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CHARACTERIZATION OF GENE EXPRESSION PROFILES IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME (IC/BPS) PATIENTS AND IDENTIFICATION OF WNT2B AS A KEY REGULATOR OF FIBROGENESIS

Hypothesis / aims of study
Interstitial cystitis/bladder pain syndrome (IC/BPS) is a distressing, chronic bladder disorder of pathologically unknown cause. However, crucial genes responsible for pathogenesis remain to be determined. We already found out the expression of sonic hedgehog (Shh) and WNT family genes in our previous IC/BPS animal model. Here, we investigated whether WNT2B were involved in the initiation of bladder tissue fibrosis IC/BPS patients.

Study design, materials and methods
A total of 15 patients, including 5 NHIC (non-Hunner-type IC), 5 HIC (Hunner-type IC), and 5 non-IC (control) cases, were enrolled. Employing quantitative RT-PCR, the expression of genes which had been previously reported as biomarkers for IC/BPS patients were examined in patients with bladder IC/BPS and in controls (non-IC) as well. Furthermore, we investigated the expression of sonic hedgehog (Shh) and WNT family genes which were involved in IC/BPS pathology in our previous IC/BPS animal model studies. Particularly, the function study of WNT2B was evaluated by infection of its specific shRNA containing lentivirus into HBIEpC, a normal human bladder epithelial cells.

Results
According to our qPCR data, the expression of WNT2B in the bladder tissue was characteristically increased in HIC patients, compared with NHIC and control patients. Silencing of WNT2B in HBIEpC bladder epithelial cells resulted in the fibrotic changes including fibrotic morphology, localization of phospho-Smad2 or -Smad3 proteins, increased vimentin protein, a mesenchaymal marker, and up-regulation of genes related epithelial mesenchymal transition.

Interpretation of results
Through integrative data analysis, functional experiments demonstrated that WNT2B was a key regulator of fibrogenesis.

Concluding message
Conclusively Shh-WNT pathway play a crucial role in pathogenesis of IC/BPS. Particularly, mis-regulation of WNT2B impaired the balance between bladder epithelial regeneration and tissue fibrosis in IC/BPS patient. Taken together, WNT2B is a novel finding that may have new treatment implications in IC/BPS.

Disclosures
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