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ONE-PAGE REPORT OF NEW ALLELES OR ANTIGENS

TRANSFUSION

A novel *FUT1*932A* allele associated with the para-Bombay A phenotype in a Chinese individual

Lili Shi[1] | **Ling Ma**[1] | **Chenchen Feng**[1] | **Qinping Yang**[2]

[1]Department of Transfusion Research, Jiangsu Province Blood Center, Nanjing, China

[2]Department of Transfusion Medicine, Bengbu Blood Center, Bengbu, China

Correspondence

Ling Ma, Department of Transfusion Research, Jiangsu Province Blood Center, 179 Longpan Road, Nanjing, Jiangsu 210042, China.
Email: mlinsmile@hotmail.com

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1 | BRIEF BACKGROUND

The H antigen serves as a precursor to both A and B antigens; H antigen deficiency causes rare Bombay and para-Bombay phenotypes within the H blood group systems. The type 2 chain H antigen status on red blood cells (RBCs) is determined by the α-(1,2)-fucosyltransferase gene *FUT1* (also known as the *H* gene), while *FUT2* (also known as the *Se* gene) determines the expression of soluble type 1 chain H antigen in secretions. Bombay phenotypes are characterized by H-deficient nonsecretors with silencing mutations in both *FUT1* and *FUT2*. The para-Bombay phenotypes are H-deficient secretors, which means they have silenced *FUT1* genes but active *FUT2* genes, and soluble type 1 chain ABH antigens may be adsorbed on RBCs. Para-Bombay phenotypes may include individuals with mutations in the *FUT1* gene that weaken the expression of H antigens on RBCs, which can be secretors or nonsecretors.[1] A para-Bombay A phenotype associated with the c.932G>A mutation in the *FUT1* gene is reported.

Abbreviations: ASP, aspartate; BP, base – pair; DNA, deoxyribonucleic acid; GLY, glycine; INC, incorporated.

2 | BRIEF METHODS

The ABO phenotype of RBCs was routinely detected via tube testing, and in the case of a discrepancy, further investigations were conducted to assess the H antigen and Lewis blood groups (anti-A, anti-B, and Anti-H, clone no. SRBC-B3 + 9113D10, SRBC-C1 + 9621A8 and H5B12, respectively; ABO Reverse Grouping Reagent Kit; Shanghai Hemo-Pharmaceutical and Biological, Inc., Shanghai, China; Anti-Le^a and Anti-Le^b, clone no. LEA2, and P3F234MD4; Sanquin, Netherlands). An absorption–elution test (using anti-A and anti-H, as mentioned above) was used to detect weak A and H antigens on the surface of RBCs.

Genomic DNA was extracted from peripheral blood using a commercially available extraction kit (TaKaRa, Dalian, China). A 1198-bp fragment of *FUT1* was analyzed using direct Sanger sequencing (ABI3500xl, ABI, USA).[2] *FUT2* and exons 6 and 7 of *ABO* were amplified and sequenced.[3,4] Third-generation single-molecule real-time DNA (SMRT) sequencing (PacBio Sequel II, Pacific Biosciences, Inc. USA) was performed to identify heterozygous mutations (performed by Haorui Genomics Company, Xi'an, China). All sequences were compared with the reference sequences (*FUT1*: NG_007510.1; *FUT2*: NG_007511.1; *ABO*: NG_006669.1). The donors provided informed consent prior to sample collection.

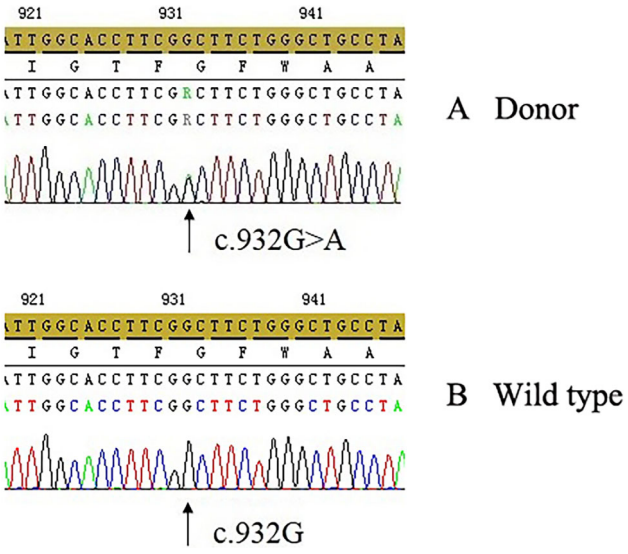

FIGURE 1 *FUT1* gene sequencing results. (A) Direct Sanger sequencing showed a novel heterozygous mutation, c.932G>A of the donor (another deletion mutation, c. 551_552delAG, was not shown); (B) wild-type control.

3 | RESULTS

A discrepancy in ABO blood group results was observed between forward and reverse typing. The RBCs of the donor exhibited no agglutination with anti-A, anti-B, or anti-H antibodies, whereas the serum grouping exhibited only strong agglutination with B cells. Absorption–elution tests indicated trace amounts of the A antigen on red cells, whereas the H antigen was not detected. The donor was demonstrated to be a secretor by his Le(a–b+) blood group phenotype. Based on these serological characteristics, a para-Bombay A phenotype was identified.

Direct sequencing analysis of the *ABO* gene confirmed the genotype as *ABO*A1.02/O.01.02*, which was consistent with the serological phenotypes. *FUT2* was homozygous for functional Se^{357}, which is common in Asian populations and indicated the secretor status. *FUT1* genotyping showed heterozygosity for a known deletion mutation, c.551_552delAG (*FUT1*01N.06*), and a novel missense mutation, c.932G>A (Figure 1). SMRT technology confirmed that the two mutations were present on two separate strands. The novel missense mutation, c.932G>A, resulted in an amino acid substitution from Gly to Asp at residue 311 (p.Gly311Asp). According to https://www.mutationtaster.org/,[5] this missense mutation is predicted to be "disease-causing" and defined as a new molecular basis for the para-Bombay phenotype. The relevant sequence has been submitted to GenBank (accession number OQ401875).

4 | BRIEF SUMMARY

The *FUT1*932A/01N.06* genotype was identified in a Chinese individual with the para-Bombay A phenotype. The novel c.932G>A nucleotide mutation of the *FUT1* gene might abolish or weaken the activity of the α1,2-fucosyltransferase to cause H antigen deficiency.

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CONFLICT OF INTEREST STATEMENT

The authors have disclosed no conflicts of interest.

ORCID

Lili Shi https://orcid.org/0000-0002-7374-8322
Ling Ma https://orcid.org/0000-0001-8981-2483
Chenchen Feng https://orcid.org/0000-0003-4075-5208

REFERENCES

1. Fung MK. Technical manual. 19th ed. Bethesda, MD: American Association of Blood Banks; 2017. p. 280.
2. Yan L, Zhu F, Xu X, Hong X, Lv Q. Molecular basis for para-Bombay phenotypes in Chinese persons, including a novel non-functional FUT1 allele. Transfusion. 2005;45(5):725–30.
3. Anukul N, Wita R, Leetrakool N, Sirikul C, Veeraphan N, Wongchai S. Two novel alleles on Fucosyltransferase 2 from northern Thai para-Bombay family and computational prediction on mutation effect. Transfusion. 2021;61(11):3247–57.
4. Zhu F, Tao S, Xu X, Ying Y, Hong X, Zhu H, et al. Distribution of ABO blood group allele and identification of three novel alleles in the Chinese Han population. Vox Sang. 2010;98(4):554–9.
5. Schwarz JM, Rödelsperger C, Schuelke M, Seelow D. MutationTaster evaluates disease-causing potential of sequence alterations. Nat Methods. 2010;7(8):575–6.

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