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The Ancient, Present and Future of Genetics on Korean population

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Korean population is regarded as one ancestral origin and the same geographical distribution in large scale. In order to clarify the genetic structure of Korean population, protein polymorphism have widely been used as genetic marker. In our study, acid phosphatase (AcP) and esterase D (EsD) polymorphism were analyzed on unrelated individuals of Korea by horizontal starch gel electrophoresis. The allele frequencies of two gene were: AcP^a=0.4037, AcP^b=0.5963, EsD^1=0.6702, EsD^2=0.3298. They were agreement with the Hardy-weinberg equilibrium. In the case of AcP polymorphism, AcP^a allele frequency in Asiantic population including our result was higher than those of other Europe and African population. Also, AcP^a allele frequency in Korean population is higher than that of Japanese population. With respect to EsD polymorphism, the Far East population show considerable homogeneity, and the elevated allele frequency of EsD^2 seems to be a characteristic of East Asians. Frequency of the EsD^2 in Korea (Seoul) population is lower than that of Japanese (Tokyo) population. There is a clear increase in frequency of the EsD^2 allele as one move from Europe to Asia.

Recent advances in technique of molecular genetics field such as polymerase chain reaction method, enable research into the molecular basis of many genetic disease. The genetic diseases were classified as three categories by number of gene involved: monogenic, oligogenic, or polygenic multifactorial.

Monogenic disease are the result of a mutation at a single gene. Our study group focus on familial hypercholesterolemia (FH) by mutations in the LDL receptor gene. Mutations of LDL receptor gene are genetically heterogeneous, and a large number of mutations have been reported in various populations and ethnic groups. In our study, four novel point mutations were detected in 5 FH patients and chracterized by sequence analysis. Of them, one is a nonsense mutation, Glu→ Stop (CAG→TAG) at codon 161, and results in a large deletion. The other three, which were a Ala→Glu (GCG→GAG) mutation at single peptide, Cys→Tyr (TGC→

TAC) at codon 210, and Pro→Leu(CTG→CCG) at codon 584, were novel missense mutations, which modified the highly conserved region of the LDL receptor gene. Identification of these novel mutations imply the molecular heterogeneity of the LDL receptor gene mutations causing FH.

Oligogenic disease is a genetically heterogeneous disease that can be caused by an alteration in at least two genes, and autosomal dominant polycystic kidney disease (ADPKD) is a good example on this kind of disease. Linkage analysis have revealed that the molecular defect of ADPKD cases are due to mutations in PKD1, PKD2 or unknown third loci. In order to characterize the genetic heterogeneity of ADPKD in Korean population, linkage analysis with microsatellite marker was performed on Korean family samples. Of 63 Korean families tested, 39 families (61.9%) showed the closed linkage with PKD1 gene, whereas 22 families (34.9%) indicated the significant linkage with PKD2, showing remarkably higher proportion of PKD2 gene in Korean ADPKD families than those of Caucasians.

Polygenic multifactorial disease occurs as a consequence of the interactions between a number of genes and environmental factors. Coronary artery disease (CAD) is a kind of polygenic multifactorial disease. Common genetic variants of proteins participating in lipid metabolism have been suggested to be associated with the pathogenesis of CAD. Of plasma lipids, lipoprotein(a) (Lp(a)) has been considered as independent risk factor on the ethiology of CAD. In view of the clinical importance of Lp(a), we investigated the genetic polymorphism of apolipoprotein(a) (apo(a)), only protein component of Lp(a). In our study design, the apo(a) polymorphism was examined in 184 Korean patients with CAD and 121 healthy subjects. For (TTTTA)n sequence polymorphism, subjects with 9/9 genotypes were significantly associated with Korean CAD group ($P<0.05$). Thus, our result suggests that the genetic variation of apo(a) gene may be responsible for the pathogenesis of CAD in Korean population.

Until now, our study group investigated the genetic makeup of Korean population and the molecular aspect of genetic diseases such as FH, ADPKD and CAD. However, it is foreseeable that in the coming years, the study on the molecular basis of the genetic disease and the ethnic characteristics of Korean population will be advanced by the development of DNA chip technique and bioinformatics.