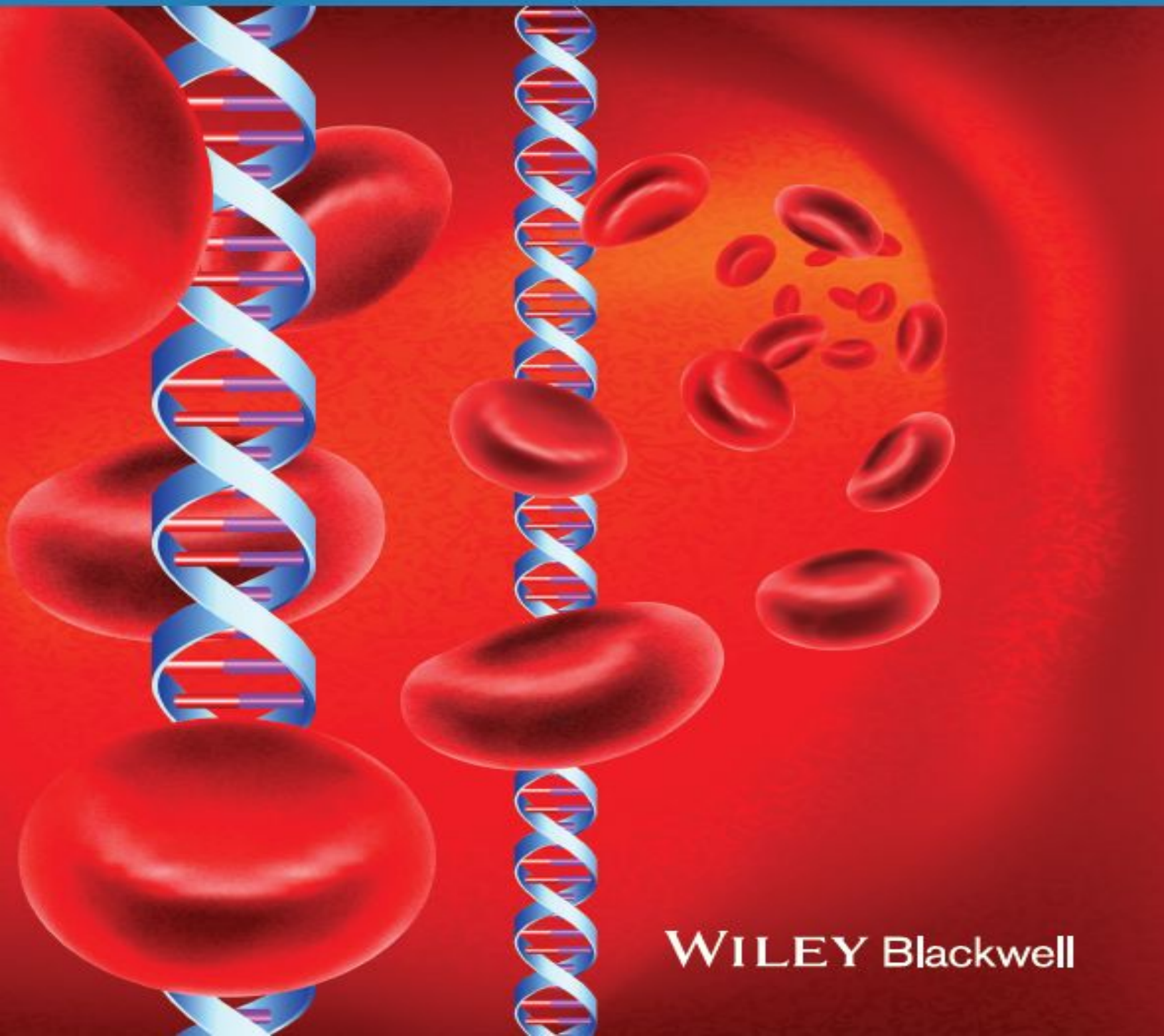
THIRD EDITION

Essential Guide to Blood Groups

GEOFF DANIELS AND IMELDA BROMILOW



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Abbreviations

2ME	2-mercaptoethanol
ADCC	antibody dependent cell-mediated cytotoxicity
AET	2-aminoethylisothiouronium bromide
AHG	anti-human globulin
AIHA	autoimmune haemolytic anaemia
AML	acute myeloid leukaemia
CAPA	corrective and preventive action
CGD	chronic granulomatous disease
CHAD	cold haemagglutinin disease
CLT	chemiluminescence test
CMV	cytomegalovirus
cv	co-efficient of variation
DAF	decay accelerating factor
DARC	Duffy antigen receptor for chemokines
DAT	direct antiglobulin test
DTT	dithiothreitol
EDTA	ethylenediaminetetraacetic acid
ETC	enzyme treated cells
FMH	feto-maternal haemorrhage
GP	glycophorin
GPI	glycosylphosphatidylinositol
HA	haemolytic anaemia

Hb	haemoglobin
HCT	haematocrit
HDFN	haemolytic disease of the fetus and newborn
HFA	high frequency antigen
HLA	human leucocyte antigen
HTR	haemolytic transfusion reaction
IAT	indirect antiglobulin test
ICAM	intercellular adhesion molecule
Ig	immunoglobulin
IL	interleukin
IS	immediate spin
ISBT	International Society of Blood Transfusion
IUT	intrauterine transfusion
LFA	low frequency antigen
LISS	low ionic strength saline
MAC	membrane attack complex
MCA	middle cerebral artery
MGSA	melanoma growth stimulatory activity
MMA	monocyte monolayer assay
NANA	N-acetylneuraminic acid
NISS	normal ionic strength saline
PBS	phosphate buffered saline
PCH	paroxysmal cold haemoglobinuria
PCR	polymerase chain reaction
PEG	polyethylene glycol

PNH	paroxysmal nocturnal haemoglobinuria
QA	quality assurance
QC	quality control
RBC	red blood cell
RCA	root cause analysis
SNP	single nucleotide polymorphism
SOP	standard operating procedure
TQM	total quality management
WAIHA	warm auto-immune haemolytic anaemia

CHAPTER 1

An introduction to blood groups

What is a blood group?

In 1900, Landsteiner showed that people could be divided into three groups (now called A, B, and O) on the basis of whether their red cells clumped when mixed with separated sera from other people. A fourth group (AB) was soon found. This is the origin of the term ‘blood group’.

A blood group could be defined as, ‘An inherited character of the red cell surface, detected by a specific alloantibody’. Do blood groups have to be present on red cells? This is the usual meaning, though platelet- and neutrophil-specific antigens might also be called blood groups. In this book only red cell surface antigens are considered. Blood groups do not have to be red-cell specific, or even blood-cell specific, and most are also detected on other cell types. Blood groups do have to be detected by a specific antibody: polymorphisms suspected of being present on the red cell surface, but only detected by other means, such as DNA sequencing, are not blood groups. Furthermore, the antibodies must be alloantibodies, implying that some individuals lack the blood group.

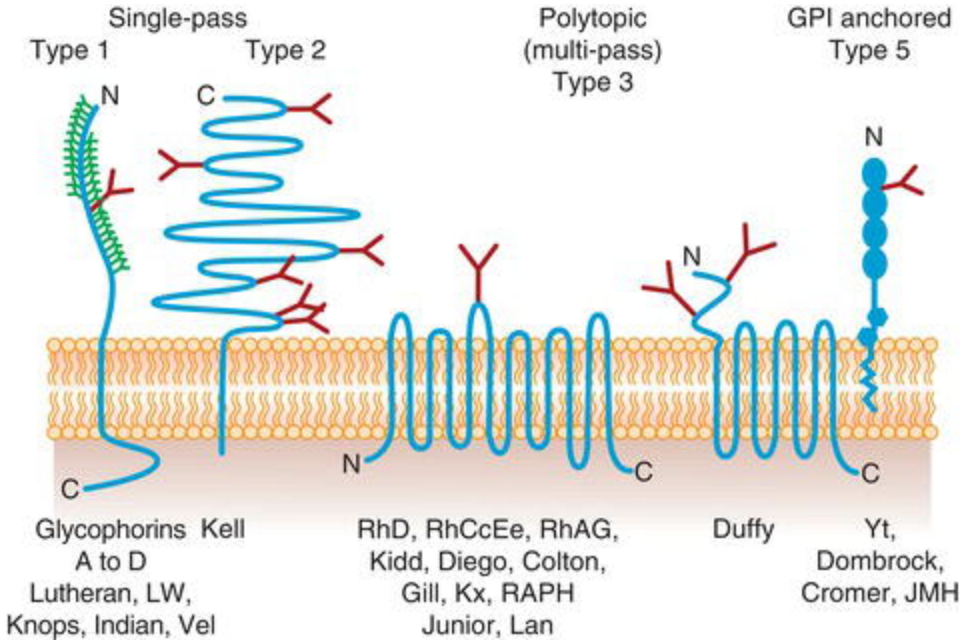
Blood group antigens may be:

- proteins;
- glycoproteins, with the antibody recognising primarily the polypeptide backbone;

- glycoproteins, with the antibody recognising the carbohydrate moiety;
- glycolipids, with the antibody recognising the carbohydrate portion.

Blood group polymorphisms may be as fundamental as representing the presence or absence of the whole macromolecule (e.g. RhD), or as minor as a single amino acid change (e.g. Fy^a and Fy^b) or a single monosaccharide difference (e.g. A and B).

Fig. 1.1 Diagram of different types of blood group active proteins and glycoproteins based on their integration into the red cell surface membrane. Listed are examples of blood group antigens for each type. (Type 4 proteins are cytoplasmic and not present in red cells.)



Blood group proteins and glycoproteins are integral structures of the red cell membrane. Diagrammatic representations of some blood group proteins and glycoproteins in the membrane are shown in Fig. 1.1. Some pass through the membrane once. These generally have an external N-terminal domain and a cytoplasmic C-terminal domain (Type 1), though in one case (the Kell glycoprotein)

the C-terminus is external and the N-terminus internal (Type 2). Some are polytopic (Type 3); that is, they cross the membrane several times. Usually both termini are cytoplasmic, but the Duffy glycoprotein has an odd number of membrane-spanning domains and an extracellular N-terminal domain. Finally, some have no membrane-spanning domain, but are anchored to the membrane by a lipid tail (called a glycosylphosphatidylinositol or GPI anchor), which is attached to the C-terminus of the protein through carbohydrate (Type 5). There are no Type 4 glycoproteins, which have no external domain, in the red cell membrane.

Most red cell surface proteins are glycosylated, the only exceptions being the Rh and Kx proteins. This glycosylation may be (1) N-glycosylation, large, branched sugars attached to asparagine residues of the amino acid backbone, or (2) O-glycosylation, smaller glycans (usually tetrasaccharides) attached to serine or threonine residues.

Blood group antibodies

Blood groups are antigens and, by definition, a molecule cannot be an antigen unless it is recognised by an antibody (or T cell receptor); therefore, all blood group specificities are defined by antibodies. Most adults have antibodies to the A or B antigens, or to both; that is, they have ‘naturally occurring’ antibodies to those ABO antigens they lack. For most other blood groups, corresponding antibodies are not ‘naturally occurring’, but are only formed as a result of immunisation by transfused red cells or by fetal red cells leaking into the maternal circulation during pregnancy or childbirth.

Blood group antibodies are usually IgM or IgG, although some may be IgA (Chapter 6). ‘Naturally occurring’ antibodies are usually predominantly IgM, whereas ‘immune’ antibodies are predominantly IgG. As a general

rule, IgM antibodies will directly agglutinate antigen-positive red cells in a saline medium, whereas most IgG antibodies require potentiators or anti-human globulin to effect agglutination (Chapter 2).

Clinical importance of blood groups

Blood groups are of great clinical importance in blood transfusion and in transplantation. In fact, the discovery of the ABO system was one of the most important factors in making the practice of blood transfusion possible. Many blood group antibodies have the potential to cause rapid destruction of transfused red cells bearing the corresponding antigen, giving rise to a haemolytic transfusion reaction (HTR), either immediately or several days after the transfusion. At their worst, HTRs give rise to disseminated intravascular coagulation, renal failure, and death. At their mildest, they reduce the efficacy of the transfusion (Chapter 6).

IgG blood group antibodies can cross the placenta during pregnancy and haemolyse fetal red cells expressing the corresponding antigen. This may cause alloimmune fetal haemolytic anaemia, more commonly known as haemolytic disease of the fetus and newborn (HDFN). Many blood group antibodies have the potential to cause HDFN, but the most common culprits are D and c of the Rh system and K of the Kell system.

Biological importance of blood groups