Letter to the Editor
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Identification of the *ABO*cis-AB04* Allele With a Unique Substitution C796A: The First Case in Korea

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Dear Editor,

Herein, we describe a family carrying the *cis-AB04* allele through two generations; this is the first report of such a case in the Korean population.

Cis-AB is a very rare phenotype in the ABO blood group system and is characterized by the inheritance of an allele encoding an enzyme with both A and B activity [1]. *Cis*-AB red blood cells (RBCs) show various phenotypes depending on the partnering alleles, resulting in serological discrepancies. Blood group cis-AB is relatively more common in the Korean population and is reported to be the most common ABO subgroup in Korea [2]. At present, nine *cis*-AB alleles have been identified according to the Blood Group Antigen Gene Mutation Database. Among the *cis-AB* alleles, *cis-AB01* is the most frequently observed allele in the Korean population [2] and *cis-AB09* has also been reported [3], but reports on the other alleles are scarce.

A 46-yr-old woman (II-3, Fig. 1) visited the outpatient clinic of the Korea University Ansan Hospital for submucosal turbinectomy and septoplasty for chronic pansinusitis. Routine ABO typing of the proband's blood revealed an ABO discrepancy. ABO genotyping using peripheral blood from the proband was performed along with serological and molecular ABO typing of her family.

RBCs of the proband showed the A2B phenotype, characterized by 4+ agglutination with anti-A, anti-B, and anti-AB antisera, no agglutination with anti-A_1 lectin, and an almost undetectable signal with anti-H antiserum. In the proband's serum, only traces of anti-A antibodies were found. She had negative results of irregular antibody screening. The RBCs of the proband's sister (II-2), nephew (III-1), and daughter (III-4) also showed the A_2B phenotype.

For ABO genotyping, genomic DNA was extracted by using a DNA Extraction Kit (Qiagen Inc., Chatsworth, CA, USA) from peripheral blood. DNA fragments covering exons 6 and 7 of the *ABO* gene were amplified as previously described [4] by using a GeneAmp PCR System 9700 (Applied Biosystems, Foster City, CA, USA). The amplified PCR products were digested with re-

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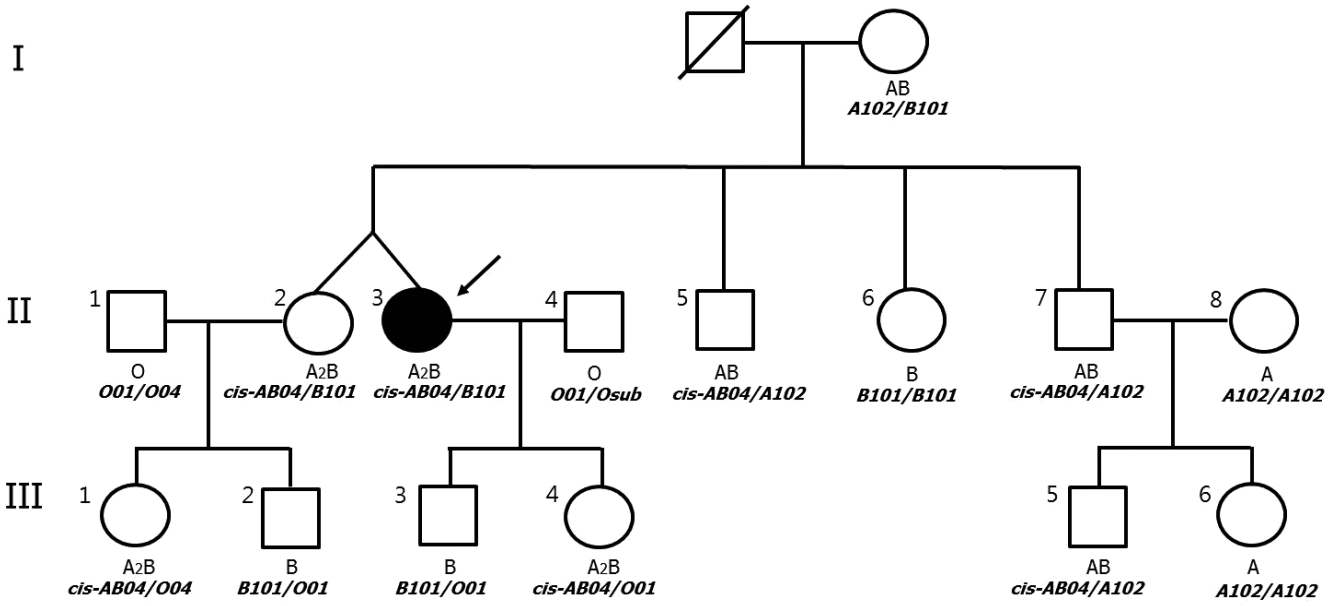

Fig. 1. Pedigree of the proband's family, showing inheritance of allele *cis-AB04*. The ABO blood group phenotype and genotype of each person are shown. The filled circle with the arrow indicates the proband.

striction enzymes *Kpn*I and *Alu*I and fractionated by electrophoretic separation on agarose gels. Direct sequencing of the PCR product was carried out by using previously described methods [5, 6] on an ABI 3130 Genetic Analyzer (Applied Biosystems), and the data were analyzed in the SEQUENCHER software (Gene Codes Corp., Ann Arbor, MI, USA) v.4.9. Direct sequencing of *ABO* exons 6 and 7 from the clones of the proband showed the c.796C>A substitution (p.Met266Leu) based on allele *ABO*A102* and confirmed the presence of *cis-AB04* (Fig. 2). The other allele corresponded to *ABO*B101*. Pedigree analysis revealed that three siblings (II-2, II-5, and II-7), the daughter (III-4), and two nephews (III-1, III-5) of the proband also carried the *cis-AB04* allele (Fig. 2).

Allele *cis-AB04* was first reported by two separate Taiwanese groups [7, 8]. This allele is similar to allele *A102* bearing the 796C>A substitution, which causes the Leu266Met mutation. The *A102* allele is common among Asians and differs from the *A101* allele by one nucleotide polymorphism, 467C>T (Pro-156Leu) and this amino acid substitution is unlikely to be deleterious to the activity of glycosyltransferase A (GTA) encoded by *A102*. On the other hand, amino acid residue 266 is known to be one of two critical positions determining A and B transferase specificity via complementary stereochemical relations between the side chains of these amino acid residues and the size of the donor sugar [1].

Phenotype *cis*-AB may be affected by a coinherited allele. In our case, *cis-AB04* that was inherited with an *O01* or *O04* allele,

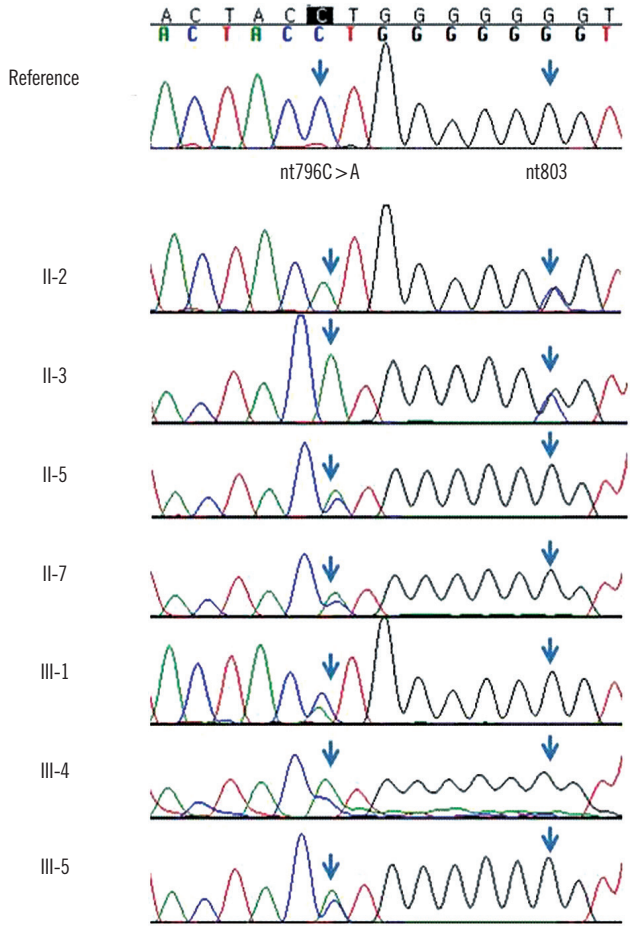

Fig. 2. Sequence analysis at and around nucleotide (nt) 796 of exon 7 of allele *cis-AB04*.

A101 allele, and *B101* allele yielded phenotypes A_2B, AB, and A_2B, respectively. Other authors reported *cis-AB04* in combination with *O* alleles and *B101* resulting in the A_2B phenotype, which matches our case [7, 8]. In reverse grouping, there was one report describing the presence of an anti-A_1 antibody of varying strength [7], and our results also showed the presence of a weak anti-A antibody in the proband and her family.

Transfusion for a patient with allele *cis-AB04* can be challenging because blood type ABO can be misclassified. When blood type *cis*-AB04 is confirmed, theoretically, blood type O or B RBCs can be transfused, considering the presence of anti-A in serological tests of previously reported cases and our case. For platelet and fresh frozen plasma transfusion, blood type AB should be considered.

This case suggests that the possibility of *cis*-AB04 should be considered when diagnosing blood group *cis*-AB in the Korean population.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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