

쥐사이질세포에서 시클로스포린에 의해 증가된 섬유결합소 합성에 대한 mycophenolic acid의 억제 효과

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Prevention of Cyclosporin A-Induced Fibronectin Upregulation by Mycophenolic Acid in Rat Mesangial Cell

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Background : The usefulness of Cyclosporin A (CsA) is limited by its potential nephrotoxicity, in which transforming growth factor- β (TGF- β) may play a pivotal role. Mycophenolic acid (MPA), the active metabolite of mycophenolate mofetil (MMF), is a specific inhibitor of inosine monophosphate dehydrogenase during de novo purine synthesis, and may decrease the production of many cytokines and growth factors, especially TGF- β 1. The aim of this study was to investigate whether the pro-fibrotic action of CsA may be prevented by MPA in rat mesangial cells (RMC).

Methods : Primary cultures of RMCs were obtained from outgrowths of collagenase-treated rat renal isolated glomeruli. RMCs at passages 5 to 15 were exposed to CsA 1 μ M or CsA 1 μ M+MPA 1 μ M for 72 h and were compared with the untreated control. Expression levels of fibronectin, TGF- β , Smad3, and Smad7 proteins were estimated by western blot analysis.

Results : After treatment with CsA the expression of TGF- β protein showed an increasing tendency (1.54 \pm 0.24-fold), but without a statistical significance. However, the protein abundances of fibronectin (2.84 \pm 0.14-fold, p<0.05), phosphorylated Smad3 (2.74 \pm 0.43-fold, p<0.05) and Smad7 (2.42 \pm 0.74-fold, p<0.05) were significantly increased by CsA. When MPA was co-incubated with CsA, the protein abundances of fibronectin (1.32 \pm 0.34-fold, p<0.05) and phosphorylated Smad3 (0.68 \pm 0.38-fold, p<0.05) were significantly reduced. Interestingly, Smad7 protein expression was more increased (4.44 \pm 0.58-fold, p<0.05) as compared with CsA treatment.

Conclusion : We demonstrate that in RMCs MPA may ameliorate CsA-induced fibronectin synthesis by modulating the TGF- β /Smad signaling pathway. These results suggest that MMF may be a novel candidate for the prevention of CsA nephrotoxicity after kidney transplantation.

Key Words : 시클로스포린, 섬유결합소, Mycophenolic acid
Cyclosporine, Fibronectin, Mycophenolic acid