S2-03

Some Consideration in Disease Association Study on the HapMap Era

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Single nucleotide polymorphisms (SNP) are the most abundant form of human genetic variation and a resource for mapping complex genetic traits. A genome covered with millions of these markers, researchers are able to compare which SNPs predominate in people with a certain disease. Thus, it is important to select a particular subset of SNPs which maximize the power of detecting a significant association. As International HapMap Project progresses it is expected by 2005 that one SNP every 1 kb in human chromosomes discloses, which will describe the common patterns of human DNA sequence variation. With linkage disequilibrium (LD) analysis by evaluating population frequencies of specific haplotypes, the project aims to identify LD segments that will help in the discovery of the etiological basis of common disease. Common human diseases such as birth defects, diabetes, cardiovascular disease, infectious disease, psychiatric illness or neurodegenerative disease arise from a combination of multiple genes and non-genetic factors. By combining information from human genetics, genomics and epidemiology we are searching for robust methods finding mutations contributing to common, polygenic diseases, and applying these tools to discover specific diseases. Development and application of molecular genetic, genomic and computational methods for the dissection and identification of the multiple genes, and their characteristics are summarized.

S2-04

Mutational Screen of Peripheral Neuropathy-Related Genes in Korean Patients

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Charcot-Marie-Tooth (CMT) disease is the most common form of inherited peripheral neuropathy. CMT is a genetically heterogeneous disorder of the PNS, thus many genes have been identified as CMT-causative genes. We examined CMT1A duplication of 17p11.2-p12, mutations of PMP22, MPZ, Cx32, EGR2 and NEFL genes in 57 Korean families having CMT disease. We found 15 CMT1A duplication families among 28 CMT1 cases. The duplication frequency (53.6%) in Korean patients is slightly lower than, or similar to those of European CMT1 cases. In the 42 CMT families without CMT1A duplication, 10 pathogenic mutations were found in 9 families: one PMP22 mutation, three MPZ mutations, three Cx32 mutations, one EGR2 mutation and two NEFL mutations, respectively. Seven mutations (318delT(A106fs) in PMP22, 352G>A(D118N), 449-1G>T(3-splice site), 706A>G(K236E) in MPZ, 407T>C(V136A), 502T>C(C168R) in Cx32, and 1001T>C(L334P) in NEFL) were determined to be novel. The mutation frequency in Cx32(7.1%) in this study was considerably lower than in several European groups, i.e., Spain 21.3%, Finland 19.0%, Russia 13.0%, Italy 16.7% and Germany 11.9%, but similar to that of the Japanese 5.6-5.7%. Thus, it appears that mutations in Cx32 are less frequent in East Asian CMT patients than in European patients.