

## Advances in Leukemia Treatment with Bone Marrow Transplantation

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Bone Marrow Transplantation (BMT) is a useful strategy for the treatment of leukemia, severe combined immune deficiency, enzyme deficiencies, autoimmune disease, and osteoporosis [1-3]. Furthermore, BMT plays an important role in the induction of immune tolerance in organ transplantation [4]. Bone marrow is a spongy tissue, and is made up of Hematopoietic Stem Cells (HSCs), Mesenchymal Stem Cells (MSCs), and various blood cells. HSCs differentiate into common myeloid- and lymphoid-precursor cells and then terminally differentiate into erythrocytes, monocytes, platelets, neutrophils, dendritic cells and other cells. MSCs can differentiate into not only mesoderm derived-cells such as adipocytes, osteoblasts, and osteoclasts, but also endoderm- and ectoderm-derived cells [5]. Intra-Bone Marrow-BMT (IBM-BMT) has been proven to be the best strategy for allogeneic BMT as it results in the rapid recovery of hemopoietic function and the restoration of T cell functions since it can replace not only HSCs but also MSCs [6]. We have reported that IBM-BMT plays an important role in therapies for various diseases in animal models such as those of rheumatoid arthritis, Alzheimer's disease and diabetes [7-10]. Moreover, IBM-BMT has induced persistent donor-specific tolerance, and enables the use of reduced radiation doses as conditioning regimens in organ transplantation [11,12].

Leukemia is a kind of HSC disorder in which various stages of incomplete mature cells accumulate. Allogeneic BMT is an effective immunotherapy for childhood leukemia. One report has demonstrated that BMT can be used to treat all subtypes of pediatric leukemia and provides consensus guidelines for the transplantation of acute leukemia [13]. We have found that allogeneic IBM-BMT plus adult Thymus Transplantation (TT) significantly increased numbers of CD8<sup>+</sup> T cells that infiltrated the tumors and apoptotic tumor cells, and preserved strong graft-versus-tumor effects [14]. EL-4 cells are derived from the thymoma of mice, and can induce the mimicking of leukemia in mice. We recently reported that IBM-BMT plus adult TT prevented the growth of leukemia as a result of the improved mitogen responses to both T and B cells, and significantly increased IL-2 production, and the number of donor-derived T cells [15]. Our results indicate that allogeneic IBM-BMT plus TT can induce a strong graft-versus-leukemia effect with mild graft-versus-host disease, suggesting it may be a viable strategy for the treatment of leukemia in humans.

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