Identification of Quantitative Trait Loci Underlying Proteome Variation in Human Lymphoblastoid Cells


Population-based variability in protein expression patterns, especially in humans, is often observed but poorly understood. Moreover, very little is known about how interindividual genetic variation contributes to protein expression patterns. To begin to address this knowledge gap, we describe elements of technical and biological variations contributing to the expression of 544 proteins in a population of 24 individual human lymphoblastoid cell lines that have been extensively genotyped as part of the International HapMap Project.

We determined that expression levels of 10% of the proteins were tightly correlated to cell doubling rates. Using the publicly available genotypes for these lymphoblastoid cell lines, we applied a genetic association approach to identify quantitative trait loci associated with protein expression variation.

The study identified 24 protein forms corresponding to 15 proteins for which genetic elements were responsible for >50% of the expression variation. The genetic variation associated with protein expression levels were located in cis with the gene coding for the transcript of the protein for 19 of these protein forms. Four of the genetic elements identified were coding nonsynonymous single nucleotide polymorphisms that resulted in migration pattern changes in the two-dimensional gel.

This is the first description of large-scale proteomics analysis demonstrating the direct relationship between genome and proteome variations in human cells.