Organ fibrosis is caused commonly by an excessive deposition of collagen and other components of extracellular matrix in various organs including liver, lung, kidney and skin. Several recent studies have shown that bone marrow (BM)-derived cells express collagen and accelerate organ fibrosis. On the other hand, others have reported that BM-derived cells contribute to wound healing and the resolution of organ fibrosis. Thus, contribution of BM-derived cells to the progression and regression of organ fibrosis has been a matter of controversy.

Liver fibrosis is usually progressive, but it can be occasionally reversed if the causative agents are removed or patients are treated effectively. We have recently demonstrated contribution of autologous BM cells to the spontaneous regression of liver fibrosis (Hepatology, 2007). Repeated carbon tetrachloride injections after hematopoietic reconstitution with enhanced ß-enfluorescent protein (EGFP)-expressing BM cells caused migration of a large number of EGFP+ cells into fibrotic liver tissue. Some of them, as well as EGFP-negative liver resident cells, produced matrix metalloproteinase (MMP)-13 and MMP-9. While MMP-13 was transiently expressed in stem/progenitor cells clustering in the periportal areas, MMP-9 expression was detected over the resolution process in several different kinds of cells located in the portal areas and along the fibrous septa. Therapeutic recruitment of BM cells by granulocyte colony stimulating factor (G-CSF) treatment significantly enhanced migration of BM-derived cells into fibrotic liver tissue. Some of them, as well as EGFP-negative liver resident cells, produced matrix metalloproteinase (MMP)-13 and MMP-9. While MMP-13 was transiently expressed in stem/progenitor cells clustering in the periportal areas, MMP-9 expression was detected over the resolution process in several different kinds of cells located in the portal areas and along the fibrous septa. Therapeutic recruitment of BM cells by granulocyte colony stimulating factor (G-CSF) treatment significantly enhanced migration of BM-derived cells into fibrotic liver tissue. Some of them, as well as EGFP-negative liver resident cells, produced matrix metalloproteinase (MMP)-13 and MMP-9. While MMP-13 was transiently expressed in stem/progenitor cells clustering in the periportal areas, MMP-9 expression was detected over the resolution process in several different kinds of cells located in the portal areas and along the fibrous septa. Therapeutic recruitment of BM cells by granulocyte colony stimulating factor (G-CSF) treatment significantly enhanced migration of BM-derived cells into fibrotic liver tissue.

Transgenic mice have been established in our laboratory that harbor the tissue-specific ß2(I) collagen gene enhancer/promoter sequence linked to either EGFP or firefly luciferase gene. By using the mice as BM donors, work is now in progress to determine whether BM-derived cells migrating into liver tissue produce collagen and contribute to the progression of liver fibrosis.