HEP-04

HEPATIC STELLATE CELLS COTRANSPLANTATION PREVENT ACUTE GRAFT-VERSUS-HOST DISEASE IN ALLOGENIC BONE MARROW TRANSPLANTATION

C-H Chen [1,2], C-H Cheng [1], J-D Lian [3], M-J Wu [1], C-P Hu [2], K-H Shu [1]

[1]Section of Nephrology, Taichung Veterans General Hospital; [2]Life Science Research Center, Tunghai University, [3]Division of Nephrology, Chung Shan Medical University Hospital, Taichung, Taiwan

BACKGROUND: Graft-versus-host disease (GVHD) represents a major hurdle impeding the efficacy of allogeneic bone marrow transplantation (BMT). Hepatic stellate cells (HSCs) induce activated T cell apoptosis and secrete growth factors. In this study, we investigated HSCs-enhanced BM engraftment, and protected mice from lethal GVHD.

METHODS: Allogeneic BM mixtures, generated from MHC-mismatched B6 BM ($1.0x10^7$/mouse) plus spleen T cell ($1.0x10^6$/mouse) with or without HSCs ($1.0x10^6$/mouse) from donor (B6), was injected through the tail vein of lethal total body irradiation host (BALB/c) mice. Recipients were characterized for chimerism using flowcytometry to determine the percentage of donor-derived lineages post-BMT. The graft survival and GVHD were evaluated.

RESULTS: The spleen size was significantly enlarged in the allograft BMT group compared with that of the HSCs cotransplantation group. Histopathological examination disclosed marked hepatitis, dermatitis and enteritis in BMT only group, but not in HSCs cotransplantation group. The graft survival was 14.9±5.5 days in the BMT group and 40.9±26.7 in the HSC cotransplantation group ($p=0.009$). In addition, there were more H-2^{b+}CD34^+ cells in the HSCs cotransplantation group than in the BMT group (2.07% *versus* 1.03%).

CONCLUSIONS: HSCs may support hematopoiesis and engrafting, and contribute to the suppression of acute GVHD and prolong the survival of recipient mice. Our study will shed some lights on the immunosuppressive nature of the liver and may provide a biological manipulation of alloreactivity in transplantation medicine.

Key words: Hepatic stellate cells, bone marrow transplantation, Graft-versus-host disease