Different Genetic aspects of IBD in Asia-Pacific Region

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Although the precise etiologies of inflammatory bowel disease (IBD) (ulcerative colitis and Crohn's disease) remain obscure, several reports have indicated that dysfunction of the mucosal immune system plays an important role in its pathogenesis. Recent progress in genome-wide association studies (GWAS) has identified over 100 of IBD susceptibility genes. The panel of identified susceptible genes indicates that abnormal immune responses to gut microbiota, dysregulation of cellular responses such as autophagy, and mucosal barrier dysfunction caused by ER stress play key roles in IBD pathogenesis.

It has been well established that host genetic susceptibility plays a key role in the risk of development of IBD. Before identification of susceptible genes, it was reported that the risk of development of IBD in homozygous twins is higher than the risk in the general population. The turning point has come in 2001.Nucleotide oligomerization domain receptor 2 (NOD2), also known as CARD15, an intracellular pathogen recognition molecule, was identified as a susceptibility gene for Crohn's disease by linkage analysis. Since the discovery of NOD2, innate immunity has been highlighted in the research of IBD pathogenesis. However,unexpectedly, our study of Japanese population clearly demonstrated that NOD2 did not show any association with Japanese IBD population. Then, NOD2 have been reported to have no association with Korean and Chinese IBD population. After discovery of GWAS, many IBD susceptible genes including IL-23R and ATG16L1 have been rapidly identified in Western IBD population, while majority of themdo not show any association with the risk of IBD development in Asian population as well as NOD2. On the other hand, TNFSF15 was originally identified as a Crohn's disease susceptibility gene in a Japanese population and the association was confirmed in other Asian Crohn's disease population. Thus, research into IBD susceptibility genes demonstrates the differences in genetic risk between several human races. According to the discovery of many susceptible gens, the concept of re-classification of IBD by susceptible gene panel has been proposed, but we have to consider the differences in human races.

Identification of susceptible genes may give us the idea for discovery of novel therapeutic targets. Indeed, several molecular targeting therapies have been developed. Global clinical trials have been performed recently and will be planned in the future. However, we have to recognize that efficacy and risk of adverse effects may be different between in Western and Asian population, where genetic background is clearly different. Considering these issues, I believe that the study in cooperation with Asian countries must be planned and APDW could provide good opportunity for the future cooperative study all over the Asia.