343.78       10.07
## Trimethylamine.N.oxide        139.77       186.79  982.40      383.75
## Tryptophan                     12.30       111.05   31.82       10.91
## Tyrosine                       19.89       179.47   56.83        7.85
## Uracil                          3.10        56.26  135.64        7.24
## Valine                          7.85        34.47   35.87        9.21
## Xylose                         10.07        55.70   31.82       29.96
## cis.Aconitate                  83.10       156.02  175.91       18.54
## myo.Inositol                   16.28        54.60  167.34       15.80
## trans.Aconitate                 7.85        30.27  181.27        7.39
## pi.Methylhistidine             15.64       934.49  307.97       32.14
## tau.Methylhistidine             8.58       156.02  170.72       18.54
##                            NETL_010_V2 NETL_001_V1 NETCR_015_V2 NETCR_005_V1
## X1.6.Anhydro.beta.D.glucose       18.54       37.34        33.78        22.42
## X1.Methylnicotinamide              8.41       55.15        53.52        55.15
## X2.Aminobutyrate                   3.78        7.39        18.17        20.70
## X2.Hydroxyisobutyrate              4.85       36.23        46.53        38.47
## X2.Oxoglutarate                    8.08       75.94        81.45       164.02
## X3.Aminoisobutyrate               22.87        9.87        44.70       206.44
## X3.Hydroxybutyrate                 3.22        7.24        17.81        15.03
## X3.Hydroxyisovalerate              5.05        4.22         4.48         7.24
## X3.Indoxylsulfate                 31.19      103.54        31.82       159.17
## X4.Hydroxyphenylacetate           21.33       70.11        83.10        84.77
## Acetate                            6.82       28.79        29.96        11.13
```

```
## Acetone                          12.55       2.29       10.18       11.25
## Adipate                           3.46       5.37       14.15        6.23
## Alanine                          21.76     152.93      464.05      221.41
## Asparagine                        8.17      47.94      134.29       62.80
## Betaine                          11.25      70.11      247.15       48.42
## Carnitine                        16.95       7.92        8.41       20.09
## Citrate                         179.47    2079.74     4105.16     2540.20
## Creatine                        395.44      24.29       91.84       49.40
## Creatinine                     1064.22    6974.39     8266.78    11849.01
## Dimethylamine                    41.26     192.48      249.64      368.71
## Ethanolamine                     51.42     204.38      692.29      265.07
## Formate                          21.54      72.24      181.27       85.63
## Fucose                            5.70      91.84       87.36       37.71
## Fumarate                          0.79       2.69        5.70        4.10
## Glucose                          38.09      92.76      221.41      214.86
## Glutamine                        23.34     181.27      685.40      287.15
## Glycine                          78.26    1152.86     1261.43      906.87
## Glycolate                         5.42     320.54      441.42      327.01
## Guanidoacetate                   51.94      69.41      301.87       95.58
## Hippurate                       632.70    2921.93      383.75      464.05
## Histidine                        26.58     395.44      614.00      295.89
## Hypoxanthine                      6.11      24.53      146.94       90.92
## Isoleucine                        2.89       7.69       12.68       14.59
## Lactate                           7.85      30.88      137.00       98.49
## Leucine                          11.25      21.98       23.10       24.05
## Lysine                           19.49      44.70       85.63       87.36
## Methylamine                       4.44      26.84        4.39       17.46
## Methylguanidine                   2.92       5.00       34.47       35.16
## N.N.Dimethylglycine               3.19      20.29       31.19       42.52
## O.Acetylcarnitine                 2.08       1.97       16.44       17.99
## Pantothenate                      4.48     174.16       24.53       29.08
## Pyroglutamate                    25.28      73.70      135.64      157.59
## Pyruvate                          6.11       9.49       29.08       30.88
## Quinolinate                       7.32      54.05       40.04       43.38
## Serine                           16.12     126.47      270.43      198.34
## Succinate                         3.03      43.82       25.79       16.95
## Sucrose                           9.21      19.49       16.78       17.46
## Tartrate                          3.39       8.94       40.45       10.70
## Taurine                         175.91    1064.22      254.68      544.57
## Threonine                        10.07      64.72      157.59      129.02
## Trigonelline                     26.84      92.76      106.70       38.09
## Trimethylamine.N.oxide           92.76     196.37      107.77      273.14
## Tryptophan                       10.49      74.44      107.77       37.34
## Tyrosine                          4.22      64.72      126.47       34.81
## Uracil                            7.24      36.23       57.40       58.56
## Valine                            6.30      29.96       37.71       30.88
## Xylose                           21.54      50.40      259.82       45.60
## cis.Aconitate                    18.54      54.05      183.09      242.26
## myo.Inositol                     11.59     135.64      100.48       30.27
## trans.Aconitate                  11.36      15.03       21.76       29.37
## pi.Methylhistidine               30.27     126.47      259.82     1187.97
## tau.Methylhistidine              16.78      20.09      113.30      184.93
##                              PIF_111  PIF_171 NETCR_008_V1 NETCR_008_V2
## X1.6.Anhydro.beta.D.glucose  146.94    64.07        32.46       113.30
```

```
## X1.Methylnicotinamide         10.07     6.42       14.01       43.38
## X2.Aminobutyrate               6.30    28.79        2.97        4.66
## X2.Hydroxyisobutyrate         27.94    18.92        5.16       27.11
## X2.Oxoglutarate               24.05    85.63        8.08       22.42
## X3.Aminoisobutyrate           14.88    31.82        5.99       27.11
## X3.Hydroxybutyrate             8.76    26.31        3.29        9.49
## X3.Hydroxyisovalerate          6.55     9.39        1.67        2.94
## X3.Indoxylsulfate            126.47   614.00       41.26      202.35
## X4.Hydroxyphenylacetate       38.86   172.43       15.49       60.34
## Acetate                       65.37    95.58        9.39       55.15
## Acetone                        4.14     5.70        5.42        6.36
## Adipate                       16.12     8.00        1.99        8.58
## Alanine                      105.64   278.66       16.78       61.56
## Asparagine                    26.05    34.47        6.69       29.96
## Betaine                       13.33    42.52        2.29       14.73
## Carnitine                     70.11    22.87        2.72       26.84
## Citrate                     1074.92   735.10       59.74     1118.79
## Creatine                      20.91    20.49        4.26       29.67
## Creatinine                  3827.63 10614.75     1339.43     7785.36
## Dimethylamine                120.30   459.44       56.26      304.90
## Ethanolamine                 206.44   196.37       40.45      144.03
## Formate                      112.17   167.34        6.42       45.15
## Fucose                        25.79   137.00       15.18       91.84
## Fumarate                       3.60     8.08        1.46        1.14
## Glucose                      164.02   304.90       57.97      139.77
## Glutamine                     75.19   273.14       32.14       91.84
## Glycine                      383.75   482.99       38.09      307.97
## Glycolate                    103.54    41.68       28.79      112.17
## Guanidoacetate                64.72    35.52        7.46       72.24
## Hippurate                    235.10  3904.95      262.43     5710.15
## Histidine                     28.50    98.49       16.28      103.54
## Hypoxanthine                  44.70    59.74       15.18       75.19
## Isoleucine                     2.12    16.28        1.79        2.80
## Lactate                       63.43   174.16       24.05       47.94
## Leucine                        8.50     8.50        3.29       14.44
## Lysine                        34.81    36.97       17.46       82.27
## Methylamine                   20.29    16.44        3.53        3.67
## Methylguanidine                3.39     4.31        2.92        4.39
## N.N.Dimethylglycine           13.46    11.59        1.23        3.46
## O.Acetylcarnitine             16.12    23.57        2.53       10.07
## Pantothenate                   7.32    19.30        9.49       46.06
## Pyroglutamate                 85.63   441.42       21.33      179.47
## Pyruvate                       1.77    17.29        1.62        7.10
## Quinolinate                   83.93    87.36        9.39       47.47
## Serine                        39.25   160.77       46.53      217.02
## Succinate                     59.74     5.31        3.19       34.12
## Sucrose                       55.15   254.68       17.99       10.91
## Tartrate                       3.53    10.91        3.90       11.82
## Taurine                       64.72   247.15       27.94      137.00
## Threonine                     44.70    62.18       12.06       39.25
## Trigonelline                 415.72   450.34       33.12      141.17
## Trimethylamine.N.oxide       134.29   620.17      101.49     1540.71
## Tryptophan                    35.87    27.94       13.46       33.12
## Tyrosine                      48.91   129.02        5.58       24.05
```

```
## Uracil                          15.80    22.42        14.59        55.15
## Valine                          18.17    25.28         4.10        17.12
## Xylose                          27.94    75.94        19.49        46.53
## cis.Aconitate                   23.10    27.39        28.22       160.77
## myo.Inositol                    41.68   181.27        20.29        29.67
## trans.Aconitate                 12.43    81.45         4.90        20.49
## pi.Methylhistidine              46.53    72.97        67.36        67.36
## tau.Methylhistidine             26.31   100.48        16.12        79.84
##                              NETL_017_V1 NETL_017_V2 NETL_002_V1 NETL_002_V2
## X1.6.Anhydro.beta.D.glucose        22.20       46.53      192.48      528.48
## X1.Methylnicotinamide              20.70        9.78      108.85      225.88
## X2.Aminobutyrate                    7.85        3.10        7.77       13.46
## X2.Hydroxyisobutyrate              19.69        9.30       46.06       93.69
## X2.Oxoglutarate                    38.47       10.59       55.15      230.44
## X3.Aminoisobutyrate                 9.30       13.20        7.03       10.80
## X3.Hydroxybutyrate                  3.74        5.31        3.29       15.03
## X3.Hydroxyisovalerate               3.56        1.70       30.27       60.95
## X3.Indoxylsulfate                  64.07       27.66      152.93      167.34
## X4.Hydroxyphenylacetate            29.96       26.84      123.97      202.35
## Acetate                             5.70        4.85       39.65       47.47
## Acetone                            21.76       23.81        6.75        7.10
## Adipate                             2.53        1.55       11.47       58.56
## Alanine                            56.26       20.49      186.79      372.41
## Asparagine                         20.49       12.81       38.47       55.15
## Betaine                            37.71       43.82       21.76       44.26
## Carnitine                          46.06       11.70       34.47       54.60
## Citrate                           972.63      254.68     1719.86     2416.32
## Creatine                            7.39        4.35        8.00       30.88
## Creatinine                       5115.34     1571.84     6768.26    13359.73
## Dimethylamine                     151.41       87.36      219.20      419.89
## Ethanolamine                      131.63       40.85      145.47      239.85
## Formate                            28.22       24.05      113.30      100.48
## Fucose                             24.53        6.89       52.46      131.63
## Fumarate                            2.05        3.35        4.26        6.69
## Glucose                            76.71       71.52      162.39      281.46
## Glutamine                          41.26       41.26      122.73      275.89
## Glycine                           186.79       75.94      450.34      788.40
## Glycolate                          29.67       20.70      284.29      720.54
## Guanidoacetate                     15.18       11.36       50.40       79.04
## Hippurate                        1107.65      372.41     1224.15     1826.21
## Histidine                          56.26       35.52      399.41      720.54
## Hypoxanthine                       39.25        9.30       31.82      175.91
## Isoleucine                          6.30        2.25        8.33       21.33
## Lactate                            15.03        7.32       60.34      131.63
## Leucine                             6.42        4.31       17.46       38.09
## Lysine                             28.79       21.76       63.43       91.84
## Methylamine                         5.75        2.56        9.03       14.73
## Methylguanidine                     6.89        3.67       26.58       44.26
## N.N.Dimethylglycine                 6.89        1.62        4.57        6.23
## O.Acetylcarnitine                  21.54        3.71       11.59       17.29
## Pantothenate                       11.25        3.10       27.11       71.52
## Pyroglutamate                      65.37       26.31      127.74      314.19
## Pyruvate                           10.38        6.75        4.35       59.15
## Quinolinate                        25.28       22.20       46.99       49.90
```

```
## Serine                            84.77       33.45      105.64      383.75
## Succinate                          8.50        1.72       66.69       50.91
## Sucrose                           17.29       17.64       36.97      109.95
## Tartrate                           7.39       33.78       11.25       16.61
## Taurine                          428.38      127.74      671.83     1211.97
## Threonine                         26.31       10.59       52.46      117.92
## Trigonelline                      80.64       59.15       12.55       62.18
## Trimethylamine.N.oxide           336.97      478.19      437.03      972.63
## Tryptophan                        19.30       14.44       56.26       97.51
## Tyrosine                          23.57        9.78       58.56      135.64
## Uracil                            20.29        5.81       23.10       51.94
## Valine                            10.59        5.75       25.53       56.83
## Xylose                            13.07       38.86       49.90      407.48
## cis.Aconitate                     73.70       22.20      157.59      270.43
## myo.Inositol                      26.58       23.57       36.23      129.02
## trans.Aconitate                   13.60       21.12       30.27       56.26
## pi.Methylhistidine               200.34       72.24       32.46      403.43
## tau.Methylhistidine               55.70       15.96       71.52      287.15
##                                PIF_190 NETCR_009_V1 NETCR_009_V2 NETL_007_V1
## X1.6.Anhydro.beta.D.glucose      28.79       181.27        47.47       15.96
## X1.Methylnicotinamide             9.21        48.42         7.69       16.12
## X2.Aminobutyrate                  5.53         8.94         4.06        1.93
## X2.Hydroxyisobutyrate            17.64        51.94         9.30       15.80
## X2.Oxoglutarate                  14.44       982.40        65.37       25.28
## X3.Aminoisobutyrate              15.49       198.34        50.40       13.46
## X3.Hydroxybutyrate                6.82        20.70         4.22        4.01
## X3.Hydroxyisovalerate             9.30        57.40         0.92        4.18
## X3.Indoxylsulfate               104.58       502.70        54.60       37.34
## X4.Hydroxyphenylacetate          29.08       796.32        93.69       33.78
## Acetate                          14.88        55.15        14.30       26.84
## Acetone                          22.42         3.10         4.35        7.46
## Adipate                           9.21         9.03         5.75        8.50
## Alanine                          56.26       601.85        93.69       58.56
## Asparagine                       17.46       152.93        37.34       15.49
## Betaine                         102.51       137.00        20.70       27.39
## Carnitine                        21.12        12.94         3.06       19.49
## Citrate                         432.68      3133.79      1790.05     1012.32
## Creatine                         22.65       202.35         9.30       11.94
## Creatinine                     2121.76     13493.99      2298.47     3165.29
## Dimethylamine                   104.58       454.86        89.12      130.32
## Ethanolamine                     86.49       555.57       114.43      138.38
## Formate                          61.56        47.94        20.70       71.52
## Fucose                           22.87        86.49        31.82       52.46
## Fumarate                          3.10        36.23         3.42        1.21
## Glucose                          75.19       275.89        68.72       75.94
## Glutamine                        45.60       862.64       121.51      123.97
## Glycine                         184.93      2038.56       845.56      492.75
## Glycolate                        51.42       186.79        66.02       90.02
## Guanidoacetate                    7.03       242.26        45.60       42.52
## Hippurate                      1012.32       492.75       122.73      572.49
## Histidine                        39.25       544.57        27.39       78.26
## Hypoxanthine                     11.70       154.47        17.81       27.11
## Isoleucine                        4.44        17.64         4.66        4.18
## Lactate                          35.16       198.34        35.52       17.81
```

```
## Leucine                          7.10        31.50         7.54         8.94
## Lysine                          24.53       292.95        17.12        35.87
## Methylamine                      4.18        17.29         3.42         6.49
## Methylguanidine                  3.49        36.60        17.29         1.77
## N.N.Dimethylglycine             24.05        42.95         8.67        11.59
## O.Acetylcarnitine               23.81         3.86         1.60         3.94
## Pantothenate                     4.06        41.68         6.05         9.49
## Pyroglutamate                  160.77       247.15        40.04        44.70
## Pyruvate                         4.44        66.69         4.81         6.30
## Quinolinate                     25.53        51.42         5.21        12.18
## Serine                          51.94       219.20        57.97        90.92
## Succinate                        3.03       104.58         5.10         8.58
## Sucrose                         11.94        39.65        83.93        17.12
## Tartrate                         6.89        20.29         4.71         4.90
## Taurine                         66.02       347.23        63.43       259.82
## Threonine                       17.64       249.64        20.09        38.09
## Trigonelline                   114.43       376.15       134.29        67.36
## Trimethylamine.N.oxide         340.36      1118.79        72.97       130.32
## Tryptophan                      24.05       184.93        17.99        17.81
## Tyrosine                        84.77       139.77        13.74        20.70
## Uracil                           5.26       138.38         9.58        28.22
## Valine                           9.30        53.52         5.93        12.18
## Xylose                          42.52        58.56        11.82        26.05
## cis.Aconitate                   65.37       298.87        19.30        34.47
## myo.Inositol                    31.19       177.68        12.81        48.42
## trans.Aconitate                 11.02        30.57        35.52         6.55
## pi.Methylhistidine              98.49       943.88        11.36        62.18
## tau.Methylhistidine             52.46        48.42         9.03        29.67
##                               PIF_112 NETCR_019_V2 NETL_012_V1 NETL_012_V2
## X1.6.Anhydro.beta.D.glucose     22.87        35.16        16.95         9.39
## X1.Methylnicotinamide           10.38        52.46        15.80        14.01
## X2.Aminobutyrate                 1.28        13.87        10.49         5.16
## X2.Hydroxyisobutyrate            5.58        44.26        22.42        23.57
## X2.Oxoglutarate                  8.50        99.48        62.80        46.99
## X3.Aminoisobutyrate             13.74       208.51        10.91        13.33
## X3.Hydroxybutyrate               3.56        11.25         6.96         3.35
## X3.Hydroxyisovalerate            6.36         6.49         3.46         2.69
## X3.Indoxylsulfate               68.72       179.47       164.02        82.27
## X4.Hydroxyphenylacetate         23.81        82.27        31.50        36.97
## Acetate                         18.36        25.03        33.45         3.56
## Acetone                          2.32        10.28         4.95         7.03
## Adipate                          2.94         8.33         4.95         4.14
## Alanine                         47.47       181.27        78.26        56.26
## Asparagine                      16.78        31.19        17.46        29.08
## Betaine                          9.58       107.77        18.73        43.38
## Carnitine                       44.70        11.94         5.31        13.60
## Citrate                        626.41      2921.93      1719.86      1366.49
## Creatine                         5.42        30.57         7.17        12.94
## Creatinine                    1002.25     10097.06      3789.54      3498.19
## Dimethylamine                   44.70       314.19       127.74       365.04
## Ethanolamine                    21.54       395.44       112.17       112.17
## Formate                         46.53       149.90        42.95        61.56
## Fucose                          15.64        82.27        29.37        24.05
## Fumarate                         1.62         3.67         2.48         3.63
```

```
## Glucose                          26.84       188.67      122.73      121.51
## Glutamine                        57.97       225.88      113.30      113.30
## Glycine                         265.07       492.75      845.56      804.32
## Glycolate                        61.56       317.35       75.19       56.83
## Guanidoacetate                   11.25        83.10       17.64       44.70
## Hippurate                       464.05      1510.20      259.82      333.62
## Histidine                        66.69       267.74       64.07       43.38
## Hypoxanthine                      5.37        89.12       44.70       35.52
## Isoleucine                        2.94         9.87        7.85        3.22
## Lactate                          22.87        42.52       39.25      109.95
## Leucine                           2.51        16.95        8.85        7.39
## Lysine                           30.27        46.06       19.11       31.50
## Methylamine                       3.97        41.26        5.05        7.85
## Methylguanidine                   1.86        10.91       19.30       14.30
## N.N.Dimethylglycine               7.03        23.34       10.28        9.21
## O.Acetylcarnitine                 1.23        12.06        1.84        7.24
## Pantothenate                      3.74        20.49       14.44       11.82
## Pyroglutamate                    28.79       152.93       76.71       68.72
## Pyruvate                          5.93        15.49        5.93       12.06
## Quinolinate                      13.33        46.53       27.94       22.42
## Serine                           42.10       177.68      127.74      120.30
## Succinate                        15.03        20.91        7.24        4.57
## Sucrose                          25.03        12.06       13.46        6.49
## Tartrate                         10.80       273.14        6.69        6.49
## Taurine                          32.79       645.48       41.68      154.47
## Threonine                        18.54        49.40       40.85       17.46
## Trigonelline                     30.88        58.56       74.44       40.45
## Trimethylamine.N.oxide           82.27       202.35      307.97      943.88
## Tryptophan                       14.30        46.06       21.33       14.88
## Tyrosine                         21.12        45.15       21.33       15.18
## Uracil                            5.87        62.18       31.19       39.65
## Valine                            8.50        33.45       13.20       13.74
## Xylose                           21.33        62.80       14.30       21.76
## cis.Aconitate                    25.79       103.54       36.23       40.85
## myo.Inositol                     30.57        78.26       11.59       30.88
## trans.Aconitate                   7.85        18.17       12.30        8.50
## pi.Methylhistidine               25.53       871.31       53.52       90.02
## tau.Methylhistidine              17.46        84.77       44.70       28.22
##                             NETL_003_V1 NETL_003_V2
## X1.6.Anhydro.beta.D.glucose       37.71       38.47
## X1.Methylnicotinamide             18.17       12.55
## X2.Aminobutyrate                  26.05       15.03
## X2.Hydroxyisobutyrate             15.03       12.55
## X2.Oxoglutarate                   23.34       22.20
## X3.Aminoisobutyrate               33.45       21.33
## X3.Hydroxybutyrate                 6.05        5.99
## X3.Hydroxyisovalerate              5.26        3.42
## X3.Indoxylsulfate                105.64      113.30
## X4.Hydroxyphenylacetate           45.60       22.87
## Acetate                            7.32       11.82
## Acetone                           14.73        6.82
## Adipate                            6.82        6.36
## Alanine                           79.04       75.19
## Asparagine                        31.50       17.64
```

```
## Betaine                          24.29       21.98
## Carnitine                        40.45       32.79
## Citrate                         651.97      424.11
## Creatine                         17.64       16.28
## Creatinine                     3498.19     2864.07
## Dimethylamine                   151.41      148.41
## Ethanolamine                     61.56       53.52
## Formate                          65.37       95.58
## Fucose                           70.81       52.46
## Fumarate                          2.51        1.62
## Glucose                          78.26       72.97
## Glutamine                       122.73      123.97
## Glycine                         244.69      192.48
## Glycolate                        89.12       77.48
## Guanidoacetate                   42.10       14.30
## Hippurate                      1053.63     1043.15
## Histidine                       135.64      174.16
## Hypoxanthine                     35.87       16.61
## Isoleucine                        4.14        2.72
## Lactate                          21.76       31.50
## Leucine                          16.28       14.15
## Lysine                          788.40      478.19
## Methylamine                       5.00        2.44
## Methylguanidine                  12.43        7.17
## N.N.Dimethylglycine               3.63        3.49
## O.Acetylcarnitine                10.59        6.11
## Pantothenate                     15.03       15.80
## Pyroglutamate                    97.51       99.48
## Pyruvate                          4.14        6.55
## Quinolinate                      15.33       26.58
## Serine                           83.10       84.77
## Succinate                         3.90        4.22
## Sucrose                          34.12       39.65
## Tartrate                        141.17       30.57
## Taurine                         249.64      113.30
## Threonine                        60.34       32.46
## Trigonelline                    174.16      154.47
## Trimethylamine.N.oxide          242.26      403.43
## Tryptophan                       17.46       27.66
## Tyrosine                         29.96       23.57
## Uracil                           13.46        9.58
## Valine                           14.59       10.59
## Xylose                           36.97       19.89
## cis.Aconitate                    90.92       58.56
## myo.Inositol                     17.64       24.29
## trans.Aconitate                  12.43       13.07
## pi.Methylhistidine              897.85       83.93
## tau.Methylhistidine              90.02       27.39
```

```
head(muscle_info)
```

```
##   MuscleLoss
## 1   cachexic
## 2   cachexic
```

```
## 3   cachexic
## 4   cachexic
## 5   cachexic
## 6   cachexic
```

0.2.6 Creacion del contenedor:

```
# Crear el contenedor SummarizedExperiment

metab_contenedor <- SummarizedExperiment(assays = list(counts = metabolite_data),
                                         colData = muscle_info)
#Mostrar el contenedor:

metab_contenedor
```

```
## class: SummarizedExperiment
## dim: 63 77
## metadata(0):
## assays(1): counts
## rownames(63): X1.6.Anhydro.beta.D.glucose X1.Methylnicotinamide ...
##   pi.Methylhistidine tau.Methylhistidine
## rowData names(0):
## colnames(77): PIF_178 PIF_087 ... NETL_003_V1 NETL_003_V2
## colData names(1): MuscleLoss
```

```
#Salvar el contenedor:

save(metab_contenedor, file = "contenedor.Rda")
```

Exploración:

``` r
head(metab_contenedor)
```

```
## class: SummarizedExperiment
## dim: 6 77
## metadata(0):
## assays(1): counts
## rownames(6): X1.6.Anhydro.beta.D.glucose X1.Methylnicotinamide ...
##   X2.Oxoglutarate X3.Aminoisobutyrate
## rowData names(0):
## colnames(77): PIF_178 PIF_087 ... NETL_003_V1 NETL_003_V2
## colData names(1): MuscleLoss
```

```
#Resumen estadístico para cada metabolito:
apply(assay(metab_contenedor), 1, summary)
```

```
##         X1.6.Anhydro.beta.D.glucose X1.Methylnicotinamide X2.Aminobutyrate
```

```
## Min.                          4.7100              6.42000          1.28000
## 1st Qu.                      28.7900             15.80000          5.26000
## Median                       45.6000             36.60000         10.49000
## Mean                        105.6304             71.57364         18.15974
## 3rd Qu.                     141.1700             73.70000         19.49000
## Max.                        685.4000           1032.77000        172.43000
##         X2.Hydroxyisobutyrate X2.Oxoglutarate X3.Aminoisobutyrate
## Min.                  4.85000         5.5300             2.61000
## 1st Qu.              15.80000        22.4200            11.70000
## Median               32.46000        55.1500            22.65000
## Mean                 37.25065       145.0871            76.75636
## 3rd Qu.              54.60000        92.7600            56.26000
## Max.                 93.69000      2465.1300          1480.30000
##         X3.Hydroxybutyrate X3.Hydroxyisovalerate X3.Indoxylsulfate
## Min.               1.70000               0.92000           27.6600
## 1st Qu.            5.99000               5.26000           82.2700
## Median            11.70000              12.55000          144.0300
## Mean              21.71701              21.64779          218.8792
## 3rd Qu.           29.96000              30.27000          333.6200
## Max.             175.91000             164.02000         1043.1500
##         X4.Hydroxyphenylacetate   Acetate   Acetone   Adipate   Alanine
## Min.                     15.490   3.49000   2.29000   1.55000   16.7800
## 1st Qu.                  41.680  16.28000   4.95000   6.11000   78.2600
## Median                   70.110  39.65000   7.10000  10.18000  194.4200
## Mean                    112.021  66.14143  11.42701  24.75636  273.5623
## 3rd Qu.                 145.470  86.49000  10.49000  19.11000  399.4100
## Max.                    796.320 411.58000 206.44000 327.01000 1312.9100
##         Asparagine   Betaine Carnitine   Citrate  Creatine Creatinine
## Min.       6.69000   2.29000   2.18000    59.740    2.7500   1002.250
## 1st Qu.   20.49000  28.79000  14.44000   788.400   17.6400   3498.190
## Median    42.10000  64.72000  23.81000  1790.050   44.2600   7631.200
## Mean      62.28364  90.32468  52.08506  2235.346  126.8319   8733.972
## 3rd Qu.   89.12000 127.74000  60.95000  3071.740  117.9200  12332.580
## Max.     273.14000 391.51000 487.85000 13629.610 1863.1100  33860.350
##         Dimethylamine Ethanolamine  Formate    Fucose Fumarate   Glucose
## Min.          41.2600      16.1200    6.420   5.70000  0.79000   26.8400
## 1st Qu.      142.5900      86.4900   53.520  29.37000  2.23000   80.6400
## Median       304.9000     204.3800   95.580  61.56000  4.10000  210.6100
## Mean         358.1661     276.2604  147.403  88.66883  8.44013  559.8445
## 3rd Qu.      454.8600     407.4800  167.340 123.97000  7.85000  407.4800
## Max.        1556.2000    1436.5500 1480.300 407.48000 96.54000 8690.6200
##         Glutamine   Glycine Glycolate Guanidoacetate Hippurate Histidine
## Min.      23.3400   38.0900    5.4200        7.03000    92.760   14.1500
## 1st Qu.  113.3000  262.4300   50.9100       33.78000   492.750   66.6900
## Median   225.8800  528.4800  130.3200       64.72000  1224.150  174.1600
## Mean     306.8716  880.7174  187.9894       86.37052  2286.838  292.6375
## 3rd Qu.  445.8600 1096.6300  267.7400      108.85000  2921.930  419.8900
## Max.    1685.8100 5064.4500  720.5400      561.16000 19341.340 1863.1100
##         Hypoxanthine Isoleucine   Lactate   Leucine   Lysine Methylamine
## Min.         3.78000   1.790000    7.3200   2.51000  10.4900     1.51000
## 1st Qu.     20.70000   3.900000   35.5200   9.12000  30.2700     5.26000
## Median      40.04000   7.170000   81.4500  19.11000  69.4100    14.73000
## Mean        61.09766   8.709091  158.4565  24.36364 108.7942    17.37623
## 3rd Qu.     83.93000  11.250000  139.7700  31.19000 121.5100    24.05000
```

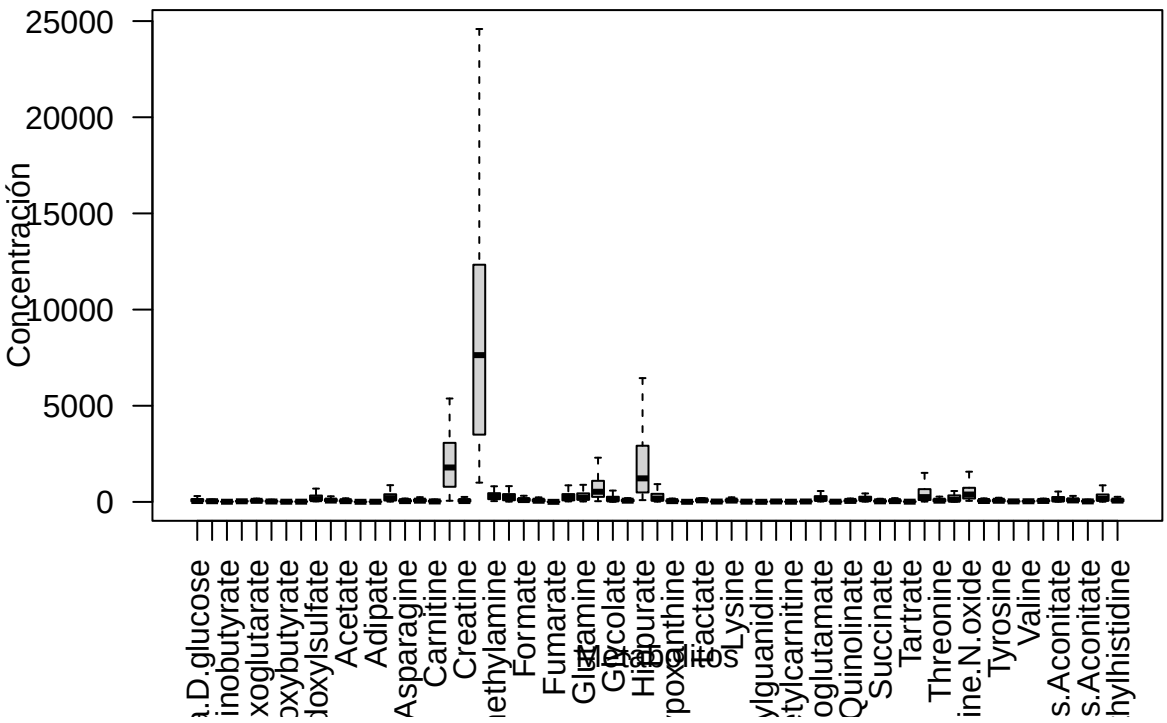
```
## Max.       265.07000  40.040000 3640.9500 103.54000 788.4000    52.46000
##         Methylguanidine N.N.Dimethylglycine O.Acetylcarnitine Pantothenate
## Min.            1.70000             0.79000           1.23000      2.59000
## 1st Qu.         4.26000             7.03000           3.94000     11.13000
## Median          7.85000            21.98000          11.47000     22.65000
## Mean           15.32455            26.34961          19.73338     44.88377
## 3rd Qu.        19.30000            40.04000          20.91000     41.26000
## Max.          141.17000           120.30000         254.68000    692.29000
##         Pyroglutamate  Pyruvate Quinolinate    Serine Succinate   Sucrose
## Min.          21.3300   0.90000     5.21000   16.1200   1.72000    6.4900
## 1st Qu.       68.7200   4.85000    26.58000   83.1000   8.58000   19.3000
## Median       157.5900  13.46000    51.42000  142.5900  30.88000   40.8500
## Mean         211.4478  21.29442    66.43948  197.6869  60.22909  113.2278
## 3rd Qu.      301.8700  29.08000    87.36000  270.4300  74.44000   94.6300
## Max.        1064.2200 184.93000   259.82000 1248.8800 589.93000 2079.7400
##          Tartrate   Taurine Threonine Trigonelline Trimethylamine.N.oxide
## Min.      2.20000   17.8100    8.2500      10.0700                55.7000
## 1st Qu.   6.89000   99.4800   31.8200      53.5200               175.9100
## Median   12.94000  249.6400   64.0700     114.4300               383.7500
## Mean     40.00403  525.1235   95.3574     270.4361               652.1569
## 3rd Qu.  25.79000  665.1400  137.0000     340.3600               735.1000
## Max.    837.15000 4272.6900  450.3400    2252.9600              5486.2500
##         Tryptophan  Tyrosine    Uracil    Valine    Xylose cis.Aconitate
## Min.       8.67000   4.22000   3.10000   4.10000   10.0700       12.9400
## 1st Qu.   21.33000  23.57000  11.94000  12.18000   29.9600       36.2300
## Median    46.99000  60.34000  27.39000  33.12000   50.4000      129.0200
## Mean      66.24312  81.75727  35.55766  35.66701  100.9334      204.2197
## 3rd Qu.   96.54000 113.30000  44.26000  50.40000   89.1200      254.6800
## Max.     259.82000 539.15000 179.47000 160.77000 2164.6200     1863.1100
##         myo.Inositol trans.Aconitate pi.Methylhistidine tau.Methylhistidine
## Min.         11.5900         4.90000            11.3600             8.00000
## 1st Qu.      30.2700        12.43000            67.3600            27.39000
## Median       78.2600        26.84000           162.3900            68.72000
## Mean        135.3975        40.63039           370.2883            89.68688
## 3rd Qu.     167.3400        57.40000           387.6100           130.32000
## Max.        854.0600       217.02000          2697.2800           317.35000
```

De este análisis se peden determinar, además de los estadístico s de cada variable las cifras de medicion que no son homogéneas para todos los metabolitos, lo cual tiene sentido ya que su funcion biológica no es exactamente la misma ni las concentraciones a las que ejercen su efecto metabólico, ni las concentraciones fisiologicamente normales. también de este analisis se puede observar, muy por arriba la posible distribucion de los valores entre pacientes de cada uno de los metabolitos, al observar los valores de media y mediana.

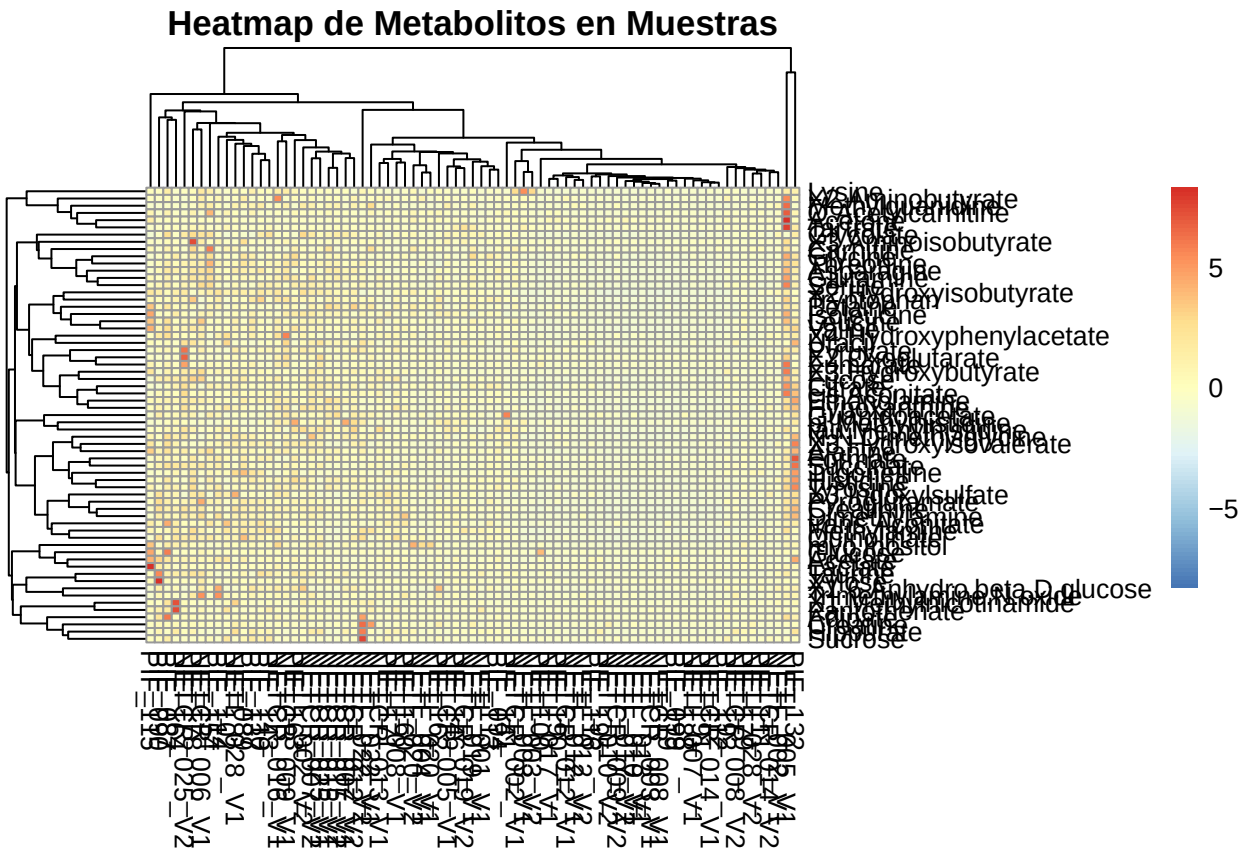
```
#Comprobar valores ausentes, aunque en el resumen comentaba que no habian missing values:

sum(is.na(assay(metab_contenedor)))
```

```
## [1] 0
```

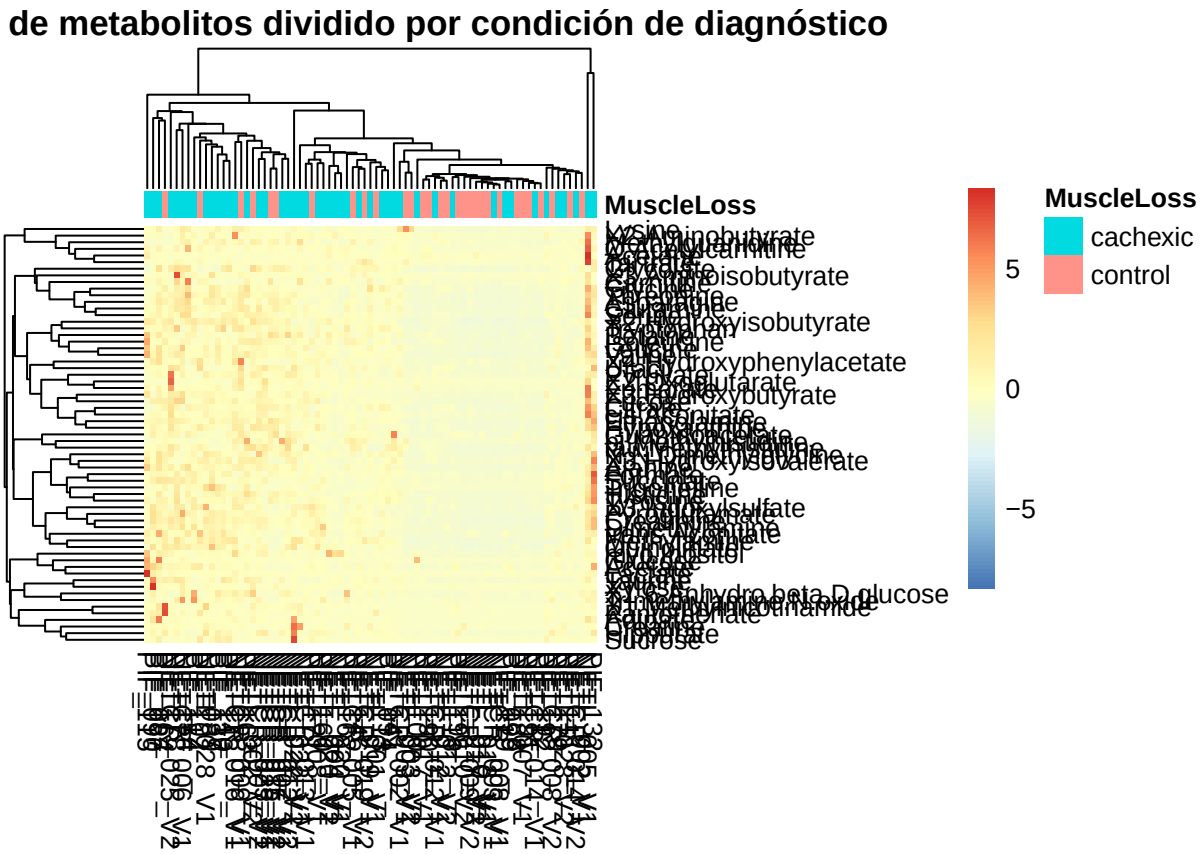
```
#Visualizaion de los datos, permite identificar posibles outliers:

boxplot(t(assay(metab_contenedor)), main = "Distribución de Metabolitos", xlab = "Metabolitos", ylab =
```




```
#Aca se transpone para que los metabolitos aparezcan graficados,
#de lo contrario saldrian los pacientes, las=2, es la dirección de las etiquetas del eje X,
#Un detalle estético para leer mas facilmente la información


library(pheatmap) #Previa instalacion del paquete en Tools/Install packages

pheatmap(assay(metab_contenedor), scale = "row", main = "Heatmap de Metabolitos en Muestras", cluster_r
```




```
#Generar un segundo heat map para tener una vision global de los metabolitos, pacientes y diagnostico d

# Crear el DataFrame de anotación para la columna MuscleLoss
annotation_col <- data.frame(MuscleLoss = colData(metab_contenedor)$MuscleLoss)
rownames(annotation_col) <- colnames(assay(metab_contenedor))
# Asegurar que los nombres de fila coincidan con las columnas de assay(metab_contenedor)

# Generar el heatmap con la anotación
pheatmap(
  assay(metab_contenedor),
  scale = "row",
  main = "Heatmap de metabolitos dividido por condición de diagnóstico",
  cluster_rows = TRUE,
  cluster_cols = TRUE,
  annotation_col = annotation_col  # Agregar la anotación de MuscleLoss en las columnas
)
```



0.2.7 Reducción de la dimension de los datos:

El análisis de componente sprincipales es una forma de reducir la dimensin de los datos, ajustandola a una combinacion lineal de las variables originales, en la que los primeros componentes son los que contribuyen mayoritariament a la variabilidad de los datos: Se escalarán los datos para realizar el PCA, pues como se observó aterioremente las medidas son dispersas y la unidades no son homogeneas

```
metabolite_matrix <- t(assay(metab_contenedor))  # Las muestras deben estar en filas para realizar el P

# Escalar los datos para que cada metabolito tenga una media de 0 y desviación estándar de 1
scaled_data <- scale(metabolite_matrix)

# Realizar el PCA
pca_result <- prcomp(scaled_data, center = TRUE, scale. = TRUE)
summary(pca_result)
```

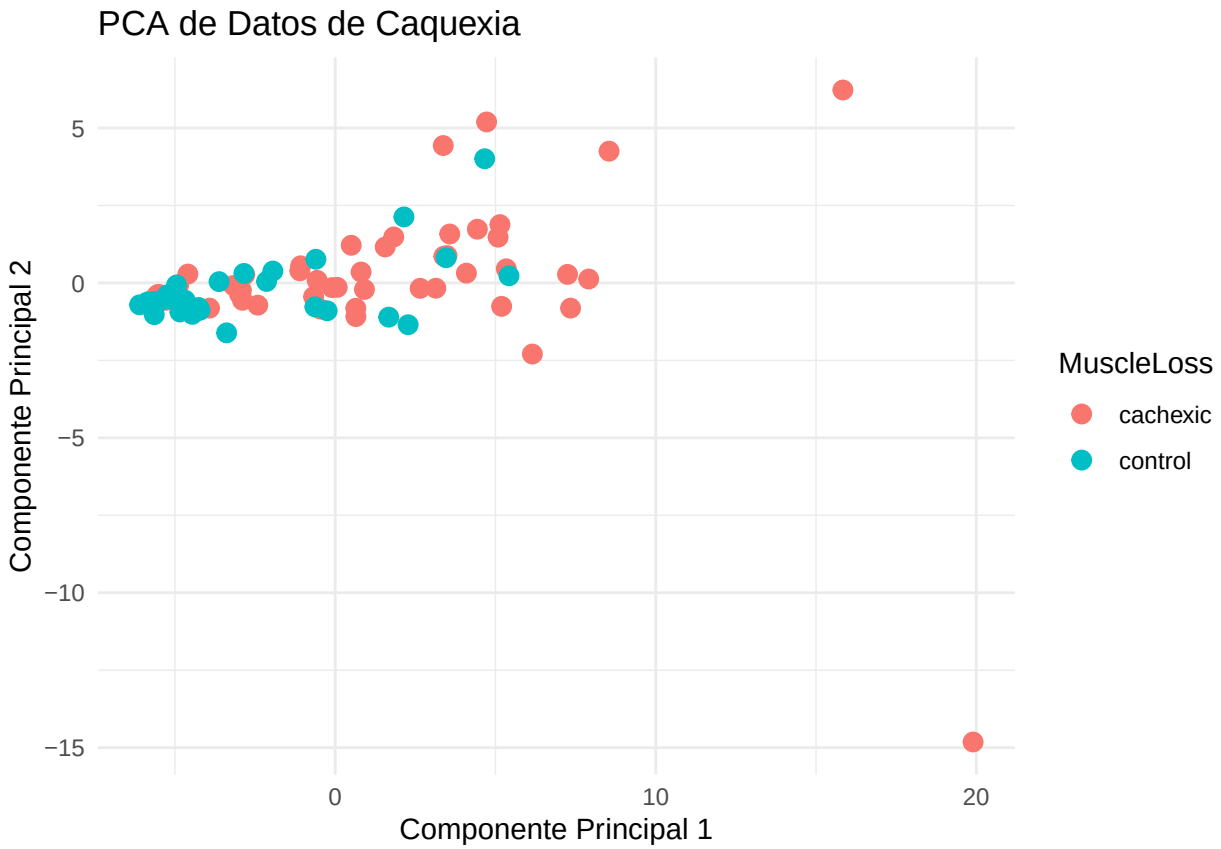
```
## Importance of components:
##                           PC1    PC2     PC3     PC4     PC5    PC6     PC7
## Standard deviation     5.0467 2.2701 1.83311 1.74728 1.65906 1.6130 1.47304
## Proportion of Variance 0.4043 0.0818 0.05334 0.04846 0.04369 0.0413 0.03444
## Cumulative Proportion  0.4043 0.4861 0.53941 0.58787 0.63156 0.6729 0.70730
##                           PC8     PC9    PC10   PC11    PC12    PC13   PC14
## Standard deviation     1.36403 1.24275 1.20650 1.1584 1.05503 1.03620 0.9914
## Proportion of Variance 0.02953 0.02451 0.02311 0.0213 0.01767 0.01704 0.0156
## Cumulative Proportion  0.73683 0.76135 0.78445 0.8057 0.82342 0.84046 0.8561
```

```
##                            PC15    PC16    PC17    PC18   PC19    PC20    PC21
## Standard deviation     0.96773 0.89551 0.86788 0.83041 0.8133 0.73918 0.72112
## Proportion of Variance 0.01487 0.01273 0.01196 0.01095 0.0105 0.00867 0.00825
## Cumulative Proportion  0.87093 0.88366 0.89562 0.90656 0.9171 0.92573 0.93399
##                            PC22    PC23    PC24   PC25   PC26    PC27    PC28
## Standard deviation     0.71053 0.64606 0.63389 0.5830 0.5442 0.50539 0.48743
## Proportion of Variance 0.00801 0.00663 0.00638 0.0054 0.0047 0.00405 0.00377
## Cumulative Proportion  0.94200 0.94863 0.95500 0.9604 0.9651 0.96916 0.97293
##                            PC29    PC30    PC31    PC32    PC33    PC34    PC35
## Standard deviation     0.42674 0.42427 0.41483 0.38653 0.35092 0.32424 0.31646
## Proportion of Variance 0.00289 0.00286 0.00273 0.00237 0.00195 0.00167 0.00159
## Cumulative Proportion  0.97582 0.97867 0.98141 0.98378 0.98573 0.98740 0.98899
##                            PC36    PC37    PC38    PC39    PC40    PC41    PC42
## Standard deviation     0.2867 0.28435 0.26060 0.25353 0.24800 0.21896 0.19537
## Proportion of Variance 0.0013 0.00128 0.00108 0.00102 0.00098 0.00076 0.00061
## Cumulative Proportion  0.9903 0.99158 0.99266 0.99368 0.99465 0.99541 0.99602
##                            PC43   PC44    PC45   PC46    PC47   PC48    PC49
## Standard deviation     0.18914 0.1767 0.16864 0.1580 0.15287 0.1380 0.13101
## Proportion of Variance 0.00057 0.0005 0.00045 0.0004 0.00037 0.0003 0.00027
## Cumulative Proportion  0.99659 0.9971 0.99753 0.9979 0.99830 0.9986 0.99888
##                            PC50    PC51    PC52    PC53    PC54    PC55    PC56
## Standard deviation     0.10759 0.10374 0.09853 0.08760 0.08258 0.08049 0.06927
## Proportion of Variance 0.00018 0.00017 0.00015 0.00012 0.00011 0.00010 0.00008
## Cumulative Proportion  0.99906 0.99923 0.99939 0.99951 0.99962 0.99972 0.99979
##                            PC57    PC58    PC59    PC60    PC61    PC62    PC63
## Standard deviation     0.05937 0.05673 0.05088 0.04001 0.02972 0.02789 0.01876
## Proportion of Variance 0.00006 0.00005 0.00004 0.00003 0.00001 0.00001 0.00001
## Cumulative Proportion  0.99985 0.99990 0.99994 0.99997 0.99998 0.99999 1.00000
```

El primer PC contribuye al 40% de la variabilidad, mientras que el segundo y tercero contribuyen al 8.18 y 5.33%, el 90% de la variabilidad esta cubiero desde el PC1 al 18. Se puede reducir la dimensionalidad de las variables de 63 a 18.

Se puede graficar usando ggplot

```r
library(ggplot2)

# Convertir los resultados del PCA a un data frame para ggplot

pca_df <- as.data.frame(pca_result$x)
pca_df$MuscleLoss <- colData(metab_contenedor)$MuscleLoss  # Añadir la información de los estados de mu

# Graficar los dos primeros componentes principales

ggplot(pca_df, aes(x = PC1, y = PC2, color = MuscleLoss)) +
  geom_point(size = 3) +
  labs(title = "PCA de Datos de Caquexia",
       x = "Componente Principal 1",
       y = "Componente Principal 2") +
  theme_minimal()
```



No se observa un efecto batch, es decir las muetras agrupadas en subgrupos, propio de una variacion más debida a la colecta de muetra mas que a un fenomeno observado en los datios biológicos per se.Se aprecian si dos valores posiblemente outliers, de pacientes con caquexia.Lo cual se había obserbado en el boxplot original para los metabolitos de creatinina, carnitina e hipurato.

0.2.7.1 Análisis estadístico del primer PC para individus enfermos y sanos

permite determinar si entre los grupos hay expresion diferencial de los metabolitos.

```
# Comparar PC1 entre los grupos MuscleLoss usando una prueba t

t.test(pca_result$x[, "PC1"] ~ colData(metab_contenedor)$MuscleLoss)
```

```
##
##  Welch Two Sample t-test
##
## data:  pca_result$x[, "PC1"] by colData(metab_contenedor)$MuscleLoss
## t = 4.2476, df = 74.968, p-value = 6.133e-05
## alternative hypothesis: true difference in means between group cachexic and group control is not equa
## 95 percent confidence interval:
##  2.230164 6.169675
## sample estimates:
## mean in group cachexic  mean in group control
##               1.636332              -2.563587
```

```r
# Comparacion de varios componentes a la vez

manova_result <- manova(pca_result$x[, 1:5] ~ colData(metab_contenedor)$MuscleLoss)
summary(manova_result)
```

```
##                                    Df  Pillai approx F num Df den Df  Pr(>F)
## colData(metab_contenedor)$MuscleLoss  1 0.18774    3.282      5     71 0.01008
## Residuals                            75
##
## colData(metab_contenedor)$MuscleLoss *
## Residuals
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Los resultados indican que hay diferencias significativas entre los individuos enfermos y el control, en el caso de la primera comoponente principal se puede afirmar que la combinacion lineal de metabolitos deteminados en la orina es significativamente superior en pacientes que en individuos sanos empleados como contro. En el caso del análisis multivariante se puede determinar que existen diferencias en los primeros 5 componentes principales. Por lo tanto se pueden emplear las dterminaciones en la orina para inferir, diagnosticar si el paciente sufre o no de caquexia.

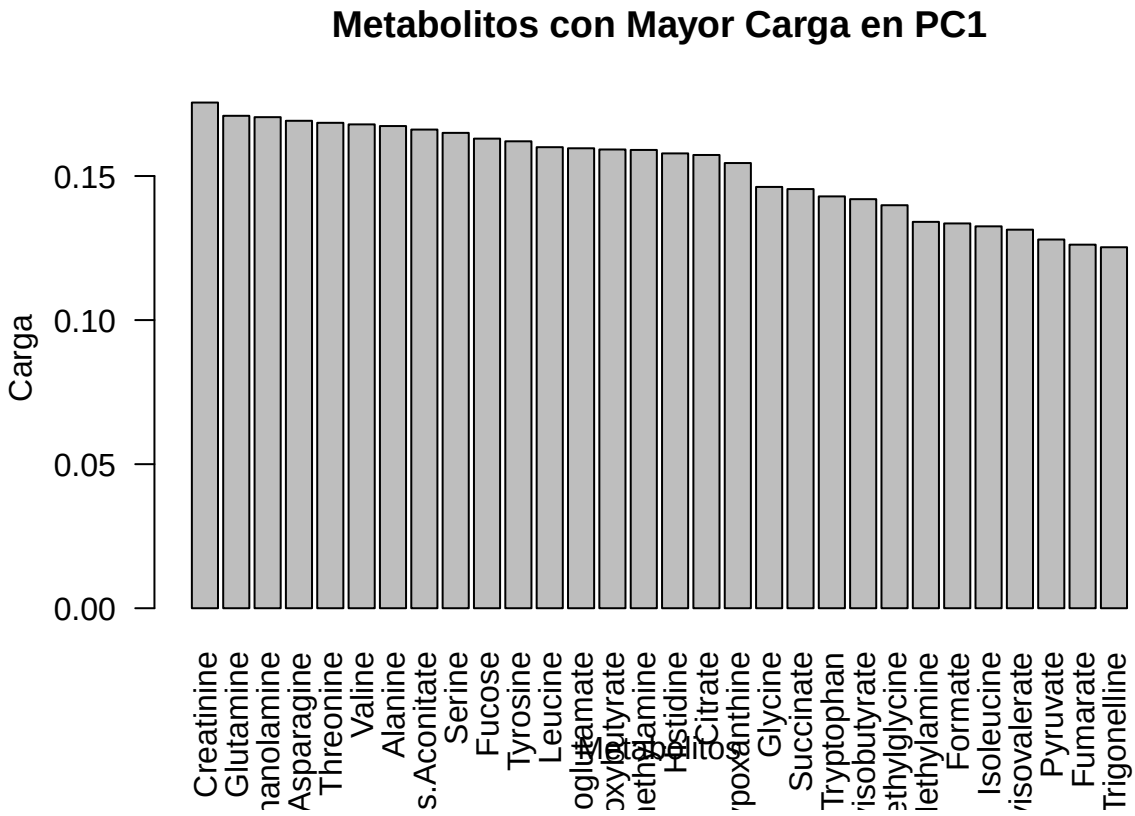
0.2.7.2 Observación de cuales variables contribuyen al primer pc: Teniendo en cuenta que el PC1, contribuye en un 40% a la varianza total, y arrojó diferencias marcadas en la prueba de t test, se extrajo que metabolitos contribuyen principalmente a este PC, se analizaron los 30 primeros, y se graficaron para observar su contribucion.

```r
# Extraer las cargas de las componentes principales
loadings <- pca_result$rotation

# Obtener las cargas de los metabolitos para PC1
loadings_PC1 <- loadings[, "PC1"]


# Ordenar los metabolitos por su contribución a PC1 (de mayor a menor)
loadings_PC1_sorted <- sort(loadings_PC1, decreasing = TRUE)


# Ver los metabolitos que más contribuyen a PC1
top_metabolites_PC1 <- names(loadings_PC1_sorted)[1:30]  # Los 30 metabolitos con mayor carga en PC1


# Imprimir resultados
top_metabolites_PC1
```

```
##  [1] "Creatinine"           "Glutamine"            "Ethanolamine"
##  [4] "Asparagine"           "Threonine"            "Valine"
##  [7] "Alanine"              "cis.Aconitate"        "Serine"
## [10] "Fucose"               "Tyrosine"             "Leucine"
## [13] "Pyroglutamate"        "X3.Hydroxybutyrate"   "Dimethylamine"
## [16] "Histidine"            "Citrate"              "Hypoxanthine"
## [19] "Glycine"              "Succinate"            "Tryptophan"
## [22] "X2.Hydroxyisobutyrate" "N.N.Dimethylglycine"  "Methylamine"
```

```
## [25] "Formate"                "Isoleucine"             "X3.Hydroxyisovalerate"
## [28] "Pyruvate"               "Fumarate"               "Trigonelline"
```

```r
# Visualizar las cargas de los metabolitos en PC1

barplot(loadings_PC1_sorted[1:30], las = 2, main = "Metabolitos con Mayor Carga en PC1", ylab = "Carga"
```



Como se puede observar, ademas de la creatinina, que es un metabolito del metabolismo de aminoácidos como Arg y Pro, la mayoría de metabolitos son aminoácidos, que se encuentran significativamentet incrementados en la caquexia, lo cual, como comentan los autores, en gan medida puede deberse a la degradación de la fibra muscular, consistente con la sintomatología principal de la enfermedad. La glutamina, por otro lado es el metabolito en el que se transporta el nitrogeno en el organismo, luego, si hay un exceso de catabolismo protéico (dada la degradación de la fibra), el incremento en Gln es reflejo de esto, pues aumentan los niveles de este transportador en el torrente sanguíneo.

0.3 Conclusiones principales:

En este examen se ha seguido un esquema similar a los vistos en clase, si bien en el preprocesado de los datos no se efectuó la conversión logaritmica que aplicaron los autores del estudio, ni se ensayaron los elementos de machine learning usados por estos. De manera general en este estudio se puede ver, a raiz de los analisis realizados, que con esta técnica, pese a los temas de resolucion bajos, que se mencionan al inicio, la determinacion de los metabolitos cuantificables permite discriminar entre sanos/enfermos.

0.4 Enlace al repositorio:

https://github.com/anaixis/del_Valle_Pena_Anaixis_PEC1/tree/main

0.5 Bibliografía principal consultada:

Se consultó adicionalmente libros como Lenhinger, clasicos del metabolismo.

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