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Rationale for Bone Marrow Transplantation in Treatment of Various Intractable Diseases

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Abstract

In this article, we provide evidence that bone marrow transplantation (BMT) can be used to treat various otherwise intractable diseases. We also show which currently incurable diseases could be treated using our novel BMT methods.

Keywords: Autoimmune diseases; Type 1 Diabetes mellitus; Bone marrow; Bone marrow cells; Bone marrow transplantation; Stem cell disorder; Hemopoietic stem cell; Mesenchymal stem cell; Primitive stem cell; Aspiration method; Perfusion method; Intra-bone marrow

Introduction

As long ago as 1985, we discovered, using animal models for autoimmune diseases, that conventional allogeneic BMT could be used to prevent and also treat not only systemic but also organ-specific autoimmune diseases (AIDs).

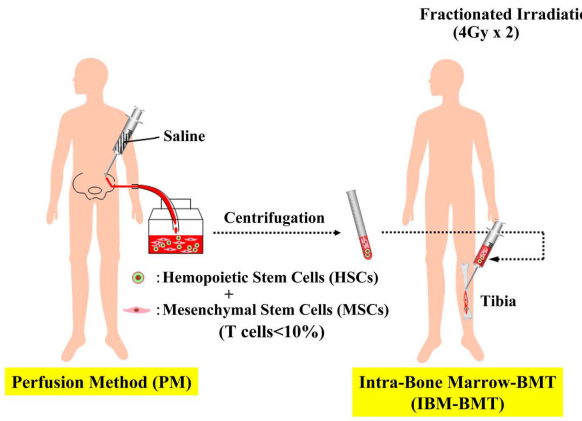

Figure 1: A new BMT method for allogeneic BMT. The new method consists of PM+IBM-BMT.

Our research at that time showed that conventional allogeneic BMT could be used to prevent not only TIDM in NOD mice [1] but also lupus nephritis in lupus mice [2]. In contrast, when BMT was carried out from autoimmune-prone mice to normal mice, the chimeras showed AIDs, strongly suggesting that AIDs were derived from BM defects, since thymus grafts from autoimmune-prone mice to athymic (nu/nu) mice did not result in the development of AIDs [3]. Based on these findings, we focused our research on the BM and eventually discovered a number of BM defects [4-7].

We developed a BMT technique that combines a "PM" for collecting BMCs with the intra-bone marrow (IBM) injection of BMCs (IBM-BMT) [8] (Figure1). As distinct from the conventional AM, the PM allows rapid (within 1 h) collection of BMCs without T cell contamination (T cells<10%). Therefore, no GvHD occurs. Moreover, the burden on donors, such as back pain, bleeding and infection, can be reduced.

Full chimerism can be achieved even with only mild conditioning regimens if IBM-BMT is carried out, since IBM-BMT replaces not only the recipient's HSCs but also MSCs with donor-derived HSCs and MSCs. The findings to date strongly suggest that all the body's cells originate in the BM, and that all diseases might therefore originate from defects in the BM. Indeed, one paper already suggests that gastric cancer originates from BM-derived cells [9].

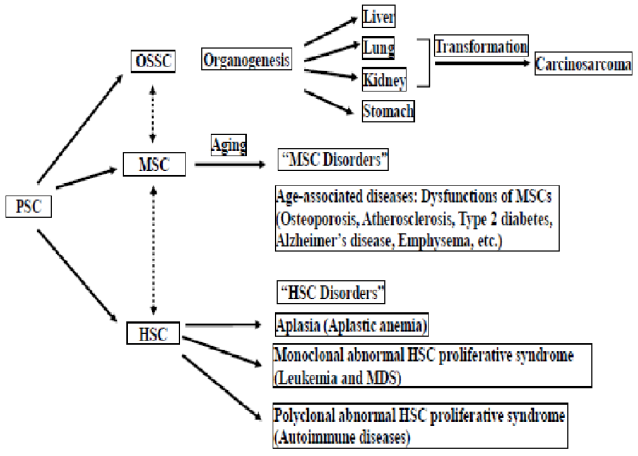

Figure 2: A novel concept of stem cell disorders.

Finally, I would like to propose a new concept of SCDs (Figure 2). On the one hand, there are HSC disorders, which include (i) aplasia of

HSCs (aplastic anemia), (ii) monoclonal or oligoclonal abnormal HSC proliferative syndromes (leukemias and myelodysplastic syndrome), and (iii) polyclonal abnormal HSC proliferative syndromes (autoimmune diseases) [10,11].

On the other hand, there are MSC disorders, which include age-associated diseases such as osteoporosis [12] and emphysema [13], Alzheimer's disease, and atherosclerosis [8,14]; it has been proposed that autoimmune mechanisms are involved in the development of atherosclerosis [15,16] and also Alzheimer's disease [17].

Conclusion

We firmly believe that the development of our BMT method heralds a revolution not only in the field of transplantation (BMT and organ transplantation) but also in the fields of cancer and regeneration.

Acknowledgments

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