Influence of other systems on ABO antigens

Description

In addition to those interactions with glycosyltransferases involved in biosynthesis described in previous chapters above (Figure 4), the effects of other blood group systems on ABO antigens deserve further mentioning. These ABO unrelated blood group systems can independently and cumulatively have consequences on ABO antigen expression either by competing for precursors and/or structurally altering the ABO antigen, thereby affecting its biological and serological characteristics.

The I blood group system is the carrier of the type 2 precursor also known as N-acetyllactosamine units (Gal?4GlcNAc?3), and is the precursor for the H type 2 antigen, and therefore is a pre-requisite of all type 2 antigens on red cells. Any variation in the structure of the I antigen is reflected in the presentation of the ABO antigens. The I blood group system is seen in two basic configurations, extended linear N-acetyllactosamine units (known as i antigen) and branched N-acetyllactosamine units known as I antigens. It is well recognized that the ABO antigens of neonates are carried on linear (i antigens) chains while those of most adults are branched (I antigens) structuresClausen & Hakomori, 1989Okada et al., 1984Koscielaj et al., 1979. These linear and branched structures may contain up to 50 – 60 saccharides and as glycolipids are called polyglycosylceramides Koscielak et al., 1976). Little is known about the contribution of these large ABO structures to serology but it is assumed that the branching and multivalency of antigens increase avidity. It has been suggested that a lack of branched glycolipids may also contribute to the mixed field reaction seen in the A3 phenotype Svensson et al., 2011. The linearity of the ABO antigen caused by the i antigen as seen in neonates reduces the avidity with antibody and has probably evolved as a consequence of protection of neonates from ABO hemolytic disease Romans et al., 1980.

The H blood group system and its resultant transferase are responsible for the synthesis of the requisite H precursor, without which the dominant type 2 antigen of red cells, built upon the I/i antigens, cannot be synthesized. H enzyme is also responsible for the synthesis of H type 3 and H type 4 but not H type 1 (see secretor below)Henry et al., 1995Mollicone et al., 1995. Individuals of the Bombay phenotype Larson Fernandez-Mateo et al., 1998 (H deficient and Secretor negative), where no H type 1, 2 or 4 antigens is synthesized, cannot express their A or B phenotype on red cells despite having a functional glycosyltransferase. Individuals with partially inactivating H mutations (e.g. para-Bombay) may result in weak-ABO phenotypes (see below). Establishing a normal H antigen basis is easily done by use of the lectin *Ulex europeaus*, and anomalies can usually be resolved by genotyping for the H gene.

The secretor system (Se) is separate from H and is responsible for expression of H type 1 antigen (and H type 2 but only in the secretory compartment and not on red cells). The enzyme encoded by the H-gene cannot utilize the type 1 precursor. H type 1 and associated type 1 and for example, ALe^b glycolipids can be found in the plasma (and secretions) of individuals with the secretor phenotype. These glycolipids will absorb into the red cell membrane and create low levels of type 1 ABO antigen expression – a mechanism that can result in a weak-ABO phenotype in an H deficient secretor positive

individual. The secretor status of an individual can be easily determined by sequencing or genotypingSvensson et al., 2000Grahn et al., 2001. The determination of ABO blood group substances in saliva was historically considered a guide in the interpretation of a weak subgroup, but due to the unreliability of this technique, particularly with monoclonal antibodies Henry et al., 1995, it should only be used for guidance.

The Lewis glycosyltransferase ?3/4 fucosyltransferase (FUT3) is able to modify certain type 1 antigens into the compound antigen ALe*b* and BLe*b*. The Le^b antigen cannot be synthesized into ALe^b or BLe^b. These glycolipid antigens absorb from the plasma into the red cell membrane and can be readily detected in individuals of the Lewis-positive secretor-positive phenotypes. In general Lewis modification of the type 1 antigen reduces its activity against anti-Le^b reagents Larson et al., 1999 and can even result in mistyping as Le(a-b-). In determining the basis of a weak phenotype it is critical to know both the Lewis and Secretor phenotype/genotype of the individual so as to accommodate for the presence of these absorbed glycolipids in the red cell membrane. Type 2 ALe^Y and BLe^Y structures, if detected, may also occur as a consequence of Lewis glycosyltransferase action, but their contribution, if any, to ABO phenotypes is uncertain.

The glycosyltransferases resulting in blood group P1 and the Globo series of antigens (Pk, P) and the glycolipid structure x2 are also competing for the precursor neolactotetraosylceramide (nLc-4) (see Figure in Biosynthesis of ABO Glycolipids) and terminate the chain with Gal?4 and GalNAc?3, respectively.

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