# The Lancet Haematology Should unrelated HPC donors be tested for CD36 in Japan? --Manuscript Draft--

Manuscript Number:	
Article Type:	Correspondence
Keywords:	CD36 deficiency; donor registry; allogeneic haematopoietic stem cell transplantation; Japan
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Manuscript Region of Origin:	JAPAN

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Manuscript word count: 400 words

No potential conflict of interest relevant to this letter was reported.

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This is a correspondence letter to the Lancet Haematology article entitled "Suitability of haematopoietic cell donors: updated consensus recommendations from the WBMT standing committee on donor issues" (Lancet Haematol. 2022 Aug;9(8):e605-e614. doi: 10.1016/S2352-3026(22)00184-3).

#### Text

Dr Worel and colleagues presented updated recommendations on the suitability of haematopoietic progenitor cell (HPC) donors for allogeneic haematopoietic stem cell transplantations (HSCT).<sup>1</sup> We would like to comment on the current situation of unrelated HPC donor registries in Japan.

The need for CD36 antigen-matching in HSCT is an issue under discussion in Japan, where the incidence of CD36 deficiency is higher compared to Caucasians, accounting for 3-11% of the population<sup>2,3</sup>. CD36 is mainly expressed on platelets and monocytes and may cause isoimmune thrombocytopenia, such as platelet transfusion refractoriness (PTR), foetal-neonatal alloimmune thrombocytopenia (FNAIT), and transfusion-related acute lung injury (TRALI)<sup>2,4</sup>, but it is also expressed on endothelial cells, erythroblast/myeloblast progenitor cells, indicating the clinical implications of CD36 antigen/antibody in HSCT. Type I deficiency, in which CD36 is absent on all cell types<sup>2</sup>, accounting for 0.5-1.0% of the Japanese population, is of special interest. Type II deficiency, where CD36 is absent only on platelets. CD36-deficient individuals have no apparent clinical symptoms, and related screening tests are limited;<sup>4</sup> it is usually diagnosed when PTR or FNAIT develop, or when blood donors are screened for CD36-antigen expression for the blood donor registry at the Japanese Red Cross Blood Services (JRCBS).

CD36 testing of HPC donors is not available at either the Japan Marrow Donor Program or the Umbilical Cord Blood Bank.<sup>2</sup> The intensive platelet transfusions during preparation for HSCT may result in PTR, leading to transfusions of HLA- and CD36compatible platelets. CD36 isoantibodies produced by the incompatible platelet transfusion not only affect platelet recovery but also may deleteriously affect HSCT. Ideally, CD36-compatible HPC should be selected for HSCT, but actually, it is not feasible due to no available information on CD36 expression. Previously, it was opted to avoid HSCT in a CD36-negative patient with the suggested risk of a TRALI-like syndrome after infusion of CD36-positive HPCs.<sup>2</sup> Despite the successful CD36incompatible HSCT cases reported from China or USA, it seemed that the appropriate management of CD36 isoantibodies was essential for the success. In Japan, the JRCBS has a registry of CD36-negative platelet donors, including type II-deficient donors, but considering the presence of concomitant HLA antibodies, securing the necessary compatible platelets is not always easy.

Taken together, considering the various risks of performing CD36-incompatible HSCT in a CD36-negative patient, discussions are ongoing in Japan regarding the need for

implementing CD36 testing of unrelated HPC donors.

#### References

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Link to the published version of this manuscript:

https://doi.org/10.1016/S2352-3026(22)00296-4