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Urosepsis Modeling on kidney and lung-on-a-chip system

EUN-JEONG KWON[1], Jeonghun Han[3], Young-Jae Cho[2], Sejoong Kim[1]
[1]Department of Internal Medicine-Nephrology, Seoul National University Bundang Hospital, Korea, Republic of
[2]Department of Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Seoul National University Bundang Hospital, Korea, Republic of
[3]Department of Regenerative Medicine and Cell Therapy Institute, Seoul National University Bundang Hospital, Korea, Republic of

Objectives : The rise of organ-on-a-chip models is spotlighting preclinical studies, yet an in vitro model for lung injury due to urosepsis remains undeveloped. Thus, we developed a 3D microfluidic chip to model urosepsis in kidney, lung, and vascular microenvironment.
Methods : The kidney and lung-on-a-chip were designed with five channels, where HK-2 (human kidney proximal tubule epithelial) cells, HUVEC (human umbilical vein endothelial) cells, lung fibroblasts, and BEAS-2B (immortalized bronchial epithelial cell) cells were co-cultured. Tubular formation induced by shear stress was assessed using confocal imaging. To induce urosepsis, LPS (lipopolysaccharide) was administered to HK-2 cells for 3 days. Following LPS treatment, cell injury was evaluated by measuring cell-to-cell distance using CK8 staining and cadherin expression of HUVEC cells to assess cell adhesion. Cell permeability and protein expression were evaluated using FITC and dot blot analysis. Using fluorescence staining, the effect of LPS induced urosepsis on Beas2B cell death was evaluated.
Results : When applying shear stress during cell culture, we observed increased cell proliferation and well-formed tubular structures. After inducing urosepsis by LPS on HK-2 cells, we confirmed an increase in FITC permeability with LPS dose-dependent. This was associated with increased cell-to-cell distance in HK-2 cells and decreased cadherin expression in HUVEC, indicating that LPS rapidly reached lung cells. Interestingly, when urosepsis-induced lung injury occurred, IL-6 and NGAL expression were increased. Cell death of Beas2B increased by LPS in urosepsis model on a chip.
Conclusions : We utilized a kidney and lung-on-a-chip system to develop a model of urosepsis and observed sequential tubular damage, vascular damage, and death of bronchial cells following LPS treatment. This innovative approach enhances our understanding of urosepsis-related lung injury and offers a new avenue for therapeutic research.