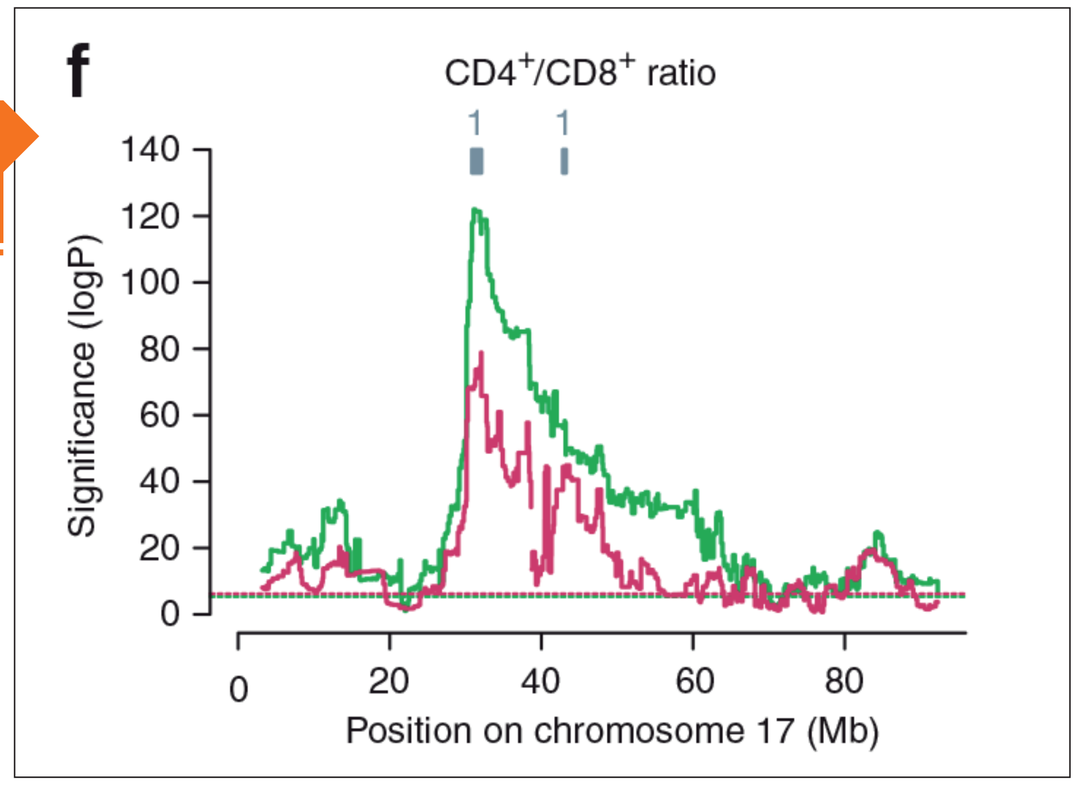
The Wellcome Trust Centre for
Human Genetics

UNIVERSITY OF OXFORD

Genetic association of complex traits in heterogeneous stock mice



Large effect QTLs controlling a variety of phenotypes in the mouse

Different strains of mice were crossed to produce the heterogeneous stock

WHAT WAS KNOWN

- The mouse is a key model organism for understanding gene function in mammals
- Many mouse phenotypes of interest to biomedical research have poorly understood and complex, polygenic origins
- A central problem that impeded the cloning of quantitative trait loci (QTLs) was the difficulty of resolving genetic effects into sufficiently small intervals to make gene identification possible

WHAT WE DID

- We set out to understand the genetic architecture and whether the genetic effect was attributable to a single, biallelic variant
- We surveyed an outbred population of mice, the heterogeneous stock, which are descended from eight known founder inbred strains, making high-resolution haplotype-based mapping possible
- We bred 2000 of these mice and phenotyped each animal at over one hundred traits, including behavior, physiology and human disease models
- We genotyped them at 15000 single nucleotide polymorphisms

WHAT THIS ADDS

- We mapped over 800 QTLs contributing to the variation of these traits
- About one third of QTLs could not be explained by single causal variants
- We also showed that the genetic variance attributable to the mapped QTLs did not explain all the heritable variance
- These data still constitute one of the largest and most comprehensive publicly-available multiple-phenotype data-sets available, and have been used in numerous other analyses of genetic architecture by groups throughout the world

REFERENCES

Genome-wide genetic association of complex traits in heterogeneous stock mice.

W Valdar, L C Solberg, D Gauguier, S Burnett, P Klenerman, W O Cookson, M S Taylor, J N P Rawlins, R Mott & J Flint.

Nature Genetics, 2006 38: 879–887