



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

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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