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UROTENSIN II ACTIVATES THE SMAD PATHWAY DURING ADVENTITIAL FIBROBLASTS PHENOTYPIC DIFFERENTIATION

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Background Urotensin II (UII) is a potent vasoconstrictive peptide. Our previous study found that UII could stimulate adventitial fibroblasts phenotypic conversion and collagen synthesis, suggesting that UII plays an important role in vascular fibrosis. The aim of this study was to test the hypothesis that smad 2/3 is involved in UII-induced adventitial fibroblasts phenotypic conversion. Design Growth-arrested adventitial fibroblasts from rat aorta were incubated in serum-free medium with UII, and SB710411, the antagonist of UII receptor. The Smad2/3 phosphorylation was evaluated by western blot. In another experiment, the adventitial fibroblasts were transfected with Smad2 and smad3-specific siRNA, and the α -smooth muscle-actin (α -SM-actin) expression was also evaluated by western blot. Results UII stimulated smad2/3

phosphorylation in cultured adventitial fibroblasts in a time-dependent manner. After 3, 6, 12 or 24 h incubation with UII (10^{-8} mol/l), the Smad 2/3 phosphorylation were increased by 21.6%, 68.1%, 117.8%, and 147.2% ($p < 0.01$), respectively, than with control treatment. UII (10^{-10} – 10^{-8} mol/l) also stimulated Smad 2/3 phosphorylation in a concentration dependent manner ($p < 0.05$). The UT antagonist SB710411 diminished the UII-induced Smad 2/3 phosphorylation ($p < 0.01$). In addition, transfection with Smad2 or Smad3 siRNA decreased the UII-induced α -SM-actin expression significantly ($p < 0.01$).

Conclusion These data show that UII activates the Smad2/3 phosphorylation via its receptor, and the Smad2/3 pathways are involved in UII-induced α -SM-Actin expression in adventitial fibroblasts. The novel finding suggests that Smad2/3 activation could be involved in the profibrogenic effects of UII in vascular diseases.