Transporter Colocalization Analysis (ImageJ Coloc2)

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M1 = occludin overlapping P-gp/Bcrp/Mrp2 M2 = P-gp/Bcrp/Mrp2 overlapping occludin

Reading in the data

P-gp

```
pgp_filelist <- list.files(path="../data/IHC/coloc2_results_pgp/",</pre>
                            pattern="*.txt", full.names = TRUE)
pgp_cols <- c("sample", "m1", "m2", "r_pearson", "Pval", "r_rand", "sd_rand")
pgp_coloc2 <- as.data.frame(matrix(,1,length(pgp_cols)))</pre>
names(pgp_coloc2) <- pgp_cols</pre>
for (i in pgp_filelist) {
  test <- read_lines(i)</pre>
  sample <- str_subset(test, "Working on") %>%
    str_extract(., "(?<=:[:space:]).*")
 r_pearson <- str_subset(test, "no threshold") %>%
    str_extract(., "(?<=,[:space:]).*")
  m1 <- str_subset(test, "tM1") %>% str_extract(., "(?<=,[:space:]).*")
  m2 <- str_subset(test, "tM2") %>% str_extract(., "(?<=,[:space:]).*")</pre>
  Pval <- str_subset(test, "P-Value") %% str_extract(., "(?<=,[:space:]).*")
  r_rand <- str_subset(test, "Costes Shuffled Mean") %>%
    str_extract(., "(?<=,[:space:]).*")
  sd rand <- str subset(test, "Costes Shuffled Std") %>%
    str_extract(., "(?<=,[:space:]).*")
  res <- c(all_of(sample), all_of(m1), all_of(m2), all_of(r_pearson),
           all_of(Pval), all_of(r_rand), all_of(sd_rand))
 pgp_coloc2 <- rbind(pgp_coloc2, res)</pre>
```

```
## Warning: Using 'all_of()' outside of a selecting function was deprecated in tidyselect
## 1.2.0.
## i See details at
## <a href="https://tidyselect.r-lib.org/reference/faq-selection-context.html">https://tidyselect.r-lib.org/reference/faq-selection-context.html></a>

pgp_coloc2 <- pgp_coloc2 %>% na.omit(pgp_coloc2) %>%
mutate(sex = as.factor(str_sub(sample, start=1L, end=1L)),
mouseID = as.factor(str_extract(sample, "(?<=-)[:digit:]+")),</pre>
```

```
#prep = as.factor(str_extract(sample, "[:lower:]{2,}")),
       prep = as.factor(str_extract(sample, "wm|section")),
       image = str_extract(sample, "[:alpha:]{2,}.*"), .before=m1)
pgp_coloc2$prep
## [1] section section section section section wm
                                                              wm
                                                                      wm
## [10] wm
               wm
                                                              wm
                                                                      wm
## [19] wm
               wm
                       wm
                                                      section section
                               wm
                                       wm
                                               wm
## [28] section section section section section section section
## [37] section section section section section wm
## [46] wm
              wm
                       wm
                               wm
                                       wm
## Levels: section wm
pgp_coloc2 <- pgp_coloc2 %>% select(-sample) %>%
 mutate(m1 = as.double(m1),
       m2 = as.double(m2),
       r_pearson = as.double(r_pearson),
       Pval = as.double(Pval),
       r rand = as.double(r rand),
       sd rand = as.double(sd rand),
       coloc = Pval>0.95)
#write.xlsx(pgp_coloc2, "../data/IHC/coloc2-pgp-totals.xlsx")
head(pgp coloc2)
                                                      m2 r_pearson Pval r_rand
    sex mouseID
                   prep
                                        image
## 2
      F
             20 section slide1-section2-20x-1 0.816 0.760
                                                              0.64
## 3
      F
             20 section slide1-section2-20x-2 0.789 0.770
                                                              0.58
                                                                      1
                                                                             0
## 4
             20 section slide1-section3-20x-1 0.845 0.640
                                                              0.50
                                                                             0
             20 section slide1-section3-20x-2 0.063 0.057
                                                              0.61
                                                                             0
## 5
    F
                                                                      1
             20 section slide2-section2-20x-1 0.613 0.361
## 6
      F
                                                              0.62
                                                                             0
## 7
      F
             20 section slide2-section2-20x-2 0.778 0.772
                                                              0.62
                                                                             0
    sd rand coloc
## 2
          O TRUE
## 3
          O TRUE
## 4
          O TRUE
## 5
          O TRUE
          O TRUE
## 6
## 7
          O TRUE
Bcrp
```

```
for (i in bcrp_filelist) {
  test <- read_lines(i)</pre>
  sample <- str_subset(test, "Working on") %>%
    str_extract(., "(?<=:[:space:]).*")
  r_pearson <- str_subset(test, "no threshold") %>%
    str_extract(., "(?<=,[:space:]).*")
  m1 <- str_subset(test, "tM1") %>% str_extract(., "(?<=,[:space:]).*")</pre>
  m2 <- str subset(test, "tM2") %>% str extract(., "(?<=,[:space:]).*")</pre>
  Pval <- str_subset(test, "P-Value") %>% str_extract(., "(?<=,[:space:]).*")
 r_rand <- str_subset(test, "Costes Shuffled Mean") %>%
    str_extract(., "(?<=,[:space:]).*")
  sd_rand <- str_subset(test, "Costes Shuffled Std") %>%
    str_extract(., "(?<=,[:space:]).*")
  print(sample)
  res <- c(all_of(sample), all_of(m1), all_of(m2), all_of(r_pearson),
           all_of(Pval), all_of(r_rand), all_of(sd_rand))
  bcrp_coloc2 <- rbind(bcrp_coloc2, res)</pre>
```

```
## [1] "F-22-section1-40x-1-avg4"
## [1] "F-22-section1-40x-2-avg4"
## [1] "F-22-section1-40x-3-avg4"
## [1] "F-22-section3-40x-1-avg4"
## [1] "F-22-section3-40x-2-avg4"
## [1] "F-22-section3-40x-3-avg4"
## [1] "F-GTL-section1-40x-1-avg4"
## [1] "F-GTL-section1-40x-2-avg4"
## [1] "F-GTL-section1-40x-3-avg4"
## [1] "F-GTL-section3-40x-1-avg4"
## [1] "F-GTL-section3-40x-2-avg4"
## [1] "F-GTL-section3-40x-3-avg4"
## [1] "F-McKO-98-section1-40x-1-avg4"
## [1] "F-McKO-98-section1-40x-2-avg4"
## [1] "F-McKO-98-section1-40x-3-avg4"
## [1] "F-McKO-98-section3-40x-1-avg4"
## [1] "F-McKO-98-section3-40x-2-avg4"
## [1] "F-McKO-98-section3-40x-3-avg4"
## [1] "M-80-section1-40x-1-avg4"
## [1] "M-80-section1-40x-2-avg4"
## [1] "M-80-section1-40x-3-avg4"
## [1] "M-80-section3-40x-1-avg4"
## [1] "M-80-section3-40x-2-avg4"
## [1] "M-80-section3-40x-3-avg4"
## [1] "M-81-section1-40x-1-avg4"
## [1] "M-81-section1-40x-2-avg4"
## [1] "M-81-section1-40x-3-avg4"
## [1] "M-81-section3-40x-1-avg4"
## [1] "M-81-section3-40x-2-avg4"
## [1] "M-81-section3-40x-3-avg4"
## [1] "M-82-section1-40x-1-avg4"
## [1] "M-82-section1-40x-2-avg4"
## [1] "M-82-section1-40x-3-avg4"
## [1] "M-82-section3-40x-1-avg4"
```

```
## [1] "M-82-section3-40x-2-avg4"
## [1] "M-82-section3-40x-3-avg4"
## [1] "M-McKO-92-section1-40x-1-avg4"
## [1] "M-McKO-92-section1-40x-2-avg4"
## [1] "M-McKO-92-section1-40x-3-avg4"
## [1] "M-McKO-92-section3-40x-1-avg4"
## [1] "M-McKO-92-section3-40x-2-avg4"
## [1] "M-McKO-92-section3-40x-3-avg4"
bcrp_coloc2 <- bcrp_coloc2 %>% na.omit(bcrp_coloc2) %>%
  mutate(sex = as.factor(str sub(sample, start=1L, end=1L)),
        mouseID = as.factor(str_extract(sample, "(?<=-)[:digit:]+")),</pre>
        prep = as.factor(str extract(sample, "[:lower:]{2,}")),
        image = str_extract(sample, "[:alpha:]{2,}.*"), .before=m1)
bcrp_coloc2 <- bcrp_coloc2 %>% select(-sample) %>%
  mutate(m1 = as.double(m1).
       m2 = as.double(m2),
        r_pearson = as.double(r_pearson),
        Pval = as.double(Pval),
        r_rand = as.double(r_rand),
        sd rand = as.double(sd_rand),
        coloc = Pval>0.95)
write.xlsx(bcrp_coloc2, "../data/IHC/coloc2-bcrp-totals.xlsx")
head(bcrp_coloc2)
##
     sex mouseID
                                       image
                                                      m2 r_pearson Pval r_rand
                    prep
                                                m1
## 2
              22 section section1-40x-1-avg4 0.618 0.229
                                                               0.32
                                                                       1
                                                                              0
## 3
      F
              22 section section1-40x-2-avg4 0.787 0.359
                                                              0.63
                                                                      1
                                                                              0
## 4
              22 section section1-40x-3-avg4 0.782 0.290
                                                              0.51
                                                                      1
                                                                              0
## 5 F
              22 section section3-40x-1-avg4 0.517 0.461
                                                              0.49
                                                                      1
                                                                              0
              22 section section3-40x-2-avg4 0.687 0.541
## 6 F
                                                              0.58
                                                                      1
                                                                              0
## 7
              22 section section3-40x-3-avg4 0.555 0.431
                                                              0.58
                                                                       1
                                                                              0
   sd rand coloc
##
## 2
          O TRUE
## 3
           O TRUE
          O TRUE
## 4
          O TRUE
## 5
```

Mrp2

6

7

O TRUE

O TRUE

```
for (i in mrp2_filelist) {
  test <- read_lines(i)</pre>
  sample <- str_subset(test, "Working on") %>%
    str_extract(., "(?<=:[:space:]).*")
  r_pearson <- str_subset(test, "no threshold") %>%
   str_extract(., "(?<=,[:space:]).*")
  m1 <- str_subset(test, "tM1") %>% str_extract(., "(?<=,[:space:]).*")
  m2 <- str subset(test, "tM2") %>% str extract(., "(?<=,[:space:]).*")</pre>
  Pval <- str_subset(test, "P-Value") %>% str_extract(., "(?<=,[:space:]).*")
  r_rand <- str_subset(test, "Costes Shuffled Mean") %>%
    str_extract(., "(?<=,[:space:]).*")
  sd_rand <- str_subset(test, "Costes Shuffled Std") %>%
   str_extract(., "(?<=,[:space:]).*")
  res <- c(all_of(sample), all_of(m1), all_of(m2), all_of(r_pearson),
           all_of(Pval), all_of(r_rand), all_of(sd_rand))
 mrp2_coloc2 <- rbind(mrp2_coloc2, res)</pre>
mrp2_coloc2 <- mrp2_coloc2 %>% na.omit(mrp2_coloc2) %>%
  mutate(sex = as.factor(str_sub(sample, start=1L, end=1L)),
          mouseID = as.factor(str_extract(sample, "(?<=-)[:digit:]+")),</pre>
          image = str_extract(sample, "s.*(?=_)"),
          roi = str_extract(sample, "(?<=_).*"), .before=m1)</pre>
mrp2 coloc2 <- mrp2 coloc2 %>% select(-sample) %>%
 mutate(m1 = as.double(m1),
       m2 = as.double(m2),
        r_pearson = as.double(r_pearson),
       Pval = as.double(Pval),
        r_rand = as.double(r_rand),
        sd_rand = as.double(sd_rand),
        coloc = Pval > 0.95)
#write.xlsx(mrp2_coloc2, "../data/IHC/coloc2-mrp2-totals.xlsx")
head(mrp2_coloc2)
     sex mouseID
##
                          image roi
                                               m2 r_pearson Pval r_rand sd_rand
                                        m1
## 2
              22 section2-40x-1 gcl1 0.063 0.360
                                                       0.12 1.00 -0.01
                                                                           0.04
## 3 F
              22 section2-40x-1 inl1 0.000 0.087
                                                      -0.01 0.34
                                                                  0.00
                                                                           0.02
## 4
      F
              22 section2-40x-1 inl2 0.000 0.097
                                                      -0.03 0.12
                                                                  0.00
                                                                           0.02
## 5
       F
              22 section2-40x-2 gcl1 0.111 0.001
                                                                   0.00
                                                                           0.01
                                                       0.01 0.77
## 6
       F
              22 section2-40x-2 inl1 0.000 0.183
                                                      -0.02 0.18
                                                                   0.00
                                                                           0.03
                                                      -0.02 0.14 0.00
## 7
      F
              22 section2-40x-3 gcl1 0.000 0.181
                                                                           0.02
##
   coloc
## 2 TRUE
## 3 FALSE
## 4 FALSE
## 5 FALSE
## 6 FALSE
## 7 FALSE
```

Generating summary statistics

P-gp

```
pgp sumstats <- pgp coloc2 %>% summarise(m1 mean = mean(m1),
                     m1_sd = sd(m1),
                     m2 mean = mean(m2),
                     m2_{sd} = sd(m2),
                     r_mean = mean(r_pearson),
                     r_{sd} = sd(r_{pearson}),
                     n total = n(),
                     n_{coloc} = sum(coloc)
                     )
pgp_sumstats
                                                           r_sd n_total n_coloc
                         m2_{mean}
##
     m1_{mean}
                 m1\_sd
                                      m2_sd r_mean
## 1 0.298 0.3149236 0.2291373 0.2644154 0.324902 0.1636261
                                                                     51
bcrp_sumstats <- bcrp_coloc2 %>% summarise(m1_mean = mean(m1),
                     m1 sd = sd(m1),
                     m2_{mean} = mean(m2),
                     m2 sd = sd(m2),
                     r_mean = mean(r_pearson),
                     r_{sd} = sd(r_{pearson}),
                     n_{total} = n(),
                     n_{coloc} = sum(coloc)
bcrp_sumstats
       m1_{mean}
                   m1_sd m2_mean
                                         m2\_sd
                                                              r_sd n_total n_coloc
                                                  r_{mean}
## 1 0.7374762 0.1322315 0.2660952 0.08701775 0.4604762 0.104437
mrp2 sumstats <- mrp2 coloc2 %>% summarise(m1 mean = mean(m1),
                     m1 sd = sd(m1),
                     m2 mean = mean(m2),
                     m2_sd = sd(m2),
                     r_mean = mean(r_pearson),
                     r_{sd} = sd(r_{pearson}),
                     n_{total} = n(),
                     n_{coloc} = sum(coloc)
                     )
mrp2_sumstats
##
                   m1_sd m2_mean
                                        m2\_sd
                                                                r_sd n_total n_coloc
                                                  r_{mean}
## 1 0.1098828 0.1436731 0.2081172 0.1569569 0.03496552 0.07127923
                                                                         145
mrp2_sumstats_image <- mrp2_coloc2 %>% group_by(image,mouseID,sex,coloc) %>%
  summarise(m1_mean = mean(m1),
             m1_sd = sd(m1),
             m2 mean = mean(m2),
```

```
m2_sd = sd(m2),
           r_mean = mean(r_pearson),
           r_{sd} = sd(r_{pearson}),
           n_{total} = n(),
           n_{coloc} = sum(coloc)
## 'summarise()' has grouped output by 'image', 'mouseID', 'sex'. You can override
## using the '.groups' argument.
mrp2 sumstats image
## # A tibble: 59 x 12
## # Groups: image, mouseID, sex [40]
     image mouseID sex coloc m1_mean m1_sd m2_mean m2_sd r_mean
##
                                                                        r_sd
##
     <chr>
             <fct> <fct> <fct> <lgl>
                                <dbl>
                                         <dbl> <dbl>
                                                       <dbl>
                                                              <dbl>
                                                                        <dbl>
## 1 section~ 40
                     F
                          FALSE 0.0527 0.0352 0.0933 0.107
                                                              0.0167 0.00577
## 2 section~ 92
                          FALSE 0
                                        0
                                                0.204 0.0566 -0.055
                                                                      0.0778
## 3 section~ 40
                   F
                        FALSE 0.155 NA
                                                0.023 NA
                                                              0.02
                                                                     NA
                   F TRUE
## 4 section~ 40
                                 0.127
                                        0.0396 0.129
                                                      0.0465 0.0533 0.00577
                   M FALSE 0.019
## 5 section~ 92
                                       0.0329 0.213 0.0721 0
                                                                      0.0346
## 6 section~ 40
                   F FALSE 0
                                                0.079 NA
                                       NA
                                                              0
                                                                     NA
                    F TRUE
## 7 section~ 40
                                 0.0465 0.0573 0.102
                                                      0.0983 0.025
                                                                     0.00707
                    M
## 8 section~ 92
                          FALSE 0
                                                0.352 NA
                                                              -0.02
                                       NA
                                                                     NA
## 9 section~ 92
                          TRUE
                                       0.0629 0.258
                     M
                                 0.308
                                                     0.0643 0.11
                                                                     0.0283
## 10 section~ 40
                   F
                          FALSE 0.013 NA
                                                0.362 NA
                                                              0.02
## # ... with 49 more rows, and 2 more variables: n_total <int>, n_coloc <int>
pgp_sumstats_animals <- pgp_coloc2 %>% group_by(mouseID,sex,prep) %>%
 summarise(m1\_mean = mean(m1),
           m1_sd = sd(m1),
           m2_{mean} = mean(m2),
           m2_sd = sd(m2),
           r_mean = mean(r_pearson),
           r_{sd} = sd(r_{pearson}),
           n total = n(),
           n_{coloc} = sum(coloc)
## 'summarise()' has grouped output by 'mouseID', 'sex'. You can override using
## the '.groups' argument.
pgp_sumstats_animals
## # A tibble: 10 x 11
## # Groups: mouseID, sex [10]
     mouseID sex prep
##
                         m1_mean m1_sd m2_mean m2_sd r_mean r_sd n_total
##
     <fct>
            <fct> <fct>
                          <dbl>
                                  <dbl> <dbl> <dbl> <dbl> <int>
                                 0.00784 0.043 0.0168 0.128 0.0295
## 1 10
            M wm
                          0.01
                                                                        5
```

F section 0.651 0.299 0.56 0.293 0.595 0.0505

0.0258 0.0409 0.0503 0.0192 0.145 0.0191

6

2 11

3 20

wm

```
0.0782 0.135 0.375 0.0947
## 4 39
                         0.227 0.258
                 wm
## 5 80
                 section 0.320 0.282
                                       0.246 0.290 0.37 0.140
                                                                      6
            М
               section 0.283 0.251
                                                                      6
## 6 81
                                       0.204 0.286 0.377 0.0838
                 section 0.381 0.325
                                        0.208 0.270 0.352 0.183
                                                                      6
## 7 82
            М
## 8 83
            М
                 wm
                         0.430 0.373
                                        0.368 0.274 0.328 0.0804
                                                                      5
## 9 87
            F
                         0.416 0.366
                                        0.297 0.247
                                                     0.3 0.0628
                                                                      5
                 wm
## 10 9
            М
                         0.0265 0.0155
                                        0.0812 0.0538 0.138 0.0419
                                                                      4
                 wm
## # ... with 1 more variable: n_coloc <int>
```

'summarise()' has grouped output by 'mouseID', 'sex'. You can override using
the '.groups' argument.

bcrp_sumstats_animals

```
## # A tibble: 7 x 11
## # Groups: mouseID, sex [7]
##
    mouseID sex prep m1_mean m1_sd m2_mean m2_sd r_mean r_sd n_total
    <fct> <fct> <fct>
                      <dbl> <dbl> <dbl> <dbl> <dbl> <dbl> <int>
## 1 22
          F
               section 0.658 0.114
                                      0.385 0.115
                                                  0.518 0.110
                                                                   6
         F
## 2 40
               section 0.774 0.0717 0.274 0.0454 0.502 0.117
                                                                   6
## 3 80
         M section 0.775 0.0587 0.162 0.0183 0.443 0.0638
                                                                   6
## 4 81
         M section 0.663 0.127 0.276 0.0642 0.42 0.103
                                                                   6
               section 0.754 0.0375 0.275 0.0144 0.408 0.0337
         M
## 5 82
                                                                   6
## 6 92 M
## 7 98 F
               section 0.806 0.0483 0.264 0.0486 0.503 0.0403
                                                                   6
           F
               section 0.732 0.280
                                      0.226 0.0874 0.428 0.177
                                                                   6
## # ... with 1 more variable: n_coloc <int>
```

'summarise()' has grouped output by 'mouseID', 'sex'. You can override using
the '.groups' argument.

```
uneven <- mrp2_sumstats_animals %>% group_by(mouseID) %>%
  summarise(n = n(), coloc = coloc, sex=sex) %>%
  filter(n==1) %>% select(-n) %>%
  mutate(coloc = toString(as.integer(coloc))) %>%
  mutate(coloc = str_replace(toString(coloc), pattern = "0", replacement = "1")) %%
  mutate(coloc = as.logical(as.integer(coloc)))
## 'summarise()' has grouped output by 'mouseID'. You can override using the
## '.groups' argument.
mrp2_sumstats_animals <- rbind(mrp2_sumstats_animals, uneven) %>% arrange(., mouseID)
mrp2_sumstats_animals
## # A tibble: 16 x 11
## # Groups: mouseID, sex [8]
##
     mouseID sex
                   coloc m1_mean
                                     m1_sd m2_mean
                                                     m2\_sd
                                                             r_{mean}
                                                                       r_sd
##
      <fct>
              <fct> <lgl>
                             <dbl>
                                     <dbl>
                                             <dbl>
                                                     <dbl>
                                                              <dbl>
                                                                      <dbl>
                                            0.202 0.118 -0.0262
## 1 22
             F
                   FALSE 0.0234
                                   0.0497
                                                                     0.0421
## 2 22
             F
                   TRUE
                          0.04
                                   0.0325
                                            0.244
                                                    0.164
                                                            0.08
                                                                     0.0566
## 3 40
             F
                   FALSE 0.0543
                                   0.0658
                                            0.115
                                                    0.117
                                                            0.0122
                                                                     0.0109
## 4 40
             F
                   TRUE
                          0.0796
                                   0.0552
                                            0.136
                                                    0.0669 0.0486
                                                                     0.0177
## 5 62
                   FALSE 0.0655
                                  0.0959
                                            0.0723 0.0747 -0.0174
             Μ
                                                                     0.0254
## 6 62
                   TRUE NA
             М
                                  NA
                                           NA
                                                   NA
                                                           NA
                                                                    NA
## 7 77
                                                    0.0385 0.00933 0.0249
             М
                   FALSE 0.035
                                   0.0492
                                            0.135
## 8 77
             М
                   TRUE
                          0.242
                                   0.142
                                            0.200
                                                    0.0504 0.08
                                                                     0.0486
## 9 81
                   FALSE 0.00646 0.00785 0.434
                                                    0.239 -0.00385 0.0112
             M
## 10 81
                   TRUE
                          0.029
                                   0.0428
                                            0.420
                                                    0.291
                                                            0.044
                                                                     0.0313
             Μ
## 11 82
             М
                   FALSE 0.0468
                                   0.0604
                                            0.143
                                                    0.0994 0.024
                                                                     0.0397
## 12 82
             М
                   TRUE
                          0.326
                                   0.170
                                            0.218
                                                   0.116
                                                            0.128
                                                                     0.0669
## 13 92
             Μ
                   FALSE 0.0406
                                   0.0896
                                            0.198
                                                   0.103 -0.0167
                                                                     0.0424
## 14 92
                   TRUE
                          0.306
                                   0.0802
                                            0.306
                                                    0.0831 0.115
                                                                     0.03
             М
## 15 98
             F
                   FALSE 0.056
                                   0.0752
                                            0.251
                                                    0.0982 0.005
                                                                     0.0404
## 16 98
             F
                   TRUE
                          0.253
                                   0.124
                                            0.262
                                                    0.0856 0.131
                                                                     0.0752
## # ... with 2 more variables: n_total <int>, n_coloc <int>
pgp_sumstats_sex <- pgp_coloc2 %>% group_by(sex) %>%
  summarise(m1\_mean = mean(m1),
            m1_sd = sd(m1),
            m2_{mean} = mean(m2),
            m2_sd = sd(m2),
            r_mean = mean(r_pearson),
            r_{sd} = sd(r_{pearson}),
            n_{total} = n(),
            n_{coloc} = sum(coloc)
pgp_sumstats_sex
## # A tibble: 2 x 9
          m1_mean m1_sd m2_mean m2_sd r_mean r_sd n_total n_coloc
##
##
     <fct>
            <dbl> <dbl>
                          <dbl> <dbl> <dbl> <dbl> <
                                                     <int>
                                                             <int>
## 1 F
            0.459 0.341
                          0.344 0.305 0.438 0.150
                                                                15
                                                        15
## 2 M
            0.231 0.282 0.181 0.234 0.278 0.147
                                                        36
                                                                36
```

```
bcrp_sumstats_sex <- bcrp_coloc2 %>% group_by(sex) %>%
 summarise(m1\_mean = mean(m1),
           m1_sd = sd(m1),
           m2_{mean} = mean(m2),
           m2_sd = sd(m2),
           r_mean = mean(r_pearson),
           r_sd = sd(r_pearson),
           n total = n(),
            n_{coloc} = sum(coloc)
bcrp_sumstats_sex
## # A tibble: 2 x 9
          m1_mean m1_sd m2_mean m2_sd r_mean r_sd n_total n_coloc
   <fct> <dbl> <dbl> <dbl> <dbl> <dbl> <dbl> <dbl> <int>
## 1 F
            0.721 0.176
                          0.295 0.107 0.483 0.136
                                                       18
                                                               18
## 2 M
           24
                                                               24
mrp2_sumstats_sex <- mrp2_coloc2 %>% group_by(sex) %>%
 summarise(m1\_mean = mean(m1),
           m1_sd = sd(m1),
           m2 mean = mean(m2),
           m2_sd = sd(m2),
           r_mean = mean(r_pearson),
           r_sd = sd(r_pearson),
           n total = n(),
           n coloc = sum(coloc)
            )
mrp2_sumstats_sex
## # A tibble: 2 x 9
    sex m1_mean m1_sd m2_mean m2_sd r_mean r_sd n_total n_coloc
    <fct> <dbl> <dbl> <dbl> <dbl> <dbl> <dbl> <int> <int>
##
## 1 F
           0.104 0.124 0.201 0.113 0.0411 0.0794
                                                             24
                                                     53
           0.113 0.154 0.212 0.178 0.0314 0.0664
## 2 M
                                                     92
                                                             31
pgp_sumstats_prep <- pgp_coloc2 %>% group_by(prep) %>%
 summarise(m1_mean = mean(m1),
           m1_sd = sd(m1),
           m2_{mean} = mean(m2),
           m2_sd = sd(m2),
           r_mean = mean(r_pearson),
           r_{sd} = sd(r_{pearson}),
           n_{total} = n(),
            mean_P = mean(Pval)
pgp_sumstats_prep
## # A tibble: 2 x 9
          m1_mean m1_sd m2_mean m2_sd r_mean r_sd n_total mean_P
    prep
           <dbl> <dbl> <dbl> <dbl> <dbl> <dbl> <dbl> <dbl>
   <fct>
## 1 section 0.408 0.308 0.304 0.306 0.423 0.155
            ## 2 wm
                                                      27
```

```
mrp2_sumstats_coloc <- mrp2_coloc2 %>% group_by(coloc) %>%
  summarise(m1_mean = mean(m1),
            m1_sd = sd(m1),
            m2_{mean} = mean(m2),
            m2_sd = sd(m2),
            r_mean = mean(r_pearson),
            r_{sd} = sd(r_{pearson}),
            n \text{ total} = n(),
            mean_P = mean(Pval)
mrp2_sumstats_coloc
## # A tibble: 2 x 9
     coloc m1_mean m1_sd m2_mean m2_sd r_mean r_sd n_total mean_P
           <dbl> <dbl> <dbl> <dbl> <
                                           <dbl> <dbl>
                                                        <int> <dbl>
     <lgl>
## 1 FALSE 0.0393 0.0672 0.187 0.166 -0.00622 0.0329
                                                             90 0.431
## 2 TRUE 0.225 0.160 0.243 0.136 0.102 0.0656
                                                             55 0.996
Statistical Tests
pgp_sumstats_animals$prep <- as.factor(pgp_sumstats_animals$prep)</pre>
coin::wilcox_test(pgp_sumstats_animals$r_mean ~ pgp_sumstats_animals$prep, conf.int=TRUE, distribution=
##
## Exact Wilcoxon-Mann-Whitney Test
## data: pgp_sumstats_animals$r_mean by pgp_sumstats_animals$prep (section, wm)
## Z = 2.132, p-value = 0.0381
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## 0.001666667 0.450000000
## sample estimates:
## difference in location
                0.2218333
coin::wilcox_test(pgp_sumstats_animals$m1_mean ~ pgp_sumstats_animals$prep, conf.int=TRUE, distribution
##
## Exact Wilcoxon-Mann-Whitney Test
## data: pgp_sumstats_animals$m1_mean by pgp_sumstats_animals$prep (section, wm)
## Z = 1.2792, p-value = 0.2571
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
```

-0.1103000 0.6241667
sample estimates:
difference in location

0.256375

##

```
coin::wilcox_test(pgp_sumstats_animals$m2_mean ~ pgp_sumstats_animals$prep, conf.int=TRUE, distribution
##
## Exact Wilcoxon-Mann-Whitney Test
##
## data: pgp_sumstats_animals$m2_mean by pgp_sumstats_animals$prep (section, wm)
## Z = 1.2792, p-value = 0.2571
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## -0.1212667 0.4817500
## sample estimates:
## difference in location
               0.1592083
##
coin::wilcox_test(pgp_sumstats_animals$r_mean ~ pgp_sumstats_animals$sex, conf.int=TRUE, distribution="
##
## Exact Wilcoxon-Mann-Whitney Test
##
## data: pgp_sumstats_animals$r_mean by pgp_sumstats_animals$sex (F, M)
## Z = 1.2536, p-value = 0.2667
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## -0.0700 0.4575
## sample estimates:
## difference in location
                    0.172
coin::wilcox_test(pgp_sumstats_animals$m1_mean ~ pgp_sumstats_animals$sex, conf.int=TRUE, distribution=
##
## Exact Wilcoxon-Mann-Whitney Test
##
## data: pgp_sumstats_animals$m1_mean by pgp_sumstats_animals$sex (F, M)
## Z = 1.2536, p-value = 0.2667
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## -0.1537500 0.6249167
## sample estimates:
## difference in location
##
                 0.21725
coin::wilcox_test(pgp_sumstats_animals$m2_mean ~ pgp_sumstats_animals$sex, conf.int=TRUE, distribution=
##
## Exact Wilcoxon-Mann-Whitney Test
## data: pgp_sumstats_animals$m2_mean by pgp_sumstats_animals$sex (F, M)
## Z = 1.0256, p-value = 0.3833
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
```

```
## -0.1680833 0.5097500
## sample estimates:
## difference in location
##
                  0.0932
pgp_wm_sumstats <- pgp_sumstats_animals %>% filter(prep == "wm")
coin::wilcox_test(pgp_wm_sumstats$r_mean ~ pgp_wm_sumstats$sex, conf.int=TRUE, distribution="exact")
## Warning in cci(alpha): cannot compute confidence interval
##
## Exact Wilcoxon-Mann-Whitney Test
## data: pgp_wm_sumstats$r_mean by pgp_wm_sumstats$sex (F, M)
## Z = 1.3887, p-value = 0.2667
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## NA NA
## sample estimates:
## difference in location
##
                 0.16725
coin::wilcox_test(pgp_wm_sumstats$m1_mean ~ pgp_wm_sumstats$sex, conf.int=TRUE, distribution="exact")
## Warning in cci(alpha): cannot compute confidence interval
##
  Exact Wilcoxon-Mann-Whitney Test
## data: pgp_wm_sumstats$m1_mean by pgp_wm_sumstats$sex (F, M)
## Z = 0.92582, p-value = 0.5333
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## NA NA
## sample estimates:
## difference in location
                 0.209375
##
coin::wilcox_test(pgp_wm_sumstats$m2_mean ~ pgp_wm_sumstats$sex, conf.int=TRUE, distribution="exact")
## Warning in cci(alpha): cannot compute confidence interval
## Exact Wilcoxon-Mann-Whitney Test
## data: pgp_wm_sumstats$m2_mean by pgp_wm_sumstats$sex (F, M)
## Z = 0.46291, p-value = 0.8
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## NA NA
```

```
## sample estimates:
## difference in location
                 0.031625
pgp_sect_sumstats <- pgp_sumstats_animals %>% filter(prep == "section")
coin::wilcox_test(pgp_sect_sumstats$r_mean ~ pgp_sect_sumstats$sex, conf.int=TRUE, distribution="exact"
## Warning in cci(alpha): cannot compute confidence interval
##
## Exact Wilcoxon-Mann-Whitney Test
##
## data: pgp_sect_sumstats$r_mean by pgp_sect_sumstats$sex (F, M)
## Z = 1.3416, p-value = 0.5
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## NA NA
## sample estimates:
## difference in location
##
                    0.225
coin::wilcox_test(pgp_sect_sumstats$m1_mean ~ pgp_sect_sumstats$sex, conf.int=TRUE, distribution="exact
## Warning in cci(alpha): cannot compute confidence interval
## Exact Wilcoxon-Mann-Whitney Test
##
## data: pgp_sect_sumstats$m1_mean by pgp_sect_sumstats$sex (F, M)
## Z = 1.3416, p-value = 0.5
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## NA NA
## sample estimates:
## difference in location
                0.3311667
coin::wilcox_test(pgp_sect_sumstats$m2_mean ~ pgp_sect_sumstats$sex, conf.int=TRUE, distribution="exact
## Warning in cci(alpha): cannot compute confidence interval
##
## Exact Wilcoxon-Mann-Whitney Test
## data: pgp_sect_sumstats$m2_mean by pgp_sect_sumstats$sex (F, M)
## Z = 1.3416, p-value = 0.5
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## NA NA
## sample estimates:
## difference in location
               0.3523333
##
```

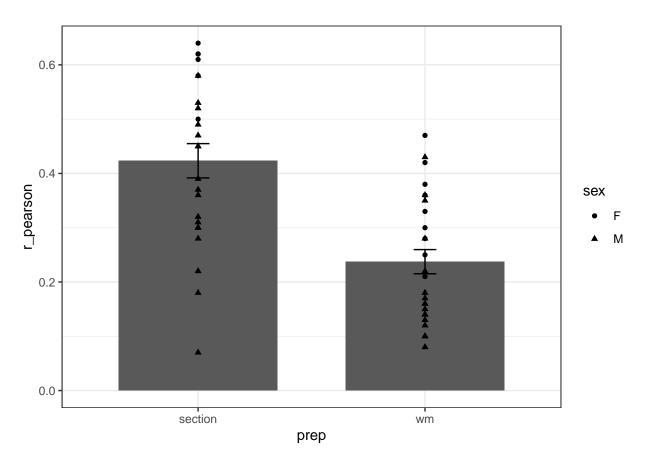
```
coin::wilcox_test(bcrp_sumstats_animals$r_mean ~ bcrp_sumstats_animals$sex, conf.int=TRUE, distribution
## Warning in cci(alpha): cannot compute confidence interval
##
## Exact Wilcoxon-Mann-Whitney Test
## data: bcrp_sumstats_animals$r_mean by bcrp_sumstats_animals$sex (F, M)
## Z = 1.0607, p-value = 0.4
\mbox{\tt \#\#} alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## NA NA
## sample estimates:
## difference in location
               0.03916667
coin::wilcox_test(bcrp_sumstats_animals$m1_mean ~ bcrp_sumstats_animals$sex, conf.int=TRUE, distribution
## Warning in cci(alpha): cannot compute confidence interval
##
## Exact Wilcoxon-Mann-Whitney Test
## data: bcrp_sumstats_animals$m1_mean by bcrp_sumstats_animals$sex (F, M)
## Z = -1.0607, p-value = 0.4
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## NA NA
## sample estimates:
## difference in location
##
                  -0.027
coin::wilcox_test(bcrp_sumstats_animals$m2_mean ~ bcrp_sumstats_animals$sex, conf.int=TRUE, distribution
## Warning in cci(alpha): cannot compute confidence interval
##
## Exact Wilcoxon-Mann-Whitney Test
## data: bcrp_sumstats_animals$m2_mean by bcrp_sumstats_animals$sex (F, M)
## Z = 0.35355, p-value = 0.8571
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## NA NA
## sample estimates:
## difference in location
               0.03708333
```

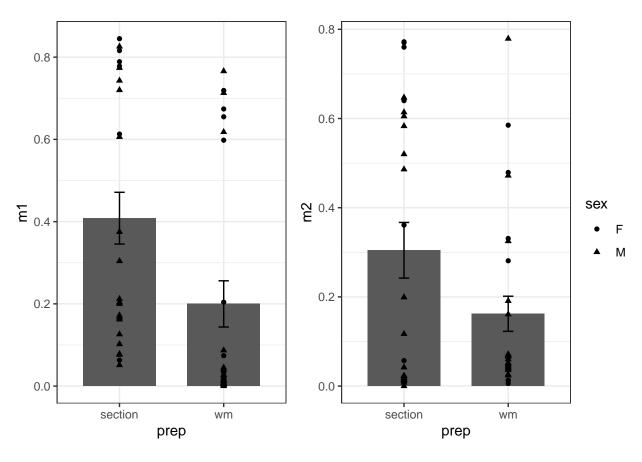
```
mrp2_sumstats_animals$coloc <- as.factor(mrp2_sumstats_animals$coloc)</pre>
mrp2_sumstats_animals$r_mean <- replace_na(mrp2_sumstats_animals$r_mean, 0)</pre>
mrp2_sumstats_animals$m1_mean <- replace_na(mrp2_sumstats_animals$m1_mean, 0)
mrp2_sumstats_animals$m2_mean <- replace_na(mrp2_sumstats_animals$m2_mean, 0)</pre>
coin::wilcoxsign_test(r_mean ~ coloc | mouseID, data=mrp2_sumstats_animals, conf.int=TRUE, distribution
##
## Exact Wilcoxon-Pratt Signed-Rank Test
##
## data: y by x (pos, neg)
## stratified by block
## Z = -2.5205, p-value = 0.007812
## alternative hypothesis: true mu is not equal to 0
coin::wilcoxsign_test(m1_mean ~ coloc | mouseID, data=mrp2_sumstats_animals, conf.int=TRUE, distribution
## Exact Wilcoxon-Pratt Signed-Rank Test
##
## data: y by x (pos, neg)
## stratified by block
## Z = -1.9604, p-value = 0.05469
## alternative hypothesis: true mu is not equal to 0
coin::wilcoxsign_test(m2_mean ~ coloc | mouseID, data=mrp2_sumstats_animals, conf.int=TRUE, distribution
##
## Exact Wilcoxon-Pratt Signed-Rank Test
##
## data: y by x (pos, neg)
## stratified by block
## Z = -1.4003, p-value = 0.1953
## alternative hypothesis: true mu is not equal to 0
mrp2_pos_sumstats_animals <- mrp2_sumstats_animals %>% filter(coloc== TRUE)
coin::wilcox_test(mrp2_pos_sumstats_animals$r_mean ~ mrp2_pos_sumstats_animals$sex, conf.int=TRUE, dist
##
## Exact Wilcoxon-Mann-Whitney Test
## data: mrp2_pos_sumstats_animals$r_mean by mrp2_pos_sumstats_animals$sex (F, M)
## Z = 0.59987, p-value = 0.6071
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## -0.06642857 0.08733333
## sample estimates:
## difference in location
              0.004571429
##
```

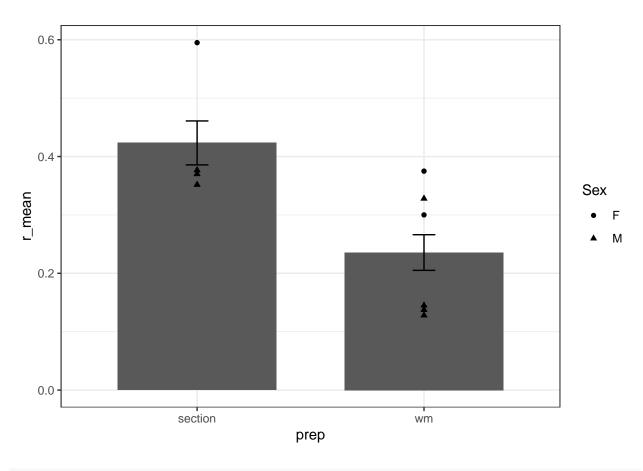
```
coin::wilcox_test(mrp2_pos_sumstats_animals$m1_mean ~ mrp2_pos_sumstats_animals$sex, conf.int=TRUE, dis
##
## Exact Wilcoxon-Mann-Whitney Test
## data: mrp2_pos_sumstats_animals$m1_mean by mrp2_pos_sumstats_animals$sex (F, M)
## Z = -0.14907, p-value = 1
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## -0.2864667 0.2530667
## sample estimates:
## difference in location
##
             -0.05243333
coin::wilcox_test(mrp2_pos_sumstats_animals$m2_mean ~ mrp2_pos_sumstats_animals$sex, conf.int=TRUE, dis
##
## Exact Wilcoxon-Mann-Whitney Test
##
## data: mrp2_pos_sumstats_animals$m2_mean by mrp2_pos_sumstats_animals$sex (F, M)
## Z = -0.14907, p-value = 1
## alternative hypothesis: true mu is not equal to 0
## 95 percent confidence interval:
## -0.2846286 0.2623333
## sample estimates:
## difference in location
             -0.04391667
##
```

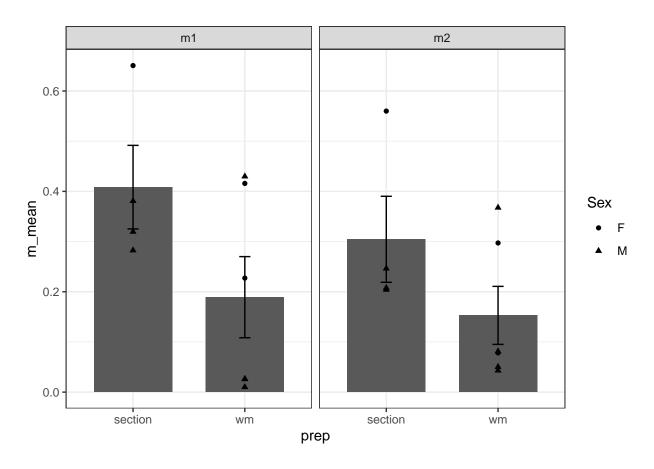
Plotting the data

pgp_coloc2 %>% ggplot(aes(x=prep, y=r_pearson)) +
 stat_summary(fun = 'mean', geom="bar", width=0.7) +

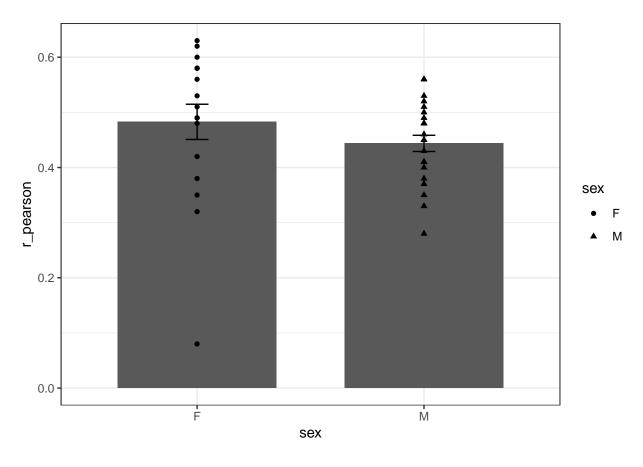


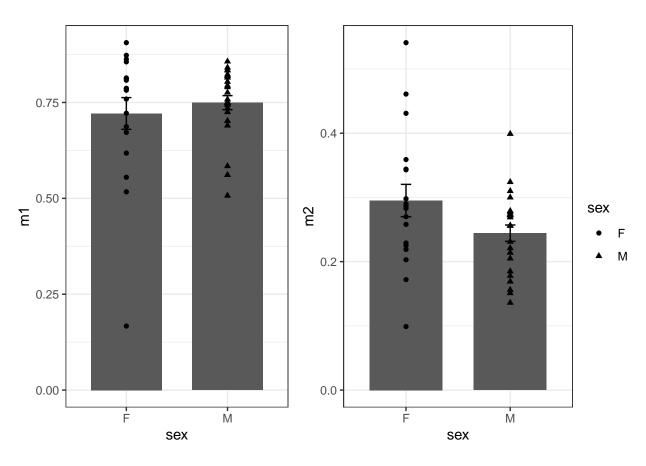


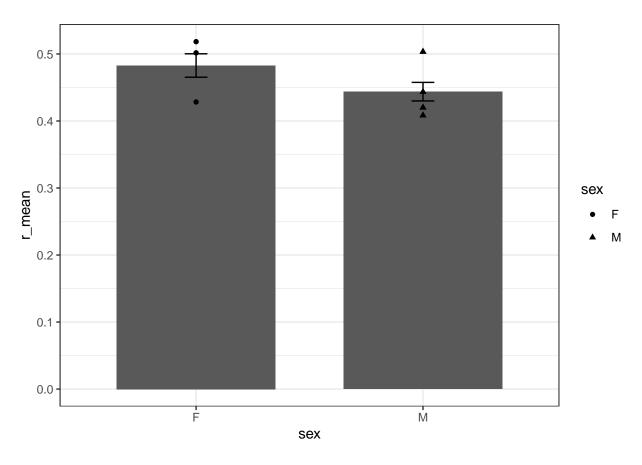


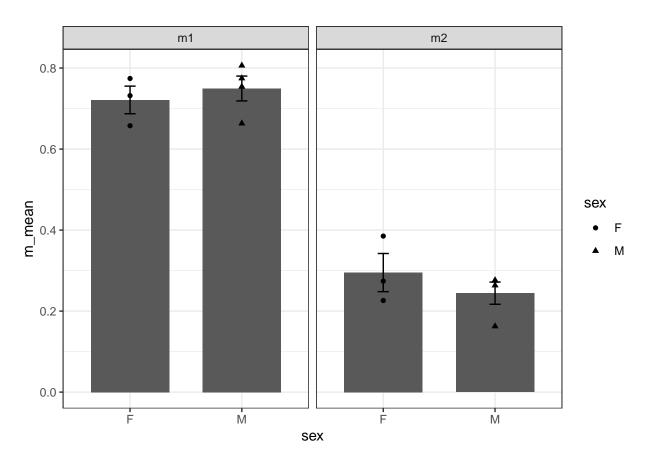


'summarise()' has grouped output by 'mouseID', 'm_stat_type'. You can override
using the '.groups' argument.

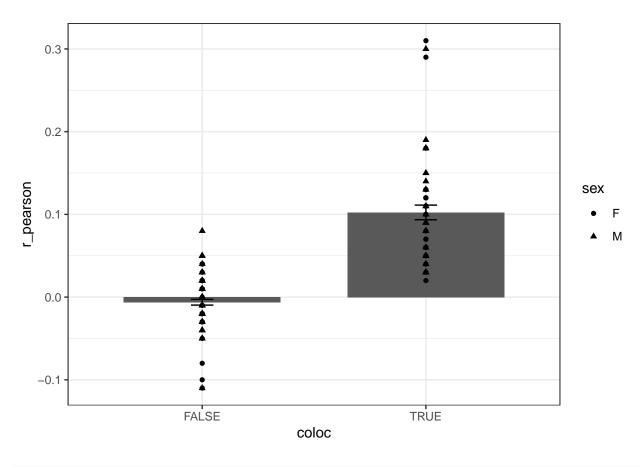


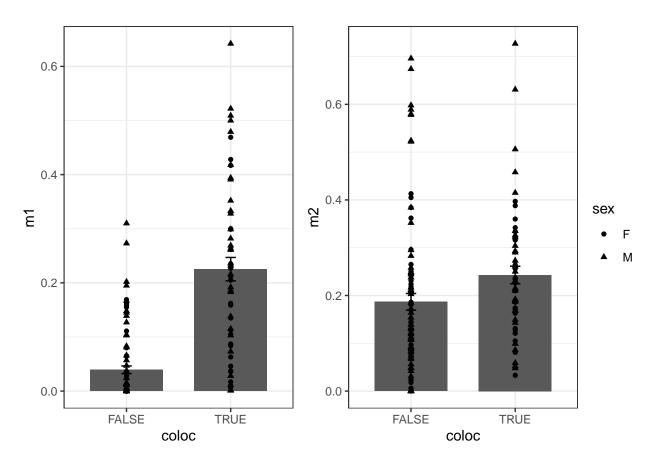


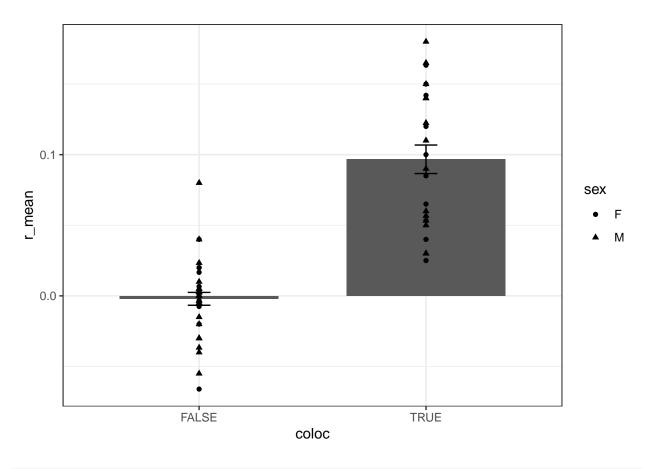


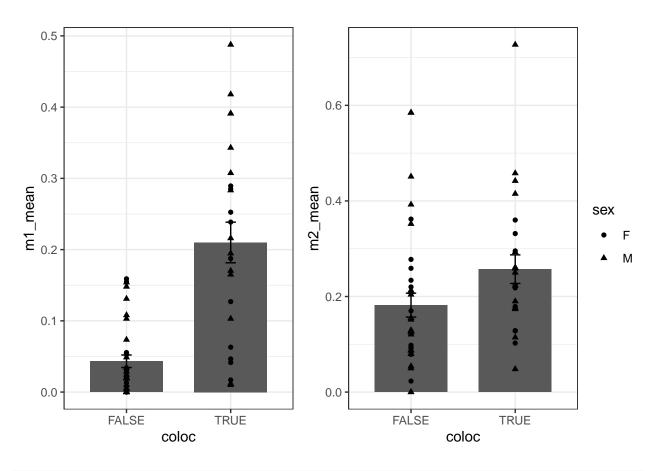


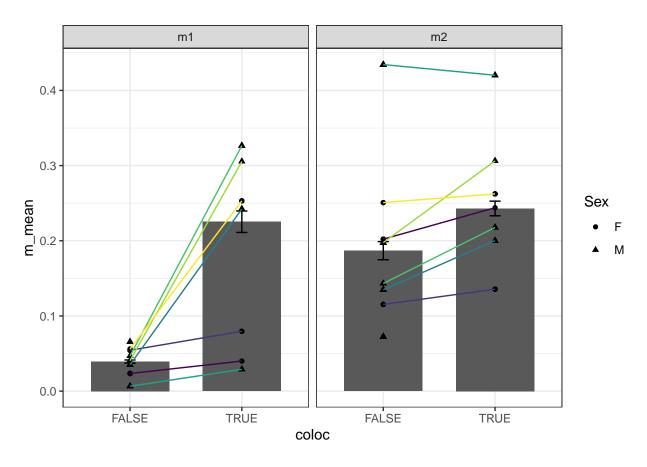
'summarise()' has grouped output by 'mouseID', 'coloc', 'm_stat_type', 'sex'.
You can override using the '.groups' argument.

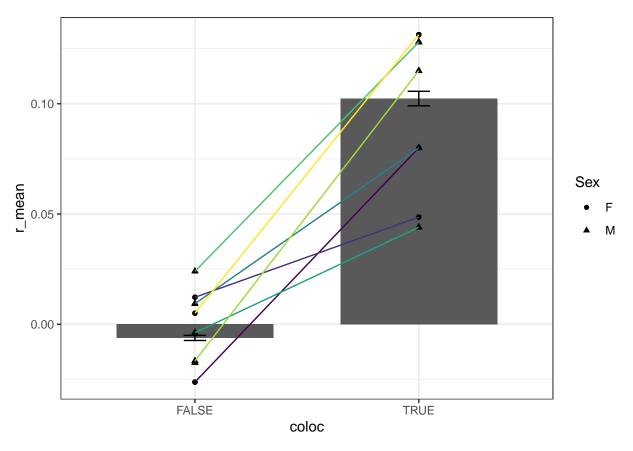












```
pgp_animal_r_plot1 <- pgp_animal_r_plot + ylim(-0.05,0.65) + ggtitle("P-gp")
bcrp_animal_r_plot1 <- bcrp_animal_r_plot + ylim(-0.05,0.65) + ggtitle("Bcrp")
mrp2_animal_r_plot1 <- mrp2_animal_r_plot + ylim(-0.05,0.65) + ggtitle("Mrp2")</pre>
all_r_plot <- ggarrange(pgp_animal_r_plot1, bcrp_animal_r_plot1, mrp2_animal_r_plot1, ncol=3, common.le
 \#ggsave("../figures/all\_r\_plot.png", plot=all\_r\_plot, width=7, height=4) \\ \#ggsave("../figures/all\_r\_plot.svg", plot=all\_r\_plot, width=7, height=4) 
pgp_animal_m1_plot <- ggplot(pgp_sumstats_animals, aes(x=prep, y=m1_mean)) +
      stat_summary(fun = 'mean', geom="bar", width=0.7) +
      stat_summary(fun.data = mean_se,
                                                   geom = "errorbar", width=0.1) +
      geom_point(color="black", aes(shape=sex)) +
      theme_bw(12) +
      ylim(0,0.9) +
      ggtitle("P-gp") +
      guides(shape=guide_legend("Sex"))
\label{lem:condition} $$ bcrp_animal_m1_plot \leftarrow ggplot(bcrp_sumstats_animals, aes(x=sex, y=m1_mean)) + $$ (aes(x=sex, y=m1_mean)) + $$ (bern_sumstats_animals, aes(x=sex, y=m
      stat_summary(fun = 'mean', geom="bar", width=0.7) +
      stat_summary(fun.data = mean_se,
                                                   geom = "errorbar", width=0.1) +
      geom_point(color="black", aes(shape=sex)) +
      scale color viridis(discrete="TRUE") +
      theme_bw(12) +
     ylim(0,0.9) +
```

```
ggtitle("Bcrp") +
  guides(shape=guide_legend("Sex"))
mrp2_animal_m1_plot <- ggplot(mrp2_sumstats_animals, aes(x=coloc, y=m1_mean)) +
  stat_summary(fun = 'mean', geom="bar", width=0.7) +
  stat_summary(fun.data = mean_se,
                 geom = "errorbar", width=0.1) +
  geom_point(color="black", aes(shape=sex)) +
  geom_line(aes(group=mouseID, color=mouseID)) +
  scale_color_viridis(discrete="TRUE") +
  theme_bw(12) +
  ylim(0,0.9) +
  ggtitle("Mrp2") +
  guides(shape=guide_legend("Sex"), color = "none")
all_m1_plot <- ggarrange(pgp_animal_m1_plot, bcrp_animal_m1_plot, mrp2_animal_m1_plot, ncol=3, common.l
#ggsave("../figures/all_m1_plot.png", plot=all_m1_plot, width=7, height=4)
#qqsave("../fiqures/all_m1_plot.svq", plot=all_m1_plot, width=7, height=4)
pgp_animal_m2_plot <- ggplot(pgp_sumstats_animals, aes(x=prep, y=m2_mean)) +
  stat_summary(fun = 'mean', geom="bar", width=0.7) +
  stat_summary(fun.data = mean_se,
                 geom = "errorbar", width=0.1) +
  geom_point(color="black", aes(shape=sex)) +
  theme_bw() +
  ylim(0,0.6) +
  ggtitle("P-gp") +
  guides(shape=guide_legend("Sex"))
bcrp_animal_m2_plot <- ggplot(bcrp_sumstats_animals, aes(x=sex, y=m2_mean)) +
  stat_summary(fun = 'mean', geom="bar", width=0.7) +
  stat_summary(fun.data = mean_se,
                 geom = "errorbar", width=0.1) +
  geom_point(color="black", aes(shape=sex)) +
  theme_bw() +
  ylim(0,0.6) +
  ggtitle("Bcrp") +
  guides(shape=guide_legend("Sex"),)
mrp2_animal_m2_plot <- ggplot(mrp2_sumstats_animals, aes(x=coloc, y=m2_mean)) +
  stat_summary(fun = 'mean', geom="bar", width=0.7) +
  stat_summary(fun.data = mean_se,
                 geom = "errorbar", width=0.1) +
  geom_point(color="black", aes(shape=sex)) +
  geom_line(aes(group=mouseID, color=mouseID)) +
  scale_color_viridis(discrete="TRUE") +
  theme_bw() +
  ylim(0,0.6) +
  ggtitle("Mrp2") +
```

```
guides(shape=guide_legend("Sex"), color = "none")

all_m2_plot <- ggarrange(pgp_animal_m2_plot, bcrp_animal_m2_plot, mrp2_animal_m2_plot, ncol=3, common.l
#ggsave("../figures/all_m2_plot.png", plot=all_m2_plot, width=7, height=4)
#ggsave("../figures/all_m2_plot.svg", plot=all_m2_plot, width=7, height=4)</pre>
```