Determining the genetic contribution to transcript variation through RNA deep sequencing

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Gene expression variation among genetically diverse individuals is one mechanism explaining the phenotypic diversity that plays a central role in susceptibility to disease and evolutionary adaptation. Like many physiological traits, gene expression is a continuous trait displaying a complex inheritance pattern that involves multiple loci. The technique of expression quantitative trait loci (eQTL) has helped understanding the genetic basis of these variations. It is a variant of QTL analysis which considers gene expression in a population of genetically diverse individuals as a quantitative trait and measures its association with a panel of genetic markers. In the framework of the European project PhenOxiGEn, we are using eQTL to investigate the mechanisms that regulate oxidative stress response. eQTL studies require knowledge about the genotype of each individual at each marker and quantification of each transcript in each individual. Here, we present a strategy for performing both the genotyping and the RNA expression quantification through a single RNA-seq experiment. In addition, our method addresses some specific requirements of eQTL studies, such as high precision of transcript measurements between individuals. This analysis pipeline allows (i) simplifying the procedure and reducing the cost of an eQTL study by skipping the experimental genotyping of the populations and, (ii) enhancing the accuracy of RNA quantification avoiding erroneous local-QTL. This method is of interest in view of future human GWAS studying gene expression as a trait.