Special Issue: Mesenchymal stem cells

Brief Review

Mesenchymal stem cells

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Adult bone marrow is composed of hematopoietic stem cells (HSCs) and tissue stem cells, which are referred to as fibroblast CFUs (CFU-Fs), marrow stromal cells/mesenchymal stem cells (MSCs), or mesenchymal progenitor cells(MPCs). As information about MSCs accumulates, parallels are often drawn between them and the extensively characterized HSCs. However, a major difference can be observed in the way the 2 stem cell types are studied.

HSCs were first identified by Till and McCulloch (1961), who called them spleen CFUs (CFU-Ss), and since then, these cells have been identified prospectively by means of surface markers, isolated using flow cytometry, and transplanted *in vivo* without being cultured *in vitro* (Smith et al., 1991; Spangrude et al., 1995; Osawa et al., 1996; Matsuzaki et al., 2004).

In contrast, MSCs, which give rise to multiple mesenchymal cell lineages (adipocytes, chondrocytes, and osteocytes), are often isolated by culturing tissues from humans and other species (Friedenstein et al., 1974; Prockop, 1997; Conget and Minguell, 1999; Pittenger et al., 1999). Therefore, most of the information about MSCs comes from *in vitro* studies on heterogeneous populations of adherent cells that contain unidentified putative stem cells.

This is a critical difference because it is the ability to isolate HSCs prospectively that has largely facilitated the rapid progress in HSC research. To understand the biology of HSCs, particularly their physiological roles *in vivo*, we and other groups previously studied and reported that different mesenchymal populations could have essential functions in the HSC niche (Morikawa et al., 2009; Méndez-Ferrer et al., 2010; Yamazaki et al., 2011).

Dr. Simón Méndez-Ferrer at Centro Nacional de Investigaciones Cardiovasculares Carlos III described their recent contributions to elucidating the functions of mesenchymal stem cells in regulating HSCs. He discussed the emerging role of MSCs as key integrators of neuro-endocrine signals, which are able to couple whole-organism demands to fine-tuned responses in remote stem cell niches.

Dr. Keiyo Takubo at Keio University also described the hematopoietic niche in a distinct context. He focused on the function of MSCs as a niche for HSCs in the bone marrow.

MSCs are currently the focus of intense investigations because of their emergence as key regulators of hematopoiesis and their potential applications in regenerative medicine.

Dr. Takumi Era at Kumamoto University presented and

discussed some recent results pertaining to ES/iPS cell-derived mesodermal cells and MSCs and the future perspectives for the application of MSCs and ES/iPS cell-derived MSCs in regenerative medicine.

We have 2 other mini reviews that describe the clinical perspectives on MSCs.

Dr. Junya Toguchida at Osaka University summarizes the recent advances in biology and the therapeutic role of the MSCs and highlights the current clinical applications of MSCs in bone diseases.

Drs. Kentaro Ishida, Masamitsu Oshima, and Takashi Tsuji review the recent studies on tooth tissue-derived MSCs and the technologies that underpin tooth regenerative therapy.

It is a pleasure for me to publish such excellent reviews on the latest developments in MSC research, which have been presented by researchers who are at the forefront of this research, in this special issue.