A new approach improves prioritization of disease-associated SNPs

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The more often a gene is differentially expressed, the more likely it is to contain disease-associated DNA variants. Research published today in BioMed Central's open access journal *Genome Biology* shows how a list of SNPs in genes that are repeatedly implicated across many publicly-available gene expression microarray experiments (so-called, 'fitSNPs'), based on differential expression rates, can be used to successfully prioritize candidate genes for further research.

Atul Butte from Stanford University School of Medicine, USA, led a team of researchers who developed the new way to prioritize candidate SNPs from genome-wide association studies (GWAS). He said, "fitSNPs successfully distinguished true disease genes from false positives in genome-wide association studies looking at multiple diseases, and can serve as a powerful and convenient tool to prioritize disease genes from this type of study."

The hypothesis that there is an association between gene expression and disease-associated variants has never before been demonstrated with such clarity and at this global scale. The authors have robustly demonstrated that the likelihood of having variants associated with disease was 12 times higher among differentially expressed genes compared to constantly expressed genes. According to Butte, "As a case study, we looked at type 1 diabetes mellitus. We derived a list of fitSNPs to analyze the top seven loci of the Wellcome Trust Case Control Consortium type 1 diabetes mellitus (T1DM) genome-wide association studies. We then rediscovered all T1DM genes, and predicted a novel

gene for a previously unexplained locus."

There are many candidate gene and SNP prioritization methods, and while the authors acknowledge that no single method is perfect, they suggest that using fitSNPs in a complementary fashion with other prioritization methods will significantly lower experimental costs.

Citation: FitSNPs: Highly differentially expressed genes are more likely to have variants associated with disease, Rong Chen, Alex A Morgan, Joel Dudley, Tarangini Deshpande, Li Li, Keiichi Kodama, Annie P Chiang and Atul J Butte, *Genome Biology* (in press) genomebiology.com/

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