Evaluation of a validated array genotyping platform for blood group antigen and allele prediction using routine and special samples pre-analysed by MALDI-TOF mass spectrometry

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Introduction: Comprehensive and accurate blood donor genotyping is crucial for reducing the risk of alloimmunisation in patients. MALDI-TOF mass spectrometry (MS) is a high-throughput platform used in our transfusion center for donor genotyping allowing the prediction of antigens on erythrocytes (HEA) and platelets (HPA). The high-throughput Axiom Universal Blood Donor Typing (UBDT_PC1) array may represent an affordable alternative in a more centralised and automated setting. We aimed to assess blood group antigen prediction on the UBDT_PC1 array with selected routine donor samples genotyped with MALDI-TOF MS. Particular samples with rare blood group alleles, often of non-European ethnicity, were additionally used to inspect the array's performance.

Methods: Up to 70 antigens were assessed in 569 routine donor samples either serologically (N=10) or inferred by MALDI-TOF MS genotyping. A further 191 samples, in which MALDI-TOF MS, PCR-SSP or Sanger sequencing revealed unusual allele combinations, were added and collectively analysed on the UBDT_PC1 array in an accredited laboratory. The array predicted 199 HEA and 54 HPA based on ~400 genetic variants. Predictions for presence of particular blood group alleles (N=17) representing RHD, GYPB, JK and FY systems were also available.

Results: Ten antigens (14%) were not predicted on the array. More than 30,000 comparisons of antigen presence vs. absence revealed no discordance in routine samples. In the group of challenging samples, concordance was 99.6% with 23 discrepancies restricted to RH, MNS, JK and DI blood group systems. Discordant results were attributable to 4 rare hemizygous *RHD* null alleles, two of which were detectable with in-house MALDI-TOF MS. One sample was interpreted as a weak C due to a wrong *RHD*/*RHCE* hybrid call on MALDI-TOF MS. Specific alleles on the homologous genes could explain two discrepancies between array and serological results: a non-inferred N in a *GYPA*M*/*N* sample with *GYPB*03N.04* and a non-inferred e in a *RHCE*E*/*e* sample with an additional *RHD*06.01*. JK and DI discrepancies were attributable to rare null alleles and a database error, respectively.

Conclusion: Results from the UBDT_PC1 array showed perfect concordance with in-house typed routine samples and very high agreement with challenging allele constellations. While the array is more comprehensive, the two very challenging blood group systems RHD and MNS show a larger panel of genetic variants for MALDI-TOF MS allowing more refined allele and antigen prediction.