Comment on Curtis et al, page 2073

Identification of the HNA-3a antigen

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In this issue of *Blood*, Curtis et al identify the human neutrophil antigen 3a (HNA-3a), which is contained within the choline transporter–like protein–2. Antibodies to HNA–3a have been implicated in significant numbers of fatal TRALI reactions, and the discovery reported by Curtis et al will lead to the identification of HNA-3a–negative donors to make transfusions safer.

Among the 5 HNA systems, HNA-3 was the only one that had yet to be characterized. This effort was critical because antibodies directed to HNA-3 are responsible for causing numerous cases of transfusion-related acute lung injury (TRALI), especially fatal TRALI. Antibodies to HNA-3a cause neutrophil (PMN) agglutination, priming of the PMN oxidase, and PMN-mediated killing of pulmonary endothelial cells in HNA-3a–PMNs and do not affect those granulocytes that do not express the antigen. A German group has also just described the identical protein as the HNA-3a antigen.

The identification of the molecular basis of HNA-3a and its allele HNA-3b should lead to the rapid manufacture of appropriate laboratory materials that will ensure the accurate identification of donors who are HNA-3a–deficient and may have antibodies against HNA-3a. Solid-phase assays to detect anti–HNA-3a should also be quickly developed.

Antibodies to HNA, especially HNA-3a, are likely to be found in multiparous female donors, and screening of female donors should be considered when the reagents are available. However, several studies of blood donors have found that HNA antibodies are rare even among multiparous females. Some blood centers are already testing multiparous apheresis platelet donors for HLA antibodies and not allowing those with high-titer antibodies to donate. It is likely that assays used to test these donors for HLA antibodies will soon include reagents to detect anti–HNA-3a. However, preventing people with leukocyte antibodies from donating platelets will not prevent all cases of TRALI, because bioactive lipids and soluble CD40 ligand, which accumulate in stored platelet components, also can cause TRALI. Ultimately, the identification of HNA-3a will make transfusions safer after appropriate screening of blood donors for antibodies to HNA-3a.

Conflict-of-interest disclosure: The authors declare no competing financial interests.

REFERENCES

1. Curtis BR, Cox NJ, Sullivan MJ, et al. The neutrophil alloantigen HNA-3a (5b) is located on choline transporter-like protein 2 (CTTL2) and appears to be encoded by an R>Q154 amino acid substitution. *Blood*. 2010;115(10): 2073–2076.


