Identification of Genetic Factors of Idiopathic Membranous Nephropathy

論文の内容の要旨

Abstract of Dissertation

Thesis Title　Identification of Genetic Factors of Idiopathic Membranous Nephropathy

(特発性膜性腎症における遺伝的解析)

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Idiopathic membranous nephropathy (IMN) is one of the major causes of adult nephrotic syndrome. Associations of phospholipase A_2 receptor 1 (*PLA2R1)* and *HLA-DQA1* with IMN have been reported in European and Asian populations. However, high-density association mapping covering the whole region of *PLA2R1* and *HLA* regions for the association with IMN has not been performed yet in the East Asian populations. In the first stage of the study, I performed genotyping of 15 SNPs in *PLA2R1* and *HLA* typing of *HLA-A*, *B*, *C*, *DRB1*, *DQB1* and *DPB1* in patients with 53 Japanese IMN patients and 419 healthy controls. In the second stage, I performed replication study with 130 Japanese IMN cases and 392 controls. I also analyzed the associations in the combined data set including both first and second sample sets. Moreover, interaction analysis of *HLA* and *PLA2R1* was conducted. In the first stage, single point analysis on *PLA2R1* identified 7 significant SNPs, and in the replication stage, 5 of which were confirmed. For *HLA* genes, strong associations were observed with *HLA-DRB1*15:01* and *HLA-DQB1*06:02*, and both were successfully replicated in the second stage. In the interaction analysis, more than additive effect was detected in patients carrying both risk alleles of *HLA-DRB1-DQB1* and *PLA2R1*. The present study identified the primary associations of *HLA* and *PLA2R1* polymorphisms with IMN in the Japanese population. Furthermore, the increased risk of IMN by combination of *PLA2R1* and *HLA* risk alleles confirmed the importance of the interaction of these two genes in the development of IMN.