Upregulation of Aquaporin 3 (AQP3) by TGF-β1 Regulates Cell Migration in Human Peritoneal Mesothelial Cell

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Background: AQPs are a family of integral membrane proteins that are widely expressed in many tissues, including the peritoneum and kidney. Recently, a novel cellular role for AQPs in cell migration was reported. The purpose of this study was to investigate the role of AQP3 in migration of TGF-β1 treated human peritoneal mesothelial cells (HPMCs).

Methods: Cultured HPMCs were exposed to TGF-β1. AQP3 mRNA and protein levels were assessed by real time PCRand Western blot. AQP3 was knocked down by transfection of siRNA in cultured HPMCs, then the cells were stimulated with TGF-β1. AQP3 and α-SMA expressions were assessed by real time RT-PCR, Western blot and immunofluorescence methods. Cell migration was determined by transwell assay and scratch test. For animal model, male Sprague-Dawley (SD) rats were divided into 2 groups; Group CC, with catheter and not dialyzed (n=12); group D, with catheter and dialyzed with 4.25% glucose solution (n=12). Dialysis exchanges were performed 2 times a day with 25mL/each exchange for 8weeks. Expressions of α-SMA, TGF-β1, and AQP3 were assessed in peritoneal tissue.

Results: The TGF-β1 induced AQP3 expression in a time- and dose-dependent manner in HPMCs. With the increased expression of AQP3, cell migration increased. AQP3 knockdown by siRNA inhibited TGF-β1-induced AQP3 expression and α-SMA. Cell migration was slowed after AQP3 siRNA transfection in HPMCs. In peritoneal dialysis rat model, the peritoneum in the group D was thickened compared to group CC ($p<0.05$). Expressions of TGF-β1, α-SMA, and AQP3 in tissue immunohistochemistry increased in the group D.

Conclusion: The results of our study provide for the first time that AQP3 plays a critical role in TGF-β1-induced HPMC migration and that AQP3 expression increases in peritoneal fibrosis. It may provide evidence for a novel role of AQP3 in peritoneal fibrosis and wound healing process.

Key Words: AQP3, TGF-β1, migration