論文の内容の要旨

論文題目 Genome-wide association studies identified new candidate regions for essential hypersomnia

（ゲノムワイド関連解析による真性過眠症の新規疾患感受性領域の同定）

氏名　　許（コー）　昔舜（セックスン）

Khor Seik Soon

Essential hypersomnia (EHS), a sleep disorder characterized by excessive daytime sleepiness (EDS), can be divided into two broad classes based on the presence or absence of the Human Leukocyte Antigen (HLA)-DQB1*06:02 allele. HLA-DQB1*06:02 positive EHS and narcolepsy with cataplexy are associated with the same susceptibility genes and orexin (hyporetin) deficiency. In contrast, there are fewer studies of HLA-DQB1*06:02 negative EHS which, I hypothesized, involves different pathophysiological pathways from narcolepsy with cataplexy. Previous studies have shown that HLA-DQB1*06:02 negative EHS shows normal orexin levels and is not associated with orexin deficiency. In order to identify susceptibility genes associated with HLA-DQB1*06:02 negative EHS, I conducted a genome-wide association study (GWAS) of 125 unrelated Japanese EHS patients lacking the HLA-DQB1*06:02 allele and 562 Japanese healthy controls. A comparative study was also performed on 268 HLA-DQB1*06:02 negative Caucasian hypersomnia patients and 1761 HLA-DQB1*06:02 negative Caucasian healthy controls. I identified three SNPs that each represented a unique locus, rs16826005 (P = 1.02E-07; NCKAP5), rs11854769 (P = 6.69E-07; SPRED1), and rs10988217 (P = 3.43E-06; CRAT) that were associated with an increased risk of EHS in this Japanese population. Interestingly, rs10988217 showed a similar tendency in its association with both HLA-DQB1*06:02 negative EHS and narcolepsy with cataplexy in both Japanese and Caucasian populations.