56. Jahrestagung der Deutschen Gesellschaft für Transfusionsmedizin und Immunhämatologie e.V. (DGTI), 20.-22. September 2023, Berlin, Deutschland (Reinhold-Eckstein-Investigator-Award)

A universal blood genotyping array tailored for transfusion services and validated in a pre-clinical study of a large, ethnically diverse cohort

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Background: Extended blood group matching substantially reduces sensitization to non-self antigens as side effect of transfusion. For broad application, affordable high-throughput typing of relevant antigens is required. Following an earlier proof-of-concept study, our consortium presents here the development of a tailored universal blood genotyping array, including the results of an international Pre-Clinical accreditation Study (PCS) comprising an ethnically highly diverse panel of samples.

Methods: The custom-designed Axiom array contains 50,000 probes tagging 20,000 variants relevant for transfusion services. It has a 384-sample format and runs on GeneTitan-MC instrument, which can generate data for 3,000 samples/week. For the PCS, DNA samples and clinical antigen typing data from 13,908 selected donors provided by seven blood services were analysed. All main ethnic groups were covered. Samples were genotyped in triplicate at three blood services in the Netherlands, USA, and UK. Array-inferred antigen types were analysed for concordance with clinical antigen types provided by the blood services. At the time of abstract submission, concordance of the first set of 6,953 samples was analysed.

Results: The array allows simultaneous typing of most clinically relevant human erythroid (HEA), platelet (HPA), and leukocyte (HLA) antigens. Perfect consistency in performance was observed among the three testing labs. The overall concordance rates for HEA, HPA, and HLA antigens with previous testing were very high. Of nearly 100,000 comparisons between blood service determined

HEA antigen types and array determined types, the concordance was at 99.4%. Over half of the discordances were caused by incorrect serology. The results of the PCS proofed a robust validation of also non-European genotype configurations. The 1,925 samples of African ancestry showed a HEA concordance rate >99.7%. Also HLA class I and class II concordance level was excellent.

Conclusions: We developed an affordable and simple-to-use DNA-based test for automated high-throughput typing of donors and patients. Our universal blood typing array was tailored for the need of transfusion services and validated in an international, ethnically highly diverse cohort. Among others, the array represents a promising new tool to facilitate a broader application practise of extended blood matching to reduce sensitization rates and to identify rare donors.