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Identification of copy number variation in the gene for autosomal dominant optic atrophy, *OPA1*, in a Chinese pedigree

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ABSTRACT. Autosomal dominant optic atrophy (ADOA) is an optic neuropathy characterized by bilateral optic nerve pallor and decreased visual acuity. It has been reported to be associated with two genes, *OPA1*, *OPA3*, and the *OPA4*, *OPA5*, and *OPA8* loci. However, mutations

in *OPA1* constitute the most prevalent cause of ADOA. The purpose of this study was to identify the underlying genetic defect in a Chinese pedigree with ADOA. DNA from six members of a Chinese pedigree was collected for testing genomic and copy number variation (CNV) by targeted region capture and next generation sequencing (targeted NGS). A new developmental CNV detection method was applied to analyze the sequence data. Further verification of CNV was performed by real-time polymerase chain reaction (PCR). Three members of the pedigree with clinically diagnosed ADOA were screened for pathogenic genes related to ophthalmic genetic disease. No eligible pathogenic point mutations associated with ADOA disease-causing genes were found in pedigree members with ADOA. Upon further analysis for CNVs, we found a heterozygous deletion in exons 1-9 of *OPA1*, which was confirmed by real-time PCR. In this study we used a new developmental method to detect CNVs associated with ADOA in a Chinese pedigree. To our knowledge, this is the first case of ADOA caused by a CNV of the *OPA1* gene in Chinese patients. The findings suggest that CNVs might be an important mutation type in Chinese patients with ADOA, and that CNV screening should be performed when point mutation screens are negative in these patients.

Key words: Autosomal dominant optic atrophy; Mutation; Pedigree; Copy number variation; Optic atrophy protein 1

