Association analysis between CDKN2B-AS1 genotype and quantitative traits of primary open-angle glaucoma

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Purpose: Several single nucleotide polymorphisms (SNPs) located in the CDKN2B-AS1 gene are reportedly associated with primary open-angle glaucoma (POAG). The purpose of this present study was to reveal the association between the genotype data of CDKN2B-AS1 and quantitative traits in POAG.

Methods: All procedures were conducted in accordance with the Helsinki Declaration. This study was approved by the Institutional Review Board of Kyoto Prefectural University of Medicine. This study involved 824 POAG patients (391 males and 433 females) who were diagnosed with the disease by glaucoma specialists based on several ophthalmic examinations, including optic disc photograph, imaging and visual field testing. The CDKN2B-AS1 genotype data was obtained by use of Affymetrix® 1000K microarray (Affymetrix, Inc., Santa Clara, CA). In this study, we analyzed the genotype data of rs7865618 SNP (AA/AG/GG), which was selected from the 5 genome-wide significant SNPs in CDKN2B-AS1 identified in our previous study (PLOS ONE, 2012). As for the quantitative traits, patient age at diagnosis of glaucoma, baseline intraocular pressure (IOP), maximum IOP in clinical follow up, optic disc area (DA), and central cornea thickness (CCT) were examined. The data of patient age at diagnosis of glaucoma and baseline IOP were got from medical documents. DA was measured by retinal tomography (HRT-II; Heidelberg Engineering GmbH, Heidelberg, Germany). CCT was measured by Pentacam® (OCULUS Optikgeräte GmbH, Wetzlar, Germany). IOP was measured by Goldmann applanation tonometer. If the above clinical data were available from both eyes, the data from the eye that showed severer visual field defects was used. Statistical analyses were performed by use of either regression analysis (AA/AG/GG, risk allele A).

Results: The number of subjects with the AA, AG, and GG genotypes were 660, 157, and 7, respectively. Among the 3 genotype groups, regression analysis revealed no significant difference for patient age at diagnosis of glaucoma, baseline IOP, maximum IOP, or CCT; however, significance was revealed for DA (p = 0.041).

Conclusions: The findings of this study show that in POAG patients, DA is a significant risk allele for CDKN2B-AS1.

This study was also submitted in 2014 ARVO meeting.

Key words: CDKN2B-AS1, GWAS, disc area