Abstract of Presentation

Presentation Titl:

Genome-wide association studies for human narcolepsy and other complex diseases

Abstract :

We have been searching human genetic factors for various complex diseases including autoimmune diseases, sleep disorders and infectious diseases. Also, we have been participating in multi-institutional collaborations for diabetes, hypertension, panic disorder, multiple system atrophy, and others. In this workshop, the results of our genome-wide association studies (GWAS) for susceptibility genes to some complex diseases are presented.

Human narcolepsy is a typical sleep disorder with an incidence of about 0.15% in Japanese. A HLA class II gene (*DQB1*0602*) is a well-established susceptibility gene, whereas the other genes are yet to be identified. We previously reported GWAS using 23K microsatellite polymorphisms and identified a new resistance gene (Kawashima et al. 2006). Recently, GWAS using new high-throughput SNP typing technologies have successfully identified susceptibility genes to a variety of complex diseases. We then performed GWAS using the 500K SNP Array and detected a number of candidate loci (Miyagawa et al. in press). Then, a second screening was performed and one SNP showed a replicated association (combined p = 4.4 x 10-7, odds ratio = 1.79). The subsequent high-density association mapping enabled to identify the primary SNPs. This significant association was also observed in Koreans, whereas the frequencies of the risk allele were much less in Caucasians and Africans. The SNP is located close to two genes and the risk allele was associated with lower mRNA levels of the genes. Interestingly, both genes were reported to have certain functions relevant to sleep regulation.

The identification of new susceptibility genes to type 2 diabetes in Japanese by a multi-institutional collaboration team is also presented briefly (Yasuda et al. in press). Based on these experiences, GWAS strategy for relatively infrequent diseases as well as ethnic differences in susceptibility genes are discussed.