

fQTLs btwn 23 phenotypes & 1452 individuals (5,312,628 variants)

Overall Scheme

Step 1: Run a nominal pass (ie, calculate QTLs in the usual way prior to FDR correction)

```
Ex6 chr1 1 1:5016315 chr1 5016315 9.80619e-06 -1 0.115741
Ex8 chr1 1 1:5016315 chr1 5016315 9.35944e-06 -1 0.116003
Ex6 chr1 1 1:5018078 chr1 5018078 7.61258e-06 -1 0.117155
Ex4 chr1 1 1:5030204 chr1 5030204 1.8558e-07 -1 -0.13629
Ex6 chr1 1 1:5030204 chr1 5030204 9.26592e-09 -1 0.150007
Ex8 chr1 1 1:5030204 chr1 5030204 1.8623e-06 -1 0.124741
In1 chr1 1 1:5030204 chr1 5030204 7.69179e-07 -1 0.129287
```

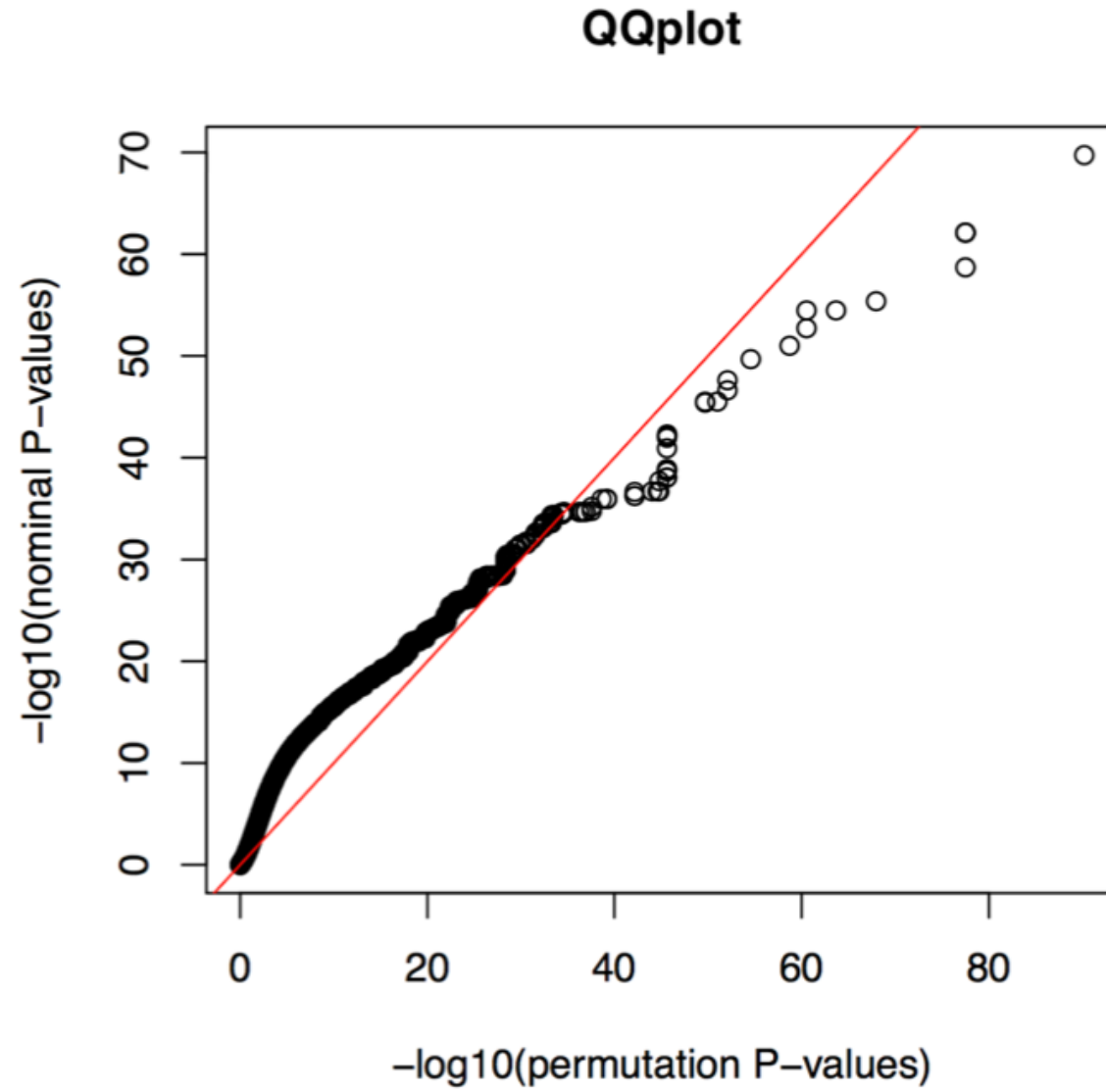
1. Phenotype ID
2. Phenotype chrID
3. Phenotype start
4. Variant ID
5. Variant chrID
6. Variant position
7. Nominal P-value of association
8. Dummy variable.
9. Regression slope

Step 2: Run a permutation pass: Randomly permute the phenotypes to generate a null

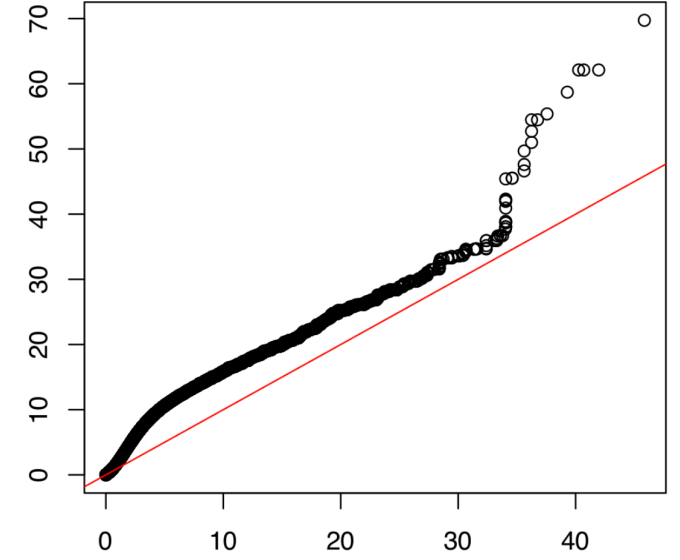
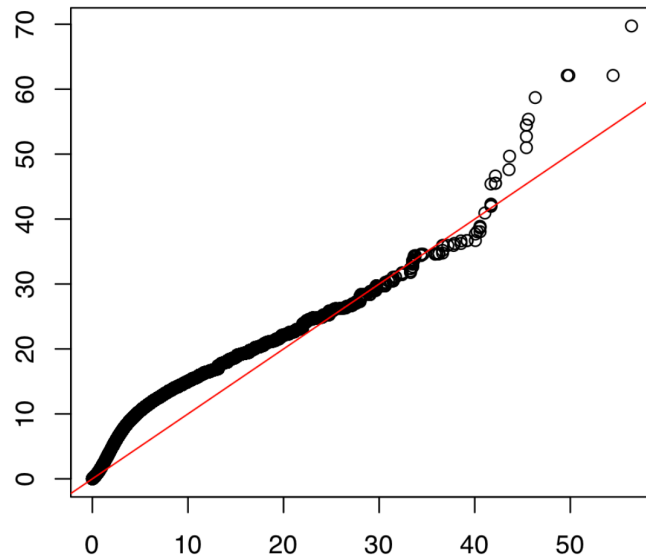
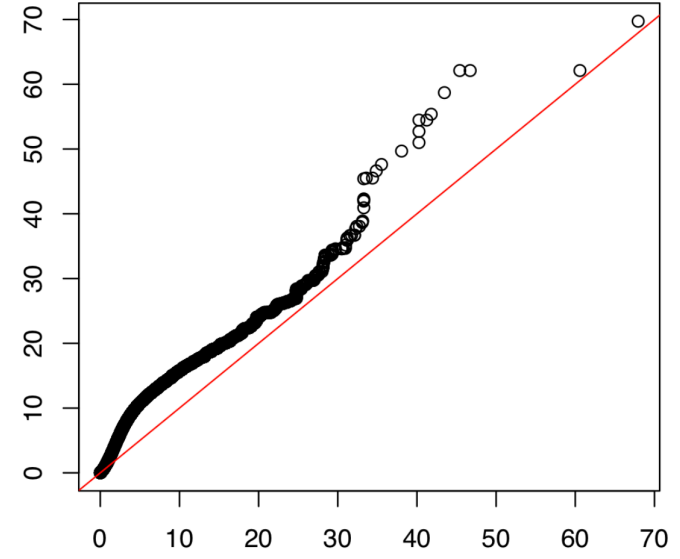
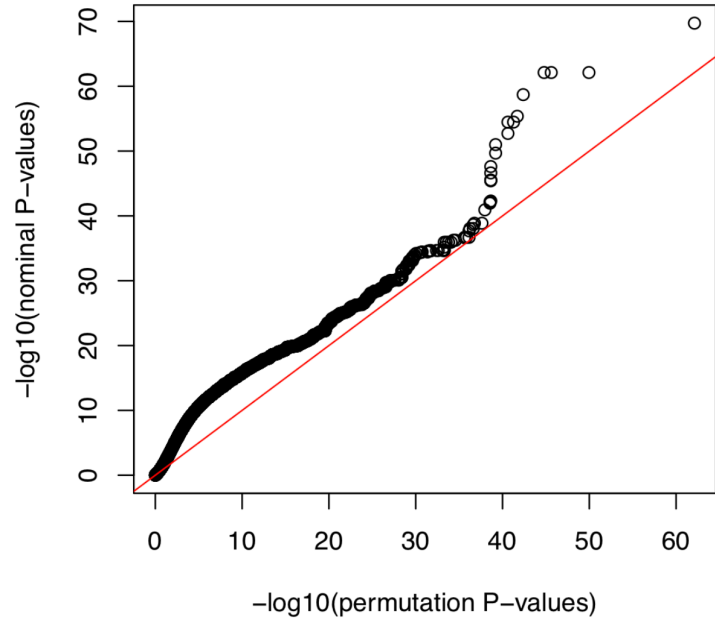
Step 3: Controlling for multiple tests

- a) Generate QQ-plots using results from steps 1 & 2
- b) Use null (from step 2) to calculate FDR for each hit (from step 1)

~75% of QQ-plots look something like this



The remaining ~25% look somewhat better



At an FDR threshold of 0.05: highly variable # of fQTLs

<u>Trial</u>	<u># fQTLs</u>	<u>Trial</u>	<u># fQTLs</u>
FDR_output__14	1003671	FDR_output__8	6
FDR_output__23	953462	FDR_output__7	5
FDR_output__22	868973	FDR_output__9	5
FDR_output__13	866959	FDR_output__29	4
FDR_output__15	835007	FDR_output__37	4
FDR_output__2	830536	FDR_output__10	1
FDR_output__38	826641	FDR_output__21	1
FDR_output__34	808353	FDR_output__25	1
FDR_output__3	753872	FDR_output__11	0
FDR_output__27	722160	FDR_output__12	0
FDR_output__4	558101	FDR_output__17	0
FDR_output__1	411041	FDR_output__20	0
FDR_output__40	404755	FDR_output__28	0
FDR_output__18	393712	FDR_output__31	0
FDR_output__16	336517	FDR_output__32	0
FDR_output__5	103139	FDR_output__33	0
FDR_output__30	4724	FDR_output__35	0
FDR_output__19	13	FDR_output__36	0
FDR_output__24	9	FDR_output__39	0
FDR_output__26	9	FDR_output__6	0

At an FDR threshold of 0.10: ~1.1 million fQTLs

<u>Trial</u>	<u># fQTLs</u>	<u>Trial</u>	<u># fQTLs</u>
FDR_output__14	1196619	FDR_output__10	1178477
FDR_output__22	1191315	FDR_output__28	1177358
FDR_output__19	1188837	FDR_output__30	1175743
FDR_output__23	1188750	FDR_output__5	1175208
FDR_output__24	1188160	FDR_output__1	1175185
FDR_output__2	1187958	FDR_output__34	1174937
FDR_output__8	1187167	FDR_output__4	1174025
FDR_output__40	1186425	FDR_output__18	1171878
FDR_output__38	1186362	FDR_output__17	1171806
FDR_output__29	1185222	FDR_output__36	1170617
FDR_output__6	1185148	FDR_output__32	1169875
FDR_output__3	1184579	FDR_output__7	1169552
FDR_output__16	1184492	FDR_output__11	1165768
FDR_output__15	1184242	FDR_output__39	1163507
FDR_output__27	1184194	FDR_output__37	1146362
FDR_output__21	1183893	FDR_output__12	1143036
FDR_output__26	1183497	FDR_output__9	1130112
FDR_output__13	1181776	FDR_output__35	1128885
FDR_output__20	1180633	FDR_output__25	1128155
FDR_output__31	1179714	FDR_output__33	1127898

Different cell types are associated w/very different numbers of fQTLs

FDR < 0.05

<i>Cell type</i>	<i>Mean # fQTLs (40 sim)</i>
Fetal-replicating	50466.625
Fetal-quiescent	45423.6
Ex6	32540.575
In5	26055.825
In3	25939.9
In4	22317.7
Ex8	16716.1
Ex7	11675.25
In1	11455.025
Ex4	8385.6
Microglia	3816.6
In8	3112.925
In2	2834.35
Ex2	2442.25
Astrocytes	1304.3
OPC	1165.725
Ex1	569.2
Oligodendrocytes	299.4
Ex3	257.35
Ex5	105.625
Endothelial	103.125
In6	54.975

FDR < 0.10

<i>Cell type</i>	<i>Mean # fQTLs (40 sim)</i>
Fetal-replicating	236793.65
Fetal-quiescent	201606.75
Ex6	150213.9
In5	115998.75
In3	110650.05
In4	96168.275
Ex8	68247.125
In1	51913.875
Ex7	50715.6
Ex4	27633.15
In2	14027.7
Microglia	11943.3
Ex2	11863.575
In8	11763.45
OPC	5078.025
Astrocytes	4158.7
Ex1	1796.875
Ex3	992.3
Oligodendrocytes	925
Endothelial	401.05
Ex5	374.075
In6	169

Most significant fQTLs for each of the 23 cell types (pre-FDR correction)

```
Ex1 -1 2.14854e-11
Ex2 -1 7.63141e-63
Ex3 -1 4.31922e-15
Ex4 -1 2.89105e-16
Ex5 -1 1.49832e-13
Ex6 -1 6.78487e-36
Ex7 -1 1.71476e-35
Ex8 -1 8.95144e-22
In1 -1 2.3385e-47
In2 -1 1.84706e-70
In3 -1 7.53105e-27
In4 -1 2.11122e-28
In5 -1 9.08316e-32
In6 -1 1.36646e-08
In7 -1 1
In8 -1 2.02036e-22
Astrocytes -1 4.59144e-20
Endothelial -1 2.62168e-16
Fetal-quiescent -1 1.22594e-26
Fetal-replicating -1 2.4596e-31
Microglia -1 7.89827e-13
OPC -1 1.09115e-42
Oligodendrocytes -1 4.54092e-09
```