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Guest editorial: Human mesenchymal stromal/stem cell (MSC)

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About 50 years ago, cells that have the ability to organize bone and marrow tissues in vivo were identified within the physiological bone marrow [1]. Investigators extended these observations and clarified the existence of precursor cells that show a fibroblast-like shape, a colony-forming potency, and a capability to differentiate into osteoblasts, adipocytes, and chondrocytes [2]. Later, these cells were called mesenchymal stem cells [3], and the characteristics of these cells in human bone marrow were analyzed in detail [4]. The important clinical event that attracted the attention of hematologists to mesenchymal stem cells was the striking improvement in serious acute graft-versus-host disease (GVHD) upon intravenous infusion of these cells [5, 6]. Currently, human bone marrow-derived mesenchymal stem cells are prepared as a cell product, which was approved for the treatment of acute GVHD in Japan in September 2015.

In this issue, five review articles by Miura, Cho, Miyamura, Matsuzaki, and Gronthos covered the basics of human mesenchymal stromal/stem cells (MSCs), their clinical applications, the present status of these cells, and the developments that are expected in the near future. Miura introduced the biological characteristics of human MSCs and their current clinical applications and potential, especially for hematological disorders [7]. Kim et al. summarized the molecular mechanisms underlying the immunomodulatory effect, one of the most important therapeutic effects, of human MSCs [8], and Miyamura introduced the clinical results of human MSCs for the treatment of acute GVHD [9]. MSCs that are currently prepared for clinical use are isolated by the adhesion method and culture-expanded in vitro. Therefore, these cells are heterogeneous with regard to their various biological characteristics, which may influence the outcomes of therapy using MSCs. Mabuchi et al. demonstrated the highly efficient purification of the stem cell population of human MSCs using unique surface marker expression profiles [10]. This prospective isolation strategy implies the development of MSC-based cell therapy in the future. Nguyen et al. summarized the interactions between Eph cell surface tyrosine kinase receptors and their ephrin ligands, which mediate hematopoiesis-associated cross-talk between MSCs and hematopoietic cells [11]. Stromal cells that show similar characteristics as MSCs contribute to hematopoiesis through an interaction with hematopoietic stem and progenitor cells in the bone marrow microenvironment [12], and an abnormality in MSC-derived osteoprogenitor cells causes pathological hematopoiesis [13]. Not only are isolated and/or culture-expanded human MSCs a source for cell therapy, but endogenous MSCs could be a therapeutic target in some hematological conditions.

The allogeneic cell product of human MSCs is expected to be available at the bedside in the near future (Fig. 1). This series of progress in hematology review articles will help us to understand the biological characteristics of human MSCs, provide patients with appropriate MSC therapy, and develop novel and innovative MSC-based therapies.

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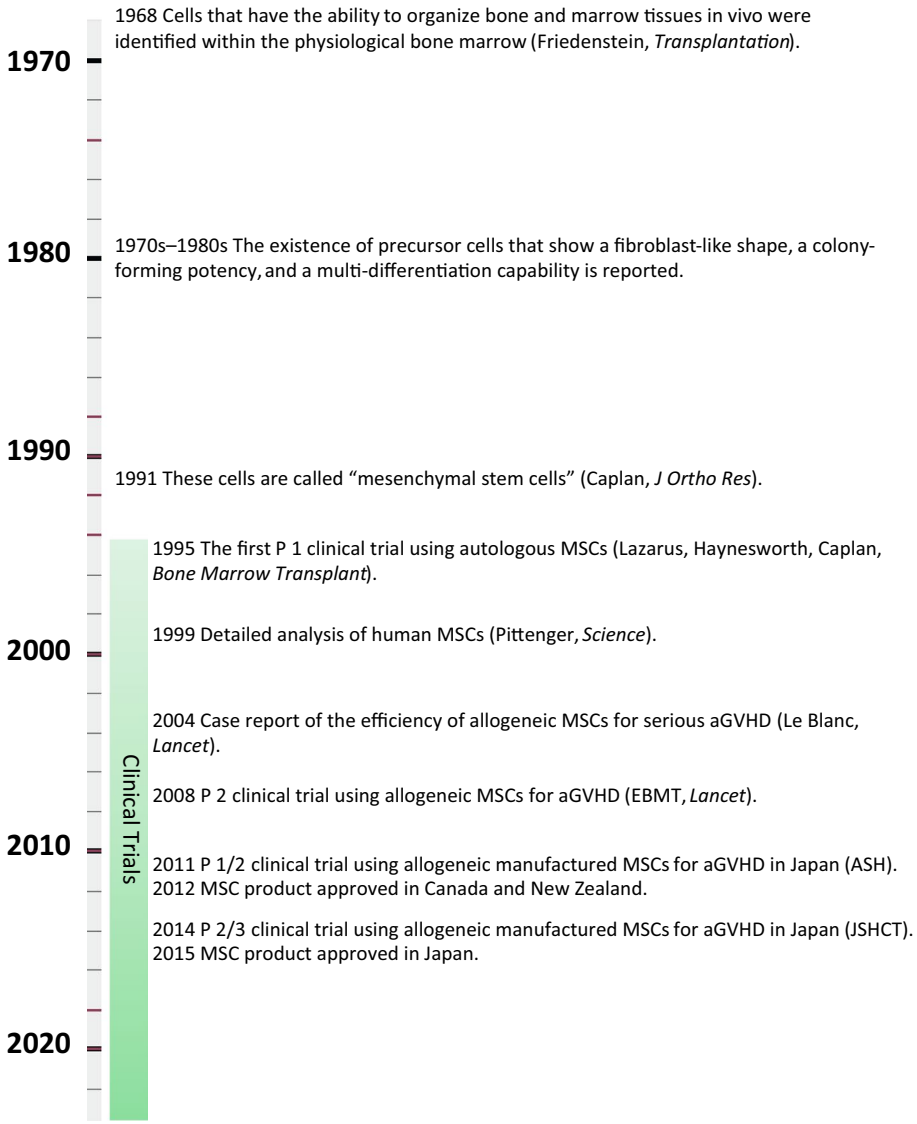

Fig. 1 Major events in the history of MSCs. *aGVHD* acute graft-versus-host disease, *ASH* The American Society of Hematology, *EBMT* The European Group for Blood and Marrow Transplantation, *JSHCT* The Japan Society for Hematopoietic Cell Transplantation, *MSC* mesenchymal stromal/stem cell, *P 1* phase 1, *P 1/2* phase 1/2, *P 2* phase 2, *P 2/3* phase 2/3

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