

Effect of TGF- β_1 stimulation on the Smad signal transduction pathway of human peritoneal mesothelial cells

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Objective: To prove whether the SMAD signal transduction pathway in human peritoneal mesothelial cells (HPMCs) influenced the process of human peritoneal fibrosis stimulated by TGF- β_1 . **Methods** HPMC's were isolated from normal human omentum and the third generation cells were stimulated by 5 ng/ml TGF- β_1 . Immunohistochemistry, Western blotting, ELISA and RT-PCR were employed to investigate the protein expression of p-Smad2/3 and the protein and mRNA expressions of SMAD 7, fibronectin(FN) and collagen-I(COL1). **Results** The protein expression of p-Smad2/3 in HPMC's was remarkably increased 15 min (29% p-Smad2/3-positive cells) after TGF- β_1 stimulation, peaking from 30 min (81%) to 1 h (84%) and dropping after 2 h (37%); Meanwhile, p-Smad2/3 mainly distributed in cytoplasm at 15 min, concentrated in cell nucleus and peri-nucleus from 30 min to 1 h, and distributed in cytoplasm again at 2 h. The protein expression of SMAD 7 in cells was obviously increased 24 h after TGF- β_1 stimulation, peaking at 48 h. The mRNA expression of SMAD7 was time-dependently increased. The expressions of extracellular FN protein, intracellular FN mRNA, as well as intracellular COL1 protein and mRNA were significantly increased and all of them displayed time dependency. **Conclusions** The SMAD signal transduction pathway of HPMC's can be specifically activated by TGF- β_1 and influence the process of human peritoneal fibrosis. The protein and mRNA expression of SMAD 7 (an inhibitor of SMAD pathway) are significantly increased as a result of feedback.

KEY WORDS: mesothelial cells; TGF- β_1 ; Smad2/3; Smad7; extracellular matrix

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