morphine_regression

nbergum

7/25/2022

Reading in and tidying the data

```
regression <- read.csv("../data/morphine__sex_diff_transporters.csv", fileEncoding = 'UTF-8-BOM')

regression$conc_wt <- (regression$raw_conc/regression$tissue_weight)

str(regression)
```

```
## 'data.frame':    48 obs. of  11 variables:
##  $ animal       : chr  "1M" "2M" "4M" "5M" ...
##  $ raw_conc     : num  56.6 22.1 49.5 87.4 36.6 ...
##  $ tissue_weight: num  20.1 10.3 15.1 31.4 14.7 14.3 20.8 15.7 43.7 14.6 ...
##  $ body_wt      : num  27.2 30.1 25.8 26.1 27.3 26.2 23.7 27.2 21.3 22.9 ...
##  $ dose         : num  20.6 18.6 21.7 20 19.1 19.9 22 19.2 20.4 19 ...
##  $ pgp          : num  2.43 2.7 2.92 2.77 2.46 ...
##  $ bcrp         : num  1.037 1.249 1.151 0.986 1.205 ...
##  $ stage        : chr  "male" "male" "male" "male" ...
##  $ group        : chr  "male" "male" "male" "male" ...
##  $ tissue       : chr  "brain" "brain" "brain" "brain" ...
##  $ conc_wt      : num  2.82 2.14 3.28 2.78 2.49 ...
```

```
regression <- regression %>% mutate(stage = as.factor(stage),
                                    group = as.factor(group),
                                    tissue = factor(as.factor(tissue), c("retina", "brain"))
                                    )
head(regression)
```

```
##   animal raw_conc tissue_weight body_wt dose      pgp      bcrp stage group
## 1     1M  56.5895          20.1    27.2 20.6 2.429027 1.0366970  male  male
## 2     2M  22.0798          10.3    30.1 18.6 2.699340 1.2487060  male  male
## 3     4M  49.5114          15.1    25.8 21.7 2.923597 1.1505545  male  male
## 4     5M  87.4161          31.4    26.1 20.0 2.770560 0.9860451  male  male
## 5     6M  36.5960          14.7    27.3 19.1 2.464103 1.2046594  male  male
## 6     7M  41.6730          14.3    26.2 19.9 2.381759 1.1407836  male  male
##   tissue  conc_wt
## 1  brain 2.815398
## 2  brain 2.143670
## 3  brain 3.278901
## 4  brain 2.783952
## 5  brain 2.489524
## 6  brain 2.914196
```

Plotting the regression

```r
pgp_plot <- ggplot(regression, aes(pgp, conc_wt)) +
  geom_point(col="black") +
  geom_smooth(method = "lm", se = T, aes(fill=tissue, col=tissue)) +
  xlim(0,5) +
  theme_bw(12) +
  ylab("[Morphine] per mg tissue (ng/mg)") +
  scale_fill_manual(values=c("dodgerblue", "goldenrod1"),
                    labels=c("retina" = "Retina", "brain" = "Brain")) +
  scale_color_manual(values=c("dodgerblue", "goldenrod1"),
                    labels=c("retina" = "Retina", "brain" = "Brain"))

bcrp_plot <- ggplot(regression, aes(bcrp, conc_wt)) +
  geom_point(col="black") +
  geom_smooth(method = "lm", se = T, aes(fill=tissue, col=tissue)) +
  xlim(0,5) +
  ylab("") +
  theme_bw(12) %+replace%
  theme(axis.text.y=element_blank()) +
  scale_fill_manual(values=c("dodgerblue", "goldenrod1"),
                    labels=c("retina" = "Retina", "brain" = "Brain")) +
  scale_color_manual(values=c("dodgerblue", "goldenrod1"),
                    labels=c("retina" = "Retina", "brain" = "Brain"))

combined_correlation_plots <- ggarrange(pgp_plot, bcrp_plot, ncol=2, common.legend = TRUE, legend="botto
```

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

```r
combined_correlation_plots
```
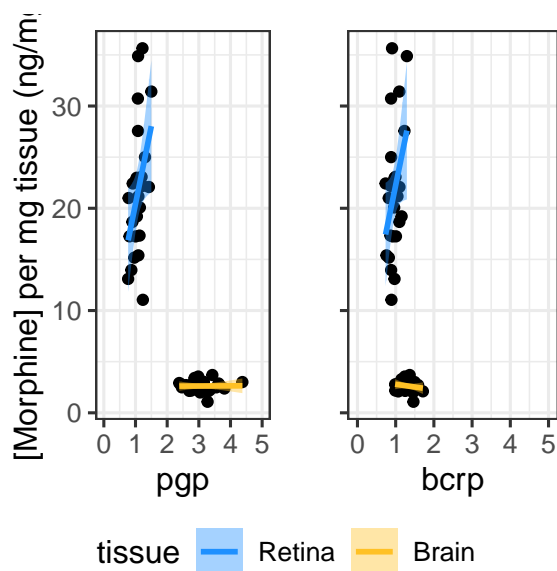
```r
#ggsave("../figures/combined_correlation_plots.png", plot=combined_correlation_plots, width=7, height=4,
#ggsave("../figures/combined_correlation_plots.svg", plot=combined_correlation_plots, width=7, height=4,
```

Statistical Analysis

P-gp in the brain

```r
regression_brain <- subset(regression, tissue == "brain")
head(regression_brain)
```

```
##   animal raw_conc tissue_weight body_wt dose      pgp      bcrp stage group
## 1     1M  56.5895          20.1    27.2 20.6 2.429027 1.0366970  male  male
## 2     2M  22.0798          10.3    30.1 18.6 2.699340 1.2487060  male  male
## 3     4M  49.5114          15.1    25.8 21.7 2.923597 1.1505545  male  male
## 4     5M  87.4161          31.4    26.1 20.0 2.770560 0.9860451  male  male
## 5     6M  36.5960          14.7    27.3 19.1 2.464103 1.2046594  male  male
## 6     7M  41.6730          14.3    26.2 19.9 2.381759 1.1407836  male  male
##   tissue  conc_wt
## 1  brain 2.815398
## 2  brain 2.143670
## 3  brain 3.278901
## 4  brain 2.783952
## 5  brain 2.489524
## 6  brain 2.914196
```
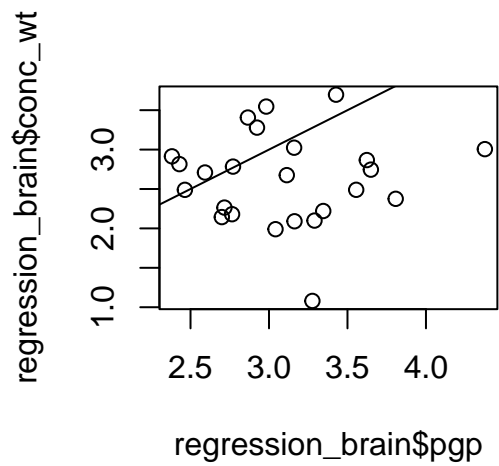
```r
shapiro.test(regression_brain$conc_wt)
```

```
##
##  Shapiro-Wilk normality test
##
## data:  regression_brain$conc_wt
## W = 0.9661, p-value = 0.5723
```
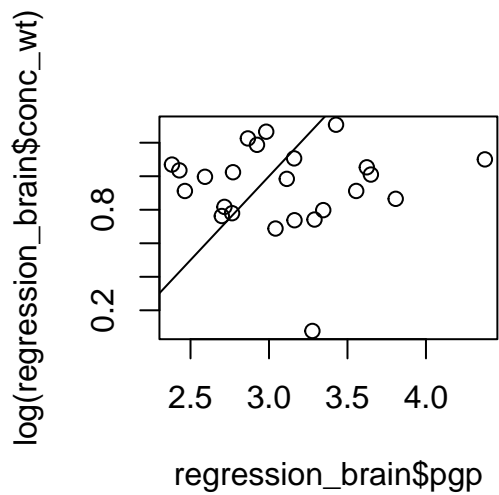
```r
shapiro.test(regression_brain$pgp)
```

```
##
##  Shapiro-Wilk normality test
##
## data:  regression_brain$pgp
## W = 0.96357, p-value = 0.5143
```
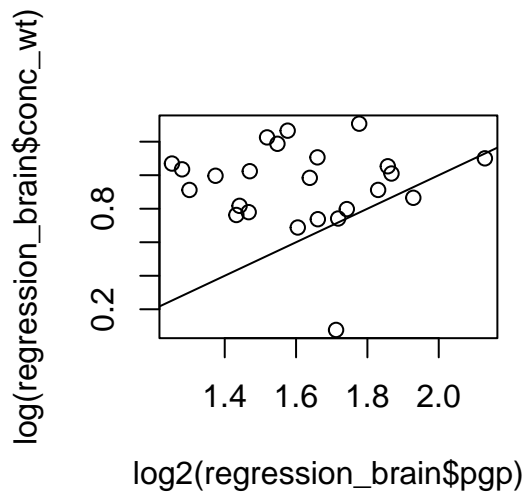
```r
plot(regression_brain$pgp, regression_brain$conc_wt)
abline(0,1)
```

```
plot(regression_brain$pgp, log(regression_brain$conc_wt))
abline(-2,1)
```



```
plot(log2(regression_brain$pgp), log(regression_brain$conc_wt))
abline(-1,1)
```

```r
cor.test(regression_brain$pgp, regression_brain$conc_wt, method = "pearson")
```

```
##
##  Pearson's product-moment correlation
##
## data:  regression_brain$pgp and regression_brain$conc_wt
## t = 0.05577, df = 22, p-value = 0.956
## alternative hypothesis: true correlation is not equal to 0
## 95 percent confidence interval:
##  -0.3933942  0.4133038
## sample estimates:
##        cor
## 0.01188931
```

```r
cor.test(regression_brain$pgp, regression_brain$conc_wt, method = "spearman")
```

```
##
##  Spearman's rank correlation rho
##
## data:  regression_brain$pgp and regression_brain$conc_wt
## S = 2306, p-value = 0.9919
## alternative hypothesis: true rho is not equal to 0
## sample estimates:
##          rho
## -0.002608696
```
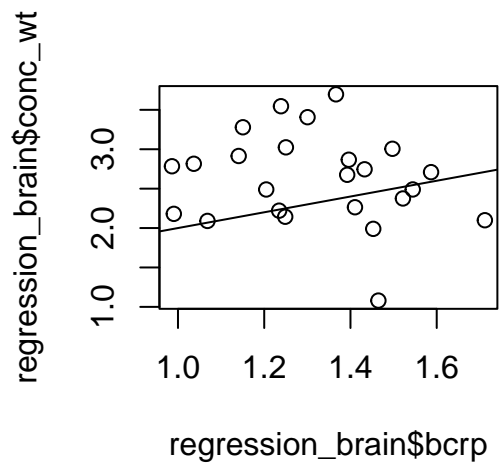
Bcrp in the brain

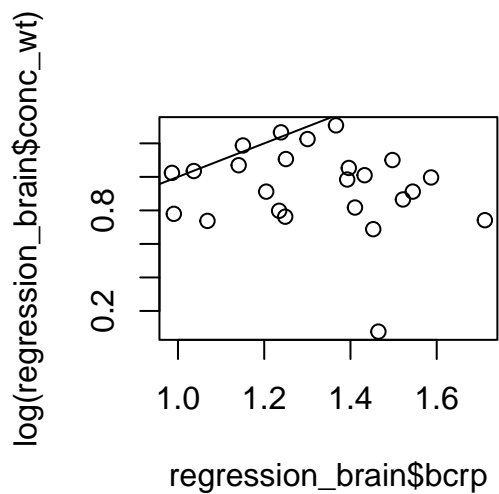```r
shapiro.test(regression_brain$bcrp)
```

```
##
##  Shapiro-Wilk normality test
```

```
## 
## data:  regression_brain$bcrp
## W = 0.9744, p-value = 0.7749
```
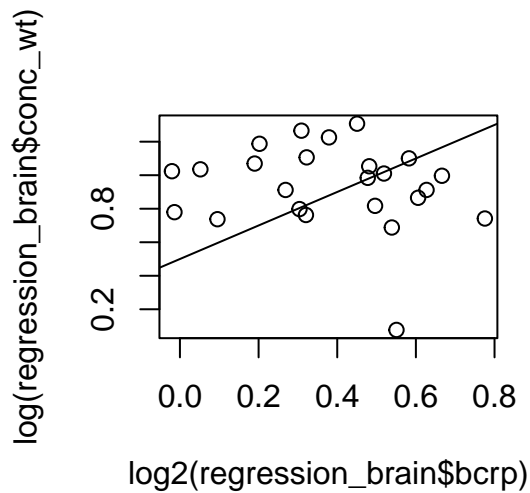
```
plot(regression_brain$bcrp, regression_brain$conc_wt)
abline(1,1)
```



```
plot(regression_brain$bcrp, log(regression_brain$conc_wt))
abline(0,1)
```



```
plot(log2(regression_brain$bcrp), log(regression_brain$conc_wt))
abline(0.5,1)
```

```r
cor.test(regression_brain$bcrp, regression_brain$conc_wt, method = "pearson")
```

```
##
##  Pearson's product-moment correlation
##
## data:  regression_brain$bcrp and regression_brain$conc_wt
## t = -0.86512, df = 22, p-value = 0.3963
## alternative hypothesis: true correlation is not equal to 0
## 95 percent confidence interval:
##  -0.5449099  0.2395396
## sample estimates:
##        cor
## -0.1813841
```

```r
cor.test(regression_brain$bcrp, regression_brain$conc_wt, method = "spearman")
```

```
##
##  Spearman's rank correlation rho
##
## data:  regression_brain$bcrp and regression_brain$conc_wt
## S = 2736, p-value = 0.3733
## alternative hypothesis: true rho is not equal to 0
## sample estimates:
##        rho
## -0.1895652
```

P-gp in the retina

```r
regression_retina <- subset(regression, tissue == "retina")
head(regression_retina)
```

```
##    animal raw_conc tissue_weight body_wt  dose       pgp      bcrp stage group
```

```
## 25       1M 104.7333          3.8     27.2 20.55 1.0782765 1.2298197  male  male
## 26       2M  86.2347          5.0     30.1 18.57 1.0045893 0.9196512  male  male
## 27       4M  88.3202          4.0     25.8 21.67 1.4228127 1.0984593  male  male
## 28       5M  99.2028          4.3     26.1 20.00 1.1925447 0.9961628  male  male
## 29       6M  97.7141          7.0     27.3 19.12 0.8683951 0.8810145  male  male
## 30       7M  99.8877          5.2     26.2 19.92 1.0440075 1.1553400  male  male
##     tissue  conc_wt
## 25 retina 27.56139
## 26 retina 17.24694
## 27 retina 22.08005
## 28 retina 23.07042
## 29 retina 13.95916
## 30 retina 19.20917
```
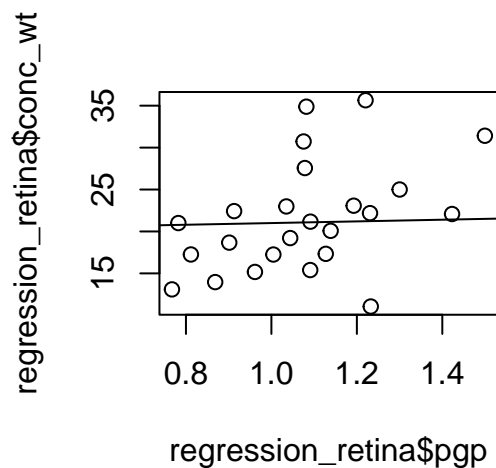
```
shapiro.test(regression_retina$conc_wt)
```

```
##
##  Shapiro-Wilk normality test
##
## data:  regression_retina$conc_wt
## W = 0.94676, p-value = 0.2303
```

```
shapiro.test(regression_retina$pgp)
```

```
##
##  Shapiro-Wilk normality test
##
## data:  regression_retina$pgp
## W = 0.973, p-value = 0.7409
```

```
plot(regression_retina$pgp, regression_retina$conc_wt)
abline(20,1)
```
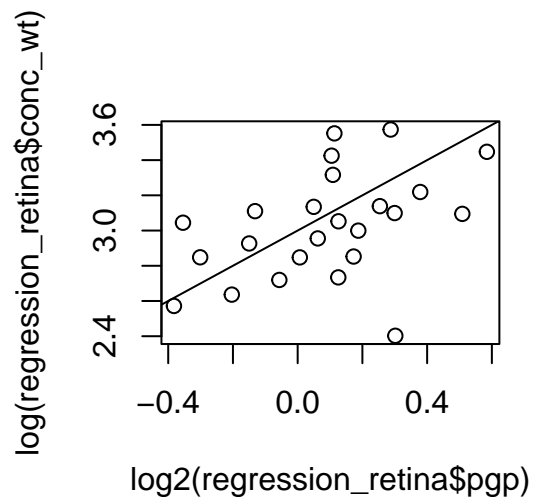
```
plot(regression_retina$pgp, log(regression_retina$conc_wt))
abline(2,1)
```



```
plot(log2(regression_retina$pgp), log(regression_retina$conc_wt))
abline(3,1)
```



```
cor.test(regression_retina$pgp, regression_retina$conc_wt, method = "pearson")
```
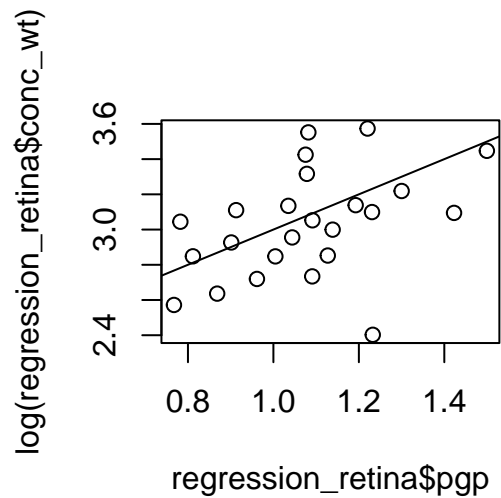
```
##
##  Pearson's product-moment correlation
##
## data:  regression_retina$pgp and regression_retina$conc_wt
## t = 2.2598, df = 22, p-value = 0.03408
## alternative hypothesis: true correlation is not equal to 0
```

```
## 95 percent confidence interval:
##  0.03714565 0.71265643
## sample estimates:
##       cor
## 0.4340385
```

```
cor.test(regression_retina$pgp, regression_retina$conc_wt, method = "spearman")
```

```
##
##  Spearman's rank correlation rho
##
## data:  regression_retina$pgp and regression_retina$conc_wt
## S = 1304, p-value = 0.03568
## alternative hypothesis: true rho is not equal to 0
## sample estimates:
##       rho
## 0.4330435
```

Bcrp in the retina

```
shapiro.test(regression_retina$bcrp)
```

```
##
##  Shapiro-Wilk normality test
##
## data:  regression_retina$bcrp
## W = 0.9579, p-value = 0.3978
```
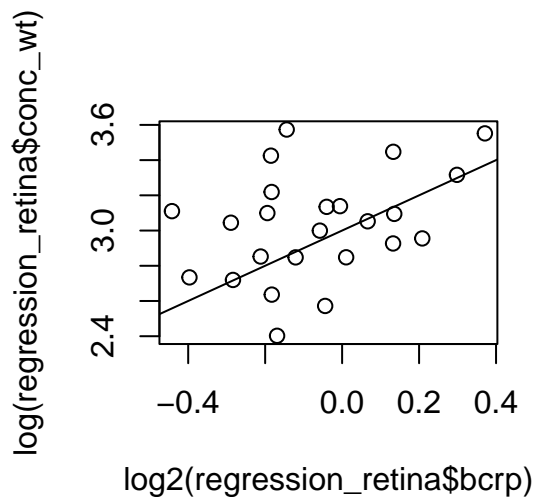
```
plot(regression_retina$bcrp, regression_retina$conc_wt)
abline(20,1)
```
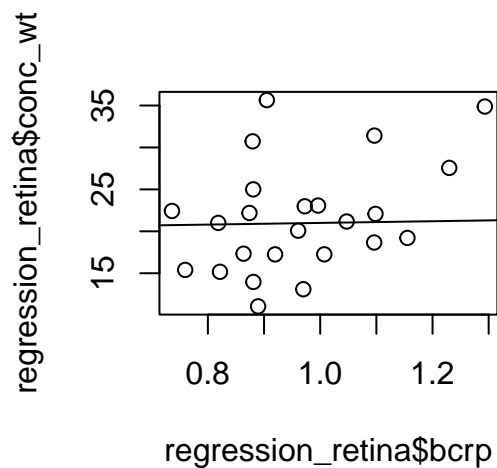
```
plot(regression_retina$bcrp, log(regression_retina$conc_wt))
abline(2,1)
```



```
plot(log2(regression_retina$bcrp), log(regression_retina$conc_wt))
abline(3,1)
```



```
cor.test(regression_retina$bcrp, regression_retina$conc_wt, method = "pearson")
```
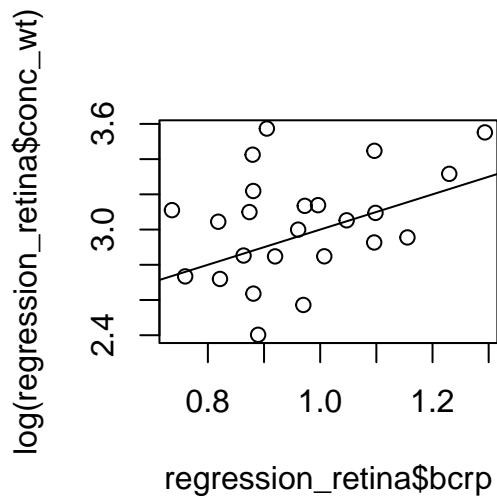
```
##
##  Pearson's product-moment correlation
##
## data:  regression_retina$bcrp and regression_retina$conc_wt
## t = 2.0013, df = 22, p-value = 0.05785
## alternative hypothesis: true correlation is not equal to 0
```
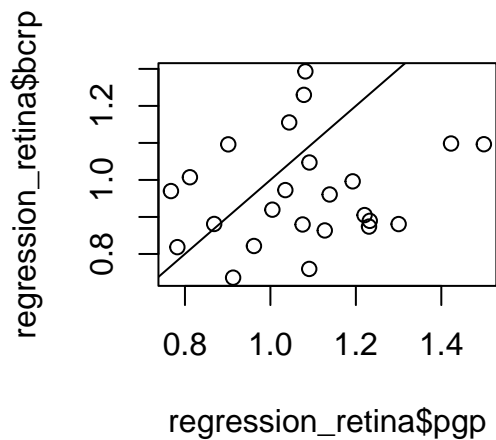
```
## 95 percent confidence interval:
##  -0.01300906   0.68707216
## sample estimates:
##       cor
## 0.3924471
```

```
cor.test(regression_retina$bcrp, regression_retina$conc_wt, method = "spearman")
```
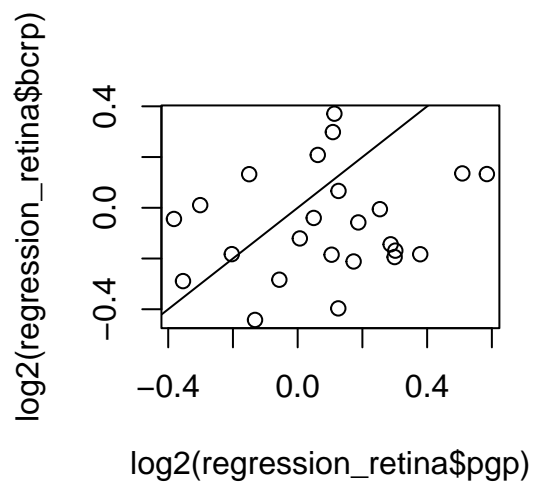
```
##
##   Spearman's rank correlation rho
##
## data:  regression_retina$bcrp and regression_retina$conc_wt
## S = 1632, p-value = 0.1682
## alternative hypothesis: true rho is not equal to 0
## sample estimates:
##       rho
## 0.2904348
```
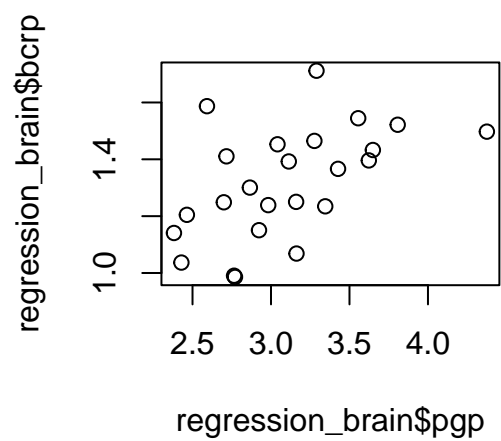
P-gp vs Bcrp

```
plot(regression_retina$pgp, regression_retina$bcrp)
abline(0,1)
```
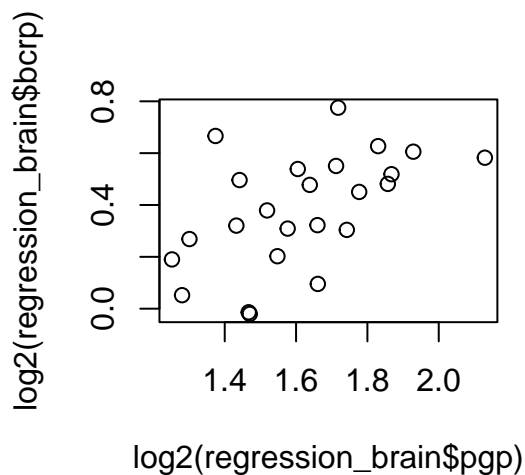


```
plot(log2(regression_retina$pgp), log2(regression_retina$bcrp))
abline(0,1)
```

```
plot(regression_brain$pgp, regression_brain$bcrp)
abline(0,1)
```



```
plot(log2(regression_brain$pgp), log2(regression_brain$bcrp))
abline(0,1)
```

```
cor.test(regression_retina$pgp, regression_retina$bcrp, method = "pearson")
```

```
##
##  Pearson's product-moment correlation
##
## data:  regression_retina$pgp and regression_retina$bcrp
## t = 0.95938, df = 22, p-value = 0.3478
## alternative hypothesis: true correlation is not equal to 0
## 95 percent confidence interval:
##  -0.2208580  0.5586306
## sample estimates:
##       cor
## 0.2003923
```

```
cor.test(regression_retina$pgp, regression_retina$bcrp, method = "spearman")
```

```
##
##  Spearman's rank correlation rho
##
## data:  regression_retina$pgp and regression_retina$bcrp
## S = 1966, p-value = 0.4967
## alternative hypothesis: true rho is not equal to 0
## sample estimates:
##       rho
## 0.1452174
```

```
cor.test(regression_brain$pgp, regression_brain$bcrp, method = "pearson")
```

```
##
##  Pearson's product-moment correlation
##
## data:  regression_brain$pgp and regression_brain$bcrp
## t = 2.9218, df = 22, p-value = 0.0079
```

```
## alternative hypothesis: true correlation is not equal to 0
## 95 percent confidence interval:
##  0.1593194 0.7682678
## sample estimates:
##       cor
## 0.5287349
```

```
cor.test(regression_brain$pgp, regression_brain$bcrp, method = "spearman")
```

```
##
##  Spearman's rank correlation rho
##
## data:  regression_brain$pgp and regression_brain$bcrp
## S = 1068, p-value = 0.007797
## alternative hypothesis: true rho is not equal to 0
## sample estimates:
##       rho
## 0.5356522
```

```
gene_plot <- ggplot(regression, aes(pgp, bcrp, col=tissue)) +
  geom_point() +
  geom_smooth(method = "lm", se = T) +
  xlim(0,5) +
  ylim(0.5,2) +
  theme_bw()

gene_plot
```

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