Biol Blood Marrow Transplant 25 (2019) e39–e40

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Commentary

KIR Genotyping Data of More Than 3 Million Individuals Are Available for Global Unrelated Stem Cell Donor Searches (Comment to: Weisdorf D, Cooley S, Wang T, et al. KIR donor selection: feasibility in identifying better donors. Biol Blood Marrow Transplant. 2018; doi: 10.1016/j.bbmt.2018.08.022.)

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Article history:
Received 10 September 2018
Accepted 13 September 2018

Weisdorf et al. [1] report on the feasibility of optimized unrelated stem cell donor selection by donor KIR genotyping during ongoing donor searches. They identify core issues of this process—including participation of transplantation centers, number of requested donors per search, donor availability for KIR genotyping, and coverage of KIR genotyping costs—and conclude that presearch donor KIR genotyping would "accelerate the search process and provide useful data to provide the best donors quickly."

We agree with that conclusion. Furthermore, we would like to add that DKMS started KIR genotyping of newly recruited potential stem cell donors (presearch donor KIR genotyping) in January 2015. For that purpose, the DKMS Life Science Lab (Dresden, Germany) developed an amplicon-based next-generation sequencing (NGS) approach on MiSeq and HiSeq devices based on a well-established high-throughput HLA genotyping process [2,3]. Characteristics of the KIR genotyping approach have been presented previously [4,5]; a complete article is in preparation.

As a result of these efforts, 3.16 million KIR-genotyped registered stem cell donors are now listed within DKMS donor centers in Germany (1.98 million), Poland (563,000), the United States (313,000), the United Kingdom (282,000), and Chile (5000) and with Bangalore Medical Services Trust in India (BMST; 19,000; date of data retrieval: August 31, 2018). Approximately one-half of these donors were genotyped at allelic resolution in most loci. Genotyping results for the remaining donors indicate presence or absence of KIR genes. For all donors, the KIR genotyping information allows the classification of "KIR best," "KIR better," and "KIR neutral" as applied by Weisdorf et al [1]. Owing to the ongoing donor recruitment and KIR genotyping efforts of DKMS, the number of KIR-genotyped registered stem cell donors currently increases by roughly 80,000 to 100,000 donors each month.

The global database of the World Marrow Donor Association (WMDA Search & Match Service; formerly known as Bone Marrow Donors Worldwide) and the European Marrow Donor Information System (EMDIS) offer the possibility of transmitting and/or displaying information on the presence or absence of each KIR gene for registered stem cell donors. A request for change to also include KIR allele-level information is pending. Via EMDIS, KIR-genotyped donors can be requested at their respective registries. More detailed information on accessing KIR information of donors from the various DKMS donor centers is available on request (pingel@dkms.de).

Regarding genotyping costs, several statements can be made. First, in the presearch high-throughput setting described above, costs per sample are much lower than in the context of individual donor searches. Second, the shift from Sanger sequencing to NGS is associated with substantial cost reductions in high-throughput HLA genotyping. Third, NGS technology generally allows the addition of further parameters to an existing workflow at low costs. As a result, we were able to extend the profile genotyped at donor recruitment (6 "classical" HLA loci at high resolution) by all KIR genes and various other parameters [6-10] while still reducing costs considerably compared with the Sanger-

Financial disclosure: See Acknowledgments on page e40.
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https://doi.org/10.1016/j.bbmt.2018.09.020

based workflow. Therefore, cost issues should not prevent presearch donor KIR genotyping, because several high-throughput HLA genotyping service providers also offer NGS-based KIR genotyping.

In summary, presearch high-throughput donor KIR genotyping seems to be more attractive than KIR genotyping of individual donors during ongoing donor searches. More than 3 million KIR-genotyped donors are currently available via the abovementioned channels. From our experience, cost issues related to presearch donor KIR genotyping should be manageable, owing mainly to NGS-related cost savings; however, we acknowledge the existence of several competing strategies for donor classification, which require validation in independent cohorts to propagate their use.

ACKNOWLEDGMENTS

Conflict of interest statement: There are no conflicts of interest to report.

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