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)
```

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
```

0.2.7 Exploración:

```
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
```

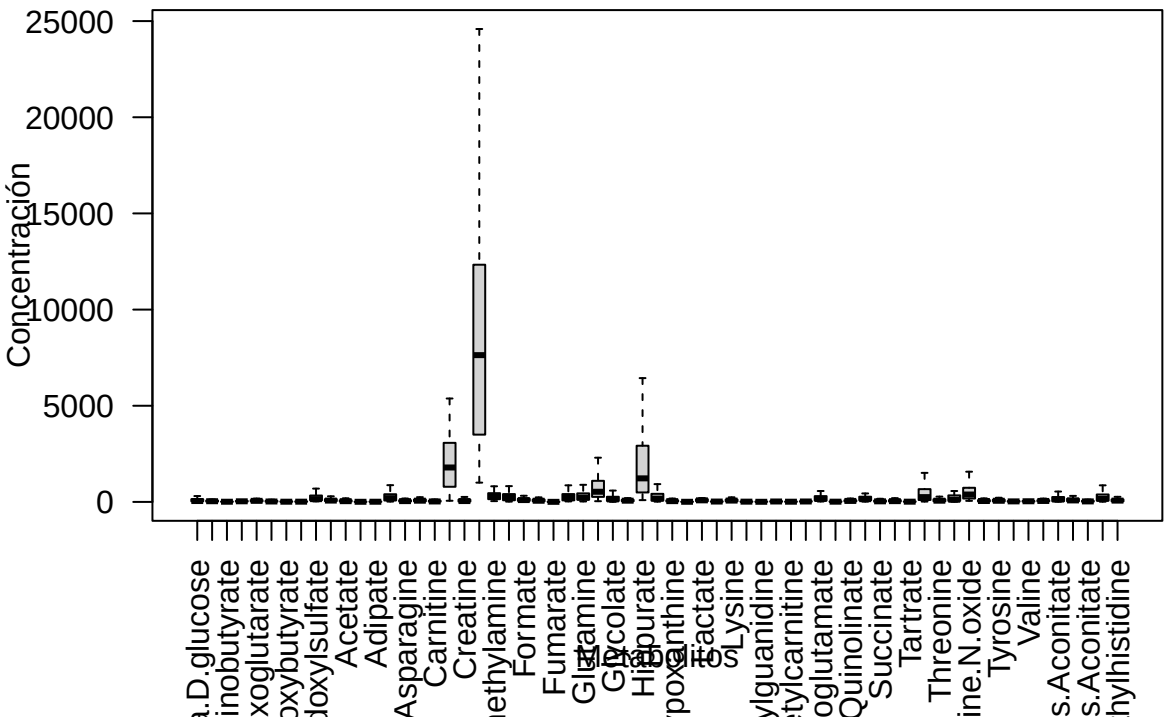
```
## Max.          141.17000           120.30000         254.68000    692.29000
##         Pyroglutamate  Pyruvate Quinolinate    Serine Succinate   Sucrose
## Min.          21.3300   0.90000     5.21000   16.1200   1.72000    6.4900
## 1st Qu.       68.7200   4.85000    26.58000   83.1000   8.58000   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.

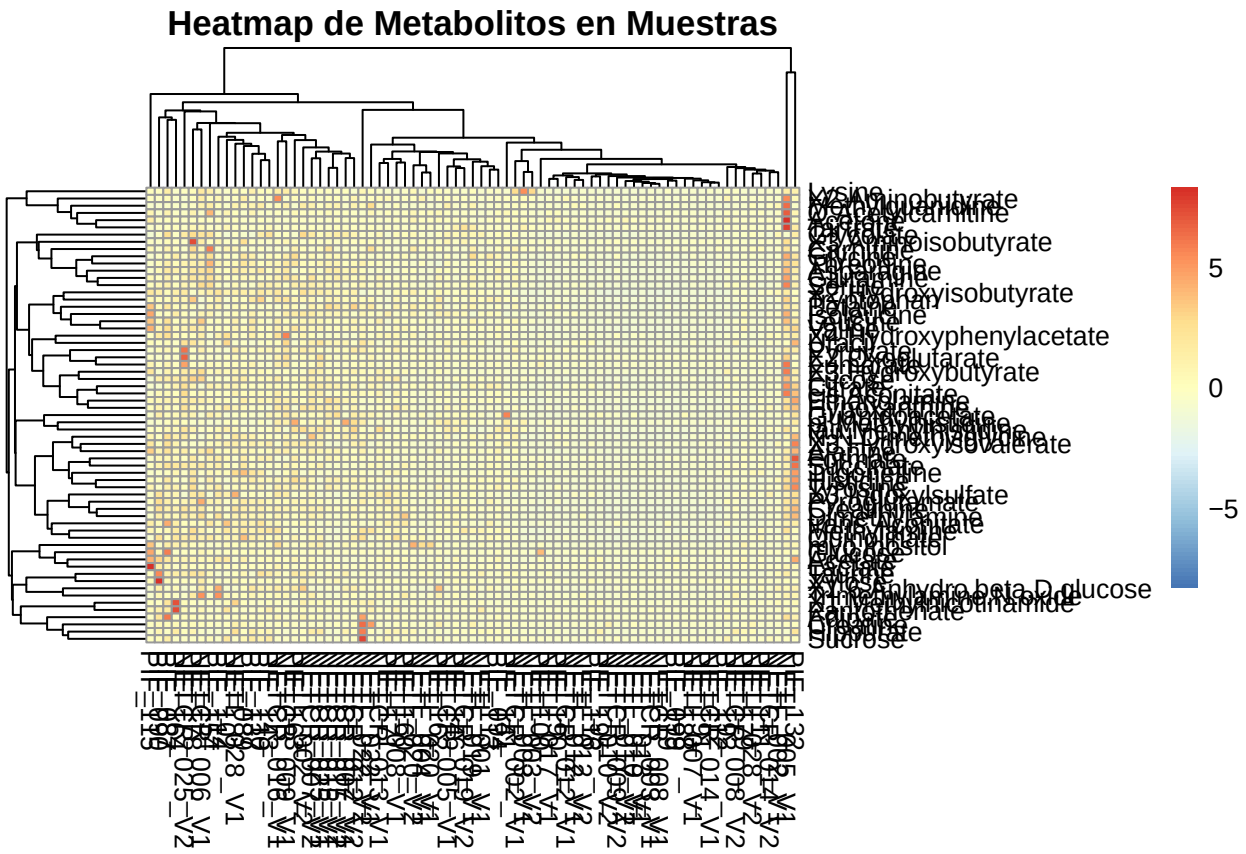
```
#Comprobar valores ausentes, aunque en el resumen comentaba que no habian missing values:

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

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

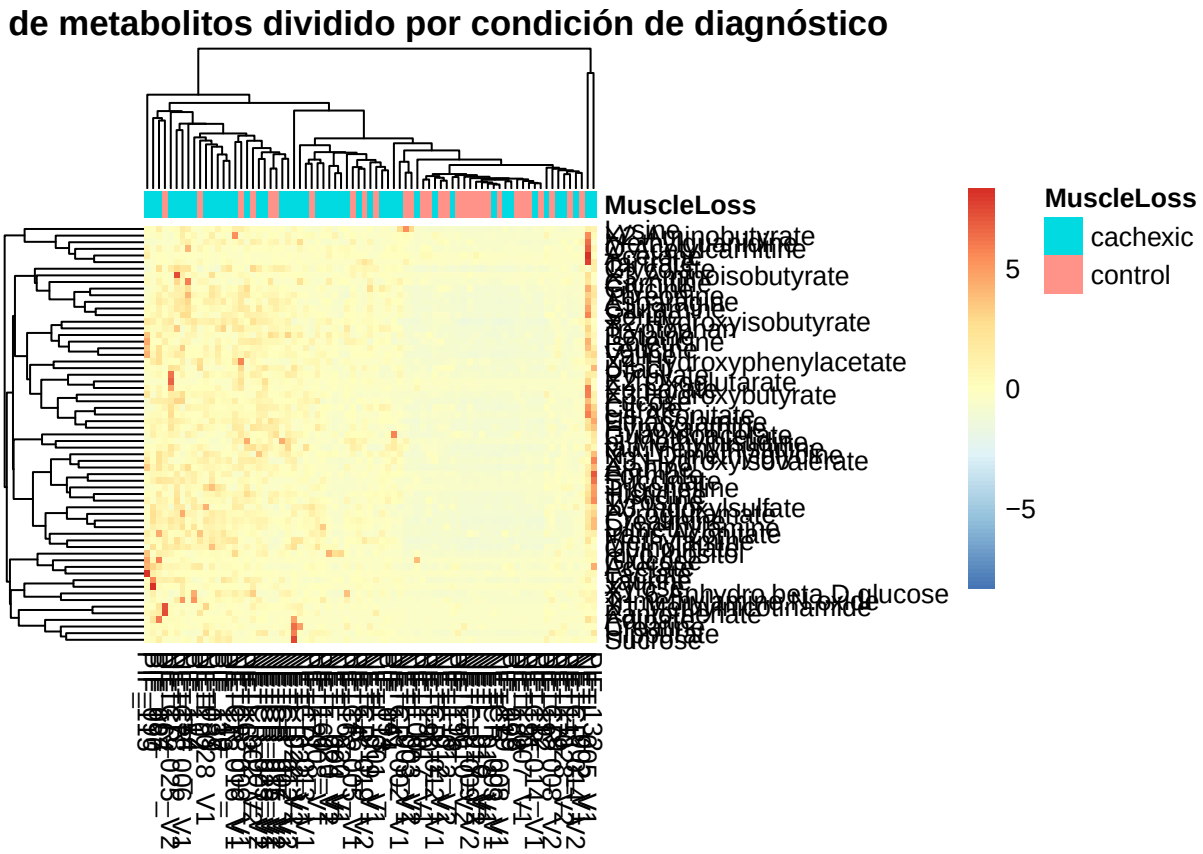
```
#Visualizaion de los datos, permite identificar posibles outliers:

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
)
```



0.2.8 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)
```

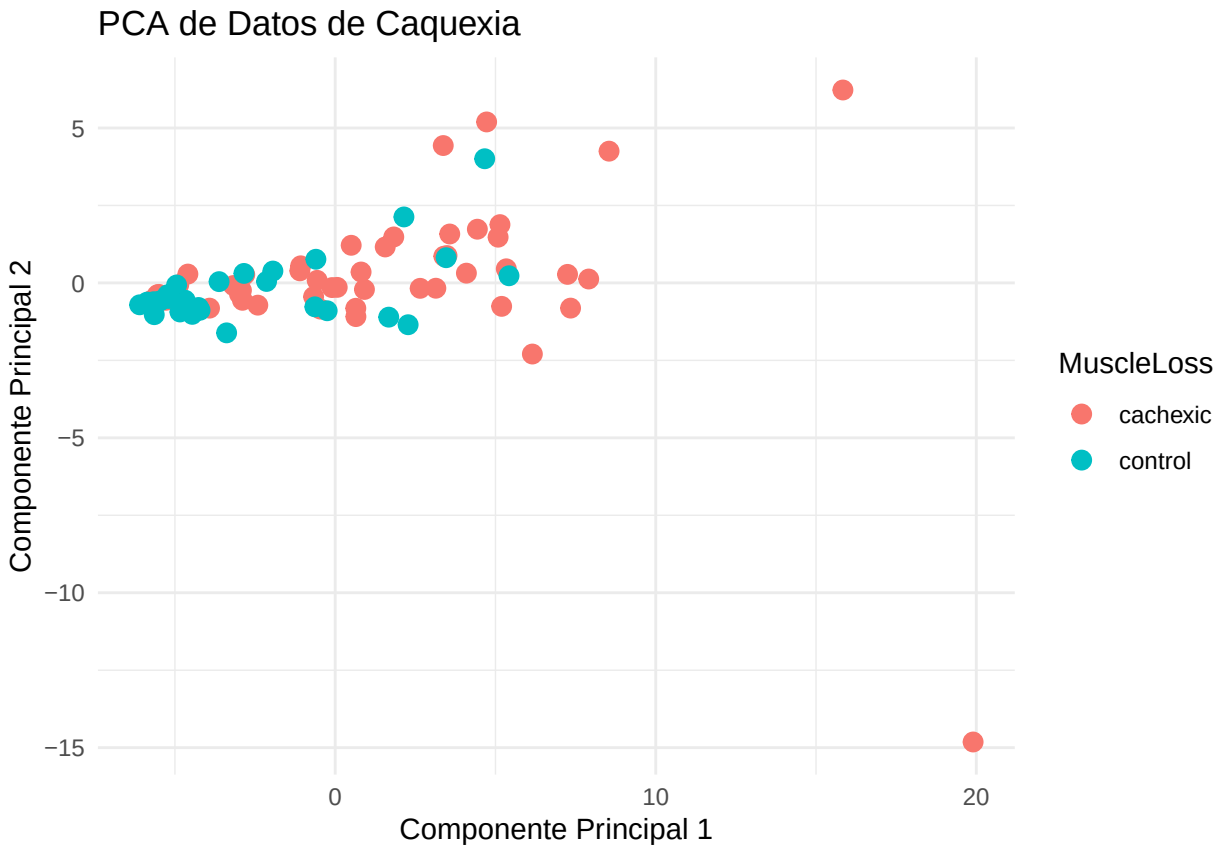
```
## Importance of components:
##                           PC1    PC2     PC3     PC4     PC5    PC6     PC7
## Standard deviation     5.0467 2.2701 1.83311 1.74728 1.65906 1.6130 1.47304
## Proportion of Variance 0.4043 0.0818 0.05334 0.04846 0.04369 0.0413 0.03444
## Cumulative Proportion  0.4043 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.

0.2.8.1 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.

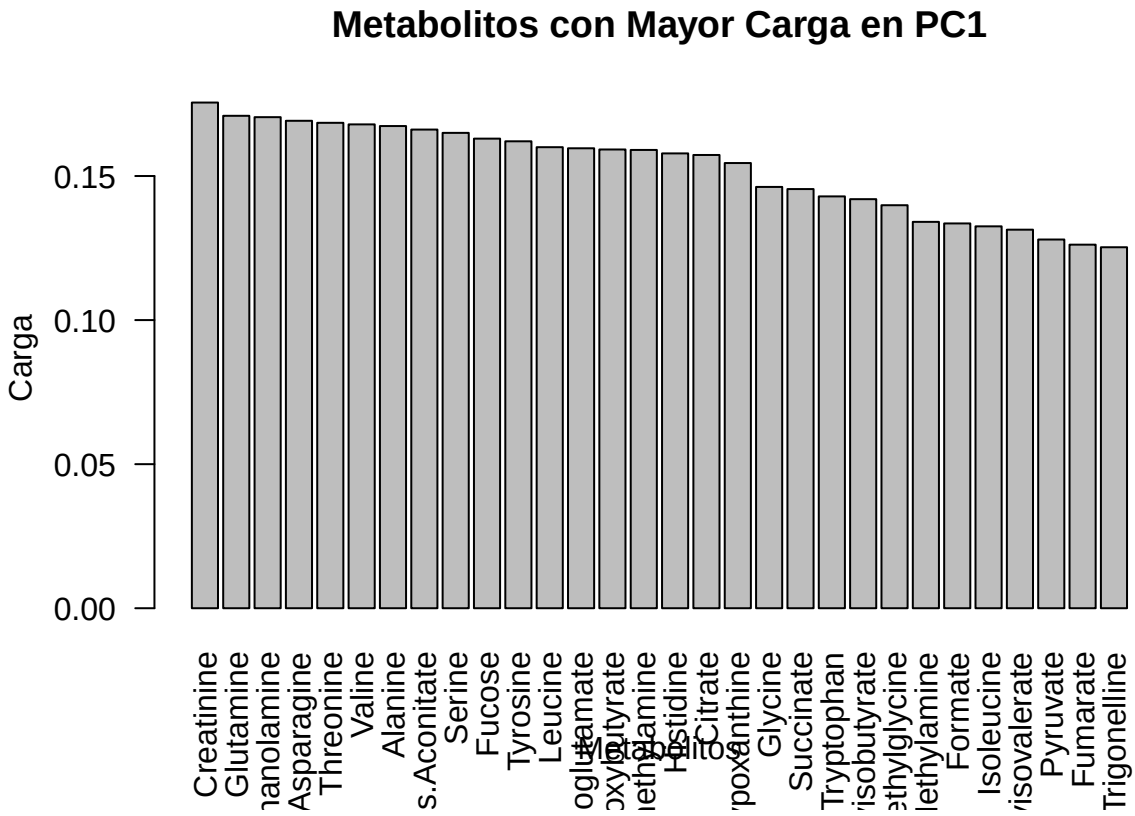
0.2.8.2 Observación de cuales variables contribuyen al primer pc: Teniendo en cuenta que el PC1, contribuye en un 40% a la varianza total, y arrojó diferencias marcadas en la prueba de t test, se extrajo que metabolitos contribuyen principalmente a este PC, se analizaron los 30 primeros, y se graficaron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

Allaire, JJ, Yihui Xie, and Jonathan McPherson. 2019. "R Markdown: Integrating a Reproducible Analysis Tool." *Journal of Statistical Software*. https://rmarkdown.rstudio.com/.

Bioconductor. n.d. "SummarizedExperiment: Extensions." https://bioconductor.org/packages/devel/bioc/vignettes/SummarizedExperiment/inst/doc/Extensions.html.

———. n.d. "SummarizedExperiment: Overview." https://www.bioconductor.org/packages/devel/bioc/vignettes/SummarizedExperiment/inst/doc/SummarizedExperiment.html.

———. 2024. *Bioconductor: Open Software Development for Computational Biology and Bioinformatics*. https://bioconductor.org/.

Eisner, Roman, Cynthia Stretch, Thomas Eastman, Jianguo Xia, David Hau, Sambasivarao Damaraju, Russell Greiner, David S Wishart, and Vickie E Baracos. 2011. "Learning to Predict Cancer-Associated Skeletal Muscle Wasting from 1 h-NMR Profiles of Urinary Metabolites." *Metabolomics* 7: 25–34.

Evans, William J, John E Morley, Josep Argilés, Connie Bales, Vickie Baracos, Denis Guttridge, Aminah Jatoi, et al. 2008. "Cachexia: A New Definition." *Clinical Nutrition* 27 (6): 793–99.

Morgan, Martin, Valerie Obenchain, Jim Hester, and Hervé Pagès. 2023. *SummarizedExperiment: Container for Summarized Experiments*. https://bioconductor.org/packages/SummarizedExperiment/.

Wickham, Hadley. 2016. "Ggplot2: Elegant Graphics for Data Analysis." https://ggplot2.tidyverse.org/.