Genomic Analysis from Candidate Genes to Association Studies

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Genetic variations have been used for the identification of disease-related genes. Among those genetic variations, single nucleotide polymorphisms (SNPs) are the most common genetic variations between individuals. Therefore, SNP can be used to facilitate genetic mapping studies that may lead to a better understanding of the genetic basis for complex diseases such as diabetes, asthma, osteoporosis and hypertension. In order to facilitate the identification of human complex disease genes which are associated with specific DNA variants (SNPs), our institute have established a pipeline system for the genomic analysis: candidate gene selection, SNP discovery, SNP genotyping, haplotyping, LD block partitioning, and statistical analysis for association studies. Initially, a large number of new SNPs have been discovered in the disease candidate genes by sequencing 24 DNA samples. In addition, many SNPs selected from disease candidate gene were also tested to determine the distribution of allele frequency in the Korean population. There were significant differences in the distribution of SNP allele frequency among diverse ethnic groups. High throughput genotyping technologies, especially high density Affymetrix or Illumina SNP chips, made genome-wide association studies possible although sophisticated statistical analyses are required to eliminate many false positive results. In addition, instead of analysis of one gene or one locus, analysis of multiple loci located separate chromosomes will increase the statistical power and thus the chance to identify the molecular basis of the multifactorial diseases resulting from the influence of multiple genes. The integrated pipeline genome analysis will facilitate the development of preventive, diagnostic, and treatment strategies for complex diseases. Furthermore, in the near future, computational genomic medicine will be feasible by understanding the detailed effects of major environmental factors and genetic factors which are conferring to the predisposition of human complex diseases.