CCL20 blockade alleviate ischemia reperfusion–induced kidney injury via oxidative stress regulation

울산대학교병원 신장내과[1], 서울대학교병원 신장내과[2], 서울대학교 의학연구원 신장연구소[3]

배진숙[1], 송제훈[1], 이종수[1], 김동기[2], 김연수[2], 양승희[3], 유경돈[1]

Background/Aims: Chemokine receptor 6 (CCR6) and its ligand, CCL20, form an axis that has pleiotropic effects for the interaction of T and B cells. By applying an ischemia reperfusion injury (IRI) model, we explored the pathogenic impact that the CCR6/CCL20 axis plays in acute kidney disease (AKD).

Methods: In order to generate this model, a unilateral renal artery pedicle was clamped in C57BL/6 mice for a period of 25 minutes in order to induce IRI. At four weeks following IRI, we examined the expression of CCR6 and CCL20. The effects of hypoxia and H2O2-induced oxidative stress were investigated using an in vitro validation study.

Results: The level of tubular epithelial cell (TEC) apoptosis that occurred in wild-type B6 mice was much higher than that which occurred in CCL20 antibody-treated mice. In primary cultured human TECs, CCR6, NGAL mRNA expression, and IL-8 levels were shown to be greater under hypoxia compared to normoxia, and these levels were inhibited by a CCL20 antibody treatment. In addition, inhibiting CCL20 reduced the amount of apoptotic damage caused by hypoxia and reactive oxygen species in a dose-dependent manner. It is interesting to note that inhibiting CCL20 resulted in a more substantial decrease in the levels of intracellular ROS, 8-OHDG, and ICAM-1. IRI induced CCR6 expression that was of a severity that was comparable to that of individuals with the AKD phenotype.

Conclusions: These mechanisms of CCR6/CCL20 axis modulation suggest a novel strategy for management of AKD.