KSN 2017 Abstract

KSN-17-P166

How to promote regeneration after ischemic reperfusion Injury: Dual role of CD 137 agonistic antibody

*Jong soo LEE[1], Jongha PARK[1], Hojong PARK[2], Kyung sun PARK[1], Hong rae CHO[2], Hyun chul CHUNG[1]

[1]Internal Medicine, Ulsan University Hospital, Korea,South, [2]Surgery, Ulsan University Hospital, Korea,South

Objectives : Acute sterile inflammation can be induced by tissue damage caused by ischemia-reperfusion. In transplantation ischemia reperfusion injury (IRI) is unavoidable procedure. IRI causes delayed graft function and increases rejection rates, finally shortens long-term graft survival. Previously we reported an inflammatory loop between tubular epithelial cells (TECs) and inflammatory cells during kidney IRI. Blocking this pathway demonstrated attenuating the severity of AKI. Although sterile inflammation plays a dominant role in damaging TECs in the early injury phase of AKI, blocking this inflammatory pathway may turn out the signal of the regeneration.

Methods : We adopted mouse kidney ischemic reperfusion injury model. CD137-/- and CD137L-/- C57BL/6 mice were used between 7 and 8 weeks of age.

Results : Here, we focused on CD 137 - CD137 ligand and reverse pathway which plays a dual role in both early inflammatory and late regenerative phase. In the early phase of IRI, CD 137 ligand signal on tubular epithelial cell amplifies inflammation and augments the intensity of tubular damage. During the healing phase, CD 137 signal promote regeneration of TEC by decreasing G2-M arrest of TEC, switching proinflammatory M1 macrophage to M2 macrophage, and expansion of regulatory T cell. Early administration of CD 137 agonistic antibody decreases the intensity of TEC injury via blocking CD 137 ligand signal of TEC. In addition, delayed treatment with CD 137 agonistic antibody promotes regeneration via enhancing CD 137 regenerative signal of immune cell

Conclusions : In this work we provide evidence that treatment with CD 137 agonistic antibody can protect from IRI and its' progression to chronic graft dysfunction by attenuating AKI severity and promoting regeneration of damaged tissue.

Keywords : ischemia reperfusion injury, AKI, regeneration