PA02-L02 | Red cell phenotyping and genotyping among blood donors

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It has been standard Transfusion Medicine practice for many years to provide patients who have clinically significant alloantibodies with red cells that lack the target antigen. In patients with simple antibodies, this is uncontroversial testing and units are readily identified by serologic phenotyping. However, for patients that require blood that is matched for two or more antibodies, serologic testing becomes more unwieldy, time-consuming and expensive. Furthermore, the increased use of 'phenotypically similar' blood for transfusion-dependent patients, for example, those with haemoglobinopathies, or following chemotherapy regimens, has meant an increased demand on phenotyped units. Many blood centres have established high-volume antigen typing using cheaper microplate methods that help them to supply the demand, however phenotyping reagents are more and more difficult to source and expensive for companies to produce.

The molecular bases for all commonly encountered and clinically significant antigens are now well-established and thus blood centres have turned their focus to blood group genotyping platforms to predict red cell phenotype. While there is not complete correlation, the risk of error lies in the blood donor's favour since the majority of available assays target the antigen-defining genetic variation. The potential presence of silencing mutations in a gene simply means that a blood donor will be falsely predicted to be positive for an antigen and thus does not provide risk to a patient. Many of the large blood suppliers now use blood group genotyping platforms to provide a large inventory of phenotyped blood, and to meet the requirements of their patients. Furthermore, rare blood programs are now often able to provide liquid units and avoid the cost of freezing, storage and thawing of rare blood. Acute and delayed transfusion reactions still remain a major source of preventable error, and while a review of the impact on alloimunisation rates by the provision of better matched blood is confounded by a reduction in the use of blood products in general, the prediction is that better matching will help to provide safer blood.

PA02-L03 | Ten years of donor RHD screening in Switzerland

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Background: Very weak RH1 (RhD) variants may be missed even by phenotyping methods including indirect antiglobulin test (IAT). However, in light of the strong immunogenicity of RH1, very low expression of the antigen may be sufficient to trigger alloimmunization in RH1 negative recipients after transfusion. Therefore, molecular routine screening for the presence of *RHD* was implemented in Switzerland for all serologically RH1 negative first-time donors in 2012 (mandatory since 2013), according to the guidelines of the Blood Transfusion Service of the Swiss Red Cross. Previous results on this screening strategy have already been published [Lejon Crottet et al., (2014) [1], Henny et al., abstract (2016)]. Herein we report on the complete data collection of this nationwide *RHD* screening in Switzerland over the last 10 years (2012–2021).

Aims: Summary of a Swiss-wide collection of *RHD* variants detected by the mandatory molecular *RHD* screening performed on all serologically RH1 negative donors.

Methods: Screening of all RH1 negative first-time donors was performed at two Swiss blood transfusion services, Berne and Zurich, using SSP–PCR (Sequence Specific Primer-Polymerase Chain Reaction). Initially, slightly different sample preparations and exon compositions were applied [1], which have now been adapted to the RBC-FluoGene D-Screen kit (Inno-Train, Germany) including specific primers for *RHD* exons 3,5 and 10. *RHD* positive samples were analysed in detail using commercially available or in-house SSP-PCR kits (Inno-Train and BAGene, Germany) and Sanger-sequencing. Extended serological phenotyping, including adsorption and elution techniques, was performed as previously described.

Results: Between 2012 and 2021 87,863 serologically RH1 negative samples were screened in total. Of these, 570 (0.65%) were genetically positive for at least one of the three analysed *RHD* exons. Overall, 323 (57%) samples comprised a *RHD* variant classified as RH1 negative according to the ISBT allele tables for *RHD* and Rhesusbase. Among these variants, different *RHD-CE* hybrid alleles were most frequent (number [*n*] = 191), followed by *RHD*08 N.01* ($n = 103$) and *RHD*01 N.08* ($n = 9$). In contrast, 237 donors harboured a *RHD* allele provoking a reclassification of the donor to serologically RH1 positive. This number represents 42% of the genetically *RHD* positive donors and in average 0.27% of all RH1 negative donors. The most common alleles detected were *RHD*11* ($n = 66$), *RHD*01EL.08* ($n = 24$), *RHD*01EL.01* ($n = 17$) and *RHD*01 W.31* ($n = 15$). The novel allele *RHD*794C* was detected in two donors (abstract Kräuchi et al., ISBT 2022). Ten samples are still under investigation. These samples were also reclassified as RH1 positive until a definitive classification can be made.

Summary/Conclusions: Here we report the outcome of a ten-year molecular *RHD* screening. In total, 237 samples, originally determined as RH1 negative, were redefined as RH1 positive, corresponding to 0.27% of all screened samples. This approach represents a cost efficient strategy to detect RH1 variants as it replaces the former mandatory RH1 determination by IAT. Furthermore, it reduces the potential risk of alloimmunization in patients.

Henny C and Engstroem C: equal contribution, Meyer S and Lejon Crottet S: equal contribution.