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OUR DEVELOPED LIVER REGENERATION THERAPIES USING AUTOLOGOUS BONE MARROW-DERIVED CELLS FOR CIRRHOTIC PATIENTS

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In our animal studies, we have reported that bone marrow cells (BMCs) infused via a peripheral vein efficiently repopulate the cirrhotic liver. Repopulated BMCs produce collagenases including matrix metalloproteinase-9. As a result, we observed reduced liver fibrosis, elevated serum albumin levels, and a significant increase in survival. Based on these data, we have begun "Autologous bone marrow cell infusion (ABMi) therapy" using non-cultured autologous whole BMCs. This therapy was officially approved as "Advanced medical technology B" in Japan. However, ABMi therapy involves bone marrow (BM) aspiration under general anesthesia.

We therefore developed a less invasive liver regeneration therapy using cultured autologous mesenchymal stem cells (MSCs) isolated from a small amount of BM fluid aspirated under local anesthesia. We showed that peripheral infusion of cultured human BMCs reduces hepatic fibrosis in immunodeficient cirrhotic mice, consistent with the maintenance of redox homeostasis in hepatic stellate cells and hepatocytes. To evaluate safety using canine models, cultured autologous MSCs were administered to the same subject in approximately three times the quantity and 10 times the concentration used in humans. We also constructed a cell-processing facility with a new isolator system to confer protection from hepatitis virus. Then we started this therapy for decompensated liver cirrhotic patients after the regulatory approval in Japan (ClinicalTrials.gov; No. CT02327832). Here, we present the current status and prospects for our liver regeneration therapy using autologous BMCs.