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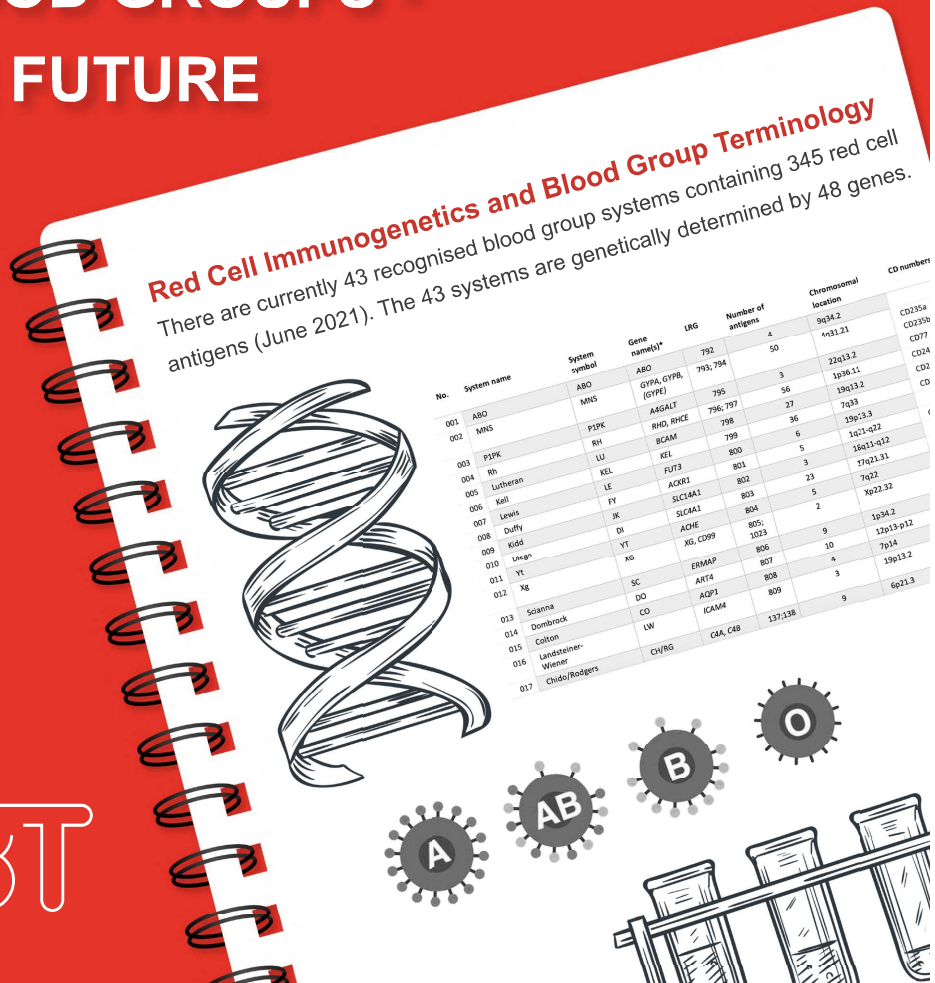
In Focus

BLOOD GROUPS - THE FUTURE



Editorial

It is a real pleasure to be able to include reports, in the ISBT Academy section, of two recent events at which delegates were able to meet in person in Pakistan and the UAE. Much as we have all come to embrace virtual meetings, I do hope this is the start of a return to face to face meetings for many more of us.

This edition's In Focus section highlights the huge impact that molecular studies have had on our understanding of blood groups and the opportunity to reduce alloimmunization for transfusion dependent patients; with fully genomics-based transfusion medicine potentially taking this to another level.

The members of the Working Party (WP) for ISBT Red Cell Immunogenetics and Blood Group Terminology are the 'custodians' of blood groups and the Co-Chairs share in their article the rigorous process for accepting a novel antigen. Their WP webpages have definitive information on blood group antigens / alleles and remain the most visited on the ISBT website. It's exciting to know that all this information and more could be available in a digital format before too long.

All of the ISBT working parties made great contributions to the live sessions for the ISBT In Focus congress in June, and reports from the congress can be found in the ISBT Central Office section. Meet the new Chairs of the Information Technology and Platelet Immunobiology WPs in this section too; congratulations to both!

In the ISBT Central Office, we are busy making a new website guided by results of a recent survey – thanks to all those of you who let us know what you like / don't like about the current site and new features you would like to see. The new website will be launched toward the end of 2021 and we hope it will become a focal point for members to interact as well as to access information.

Meanwhile, it is time to think about ISBT awards and prizes 2022 (page 18) and we look forward to your nominations!

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How a new blood group is acknowledged

The ISBT Red Cell Immunogenetics & Blood Group Terminology Working Party (RCI and BGT WP) work aims "To develop and maintain guidelines for blood group antigen and allele nomenclature for use in Transfusion Medicine and related sciences'. The WP members are charged with acknowledging and curating blood group antigens.[1]

Since the discovery of the first blood group (BG) system, in 1900, by Landsteiner a total of 43 blood group systems, containing 345 distinct antigen specificities, have been documented. These systems and antigens are registered on the WP Home Page on the ISBT website. Here we describe the steps leading to formal acknowledgement and registering of a new blood group system or to a new antigen within an existing system.

First it is important to note that a blood group system comprises antigens that are defined by a human alloantibody. BG antigen discoveries frequently are triggered through detection of a red cell antibody in a transfused patient or in a pregnant woman. As discussed in a previous Transfusion Today (number 125, December 2020) Genomic Technologies have led to a wave of recent blood group system and antigen discoveries.[2-5] The scope here is to describe how to ensure the discovery is acknowledged and registered for the global Transfusion Community.

Step 1,

Criteria to define a BG System or a new antigen in an existing system:

The first question to ask is does your finding tick the check list developed and established by the past and present WP members? This criteria can be found from the second page of the WP website under 'Criteria Used' at **isbtweb.org/working-parties/red-cell-immunogenetics-and-blood-group-terminology.**

It is of note that inheritance of the antigen has traditionally been determined by serology studies on extended family members. While family studies are still important, both genetic and genomic studies, using massively parallel sequencing (or next generation sequencing), now contribute to defining the gene and chromosome location.

Step 2,

Submission and Review by the Working Party:

The second step is to submit the findings to the WP via the Co-chairs. Many submissions are in the form of a manuscript or an abstract that will be (or has been) peer reviewed for publication. The Co-Chairs will include the submission on the agenda of the next formal Business Meeting. The person submitting will be invited to attend and present the findings to the WP members at this Business Meeting.

The presentation is followed by an enriching debate and then a vote to accept the findings as a novel BG system, or new antigen. However do not be dismayed if the antigen is not formally registered on this first presentation as it may well spark further informative studies.

As part of the acceptance process it is important to propose a name for the new BG System or new Antigen for the meeting to ratify. These will be registered on the respective ISBT Tables.

(Please note: The gene name, defining the location of the BG System, is predefined by the International HUGO Gene Nomenclature Committee.)

Step 3,

Nomenclature - naming a BG or antigen:

The WP will assign both a numerical and a common name to the BG system or antigen name. The numerical name, designed with foresight by the ISBT WP in 1980, starting with ABO ISBT 001, is designed for Bioinformatic management across clinical laboratories. The last two BG systems accepted in June 2021 by the WP were ISBT 042 EMM and ISBT 043 ABCC1.

The common name for each System and Antigen reveals a corner of rich history behind the discovery. Some names honor the patients or pregnant women who generously contributed to the findings (an early example is Mrs. Duffy).

Others may recognise the location from where the donor/patient came, a recent example being for the ISBT 039 CTL2 BG System, where the first antigen in this system, 001, is called VER after Verona (ISBT 0039 001 or VER) in Italy, where first female antibody-carrier against VER became apparent. Finally some antigen names now simply reflect the nucleotide or amino acid change causing the antigen polymorphism.

In summary, as remarked recently, the discovery of a new blood group system is a major milestone in transfusion medicine.[3] The process of acknowledging and naming is an important step to ensure these discoveries contribute to improving accurate red cell antigen antibody detection and thereby improve Transfusion Medicine practices in the future.

Appendix – extracted from ISBT web site:

Criteria for the establishment of new blood group systems

For an antigen to form a new blood group system:

- the antigen must be defined by a human alloantibody
- the antigen must be an inherited character
- the gene encoding it must have been identified and sequenced
- its chromosomal location must be known
- the gene must be different from, and not a closely-linked homologue of, all other genes encoding antigens of existing blood group systems.

Criteria for the inclusion of a new antigen specificity in an established system

All antigens awarded an ISBT number must have been shown to be inherited and at least one of the following four criteria must be met:

1 An antithetical relationship between a new antigen and one already assigned to the system.
2 Demonstration that expression of the antigen is associated with a variation in the nucleotide sequence of the gene controlling the system.
3 Evidence, from a linkage analysis of family data, that the controlling allele is probably a newly recognised form of the pertinent gene, and supporting serological or biochemical information.
4 Demonstration that an antigen is located on a protein or glycoprotein that carries other antigens belonging to the system. It must be remembered, however, that this could result from post-translational modification of a gene product, such as glycosylation, which would not support inclusion within the system.

References:

1 ISBT Terminology Committee. Red cell immunogenetics and blood group terminology Amsterdam: International Society of Blood Transfusion 2020 [Available from: http://www.isbtweb.org/working-parties/red-cell-immunogenetics-and-blood-group-terminology/.
2 Duval R, Nicolas G, Willemetz A, Murakami Y, Mikdar M, Vrignaud C, et al. Inherited glycosylphosphatidylinositol defects cause the rare Emm-negative blood phenotype and developmental disorders. Blood. 2021;137(26):3660-9.
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5 Omae Y, Ito S, Takeuchi M, Isa K, Ogasawara K, Kawabata K, et al. Integrative genome analysis identified the KANNO blood group antigen as prion protein. Transfusion. 2019;59(7):2429-35.

Other sources:

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