Introduction

- Metabolomics twin and family studies report medium-to-high heritability (h²) estimates (e.g., Kettunen et al. 2012; Draisma et al. 2013; Shin et al. 2014).
- Metabolomics GWAS report associations with explained variances which can exceed 10% (Kastenmüller et al. 2015).
- Previously, Rhee et al. (2016) investigated the contribution of common & rare variants to overall SNP h².
- Aim: Estimate both narrow-sense & SNP h² for 4 metabolomics platforms measured in NTR blood samples.

Results

- Narrow-sense and SNP h² for each of the platforms in Fig.1-4.
- Comparison with Rhee et al. in Fig.5.
- 78/94 metabolites fall within C.I. of Rhee et al. estimates.

Methods & statistics

- Participants: selection of twins and family members of NTR participating in Biobank Project.
- Samples: fasting blood samples.
- MS Platforms: Biocrates [N~1,077; M~145] & Lipidomics [N~2,248; M~131].
- NMR platforms: LUMC [N~2,320; M~44] & Brainshake [N~2,890; M~226].
- Genetic data: 1,261,818 SNPs & N = 15,110 → no ethnic outliers, autosomes only, HWE > 1x10⁻⁶, MAF > 0.01.
- GRM: Down-weighting of high-LD SNPs in GRM construction (LDAK; Speed et al. 2012).
- Statistics: Simultaneous estimation of narrow-sense & SNP h² by including two GRMs in GCTA (Yang et al. 2010; Yang et al. 2011).
  1) full GRM with both closely & distantly related pairs of individuals
  2) ‘family’ GRM with values of distantly related pairs of individuals set to zero (Zaitlen et al. 2013).

Conclusions

- Narrow-sense heritability estimates similar to those obtained in classic twin-family studies of similar platforms.
- Direct comparison with previous SNP h² difficult as both studies are underpowered and use different platforms and GRMs.
- Congruent with Rhee et al. (2016), common SNPs alone are not underpowered and use different platforms and GRMs.
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- Aim: Estimate both narrow-sense & SNP h² for 4 metabolomics platforms measured in NTR blood samples.

**Genome-wide Heritability of Metabolomics-derived Blood Metabolites**

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