ABO genotyping for diagnosis of unusual ABO blood groups: A Comparative Study in German Blood Donor Centers

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Background:
Unusual ABO typing results are a common problem in blood grouping. Rare ABO alleles have been shown to encode for the expression of aberrant ABO phenotypes, resulting in weak antigen activity as well as unexpected findings in reverse typing. Little is known about the frequency and the specificity of phenotypically relevant rare ABO alleles in a certain population.

Methods:
Among 142,000 red blood cell donations collected from first- and second-time donors in three German blood donor centers within a six-month period, we analyzed the ABO alleles of those donations in which the ABO phenotypes couldn’t be defined by automated systems and/or manual serological methods. The presence of rare ABO alleles was determined by sequence-specific priming (BAG Health Care, Lich, Germany; Figure 1) and, if necessary, further investigated by sequencing.

Results:
198 (0.14%) of the red cell donations revealed unusual ABO phenotypes. The majority of these red cell donations (n=107) exhibited an O phenotype with reduced iso-agglutinin activity: the non-deletional ABO*0 allele ABO*O03 (O') was implicated in 97, and the genotype ABO*O01/O01 (O') in 5 of these cases, while known A subgroup alleles (ABO*Ael, ABO*Aw, ABO*Ax) were detected in only 5 cases (Figures 1 and 2). The other 91 red cell donations had A and/or B phenotypes with reduced antigen expression and/or inconsistent reverse typing results; in 14 of these cases variant ABO*A and ABO*B alleles and in one case a chimerism was found. Among the variant ABO alleles, twelve known ABO*A and ABO*B alleles and two new ABO*B alleles could be identified. The two new alleles had novel single mutations in exon 6 and in the exon1/intron1 boundary, respectively (Figure 4).

Conclusion:
Rare ABO alleles are the major cause of abnormal ABO blood groups in Germany. The use of a PCR-SSP technique which is designed according to population-specific allele frequencies and occasionally supplemented with DNA sequencing is an effective and economic strategy to clarify unusual ABO phenotyping results (Figure 3).