Genetic principles are universal

Construction of a Genetic Linkage Map in Man Using Restriction Fragment Length Polymorphisms

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Different genetics for different traits

Simple: Lactose tolerance, asparagus smell, photic sneeze
Complex: T2D, CVD
Same allele: CFTR, sickle cell
Different alleles: BRCA1, hypertrophic cardiomyopathy

Complex traits: height heritability is 80%

Sizing up human height variation

Peter M Visscher

Genome-wide association studies have identified many variants affecting susceptibility to disease. Now, three studies use this approach to study adult height variation in a combined sample size of ~63,000 individuals and report a total of 54 validated variants influencing this trait.

Genome-wide association analysis identifies 20 loci that influence adult height

Michael N Weedon[1,2,23], Hana Lango[1,2,23], Cecilia M Lindgren[3,4], Chris Wallace[5], David M Evans[6], Massimo Mangino[7], Rachel M Freathy[1,2], John R B Perry[1,2], Suzanne Stevens[7], Alistair S Hall[8], Nilesh J Samani[7], Beverly Shields[2], Inga Prokopenko[3,4], Martin Farrall[9], Anna Dominiczak[10], Diabetes Genetics Initiative[21], The Wellcome Trust Case Control Consortium[21], Toby Johnson[11–13], Sven Bergmann[11,12], Jacques S Beckmann[11,14], Peter Vollenweider[15], Dawn M Waterworth[16], Vincent Mooser[16], Colin N A Palmer[17], Andrew D Morris[18], Willem H Ouwehand[19,20], Cambridge GEM Consortium[22], Mark Caulfield[5], Patricia B Munroe[5], Andrew T Hattersley[1,2], Mark I McCarthy[3,4] & Timothy M Frayling[1,2]

Association analyses of 249,796 individuals reveal 18 new loci associated with body mass index

Many sequence variants affecting diversity of adult human height

63K people

54 loci

~5% variance explained.

Calculating RISK for complex traits

- Start with your population prior for T2D: for CEU men, we use 0.237 (corresponding to LR of 0.237 / (1 − 0.237) = 0.311).

- Then, each variant has a likelihood ratio which we adjust the odds by.

dbSNP	Genotype	Imputed from	R squared	Likelihood Ratio	Running Total LR	Running Total Probability
Prior				0.311	0.311	23.700%
2283228	AA			1.031	0.320	24.252%
2237897	CC			1.023	0.328	24.675%
7903146	CC			0.753	0.247	19.789%
985694	CC			0.918	0.226	18.463%
726281	AA			0.909	0.206	17.071%
3020317	TT			0.928	0.191	16.032%

LETTER

Hundreds of variants clustered in genomic loci and biological pathways affect human height

A full list of authors and their affiliations appears at the end of the paper.
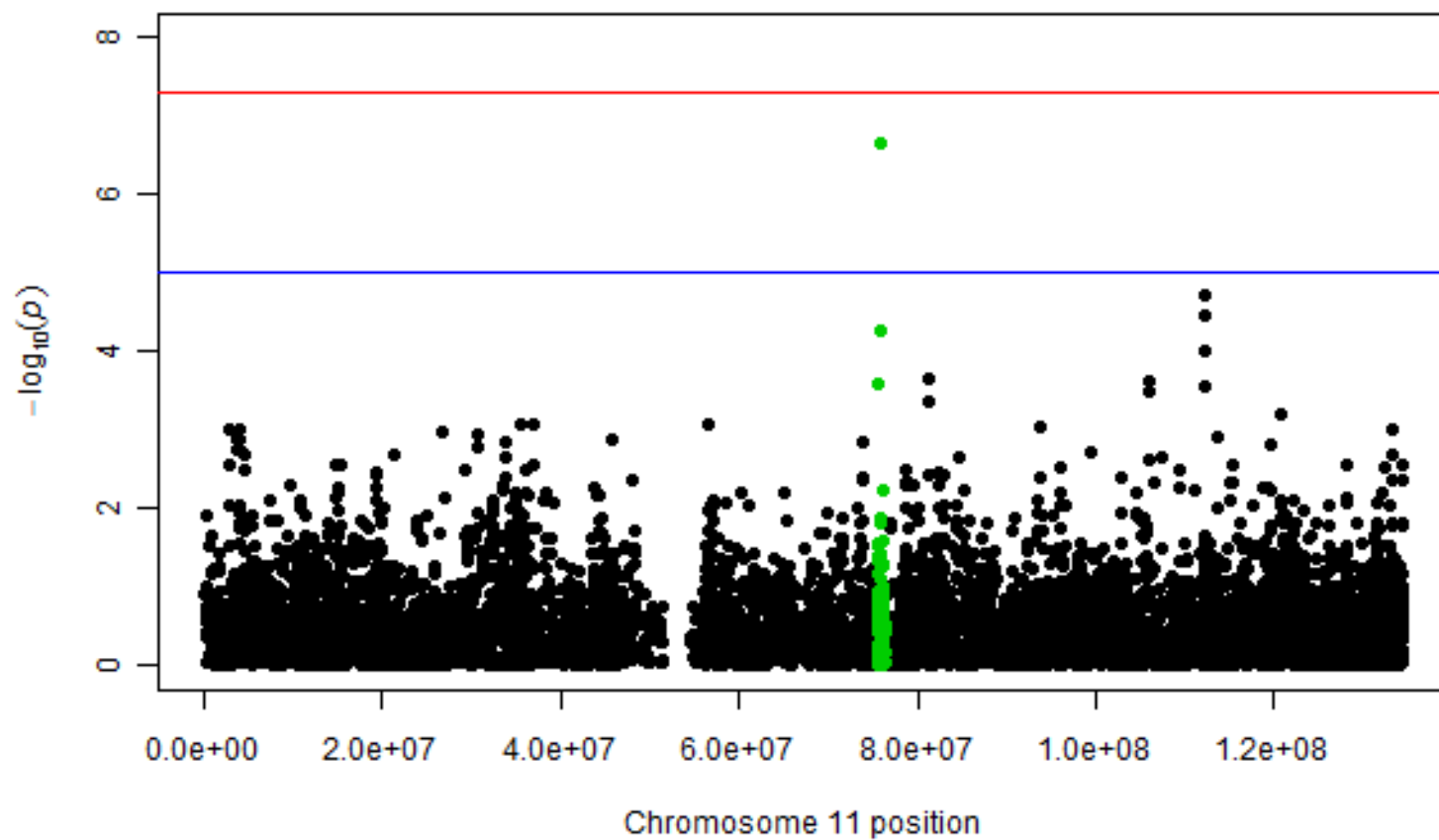
183K people
180 loci
~10% variance explained

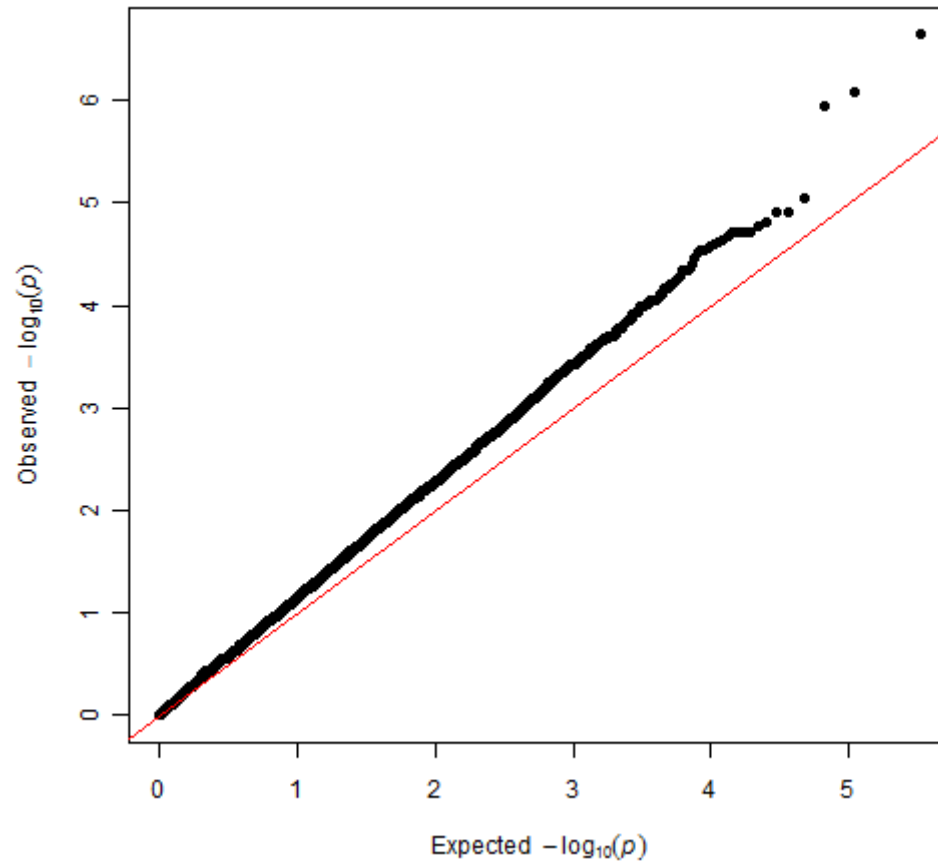# Common SNPs explain a large proportion of the heritability for human height

Jian Yang[1], Beben Benyamin[1], Brian P McEvoy[1], Scott Gordon[1], Anjali K Henders[1], Dale R Nyholt[1], Pamela A Madden[2], Andrew C Heath[2], Nicholas G Martin[1], Grant W Montgomery[1], Michael E Goddard[3] & Peter M Visscher[1]

Chromosome 11

This approach could explain 45% variance in height.

Rare alleles

1. You wont see the rare alleles unless you sequence
2. Each allele appears once, so need to aggregate alleles in the same gene in order to do statistics.

Gene-Gene

Gene-gene

Gene-environment