SNPsea: an algorithm to identify cell types affected by risk loci

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Abstract

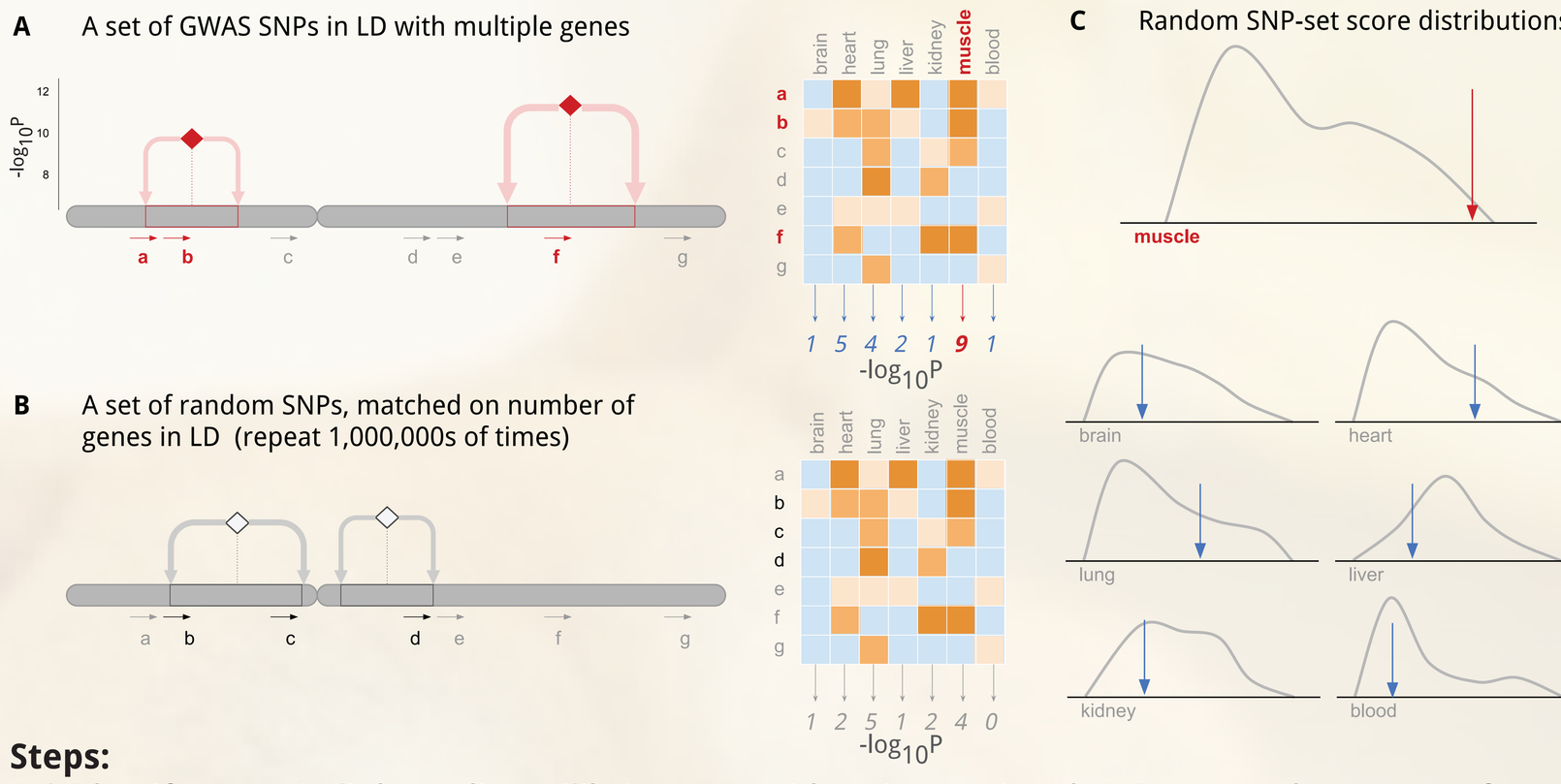
SNPsea is an algorithm to identify cell types and pathways likely to be affected by risk loci. It requires a list of SNP identifiers and a matrix of genes and conditions.

Genome-wide association studies (GWAS) have found many genomic loci associated with risk for different types of disease. SNPsea provides a simple way to determine cell types influenced by genes in these risk loci. Those cell types are likely to be
relevant to the etiology of the given disease.

Suppose disease-associated alleles influence a small number of pathogenic cell types. **We hypothesize that genes with critical functions in those cell types are likely to be within risk loci for that disease.** We assume that a gene's specificity to a cell type is a reasonable indicator of importance to the unique function of that cell type.

htttp://broadinstitute.org/mpg/snpsea

Methods



Steps:

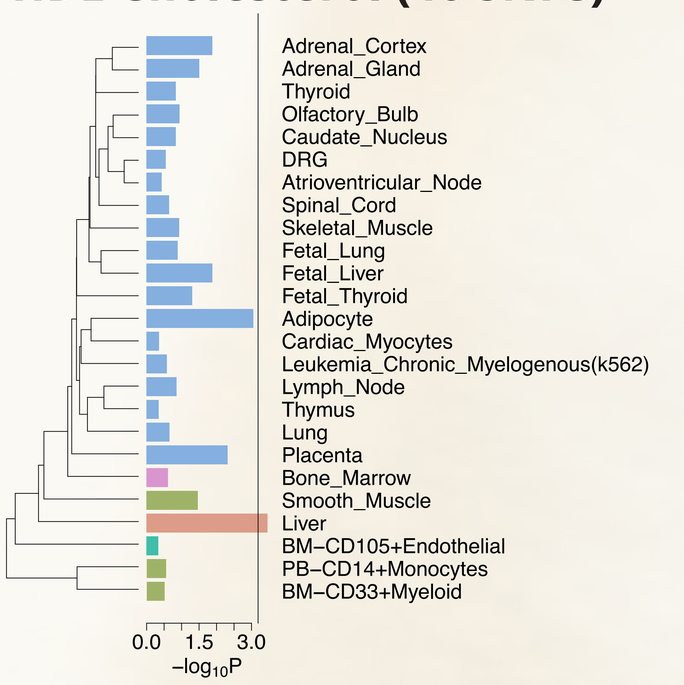
A | Identify genes in linkage disequilibrium (LD) with trait-associated SNPs. Score the gene set for specificity to each cell type.

B | Define a null distribution of scores for each cell type by sampling random SNP sets matched on the number of linked genes.

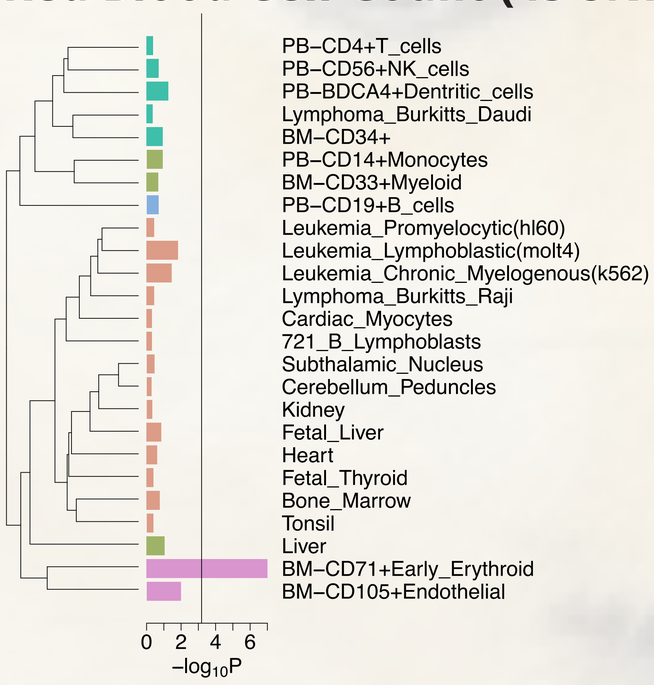
C | Evaluate significance of the original gene set's specificity by comparison to the null distributions.

Results

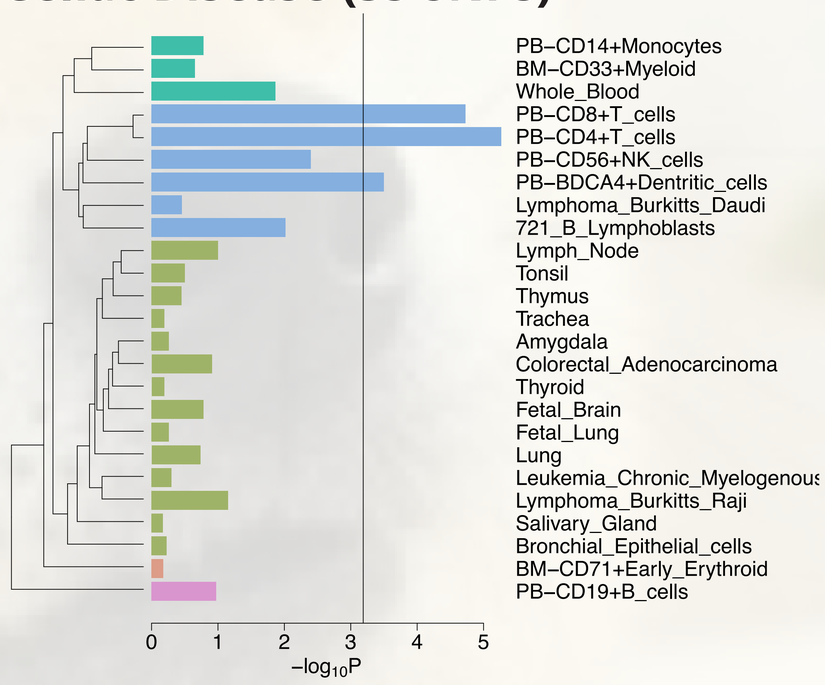
HDL Cholesterol (46 SNPs)



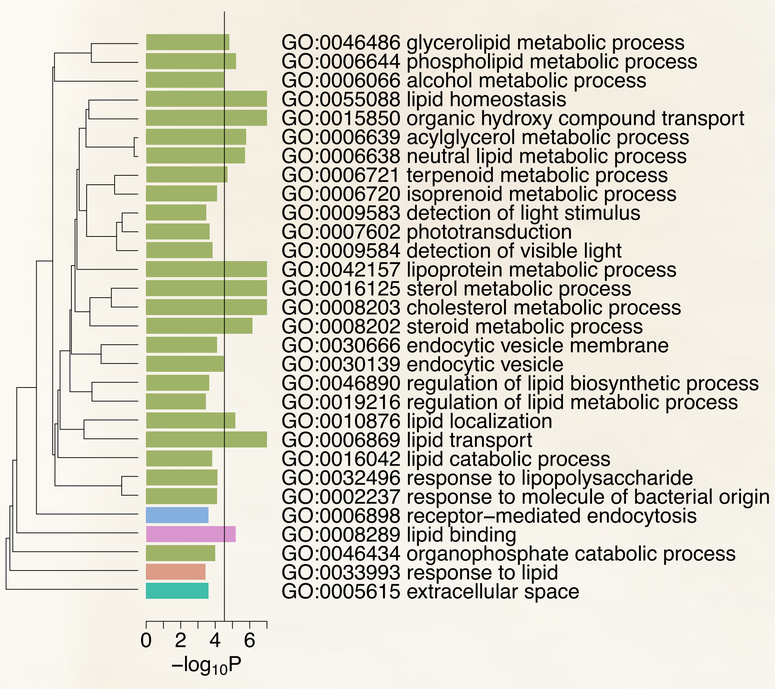
Red Blood Cell-Count (45 SNPs)

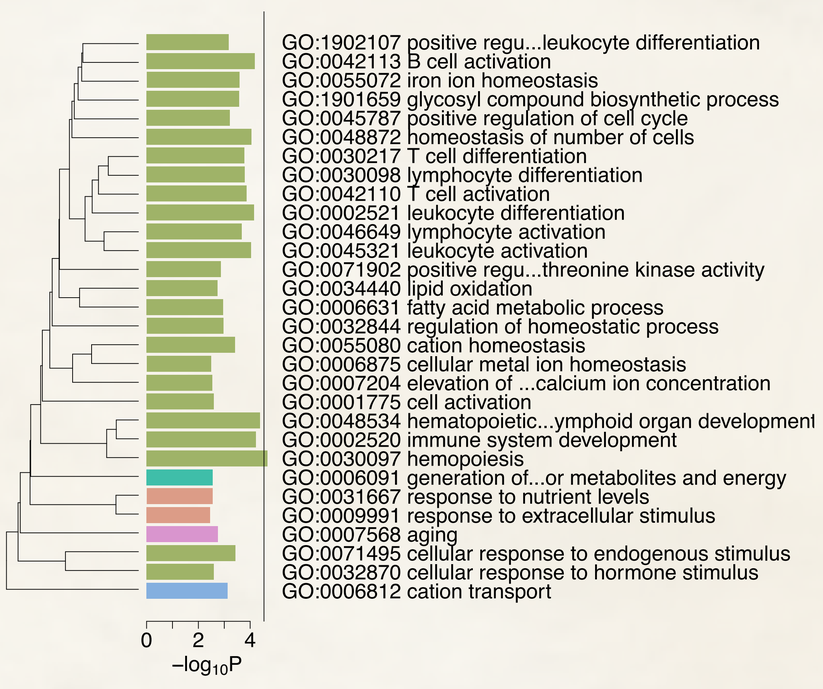


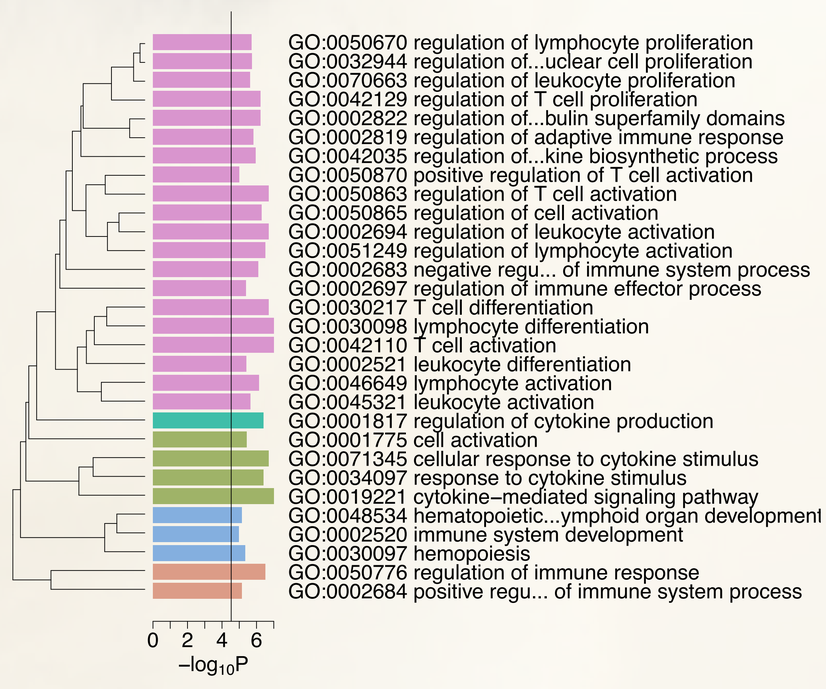
Celiac Disease (35 SNPs)



We tested each SNP set for cell type-specific gene expression relative to 78 other cell types or tissues in the **Gene Atlas** (Su et al. 2004). Top 25 are shown.







We also tested each SNP set for enrichment of gene annotations with 1,751 **Gene Ontology** (GO) terms (Botstein et al. 2000). Top 30 are shown.

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Citation

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