REVIEW

Placental/Umbilical Cord Blood (PCB) Stem Cells for Transplantation: Early Clinical Outcomes and the Status of *Ex Vivo* Expansion Strategies

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Abstract. Placental/umbilical cord blood (PCB) stem cells for transplantation provide a potentially useful alternative for patients who do not have an HLA-matched family or unrelated bone marrow donor. Concerns regarding this source of stem cells include the limited number of stem cells in a PCB unit and the delayed time to platelet engraftment. Because of the limited number of stem cells, there is a very clear cell dose effect for both success of engraftment and time to engraftment. As a result, many transplant centers will only consider PCB stem cells as a second choice for transplanting adults, despite the very favorable profile of post-transplant graft-versus-host disease (GvHD). This has resulted in considerable interest in the development of *ex vivo* stem cell expansion strategies. This review outlines the current status of PCB transplant outcomes as well as the status of our understanding of stem cell expansion with the currently available technologies. A stem cell dose-limiting effect on outcome will result in a narrower window of clinical indications for the use of this stem cell source, despite the acknowledged reduction in GvHD. The trade-offs between poor engraftment and reduction in fatal or severe chronic GvHD remain to be quantitated. (Keio J Med 49 (4): 141–151, December 2000)

Key words: umbilical cord blood transplantation, bone marrow transplantation, mobilized peripheral blood transplantation, *ex vivo* expansion

Introduction

Hematopoietic stem cell (HSC) transplantation in the form of bone marrow transplantation (BMT) to treat inherited or acquired hematologic diseases is well established.[1,2] Because not all families had an HLA-matched related donor when needed, the National Marrow Donor Program (NMDP) was established in the United States in 1986 to provide a registry of volunteer BM donors. The registry has now grown to more than 3.5 million potential donors and similar registries have been established in many other countries. Nevertheless, the length of time required to find a suitable donor (median 3.5 months; range 1 month to six years),[3] the limited numbers of donors of ethnic minorities, as well as the rigors of the BM donation process and the risk to the donor, have led to studies of alternative HSC sources.

The potential use of placental/umbilical cord blood (PCB) as a source of transplantable HSC was first suggested by Boyse in 1983, and "proof of principle" was provided by the finding that lethally-irradiated mice could be rescued and hematopoiesis completely reconstituted by transplantation of perinatal blood.[4] In 1988, Gluckman *et al.* successfully treated a patient with Fanconi anemia by using PCB from the patient's sibling.[5] That patient, the first to have received a related PCB stem cell transplantation, remains alive and free of disease to the present.

In addition, mobilization of HSC into the peripheral blood (PB) and their collection by leukapheresis became feasible and this source of HSC has been used since the late 1980's to reconstitute marrow function after high-dose chemotherapy for solid tumors or hematologic malignancies.[6–8] These advances over the past two decades have extended the field of HSC

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