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Th17세포의 분화를 이용한 허혈/재관류 손상 조절

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Transcriptional Regulation of Th17 Cell Differentiation Mediates Ischemia-reperfusion Injury

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Interleukin (IL)-17-producing $CD4^+$T cells (Th17) have been known to play an important role in the pathogenesis of acute kidney injury (AKI). IL-17 is the major cytokine of Th17 cells and signal transducer and activator of transcription3 (STAT3) is the essential transcriptional factor for Th17 cell differentiation. However, the underlying mechanisms have not been identified. We evaluated the role of STAT3/Th17 pathway focusing on IL17, STAT3 and RORγt in bilateral renal ischemia/reperfusion injury (IRI). The severity of renal injury significantly improved for T-cell specific deletion of STAT3 mice ($Stat3^{fl/fl}$Lck-$CRE^{+/-}$) compared to control mice ($Stat3^{fl/fl}$Lck-$CRE^{-/-}$) at day 2. Intra-renal mRNA expressions of IL-6, IL-12p40, IL-23, IL-23R, TGFβ, STAT3, IL-17R and IL-17 were up-regulated in control mice rendered IRI, whereas the levels of those mRNA were suppressed following the deletion of T-cell specific STAT3. Precisely, both in the kidney and spleen tissues, mRNA expressions of SOCS3 and RORγt were mitigated, while mRNA expressions of CTR9 (a component of PAFc) was elevated in T-cell specific deletion of STAT3 mice than in control mice. The expressions of CTR9 mRNA effectively decreased during the differentiation processes of Th17 cells. Blocking the JAK2/ STAT3 pathway with caffeic acid 3,4-dihydroxy-phenethyl ester (CADPE) significantly protected kidneys from IRI. CADPE decreased STAT3 phosphorylations and apoptosis of mouse tubular epithelial cells on hypoxia condition. Therefore, we conclude that STAT3/Th17 pathway mediates kidney tissue damage in murine IRI and that blocking JAK2/STAT3 may provide a potential strategy for treating AKI.

Key Words: Th17세포, 허혈재관류, STAT3
Th17 cell, Ischemia/reperfusion, STAT3