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Editorial

Novel Strategies in Hematopoietic Stem Cell Transplantation

Editorial

Hematopoietic stem cell transplantation (HSCT) is an important life-saving procedure which is applied in cases of genetic defects or malignant tumors. Hematopoietic stem cells (HSCs), reside in certain "niches" within the bone marrow allowing them to reproduce themselves and remain in undifferentiated state [1,2], whereas there are evidence that HSC population is not homogenous and can be divided into subtypes [2]. Dependent on the donor of HSC, HSCT can be autologous (if the donor and the recipient is the same person), allogeneic (HSC come from a different person) or syngeneic (HSC donor is identical twin).

The first step in HSCT requires stem cell mobilization using G-CSF or, in the autologous HSCT, various chemotherapeutics in combination with G-CSF [3]. Disruption of CXCL12 binding to CXCR4 has been shown to mobilize HSCs; this is the case in mechanisms of mobilization by G-CSF, FLt-3L, SCF, plerixafor, LECT2 and chemotherapy-driven mechanism [4-6]. Important data have been presented for plerixafor in autologous and allogeneic HSCT [7,8], in HSCT for pediatric patients [9,10], showing superior activity from established treatments such as G-CSF [11,12]. The introduction of plerixafor in clinical practice for HSC mobilization has increased the efficiency of the procedure allowing more patients, which were poorly mobilized to produce stem cells by conventional agents, to take advantage of this therapeutic strategy [13,14]. This is due mainly to the fact that more stem cells can be collected in a single session decreasing, thus, the necessary apheresis sessions [15], whereas, for NHL and multiple myeloma patients receiving autologous HSCT, plerixafor in combination with GCS-F led to an increase in the efficiency of stem cell regrowth [13,14]. Novel CXCR4 antagonists seem to be more promising than plerixafor such as POL5551 [16,17], increasing the yield of HSCs. Alternative targets such as integrin/ligand receptor interactions (VLA-4, VCAM-1) are also explored, whereas cell signaling pathways such as Rac1 have been shown to mobilize HSCs in mice. A potential target for HSCs mobilization is the activity of various proteases and their ability to degrade chemokines and other adhesive targets. Such proteases are the members of the MMP family, CD26, neutrophil elastase andcarboxypeptidase M and N [18]. Other potential targets in HSCs mobilization include the sphingosin 1-phosphate (S1P), SNS neurotransmitters and the compliment cascade.

The second step in HSCT must secure that the donor will escape immune rejection by the recipient and that the transplanted cells will have access to niche spaces in the recipient bone marrow [19-21]. Current strategies involve conditioning regimens with radiation or/and chemotherapy which lead to lymphoablation and elimination of resident HSCs. Those procedures, however, are non-specific and can cause serious complications [22,23]. A novel procedure that eliminates HSCs without radiation of chemotherapy has recently been published by Chhabra et al. [24] and Yokoi et al. [25] using anti-c-Kit monoclonal antibodies. The use of such biological agents makes the procedure safer eliminating the dangerous acute and long-term side effects including non-malignant organ dysfunction (reproductive inability, endocrinopathy, cardiopathy), secondary tumors, infections and changes in life quality [26]. An alternative strategy to secure niche spaces in the recipient bone marrow has recently been introduced by Taya et al. [27]; in their paper they presented convincing results that dietary valine starvation leads to dramatic reduction of HSCs within 1 week in the bone marrow.

Overall, those recent advances, the use of more effective mobilization regimens and the use of biological agents or valine starvation to secure niche spaces for HSCs, will transform HSCT since the procedure will become more efficient and safer. The use of HSCT in the treatment of other conditions, the combination of HSCT with gene therapy and the development of protocols for ex vivo HSCs expansion are intense fields of research and soon clinical applications will be available.

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References

1. Shizuru JA, Negrin RS, Weissman IL (2005) Hematopoietic stem and progenitor cells: Clinical and preclinical regeneration of the hematolymphoid system. Annu Rev Med 56: 509-538. Link: https://goo.gl/ge12b3

2. Crisan M, Dzierzak E (2016) The many faces of hematopoietic stem cell heterogeneity. Development, 143:4571-4581. Link: https://goo.gl/MOkAEZ

3. Hsu YM, Cushing MM (2016) Autologous stem cell mobilization and collection. Hematol Oncol Clin North Am.30:573–589. Link: https://goo.gl/I9bAU3

4. Levesque J, Hendy J, Takamatsu Y, Simmons P, Bendall L (2003) Disruption of the CXCR4/CXCL12 chemotactic interaction during hematopoietic stem cell mobilization induced by GCSF or cyclophosphamide. J Clin Invest. 111:187–196. Link: https://goo.gl/H6k6ry

5. Christopher MJ, Liu F, Hilton MJ, Long F, Link DC (2009) Suppression of CXCL12 production by bone marrow osteoblasts is a common and critical pathway for cytokine-induced mobilization. Blood 114:1331–1339. Link: https://goo.gl/HbKGiI

6. Lu XJ, Chen Q, Rong YJ, Yang GJ, Li CH, et al. (2016) LECT2 drives haematopoietic stem cell expansion and mobilization via regulating the macrophages and osteolineage cells. Nat Commun 7:12719. Link: https://goo.gl/HufK9j

7. Worel N, Fritsch G, Agis H, Böhm A, Engelich G, et al. (2016) Plerixafor as preemptive strategy results in high success rates in autologous stem cell mobilization failure. J Clin Apher (epub ahead of print). Link: https://goo.gl/3HvSWX

8. Green MM, Chao N, Chhabra S, Corbet K, Gasparetto C, et al. (2016) Plerixafor (a CXCR4 antagonist) following myeloablative allogeneic hematopoietic stem cell transplantation enhances hematopoietic recovery. J Hematol Oncol. 9:71. Link: https://goo.gl/3HvSWX

9. Teusink A, Pinkard S, Davies S, Mueller M, Jodele S (2016) Plerixafor is safe and efficacious for mobilization of peripheral blood stem cells in pediatric patients. Transfusion. 56:1402-1405 Link: https://goo.gl/dNOVrB

10. Naithani R, Sachdeva M, Rai R, Dayal N (2016) Plerixafor for Hematopoietic Stem Cell Mobilization in Children With Neuroblastoma. Exp Clin Transplant 14: 358-359. Link: https://goo.gl/H9oujn

11. Maschan AA, Balashov DN, Kurnikova EE, Trakhtman PE, Boyakova EV, et al (2015) Efficacy of plerixafor in children with malignant tumors failing to mobilize a sufficient number of hematopoietic progenitors with G-CSF. Bone Marrow Transplant 50: 1089-1091. Link: https://goo.gl/pas4Zw

12. Kosmas C, Athanasopoulos A, Dimitriadis G, Miltiadous C, Zilakos M, et al. (2014) Plerixafor added to G-CSF-supported paclitaxel-ifosfamide-cisplatin salvage chemotherapy enhances mobilization of adequate numbers of hematopoietic stem cells for subsequent autografting in hard-to-mobilize patients with relapsed/refractory germ-cell tumors: a single-center experience. Anticancer Drugs. 25:841-847. Link: https://goo.gl/GVpQv3

13. Jagirdar N, Harvey RD, Nooka A, Flowers C, Kaufman J, et al. (2015) Plerixafor in combination with granulocyte-colony-stimulating factor after chemotherapy increases mobilization efficiency in patients with lymphoma or myeloma: results of a Phase II clinical trial. Transfusion 55: 2351-2357. Link: https://goo.gl/Wh9Su7

14. Cheng J, Schmitt M, Wuchter P, Buss EC, Witzens-Harig M, et al. (2015) Plerixafor is effective given either preemptively or as a rescue strategy in poor stem cell mobilizing patients with multiple myeloma. Transfusion 55: 275-283. Link: https://goo.gl/bnXaTq

15. Goker H, Etgul S, Buyukasik Y (2015) Optimizing mobilization strategies in difficult-to-mobilize patients: The role of plerixafor. Transfus Apher Sci 53: 23-29. Link: https://goo.gl/66eKKs

16. Sison EA, Magoon D, Li L, Annesley CE, Romagnoli B, et al. (2015) POL5551, a novel and potent CXCR4 antagonist, enhances sensitivity to chemotherapy in pediatric ALL. Oncotarget 6: 30902-30918 Link: https://goo.gl/uZqZyo

17. Karpova D, Dauber K, Spohn G, Chudziak D, Wiercinska E, et al. (2013) The novel CXCR4 antagonist POL5551 mobilizes hematopoietic stem and progenitor cells with greater efficiency than Plerixafor. Leukemia, 12: 2322-2331. Link: https://goo.gl/GiBI7T

18. Bendall L (2016) Extracellular molecules in hematopoietic stem cell mobilisation. Int J Hematol. (epub ahead of print). Link: https://goo.gl/CxOrqN

19. Chan CKF, Chen CC, Luppen CA, Kim JB, DeBoer AT, et al. (2009) Endochondral ossification is required for haematopoietic stem-cell niche formation. Nature 457: 490-494. Link: https://goo.gl/HcFH4l

20. Chan CKF, Seo EY, Chen JY, Lo D, McArdle A, R. et al. (2015) Identification and specification of the mouse skeletal stem cell. Cell 160: 285–298. Link: https://goo.gl/oqWBix

21. Bhattacharya D, Ehrlich LI, Weissman IL (2008) Space-time considerations for hematopoietic stem cell transplantation. Eur J Immunol 38: 2060-2067. Link: https://goo.gl/UZcmMk

22. Deeg HJ, Seattle Marrow Transplant Team (1983) Acute and delayed toxicities of total body irradiation. Int J Radiat Oncol Biol Phys 9: 1933-1939. Link: https://goo.gl/TbnjWE

23. Socié G, Salooja N, Cohen A, Rovelli A, Carreras E, et al. (2003) Nonmalignant late effects after allogeneic stem cell transplantation. Blood 101: 3373-3385. Link: https://goo.gl/hKiaA7

24. Chhabra A, Ring AM, Weiskopf K, Schnorr PJ, Gordon S, et al. (2016) Hematopoietic stem cell transplantation in immunocompetent hosts without radiation or chemotherapy. Sci Transl Med 8: 351. Link: https://goo.gl/0Iqz45

25. Yokoi T, Yokoi K, Akiyama K, Higuchi T, Shimada Y, et al. (2016) Non-myeloablative preconditioning with ACK2 (anti-c-kit antibody) is efficient in bone marrow transplantation for murine models of mucopolysaccharidosis type II. Mol Genet Metab. 119:232-238. Link: https://goo.gl/u3kHCY

26. Mohty B, Mohty M (2011) Long-term complications and side effects after allogeneic hematopoietic stem cell transplantation: an update. Blood Cancer Journal, 1: e16. Link: https://goo.gl/xNa0oU

27. Taya Y, Ota Y, Wilkinson AC, Kanazawa A, Watarai H et al. (2016) Depleting dietary valine permits nonmyeloablative mouse hematopoietic stem cell transplantation. Science 354: 1152-1155. Link: https://goo.gl/KwtfrR

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