

Most Diseases Originate from Defects in Bone Marrow: A New Therapy for Replacing Abnormal Hemopoietic Stem Cells (HSCs) and Mesenchymal Stem Cells (MSCs) with Normal Ones

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Introduction

Bone Marrow Transplantation (BMT) is becoming a powerful strategy for the treatment of hematologic disorders (leukemia, aplastic anemia, etc.), congenital immunodeficiencies, metabolic disorders [1], and also autoimmune diseases [2]. In the case of autoimmune diseases, we have found using various animal models that BMT can be used to treat diseases such as Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), Immune Thrombocytopenic Purpura (ITP), Insulin-Dependent Diabetes Mellitus (IDDM), chronic glomerulonephritis, and also a certain type of Non-Insulin-Dependent Diabetes Mellitus (NIDDM) [2,3]. In addition, we have found that autoimmune diseases are stem cell disorders: BMT from autoimmune-prone mice to normal mice can induce autoimmune diseases in the normal mice [4,5]. However, in MRL/lpr mice, which are radiosensitive (<8.5 Gy), we found that conventional intravenous BMT (IV-BMT) had a transient effect on autoimmune diseases, which were found to recur [6]. We therefore focused on how we might prevent and treat autoimmune diseases in radiosensitive and chimeric-resistant MRL/lpr mice.

We found that stromal cells play a crucial role in preventing graft failure [7-9], since there is a Major Histocompatibility Complex (MHC) restriction between Hemopoietic Stem Cells (HSCs) and stromal cells [10]. To prevent the recurrence of autoimmune diseases in MRL/lpr mice, we found that "Intra-Bone Marrow (IBM)-BMT" (intra-bone marrow injection of whole BMCs into the bone marrow cavity) is the best strategy for allogeneic BMT [11].

To apply allogeneic BMT to humans, we extensively carried out BMT to clarify which cells were essential for successful BMT and finally found that MSCs play a crucial role in preventing graft failure, since there is a major histocompatibility complex restriction between HSCs and MSCs. These early observations gave way to studies on improved methods of not only isolating stromal cells, including Mesenchymal Stem Cells (MSCs), but also characterizing the ideal conditions for successful allogeneic BMT [7,10].

In this review article, we show that our new method can be used

to treat various intractable diseases, such as autoimmune diseases and age-associated diseases (osteoporosis and emphysema, etc.).

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