Response

Optimizing the niche conditions for maximal stem cell engraftment: human and animal model data

We appreciate the comments from Dr Zweegman and colleagues, who contribute important new data supporting our recent publication. While animal models are ideal to uncover the biologic basis of pathologic observations and therapeutic interventions, whether such scientific findings, in reality, apply to patients is always an open question. The exceptional human data of Zweegman et al corroborate our murine findings and suggest that the novel mechanisms we describe may, in fact, apply to clinical hematopoietic cell transplantation.

More than 50 years after the introduction of animal models of marrow radioablation/hematopoietic cell infusion and the first clinical bone marrow transplantation, our study and the human data of Dr Zweegman et al suggest the mechanisms by which the marrow microenvironment responds to the damaging effects of marrow ablation to favor the stem cell engraftment. We hypothesized that the damage to the hematopoietic stem cell osteoblastic niche is the driving force underlying the restoration, and the data of Zweegman et al support that notion by showing that lesser intensity regimens, which may be less damaging to the niche, have a lesser effect on stromal cell–derived factor–1 production. The homing/engraftment of transplanted donor hematopoietic cells may be diminished after nonmyeloablative conditioning regimens, which may affect the long-term outcome of these patients. Our murine model highlights the complexity of the cellular interactions within the stem cell engraftment involving not only stromal cell–derived factor–1 and hematopoietic stem cells, but cells such as the osteoblasts and megakaryocytes and other cytokines, such as platelet-derived growth factor–β and basic fibroblast growth factor.

Future work must define the relationship between conditioning intensity, niche damage and niche restoration in an effort to optimize the niche conditions for maximal stem cell engraftment. A complete understanding of niche damage/ restoration may allow targeting the niche restoration and expansion to foster stem cell engraftment after reduced intensity and nonmyeloablative conditioning regimens, which could expand the indications for this reduced toxicity approach. In addition, such targeting therapy may lessen the minimum required cell dose for routine successful cord blood transplantation, which would expand the use of this valuable source.

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

Current address of J.v.d.B.: Department of Nephrology, University Medical Center Groningen, Hanzeplein 1, 9713 GZ Groningen, The Netherlands

Correspondence: Sonja Zweegman, Department of Hematology, VU University Medical Center, de Boelelaan 1117, 1081 HV Amsterdam, The Netherlands; e-mail: s.zweegman@vumc.nl.

Reference

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

Correspondence: Edwin M. Horwitz, MD, PhD, The Children's Hospital of Philadelphia, Abramson Research Center, 1116D, 3615 Civic Center Blvd, Philadelphia, PA 19104; e-mail: horwitze@email.chop.edu; or Massimo Dominici, MD, Laboratory of Cell Biology and Advanced Cancer Therapies, University of Modena and Reggio Emilia, Via del Pozzo 71, 41100 Modena, Italy; e-mail: dominici.massimo@unimo.it.

References


Response: Optimizing the niche conditions for maximal stem cell engraftment: human and animal model data

Massimo Dominici and Edwin M. Horwitz