Exploring 1000 Genomes with Bioconductor

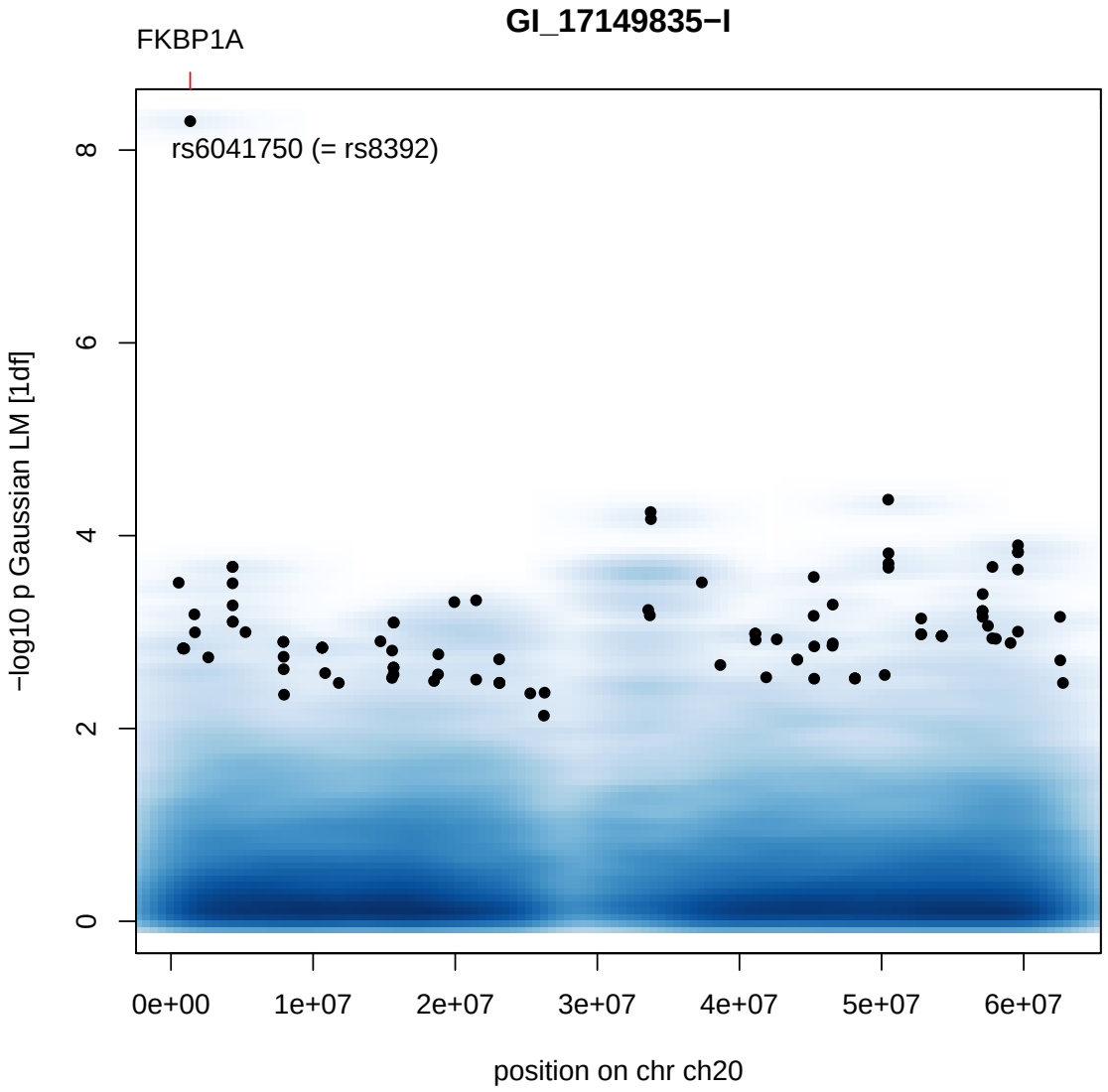
Vince Carey
Channing Lab
Harvard Medical School

- Prologue: What is an eQTL?
- Rationales: 1000 genomes; Bioconductor
- Imputation to the 1000 genomes SNP panel
- Expression arrays, RNA-seq, and eQTL identification

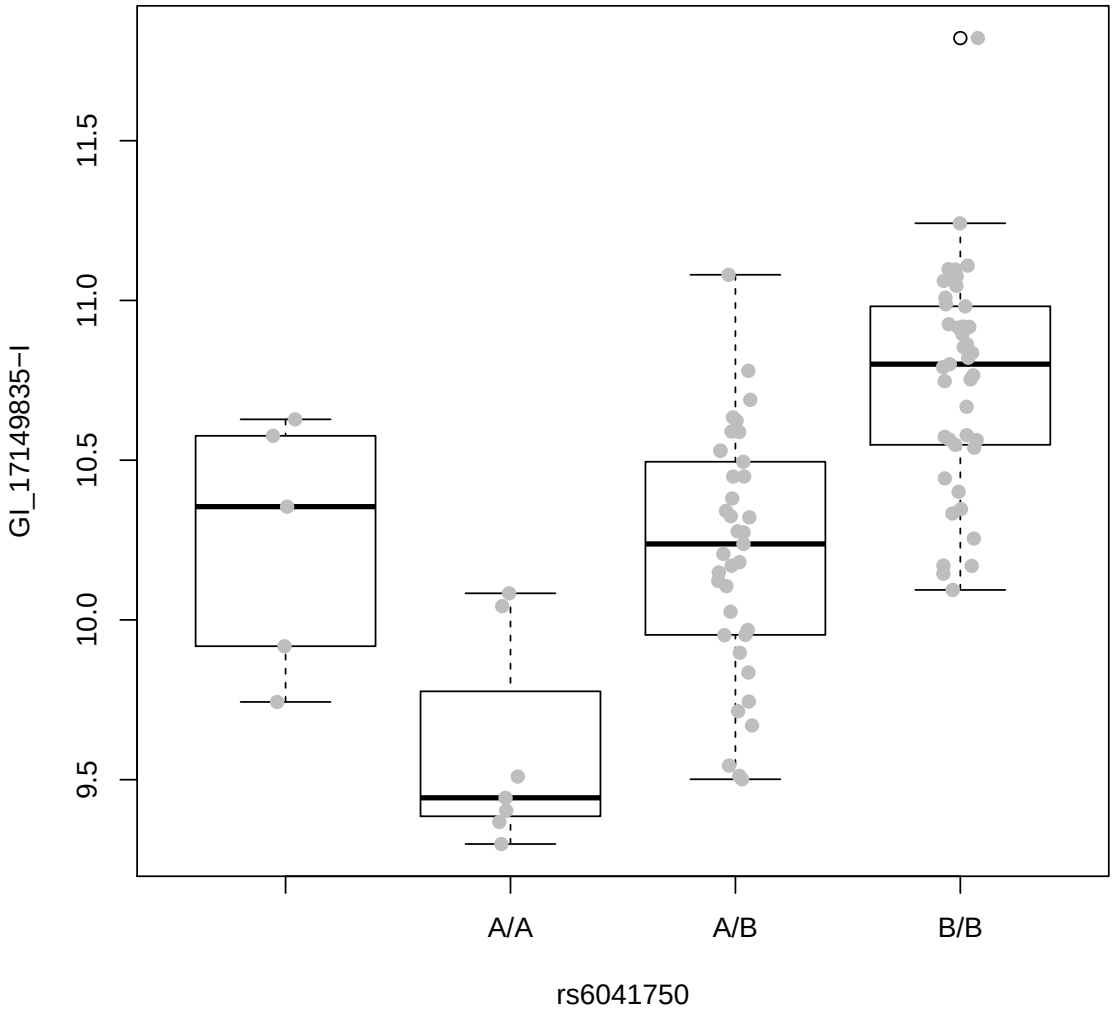
Prologue: What is an eQTL (expression quantitative trait locus)?

- Arises from a basic form of integrative genome-scale data analysis
- On a cohort of N individuals
  - SNP-chip yields allele counts for S SNP, $S \approx 10^6$
  - Expression array yields mRNA abundance measures for G genes, $G \approx 20000$
- perform $G \times S$ association tests of H_{ogs} : mean expression of g is independent of allele count for s
- the best hits are eQTL

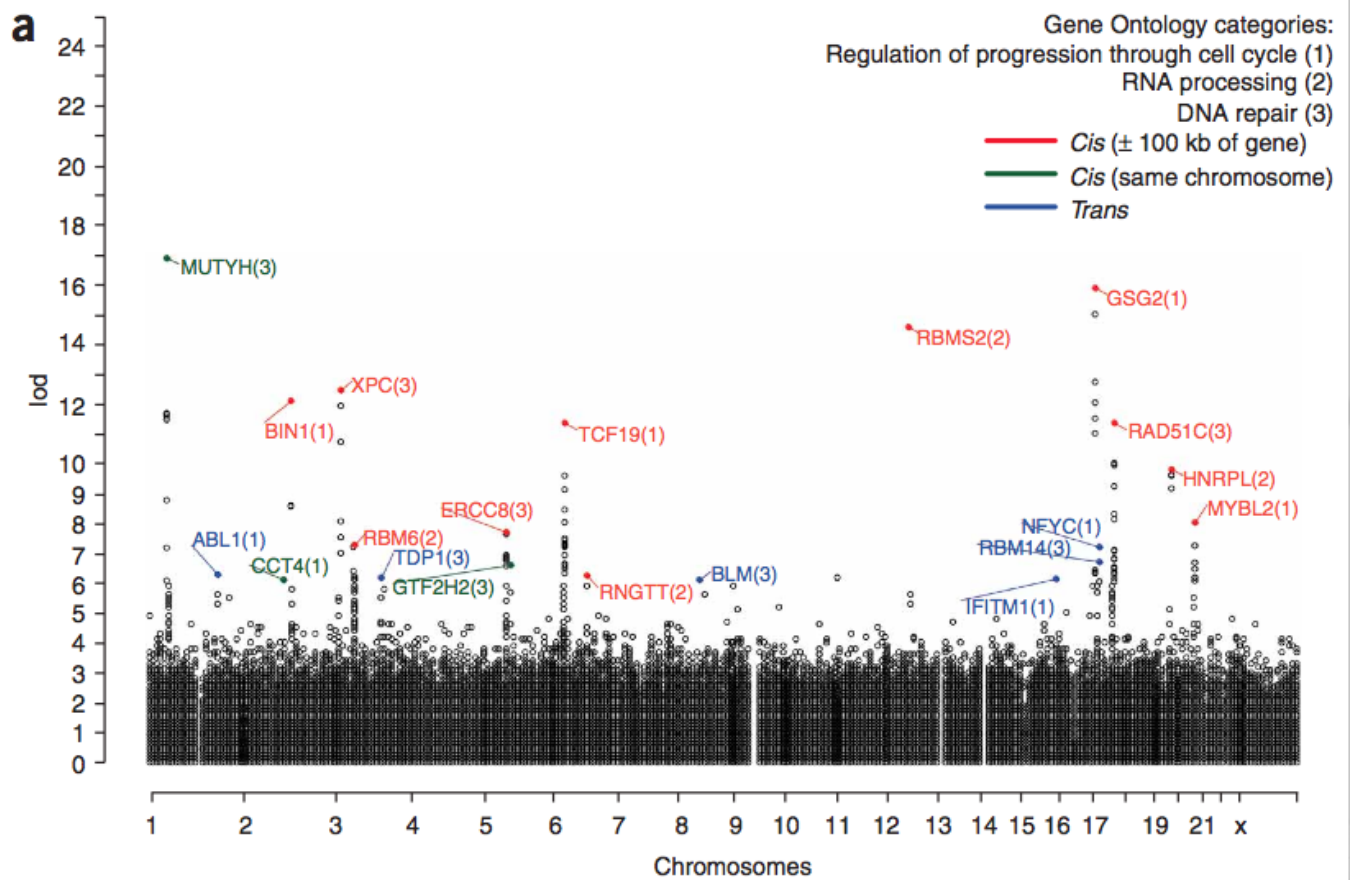
A chromosome-wide scan for a single gene



The ‘best SNP’ discriminates mean expression



Dixon 2007 Nat Genet 'global map'



Why do this? 1: Mechanisms of transcriptional control

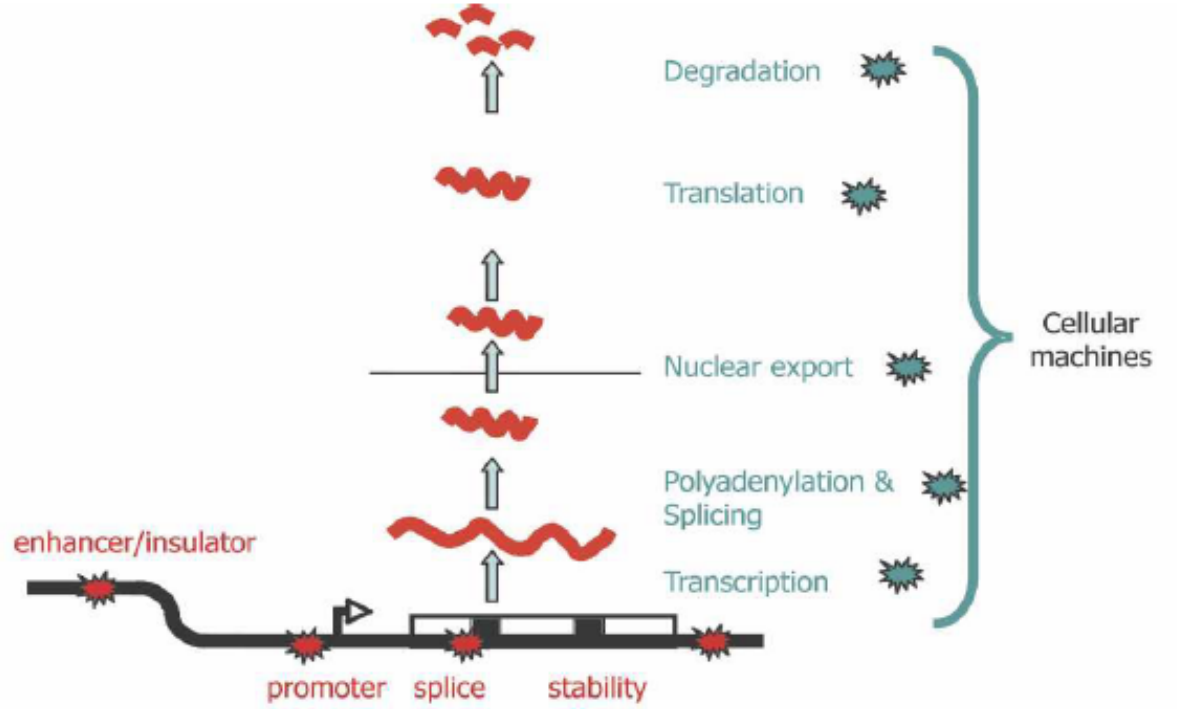
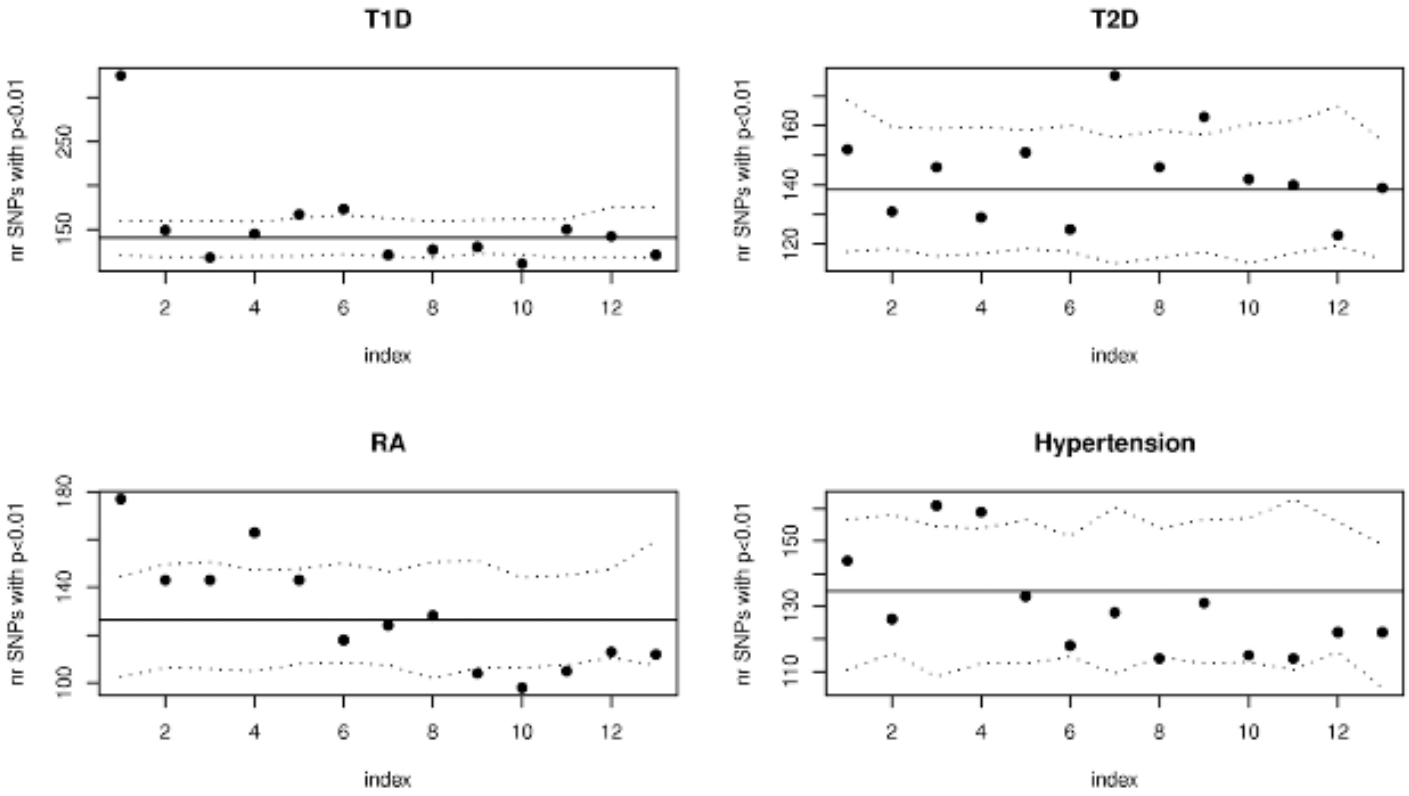


Figure 1. Plausible sites of action for genetic determinants of mRNA levels. Genetic variations influencing gene expression may reside within the regulatory sequences, promoters, enhancers, splice sites, and secondary structure motifs of the target gene and so be genetically in *cis* (red stars), or there may be variations in the molecular machinery that interact with *cis*-regulatory sequences and so act genetically in *trans* (blue stars).

(RBH Williams et al 2007 Genome Resch)

Why do this? 2: Filtering SNP for efficient GWAS

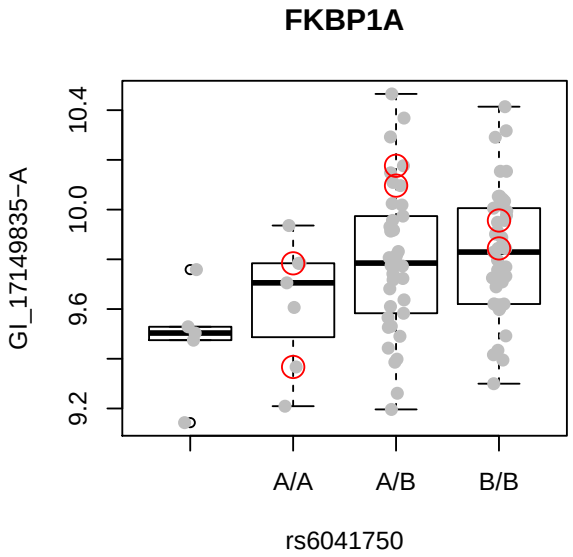
- SNPs binned left to right in decreasing order of expression regulatory capacity
- y axis: proportion SNP in bin associated with macro phenotype in WTCCC



(D Nicolae et al 2010 PLoS Genetics)

Upshots

- eQTL catalogs seem useful; can efficiencies for individual studies be gained by imputing denser SNP panels using results of institutional deep sequencing?
- How can higher-resolution measures of mRNA abundance add to value from eQTL concepts: eQTL searches based on RNA-seq/DNA-seq?
- Under the hood, things may not be so nice...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9.6
10.0
10.4
A/A
A/B
B/B
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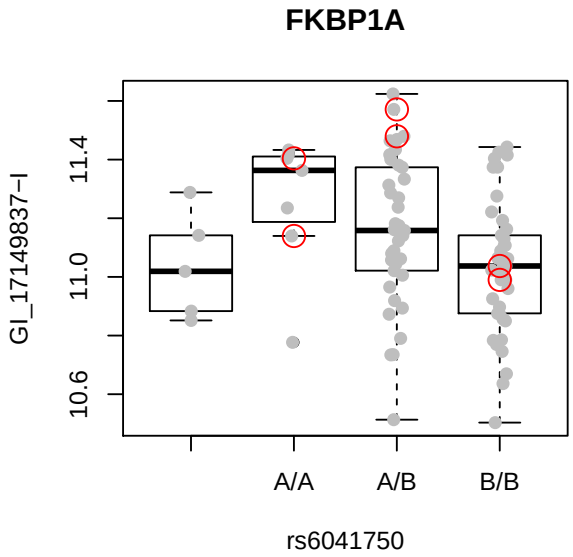
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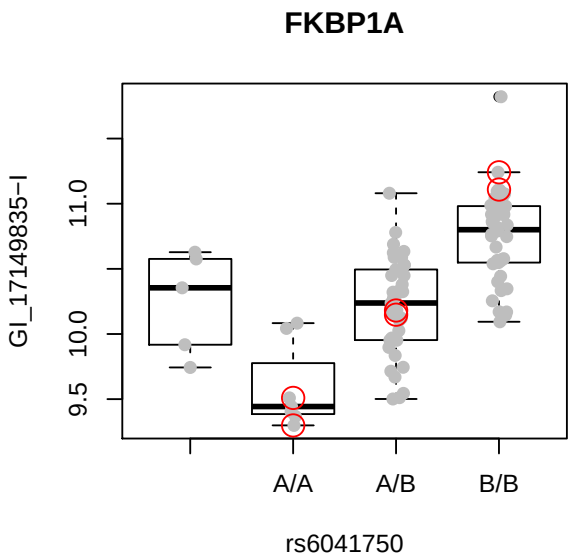
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9.5
10.0
11.0
A/A
A/B
B/B
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Rationale: 1000 genomes xyz