

# Association Testing with X Chromosome Data

## An Application to the HCHS/SOL RBC Trait

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# Outline

Gene G6PD

Autosomal Model

Autosomal Results

MLM-X Model

MLM-X Results

## Xq28, gene G6PD

- ▶ There are known associations between red blood cell count (RBC) and X chromosome loci in the gene G6PD on Xq28.
- ▶ This finding was replicated in the SOL samples when performing association tests using a mixed linear model adjusting for autosomal effects.
- ▶ We tested the X chromosome SNPs using a mixed linear model specifically accounting for X chromosome effects, and again replicated the finding.

# Sample Set and Covariates<sup>1</sup>

We include all individuals with non-missing outcome and covariates, exclude Asian outliers identified with PCA and additionally exclude samples with

- ▶ blood/lymph malignant tumor
- ▶ bone cancer
- ▶ pregnancy
- ▶ chronic kidney disease
- ▶ chemotherapy
- ▶ % blasts >5
- ▶ % immature granulocytes >5

Fixed effect covariates included are sex, age, center, and autosomal ancestry eigenvectors 1-5.

We include random effects of block group, household and autosomal kinship.

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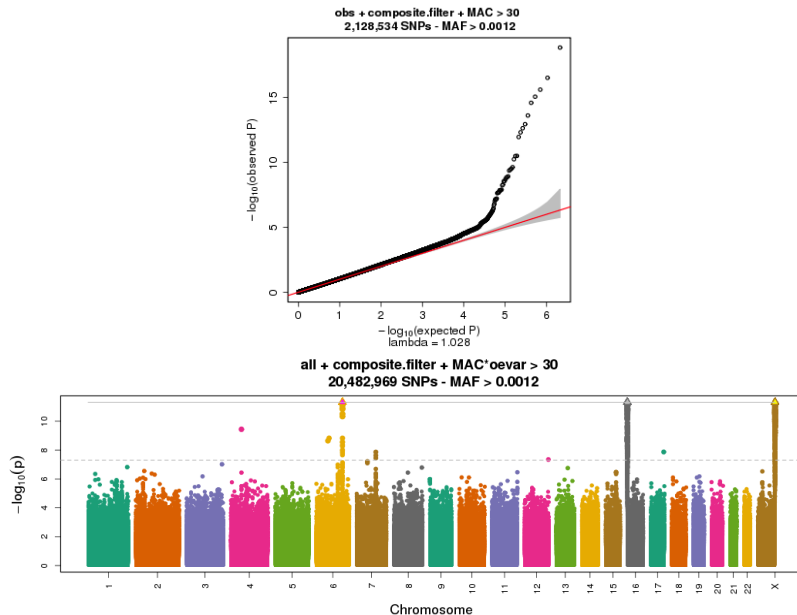
<sup>1</sup>these are as described in the working group previously

## Previous Variance Component Estimates, n=12,502

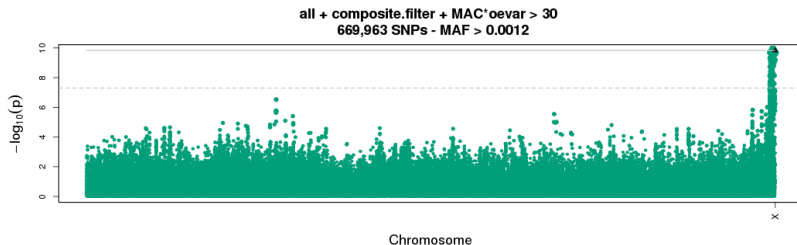
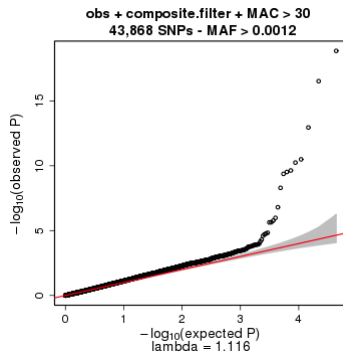
	estimate	95% CI
block group	0.00363	(-0.00177, 0.00903)
household	0.04945	(0.02113, 0.07777)
autosomal kinship	0.28473	(0.23215, 0.33732)
environment	0.66218	(0.60989, 0.71448)

**Table:** Estimate (95% CI) of the proportion variance for each of the components.

# Previous Genome-Wide Assoc Test Results, n=12,502



# Previous X Chr Assoc Test Results, n=12,502



## MLM-X Model

We include all individuals with non-missing outcome and covariates, exclude Asian outliers identified with PCA and additionally exclude samples with

- ▶ blood/lymph malignant tumor
- ▶ bone cancer
- ▶ pregnancy
- ▶ chronic kidney disease
- ▶ chemotherapy
- ▶ % blasts >5
- ▶ % immature granulocytes >5
- ▶ **an X chromosome anomaly**

Fixed effect covariates included are sex, age, center, autosomal ancestry eigenvectors 1-5, and **X chromosome ancestry eigenvectors 1-2**.

We include random effects of block group, household, autosomal kinship and **X chromosome kinship**.

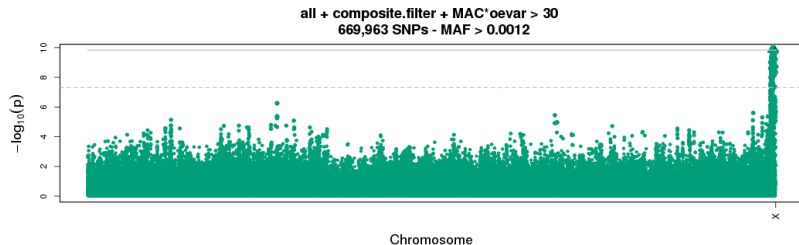
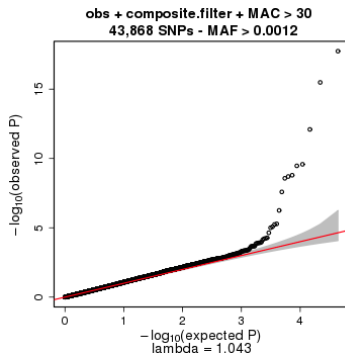


## MLM-X Variance Component Estimates, n=12,488

	MLM-X	Autosomal
block group	0.00396 (-0.0016, 0.0095)	0.00363 (-0.0018, 0.0090)
household	0.04950 (0.0209, 0.0781)	0.04945 (0.0211, 0.0778)
autosomal kinship	0.28453 (0.2316, 0.3375)	0.28473 (0.2322, 0.3373)
X kinship	0.02935 (0.0137, 0.0450)	
environment	0.63266 (0.5783, 0.6870)	0.66218 (0.6099, 0.7145)

**Table:** Estimate (95% CI) of the proportion variance for each of the components.

# MLM-X Assoc Test Results, n=12,488



## Index SNP rs1050828

	Effect Size (SE)	Stat	p-value
autosomal	0.1314 (0.0145)	81.9377	1.40447e-19
MLM-X	0.1300 (0.0148)	76.8729	1.82321e-18