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Critical Role of Bone marrow-derived Cells in the Progress of Fibrosis in Post-ischemic Kidney

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Acute kidney injury (AKI) has been recognized as a critical factor for the development of chronic kidney disease (CKD) which is characterized by fibrosis due to increases in extracellular matrix molecules and interstitial cells. However, the role of bone marrow-derived cells (BMDCs) in AKI-induced kidney fibrosis remains to be defined. Here, we investigated the role of BMDCs in kidney fibrosis following ischemia/reperfusion (I/R) injury in GFP-expressing bone marrow (BM) chimeric mice. I/R injury resulted in severe fibrotic changes in kidney tissues and dramatically increased interstitial cell numbers. GFP-expressing BMDCs accounted for over 80% of interstitial cells in fibrotic kidneys. The GFP-expressing BMDCs expressed α-smooth muscle actin (α-SMA, a myofibroblast marker), FSP-1 (a fibroblast marker), collagen III, and F4/80 (a macrophage marker). Over 20% of interstitial cells were bromodeoxyuridine (BrdU)-incorporating, proliferating, cells and these 80% cells were GFP-expressing BMDCs. Treatment with apocynin (a NADPH oxidase inhibitor which functions as an antioxidant) from the day after surgery until sacrifice inhibited these changes, resulting the reduction of kidney fibrosis. Taken together, our findings show that BMDCs make a major contribution to I/R injury-induced fibrosis, suggesting that BMDCs be considered an important target for the treatment of kidney fibrosis.

Key Words: Ischemia, Fibrosis, BMDC