PgmNr 1207: Genome-wide association studies identify two novel susceptibility loci to diabetic retinopathy in Japanese patients with type 2 diabetes.

Authors:
M. Imamura 1,2,3; M. Taira 3; A. Takahashi 4,5; Y. Kamatani 4; M. Kubo 6; S. Maeda 1,2,3

Institutes
1) Department of Advanced Genomic and Laboratory Medicine Graduate School of Medicine, University of the Ryukyus; 2) Division of Clinical Laboratory and Blood Transfusion, University of the Ryukyus Hospital; 3) Laboratory for Endocrinology, Metabolism and Kidney Diseases, RIKEN Center for Integrative Medical Sciences; 4) Laboratory for Statistical Analysis, RIKEN Center for Integrative Medical Sciences; 5) National Cerebral and Cardiovascular Center, Omics Research Center; 6) RIKEN Center for Integrative Medical Sciences

Abstract:
Several reports have shown familial aggregations of diabetic retinopathy (DR) or advanced DR among patients with type 1 or type 2 diabetes, suggesting genetic susceptibility contributes to the development and/or progression of DR. However, the genes involved in the susceptibility to DR are still unknown. To identify novel genetic loci associated with the susceptibility to DR, we performed a meta-analysis of genome-wide association studies (GWAS) for DR in Japanese patients with type 2 diabetes registered in BioBank Japan (Study-1; 4,839 DR cases and 4,041 controls, Study-2; 693 DR cases and 1,524 controls). DR cases were patients having any stages of DR and controls were type 2 diabetes patients who did not have any sign of DR with long duration of diabetes (≥5 years) or with diabetic nephropathy. We analyzed the association with DR of ~7.5 million single nucleotide polymorphisms (SNPs) from directly genotyped data (Study-1; Omni-express exome, Study-2; Illumina 610K) and genotype imputation using MACH and minimac. We have identified 85 loci showing suggestive association with DR (p < 1 × 10^{-4}) through the GWAS meta-analysis. These loci were further evaluated in an independent case-control study (Study-3; 2,260 DR cases and 723 controls, BioBank Japan). After combining all the association data (Study-1, 2 and 3) by a meta-analysis, the association of two loci reached genome-wide significance level; rs12630354 on Ch3: p = 1.62 × 10^{-9}, Odds ratio [OR] = 1.17, 95% Confidence Interval [CI] 1.11-1.23, rs140508424 on Ch9: p = 4.19 × 10^{-8}, OR = 1.61, 95% CI 1.36-1.91. None of the association with advanced DR reached genome-wide
significance \((p > 5.0 \times 10^{-8})\) in a sub-group analysis: excluding patients with simple DR (DR cases \(n = 2,003, 368\) and 1,260 for Study-1, Study-2 and Study-3, respectively).

In conclusion, we have identified two novel loci contributing to DR susceptibility, although further replication studies are required to validate the association of these loci with DR.