

## Periostin이 p38 MAPK 경로를 통해 허혈재관류손상 이후 신 섬유화에 미치는 영향

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### Periostin Induces Kidney Fibrosis after Ischemia-reperfusion Injury via p38 MAPK Pathway

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Ischemia-reperfusion injury during the transplantation procedure is associated with poor long-term allograft outcomes, such as rejection and fibrosis. Periostin, a matricellular protein, has been reported to play a crucial role in inflammatory and fibrotic mechanism. We hypothesized that periostin involves in the progression of acute kidney injury to kidney fibrosis. To establish a kidney progression model, we induced unilateral ischemia-reperfusion injury of left kidney pedicle for 30 minutes in wild type (WT) C57BL/6 mice and Postn null mice (Postn<sup>-/-</sup>), and observed during 4 to 6 weeks. In addition, inner medullary collecting duct cell line was subjected to put in the hypoxic incubator (1% O<sub>2</sub>, 5% CO<sub>2</sub>, and 94% N<sub>2</sub>) for 24 and 72 hours. After 4 to 6 weeks, the left kidneys in Postn null mice were significantly less atrophied and less small in weight compared to those of WT mice. Apparent tubular atrophic changes and collagen fiber deposition, and expressions of collagen IV, S100A4, and periostin were also remarkably alleviated in Postn null mice compared within WT mice. Furthermore, the expressions of phosphorylated p38 mitogen-activated protein kinase (p-p38 MAPK) and cleaved caspase-3 were significantly decreased in Postn null mice compared to in WT mice. Postn null mice also attenuated intra-kidney mRNA expression of TNF- $\alpha$ , MCP-1, and IL-6. In vitro, hypoxic injury during 72 hours resulted in cellular morphologic changes and increased the expressions of several fibrosis markers, periostin, and p-p38 MAPK. Treatment of recombinant periostin in hypoxic condition magnified the cellular changes and the expression of p-p38 MAPK, which were comparable to treatment with transforming growth factor- $\beta$ 1. In contrast, inhibition of p38 MAPK attenuated the periostin induced inflammation and fibrosis. In conclusion, periostin is related to the progression via p38 MAPK pathway to kidney fibrosis following acute kidney injury triggered by hypoxic or ischemic insult. Periostin ablation could have protective effects in kidney progression.

**Key Words:** 페리오스틴, 신 섬유화, 허혈재관류손상

Periostin, Renal Fibrosis, Ischemia-Reperfusion injury