Efficient Epigenetic Effect Identification in eQTL mapping with RNA-seq Data

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Abstract

Genomic imprinting is an important epigenetic phenomenon where the expression of certain genes depends on their parent-of-origin. Many imprinting genes are known to play important roles in human complex diseases such as diabetes, breast cancer and obesity. In recent years, array based eQTL studies have identified many regulatory variants that show associations with gene expression level. Nowadays, the rapid arising next-generation-sequencing is often done for eQTL mapping. We believe that parent-of-origin effect can contribute to regulating gene expression along with the overall effect from the gene. However, multicollinearlity occurs naturally when we are modeling multiple genetic components, such as additive, dominance and imprinting effects. Moreover, it has been repeatedly shown that RNA-seq data are over-dispersed which brings challenge to the modeling of the gene expression profiling. To address these issues, we introduced a novel method to test the main allelic effects along with the imprinting effect in detecting eQTL. We utilized an orthogonalization procedure, which allowed for efficient imprinting effect detection whereas maintained the power to detect the main allelic effect from eQTLs. We conducted extensive simulations to demonstrate the statistical behavior of the proposed method.

Keywords: Epigenetics, RNA sequencing, eQTL mapping, Complex diseases