

S-C15

## Pirfenidone은 복막중피세포의 상피-중간엽 세포이행을 억제한다

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### Pirfenidone Inhibits Epithelial to Mesenchymal Transition in Peritoneal Mesothelial Cells via TGF- $\beta$ /Smad-dependent and -independent Signaling Pathway

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**Background:** TGF- $\beta$  induced epithelial to mesenchymal transition (EMT) of peritoneal mesothelial cells play a key role in pathologic changes of peritoneal membrane. We investigated effectiveness of pirfenidone on the EMT processes such as TGF- $\beta$ -induced Smad dependent and independent signal transduction pathways.

**Materials and Methods:** HPMCs were isolated from human omentum specimens obtained from consenting patients undergoing elective abdominal surgery. Forty-two male SD rats weighing 200-250 g were purchased from the Orient Co. In the C group, the catheter was inserted but no dialysate was infused. The PD group was infused with a conventional 4.25% dialysis solution. The PD+PR group was infused with 4.25% dialysis solution and cotreated with pirfenidone.

**Results:** Exposure of HPMCs to TGF- $\beta$  decreased the protein level of the epithelial cell markers and increased the expression levels of the mesenchymal markers. Cotreatment with pirfenidone increased the protein levels of the epithelial cell marker and decreased those of mesenchymal markers compared with their levels in cells treated with TGF- $\beta$  alone. Exposure of HPMCs to TGF- $\beta$  significantly increased the phosphorylation of Smad2 and Smad3. Cotreatment with pirfenidone significantly decreased the phosphorylation of Smad2 and Smad 3 compared with that of cells treated with TGF- $\beta$  alone. In addition, TGF- $\beta$  lead to phosphorylation of Akt and cotreatment with pirfeindone decreased phosphorylation of Akt. After 8 weeks of experimental peritoneal dialysis in rats, the thickness of the peritoneal membrane in the PD group was significantly increased compared with that of the C group. Cotreatment with pirfenidone decreased peritoneal thickness.

**Conclusion:** Pirfenidone attenuates the TGF- $\beta$ -induced EMT in peritoneal mesothelial cells. We suggest that pirfenidone may preserve peritoneal mesothelial cells during peritoneal dialysis.

**Key Words:** 상피-중간엽 세포이행, 섬유화, 투석

Epithelial mesenchymal transition, Fibrosis, Dialysis