

Genetic architecture of cross-tissue and tissue-specific gene expression

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Modeling cross-tissue expression

Linear mixed effect model

```
library(lme4)

fit <- lmer(expression ~ (1|SUBJID) + TISSUE
+ GENDER + PEERs)

#cross-tissue expression
fitranef <- ranef(fit)

#tissue-specific expression
fitresid <- resid(fit)
```

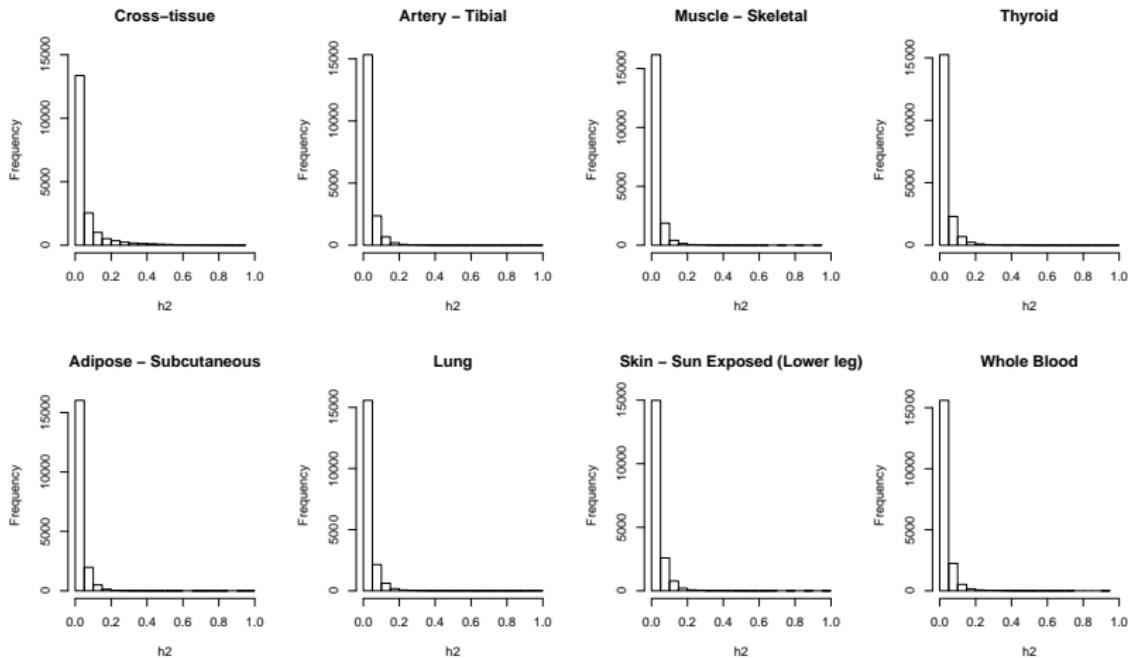
Estimating heritability with GCTA

Tested several genetic relationship matrix (GRM) models for each expressed gene

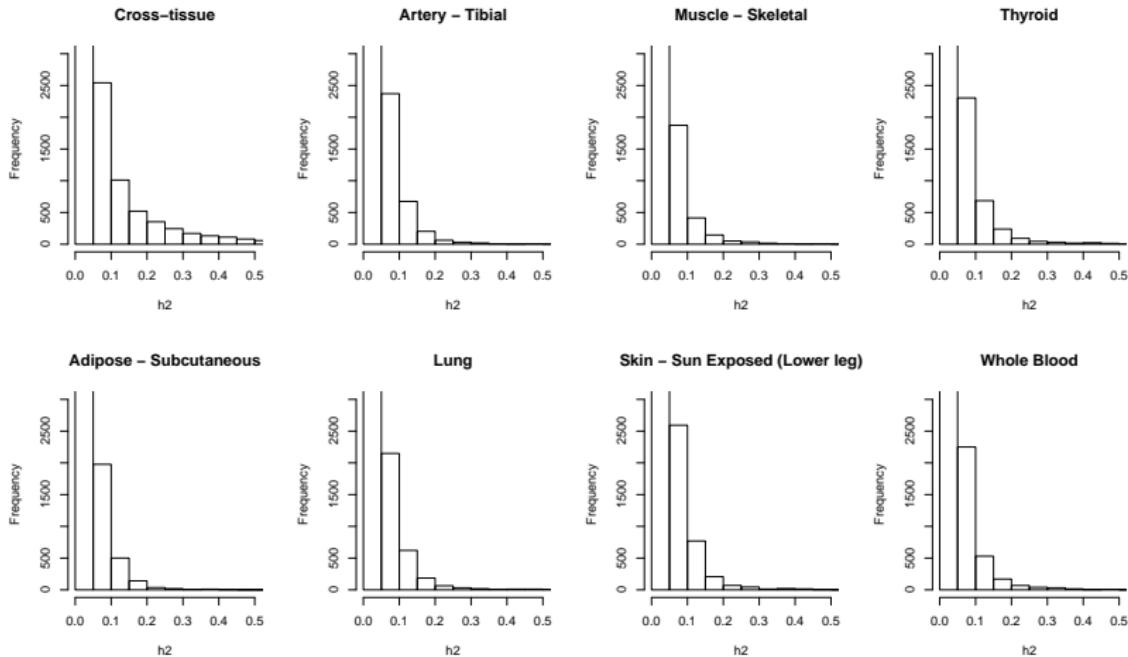
- ▶ localGRM (SNPs within 1 Mb of gene)
- ▶ localGRM + globalGRM (all SNPs)
- ▶ localGRM + chrGRM + globalGRM

First pass: estimated h^2 of cross-tissue expression and tissue-specific expression in the 7 tissues with the most samples

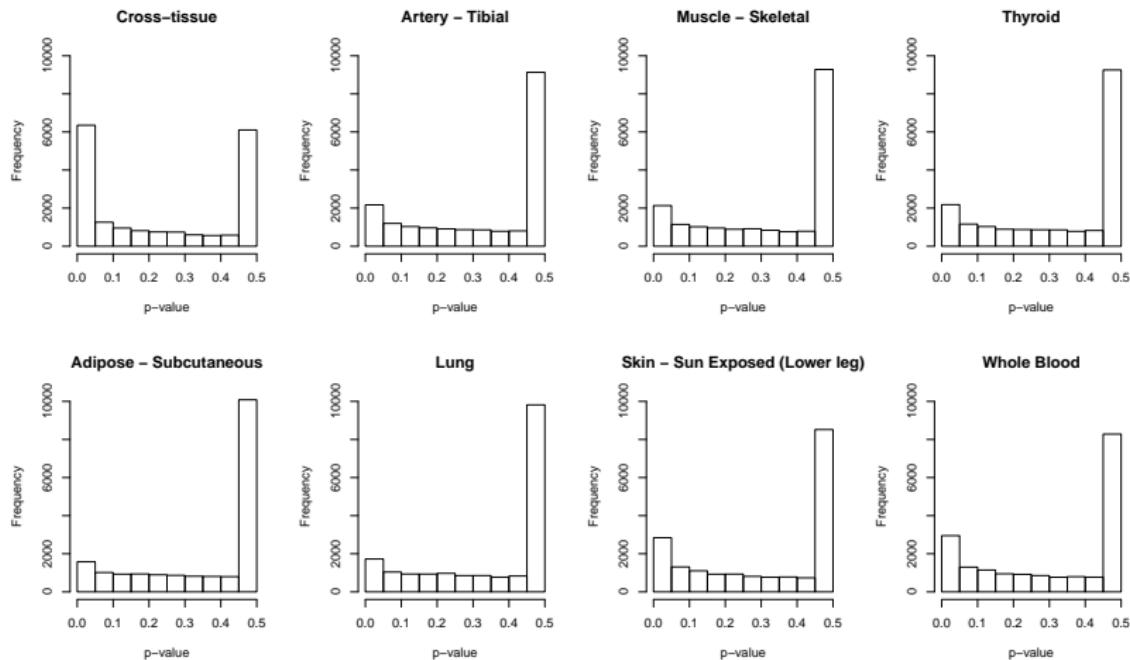
GCTA heritability: $Y \sim \text{localIGRM}$ h^2



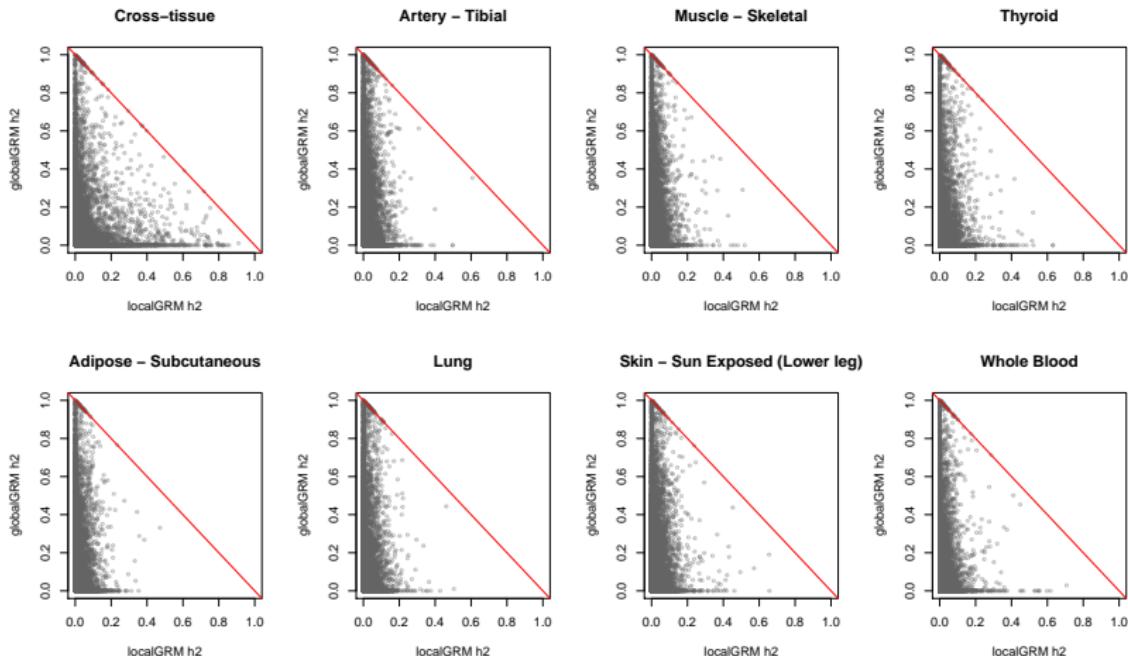
GCTA heritability: $Y \sim \text{localIGRM}$ h2 ZOOM



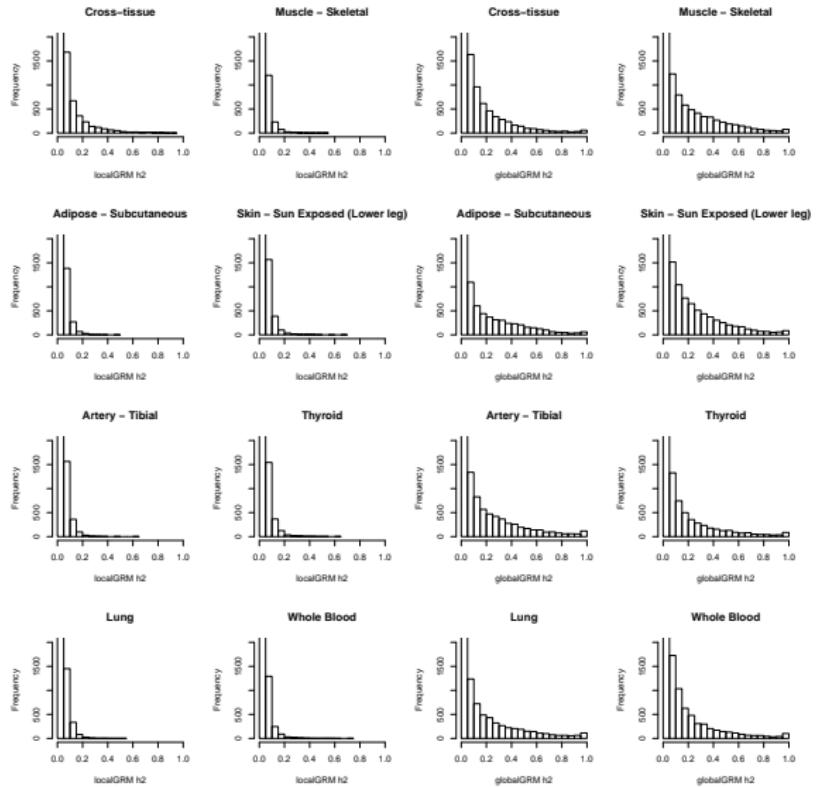
GCTA heritability: $Y \sim \text{localIGRM}$ p-values



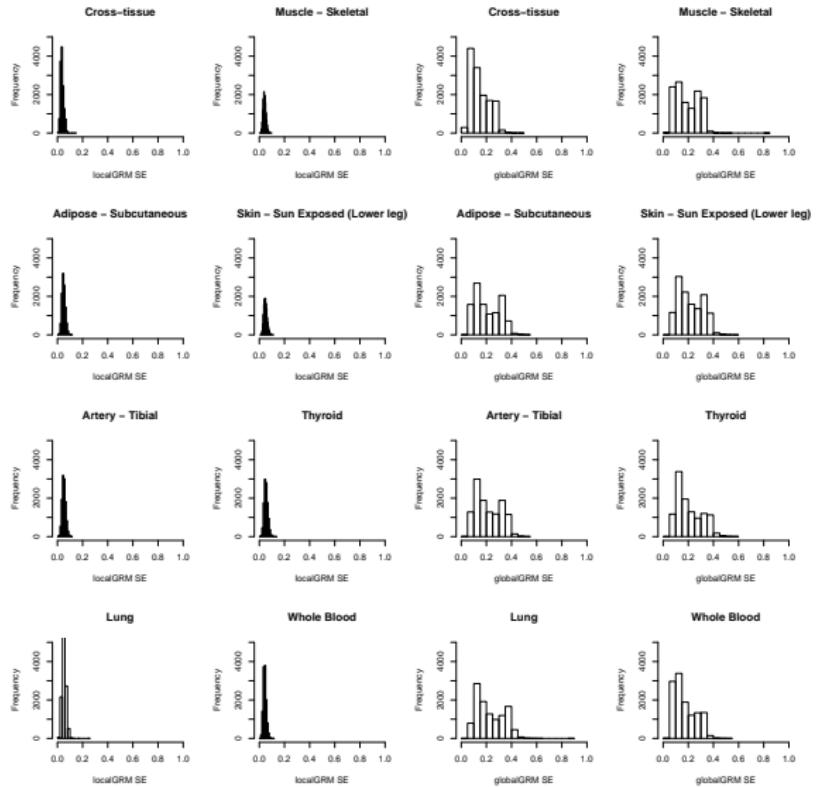
GCTA heritability: $Y \sim \text{localIGRM} + \text{globalIGRM}$ h^2



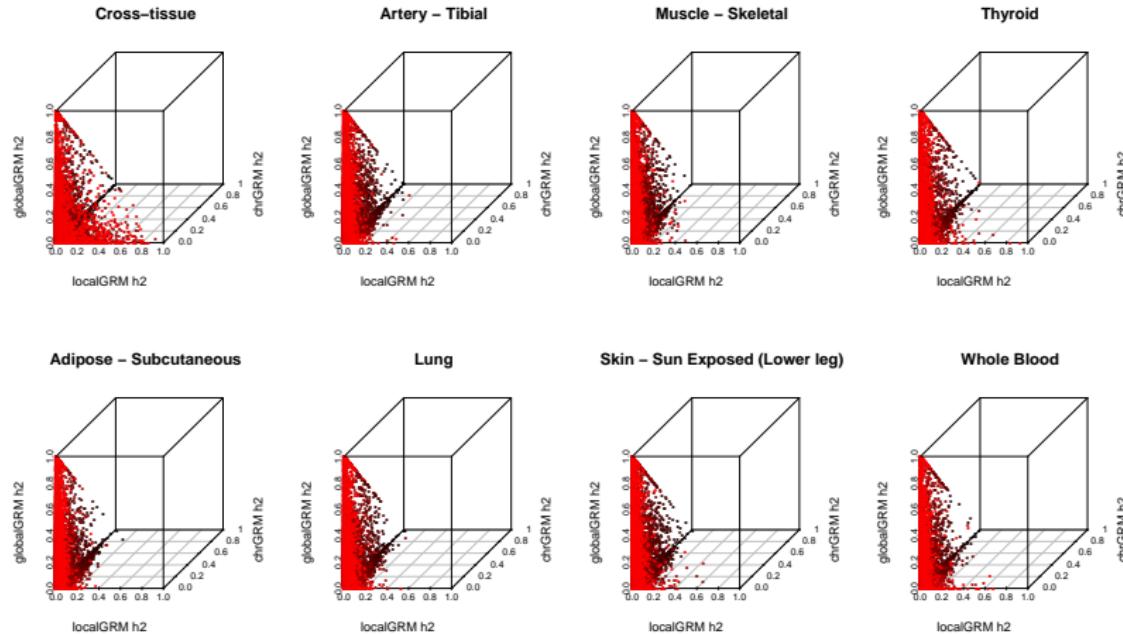
GCTA heritability: $Y \sim \text{localIGRM} + \text{globalIGRM}$ h²



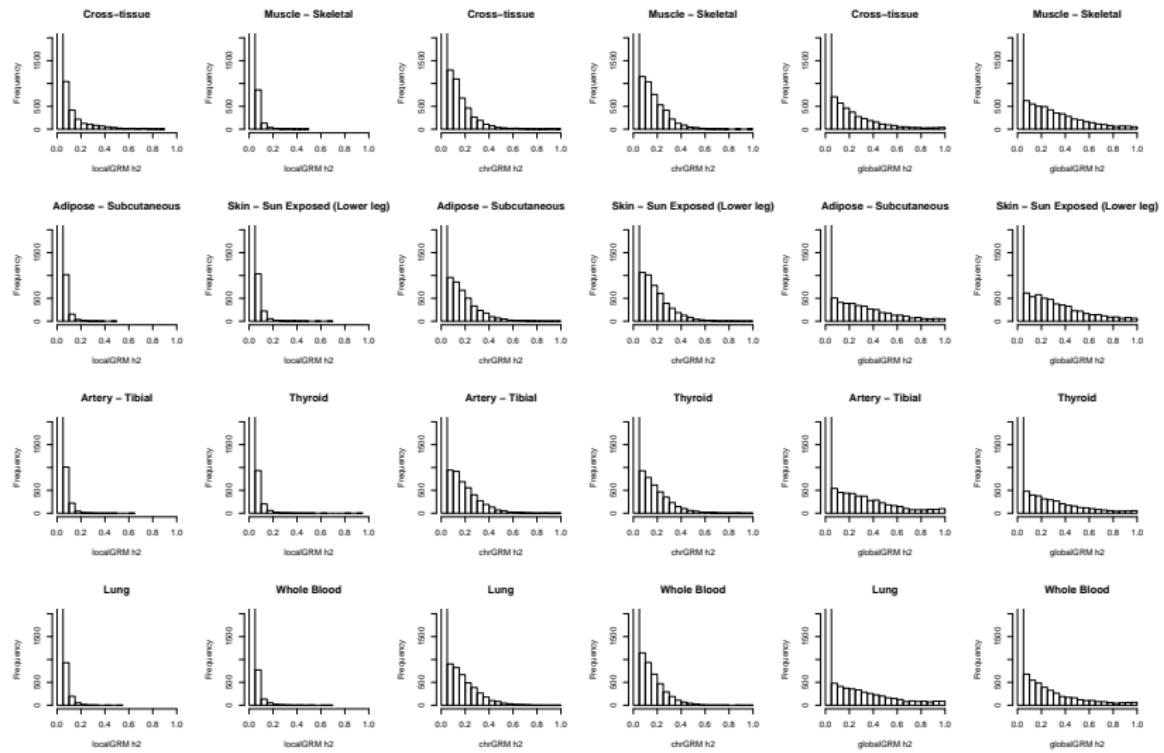
GCTA heritability: $Y \sim \text{localIGRM} + \text{globalIGRM SE}$



GCTA heritability: $Y \sim \text{localGRM} + \text{chrGRM} + \text{globalGRM}$ h^2



GCTA heritability: $Y \sim \text{localIGRM} + \text{chrGRM} + \text{globalGRM}$ h^2



GCTA heritability: $Y \sim \text{localIGRM} + \text{chrGRM} + \text{globalGRM SE}$

