ABO genetics

Description

The ABO gene was first cloned in 1990 and is located on the long arm of chromosome 9q34 Ferguson-Smith et al.,1976Yamamoto, et al., 1990and consists of seven exons and six introns, covering approximately 20 kilobase pairs from the initiation to the stop codon White, T., et al.,1995Bennett, E.P., et al.,1995 Yamamoto, 1995. The nucleotide sequence of the coding region of the gene consists of 1062 base pairs and encodes a 354 amino acid polypeptide. The gene is largely polymorphic, resulting in different defined variants of *A*- *B*– and **H-**alleles. The A^1 allele, [A101] Yamamoto et al.,1990Seltsam et al.,2003, the most frequent European A allele, is considered as the consensus (index) against which all other variants of ABO genes are compared. The A^2 allele [A201] Yamamoto et al.,1992Seltsam et al., 2003 is the second most frequent A allele in Europeans. The allele frequencies may differ in other populations worldwide. The A^2 has a nucleotide substitution at nucleotide (nt) 467 C>T, and a deletion of cysteine at nt. 1061 (1061 delC) resulting in a frame-shift and an extension of 21 amino acids of the polypeptide leading to a less efficient enzyme Yamamoto et al.,1992. The B allele [B01] Yamamoto et al.,1990 is distinguished from the A^1 allele by seven exonic mutations, four of which change the amino acids and thereby the specificity of the enzyme. The most critical amino acid changes is at 266 Leu >Met and 268 Gly > Ala Yamamoto & Hakomori,1990Yamamoto & McNeill 1996Olsson et al.,2001.

The majority of other A and B alleles, listed in Blood Group Antigen mutation database (dbRBC Website http://www.ncbi.nlm.nih.gov/projects/gv/rbc) Patnaik, 2012 are associated with other A and B phenotypes. For example for the A phenotype, these include A^3 (13 alleles), Ax (28 alleles), A^m (4 alleles), A^{finn}, A^{bantu}(1 allele) and A^{el} (12 alleles) For references and more details we refer to the dbRBC Web site.

There is a large amount of genetic polymorphism within each of these variants of ABO phenotypes, which is exemplified by the number of reported variant alleles within the brackets. However, it should be appreciated that differentiating the serology of some of these phenotypes is somewhat arbitrary and can be ambiguous. Other large groups of alleles have not been specifically associated with a named phenotype although their phenotypic serology may be identical. These alleles are simply named weak (A^w or B^w). The A weak subgroups are usually defined by A^1 or A^2 alleles with novel point mutations. Blood group B and AB also express weak phenotypes, but these are less well investigated.

The most common blood group O(H) allele, O^1 [O01], has a deletion of a guanine at nucleotide 261, which leads to a frame-shift and premature stop codon and thereby a truncated, inactive enzyme Yamamoto et al.,1990. There are many other variants of *O* alleles lacking this deletion but still causing inactive enzymes. Blood group O also has a large number of different alleles reported, including some alleles causing weak expression of A or B antigen Seltsam et al., 2003Hosseini-Maaf et al., 2005Yazer & Olsson, 2008. It can be argued that blood group O alleles resulting in low-level expression of A and/or B antigens are inappropriately named as *O* alleles, and only alleles that result in undetectable A or B antigens on red cells should be classified as *O*. But this simplistic explanation is

problematic as the definition of group O is not clearly defined or what sensitivity of the detection system is appropriate.

The presence or absence of antibodies to the ABO antigens, representing the O and A weak and B weak phenotypes, should possibly not be used to define the phenotypes as their presence or absence may be unreliable and variable.

In addition, mutations in sequences outside the coding region may decrease or abolish the enzyme activity. These sites are the “+5.8-kb site”, the erythroid cell-specific regulatory element, which is located in the first intron at positions +5653 to +6154, and serves as binding sites for the transcription factors GATA-1/2 and RUNX1. Also, the *ABO*promoter located between nt -149 and -2 before the translations start may be altered Sano et al., 2012. A large number of variant mutations in these regions and introns is also reported.

Category

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