Identification of genetic markers associated with intestinal Behçet's disease using genome-wide association and HLA analyses

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Abstract

Background: Behçet's disease (BD) is a rare, chronic, multi-systemic, inflammatory disease.[1] BD could affect oral and genital ulcers, and skin, ocular, vascular, and intestinal involvement. BD occurs mainly in the countries along the "Silk Road".[2] In addition to environmental factors, genetic factors, such as HLA-B*51, IL-10, and IL23R, are associated with BD susceptibility.[1,3,4] Especially, BD with intestinal involvement (intestinal BD) is diagnosed by a typical ulcer in gastrointestinal tract among BD patients. The prevalence of intestinal BD is higher in East Asia (5-25%) than those in the Mediterranean (0-3%).[5,6] Because of these ethnic and geographical differences, intestinal BD is likely to be distinct from BD without intestinal involvement.[7] Moreover, intestinal BD is similar to inflammatory bowel diseases in clinical manifestation and therapeutic applications.[8] Therefore, we aimed to identify genetic difference between intestinal BD and BD without intestinal involvement.

Methods: A genome-wide association study and meta-analysis were performed with 379 patients with intestinal BD, 1,310 patients with BD without intestinal involvement, and 2,327 healthy controls from South Korea and Turkey. To identify susceptible variants to intestinal BD, subset-based analysis was conducted between intestinal BD and BD without intestinal involvement using R package ASSET.[9] In addition, human leukocyte antigen (HLA) imputation using HIBAG [10] was performed to identify HLA alleles associated with intestinal BD.

Results: We confirmed that the HLA region is most significantly associated with BD in the Korean population. In addition, we found that several candidate regions on chromosome 1, 8, and 14 as well as HLA region were associated with intestinal BD in comparison with healthy control. We identified eight candidate gene regions including HLA region which have P value $\leq 1.0 \times 10^{-6}$ using subset-based analysis between intestinal BD and BD without intestinal involvement. In HLA analysis, HLA-B*51:01 and HLA-B*xx:xx[#] are associated with intestinal involvement of BD.

Conclusion: We newly identified that HLA-B*xx:xx is associated with intestinal involvement of BD. In addition to HLA-B alleles, we also found that eight candidate genes were associated with intestinal BD. Further replication study is needed to validate the candidate variants and HLA alleles.

[#] Specific gene names are concealed in view of the tense competition.

Keywords: *Behçet's disease: intestinal Behçet's disease: genome-wide association study: HLA-B*51*

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Biography

I graduated from Yonsei University College of Medicine (YUCM) in 2006. After I finished the residency training of internal medicine in Severance hospital, I got a PhD from the dept. of Pharmacology, YUCM. Then, I worked as a clinical fellow in the dept. of gastroenterology, Severance hospital. I am working as a Postdoc investigating genetics and pharmacogenetics of inflammatory bowel diseases at IKMB, Kiel University, Germany.