Platelet donor database: a study on the specialist donor database for the patients with alloimmune thrombocytopenia in the Chinese population and the assessment of completeness

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To the Editor: Due to the immunogenicity of the platelet antigens, especially blood group antigen (such as ABO antigens), human leukocyte antigen (HLA), human platelet antigen (HPA), and CD36 (platelet glycoproteins IV), which can produce corresponding alloantibodies through immune factors such as blood transfusion, pregnancy, and drugs, the immune reaction of the platelet antigens and antibodies in patients will lead to various types of alloimmune thrombocytopenia, including the immune platelet transfusion refractoriness, post-transfusion purpura, and fetal/neonatal alloimmune thrombocytopenia.[1-4] Platelet transfusion is an effective approach to treat alloimmune thrombocytopenia. Antigen-negative platelets (platelets lacking certain antigens that do not react with the alloantibodies *in vivo*) are the keys to avoid related alloimmune reactions and achieve satisfactory treatment outcomes of platelet transfusion.[1] To this end, establishing a complete platelet donor database (PDD) that has a suitable number of donors with the known platelet antigens or antigen genotypes and meets the characteristics of platelet immunohematology in the local population is the effective way for the patients with alloimmune thrombocytopenia to quickly find out the antigen-matched platelet donors.

The characteristics of the antibodies that mediate the alloimmune thrombocytopenia could be various in different populations as the polymorphisms of antigens and related genes have racial characteristics. In the Chinese population, the anti-CD36 antibody is a vital platelet alloimmune-related antibody, along with the well-known anti-HLA and anti-HPA antibodies.[3] The incidence rate of the anti-CD36-mediated alloimmune thrombocytopenia is second only to that mediated by the anti-HLA antibody, which is closely associated with the high proportion of individuals with CD36-deficient platelets (1.80%–4.13%) in the Chinese population.[3] In the Caucasian population, anti-HLA and anti-HPA are the most common platelet immune antibodies, but anti-CD36 is a rare platelet antibody due to the low proportion of CD36-deficient individuals in the population (<0.40%).[2]

Our study aims to explore how to design and establish a PDD suitable for patients with alloimmune thrombocytopenia in China. The completeness (probability) of the PDD was evaluated with the criterion that one random recipient will have at least one matched donor in the PDD. We considered the population in the Nanning area of China as the model to analyze the characteristics of the platelet antigens and the related antibodies in Chinese populations. This is because Nanning, an important transportation hub city in Southwestern China, is a multi-ethnic area with a population of over 7 million people and currently has the highest incidence rate of CD36 deficiency among the reported regions in China.[3] Among the 265 published and unpublished cases of tested and identified platelet antibody specificity in our laboratory from 2007 to 2019, there were 231 cases of anti-HLA (89.17%, 231/265), 22 cases of anti-CD36 (8.30%, 22/265), five cases of anti-HLA combined withanti-CD36 (1.89%, 5/265), three casesofanti-HPA-3a (1.13%, 3/265), two casesofanti-HLA combined with anti-HPA-5b (0.75%, 2/265), one case of anti-HPA-5b (0.38%, 1/265), andone caseofanti-HLA combined with anti-HPA-3a (0.38%, 1/265) alloantibodies involvedin the occurrence of alloimmune thrombocytopenia in the Nanning area.[2-4]

Based on the analysis of the characteristics of *HLA-A* and *-B* gene polymorphisms and the cross-reactive groups (CREGs) of the population in the Nanning area (7001 samples detected), the *HPA-1-17w* gene polymorphisms of the population in the Nanning area (4243 samples detected), and the incidence rate of CD36 deficiency in individuals and ABO blood group distribution characteristics of the apheresis platelet donors in the Nanning area

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(5081 samples detected), a PDD consisting of the database of donors with known *HLA*, *HPA*, and CD36 deficiency was constructed. All the samples were random and unrelated individuals. The completeness (probability) of the PDD was evaluated with the criterion that one random recipient will have at least one matched donor in the PDD.

The formula $c(n) = \sum \text{fi} \times [1-(1-\text{fi})^n]$, established by Müller *et al*,[5] was developed by us to calculate the probability of the established PDD, with $c(n) \times 100\%$ as the database completeness (%). In the formula, n is the number of donors with known genes or antigens, f denotes the frequency of particular antigen phenotypes or genotypes, fi represents the frequency of the i^{th} phenotype or genotype, and i denotes all the possible phenotypes or genotypes. The curve with $c(n)$ as the ordinate axis and n as the abscissa axis was plotted, the regression equation of the curve was deduced, and the completeness (%) of the PDD was calculated.

We speculated the effect of the number of donors with known *HLA-A* and *-B* genotypes, the number of donors with known *HPA* genotypes, or the number of donors with known CD36 deficiency on the completeness of the PDD, such that there will be at least one donor with matching HLA-A and -B CREGs, matching *HPA-1-17*w, or CD36 deficiency and identical ABO to those of the recipient, respectively. The changing curve of the predicted effect of the number (n) of donors on the completeness [$c(n)$] of the PDD was deduced [Figure 1] and the logarithmic regression equations could be obtained. Combining the logarithmic regression formulas with the curve, it was speculated that for a 99% completeness of the PDD, 9516 donors with known *HLA-A* and *-B* genotypes, 1728 donors with known *HPA-1-17*w genotypes, and 33 donors with CD36 deficiency were required. The currently established PDD (Nanning Platelet Donor Database [NNPDD]) covered 1813 donors with known *HLA* and *HPA* genotypes and 209 platelet donors with CD36 deficiency, and the completeness was 90.23%, 99.04%, and 100.00%, respectively, when a random local recipient has at least one donor with fully matched HLA-A and -B CREGs, fully matched *HPA-1-17w,* and CD36 deficiency and identical ABO. The NNPDD has provided services for clinical transfusion therapy in the Nanning area. For the patients with alloimmune thrombocytopenia who require platelet transfusion, matched platelets were provided according to the matching strategy that selected platelet products from NNPDD do not react with antibodies *in vivo* and have negative relevant antigens. The current NNPDD could be further improved regarding its completeness by continuously renewing and increasing the number of donors with known *HLA* and *HPA* genotypes as well as CD36 deficiency donors, and needs to be maintained by continuous financial support. The model of PDD and its completeness assessment that we designed and developed is not only suitable for the Chinese population but also other populations locally or around the world.

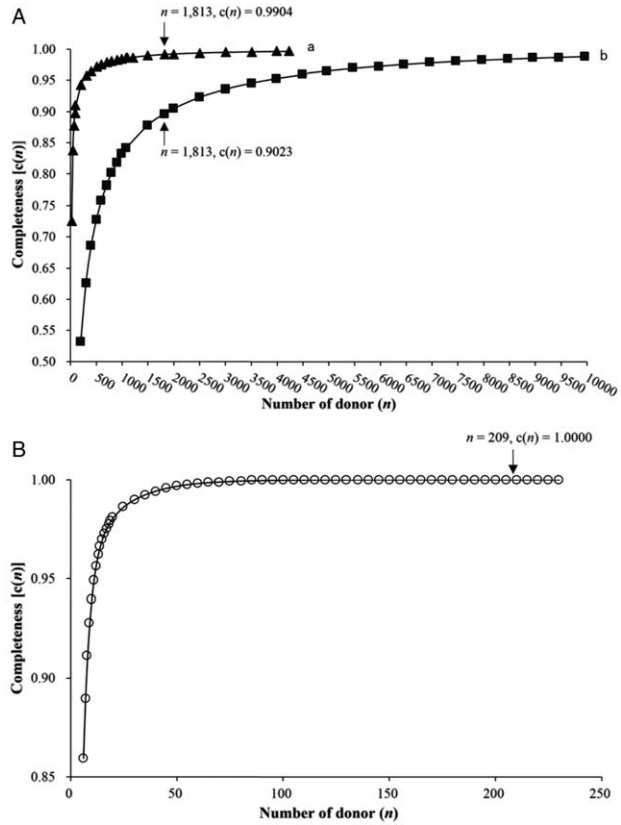

Figure 1: The changing curve of the predicted effect of the number of donors (n) on the completeness [$c(n)$] of the PDD. (Curve a) The changing curve of the predicted effect of the number of donors (n) on the completeness [$c(n)$] of the PDD, such that there will be at least one *HPA-1-17w*-matched donor for one random recipient. (Curve b) The changing curve of the predicted effect of the number of donors (n) on the completeness [$c(n)$] of the PDD, such that there will be at least one donor with HLA-A and B CREGs matched for one random recipient. (B) The changing curve of the predicted effect of the number of donors (n) on the completeness [$c(n)$] of the PDD, such that there will be at least one donor with CD36 deficiency and identical ABO for one random recipient with CD36 deficiency in the Nanning area population. CREGs: Cross-reactive groups; HLA: Human leukocyte antigen; PDD: Platelet donor database.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s)/or his/her guardian has/have given his/her/their consent for his/her/ their images and other clinical information to be reported in the journal. The patients or his/her guardian understand that his/her/their name(s) and initials will not be published and due efforts will be made to conceal his/her/their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

None.

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