Effect of erythropoietin on mesenchymal stem cell differentiation and secretion in vitro in an acute kidney injury microenvironment

N.M. Liu, J. Tian, W.W. Wang, G.F. Han, J. Cheng, J. Huang and J.Y. Zhang

Department of Nephrology, The 455th Hospital of PLA, Shanghai, China

Corresponding author: J.Y. Zhang
E-mail: jinyuanzhangcn@126.com

Received August 1, 2012
Accepted November 10, 2012
Published February 28, 2013
DOI http://dx.doi.org/10.4238/2013.February.28.14

ABSTRACT. We investigated the effect of erythropoietin (EPO) on differentiation and secretion of bone marrow-derived mesenchymal stem cells in an acute kidney injury microenvironment. Acute kidney injury mouse models were prepared. Both renal cortices were then immediately collected to produce the ischemia/reperfusion kidney homogenate supernatant. The morphological and ultrastructural changes in the cells were observed using an inverted microscope and a transmission electron microscope. Cytokeratin-18 was detected using flow cytometry. Bone morphogenetic protein-7 levels, hepatocyte growth factor, and vascular endothelial growth factor in the culture medium were detected using an enzyme-linked immunosorbent assay. The cells had high CD29 and CD44 expression, as well as low CD34 and CD45 expression. More round and oval cells with cobble-like appearances were observed after EPO treatment. In addition, an increase in the number of rough endoplasmic reticula, lysosomes, and mitochondria was observed in the cytoplasm; the intercellular junction peculiar to epithelial cells was also seen on the cell surface. After treatment with ischemia/reperfusion kidney homogenate supernatant, cytokeratin-18 expression increased significantly and EPO could magnify its expression.
Bone morphogenetic protein-7 levels, hepatocyte growth factor, and vascular endothelial growth factor levels after treatment with ischemia/reperfusion kidney homogenate supernatant significantly decreased, whereas EPO increased the cytokine secretion. The acute kidney injury microenvironment can induce the bone marrow-derived mesenchymal stem cells to partially differentiate into renal tubular epithelium-shaped cells, but weaken their secretion function. EPO intervention can boost up their differentiation function and reverse their low secretion effect.

**Key words:** Erythropoietin; Acute kidney injury; Cell differentiation; Cytokines; Bone marrow-derived mesenchymal stem cells