

## Questions on Kang et al (2010) *Nature Genetics* 42:348-354

Variance-component model to account for sample structure in genome-wide association studies.

1. Why is controlling for population structure and relatedness important in genomewide association studies?
2. How does the genomic control method account for population structure? What are its major advantages and short comings?
3. How does principal component analysis account for population structure? What are its major advantages and short comings?
4. What approach do the authors propose to account for population structure? How does their approach differ from previous suggestions?
5. What is the quantity that the authors describe as a “pseudo-heritability”?
6. In table 1, what is the message that the authors are trying to convey? Why are genomic control values so much higher for height than for other traits?
7. In Figure 5, what are the key messages that the authors are trying to convey?
8. The authors suggest that the model could be refined with additional variance components – for example, to account for genotyping platform differences. What sorts of additional variance components can you envisage?
9. What do you think some of the open questions that remain about how to model population structure in genetic association studies?