Adjusted Neutrophil Count (ANC) single marker association in PGRNseq data

Here we run a set of single marker tests on the raw phenotype. You can see its distribution in the phenotype processing report. We look at three models: simple regression on genotype on phenotype in european samples only; multiple regression of genotype + covariates in european samples only; and multiple regression of genotype on phenotype + covariates + pricipal components in ALL available samples.

In addition to summarizing the scan in a QQ plot, we happened to have captured a previously associated variant. I report the estimated effect and p-value of the variant for each model.

Known association signal

The following was pulled from the 1000 Genomes browser. UGT1A1*93: rs10929302
hg19 chr2:234,665,782 G/A
1000 Genomes allele frequencies:
A: 27%
G: 73%

The known association was referenced in PharmGKB.

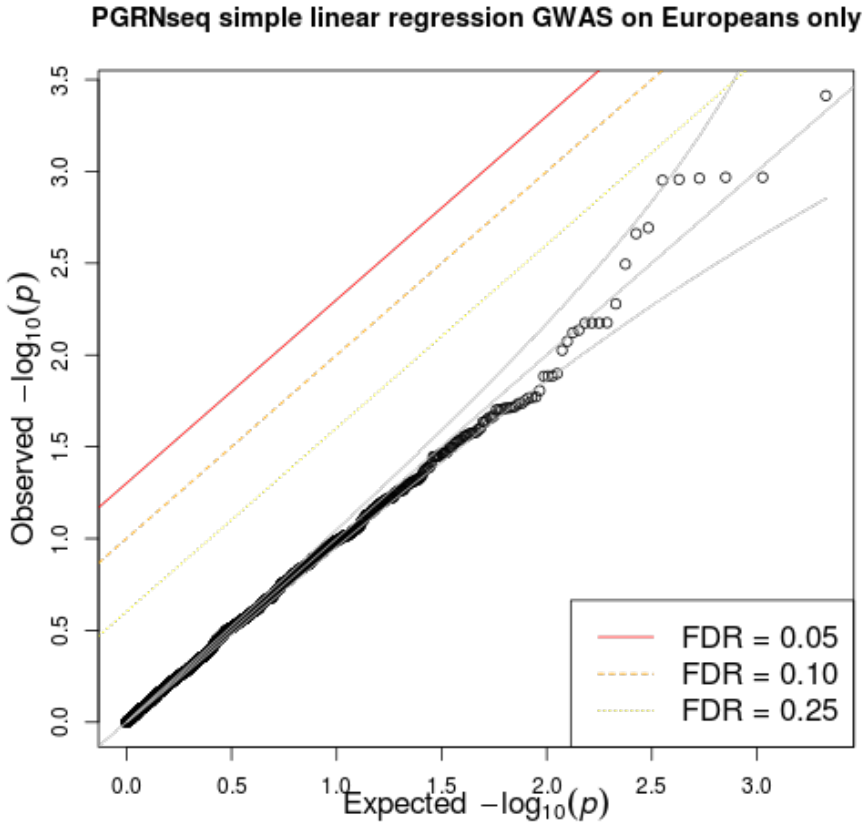
Genetic europeans

These samples were selected based on clustering analysis performed on the top two PCs of the exome chip data. This is a subset consisting of 168 samples. The subsetting is performed to remove any confouding of genetric ancestry, but ultimately may be too conservative for our sample size.

Simple regression

Regress phenotype on genotype.

```
seq.simplereg.results <- mlreg(basic.model, euro.seq.geno, trait="gaussian")
qqunif(seq.simplereg.results[,"P1df"])
title('PGRNseq simple linear regression GWAS on Europeans only')
```



Look at the association results of the previously observed signal:

```
rs10929302.res <- results(seq.simplereg.results)['chr2:234665782:G:A', c('A1', 'A2','N', 'ef
print(xtable(rs10929302.res, digits=6), include.rownames=FALSE)
```

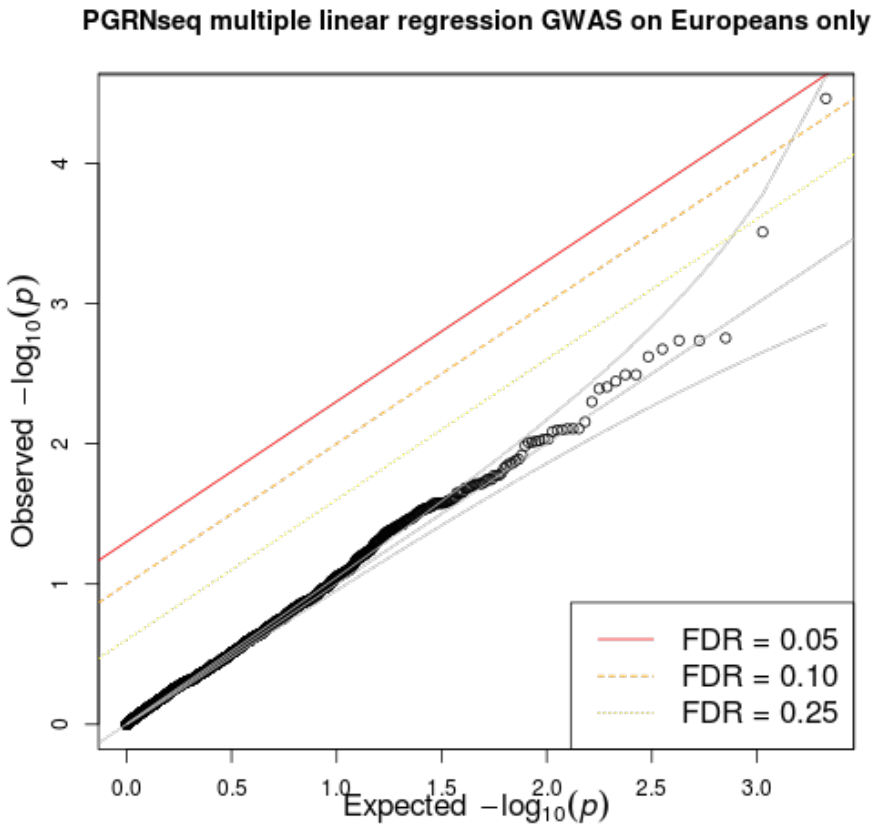
% latex table generated in R 3.1.1 by xtable 1.7-3 package % Wed Aug 27 11:20:41 2014

A1	A2	N	effB	se_effB	P1df
T	G	168.000000	-0.287127	0.175614	0.102051

Multiple regression

Regress phenotype on genotype and other sample covariates.

```
seq.multiplereg.results <- mlreg(full.model, euro.seq.geno, trait="gaussian")
qqunif(seq.multiplereg.results[,"P1df"])
title('PGRNseq multiple linear regression GWAS on Europeans only')
```



Look at the association results of the previously observed signal:

```
rs10929302.res <- results(seq.multiplereg.results)['chr2:234665782:G:A', c('A1', 'A2','N', '
print(xtable(rs10929302.res, digits=6), include.rownames=FALSE)
```

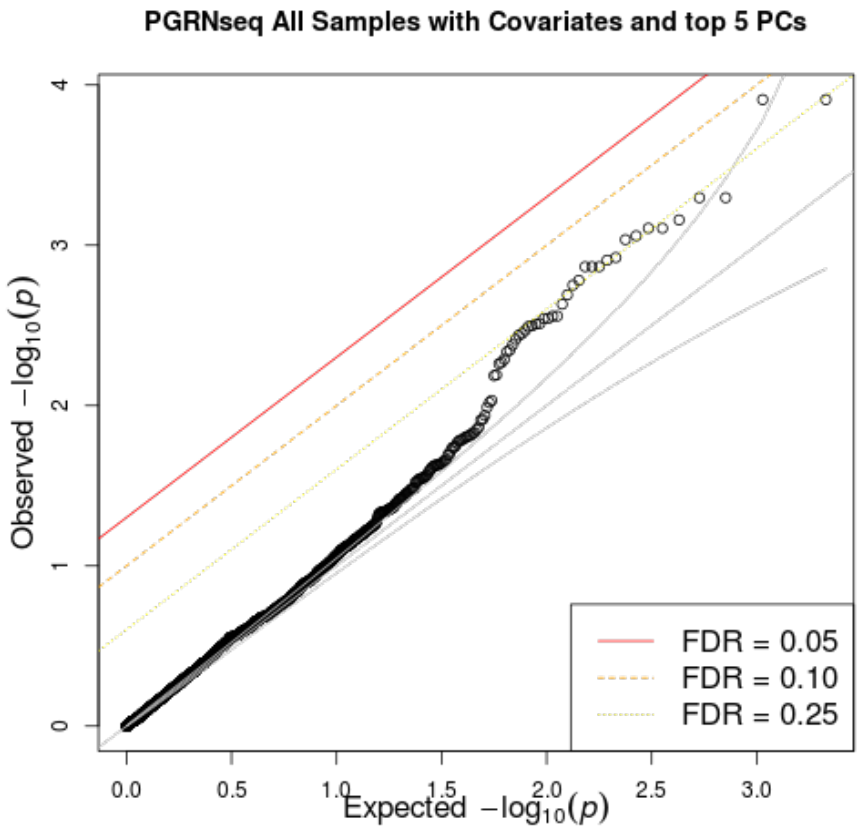
% latex table generated in R 3.1.1 by xtable 1.7-3 package % Wed Aug 27 11:20:41 2014

A1	A2	N	effB	se_effB	P1df
T	G	155.000000	-0.337503	0.180681	0.061769

Full Data with PC adjustment

Regress phenotype on genotype, sample covariates, and top five PCs using *all* samples.

```
seq.pcareg.results <- mlreg(pca.model, full.seq.geno, trait="gaussian")
qqunif(seq.pcareg.results[,"P1df"])
title('PGRNseq All Samples with Covariates and top 5 PCs')
```



Look at the association results of the previously observed signal:

```
rs10929302.res <- results(seq.pcareg.results)['chr2:234665782:G:A', c('A1', 'A2','N', 'effB
print(xtable(rs10929302.res, digits=6), include.rownames=FALSE)
```

% latex table generated in R 3.1.1 by xtable 1.7-3 package % Wed Aug 27 11:20:41 2014

A1	A2	N	effB	se_effB	P1df
T	G	206.000000	-0.398147	0.153057	0.009287