

Biological characterization of expression quantitative trait loci (eQTLs) showing tissue-specific opposite directional effects

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Interpreting the susceptible loci documented by genome-wide association studies (GWASs) is of utmost importance in the post-GWAS era. Since most complex traits are contributed by multiple tissues, analyzing tissue-specific effects of expression quantitative trait loci (eQTLs) is a promising approach. Here we describe “opposite eQTL effects”, i.e., gene expression effects of eQTLs that are in the opposite direction between different tissues, as the biologically meaningful annotations of genes and genetic variants for understanding the GWAS loci. The genes and single nucleotide polymorphisms (SNPs) associated with the opposite eQTL effects (*opp-multi-eQTL-Genes* and *opp-multi-eQTL-SNPs*) were extracted from the largest eQTL database provided by the Genotype-Tissue Expression (GTEx) project (release version 7). The opposite eQTL effects were detected even between closely related tissues such as cerebellum and brain cortex, and a significant proportion of the genes having eQTLs were annotated as the *opp-multi-eQTL-Genes* (2,323 out of 31,212; 7.4%). The *opp-multi-eQTL-SNPs* showed locational enrichment at transcription start site and also possible involvement of epigenetic regulation. The biological importance of the opposite eQTL effects was also assessed using the SNPs reported in GWASs (*GWAS-SNPs*), which demonstrated that a high proportion of the *opp-multi-eQTL-SNPs* are in linkage disequilibrium with the *GWAS-SNPs* (2,498 out of 9,290; 26.9%). Based on the results, the opposite eQTL effects can be a common phenomenon in the tissue-specific gene regulation with a possible contribution to the development of complex traits.

