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IDENTIFICATION OF SIGNALING PATHWAYS RELATED TO OVERACTIVE BLADDER IN UROTHELIUM

Hypothesis / aims of study

The bladder urothelium has important pathophysiological role to manifest overactive bladder (OAB) symptoms. However, the mechanisms of pathogenesis of OAB at the molecular level remain poorly understood, mainly as a result of lack of modern molecular analysis. In this study we tried to identify novel urothelium proteins that are related to the development of detrusor overactivity (DO) using proteomic and bioinformatic methodologies.

Study design, materials and methods

The study was conducted using male Sprague-Dawley rats, subdivided into sham operated (n=40) and partial BOO groups (n=60). Partial BOO was induced for 2 weeks and DO was confirmed with measuring cystometry. The identification of protein was assessed with LC-MS/MS using LTQ-Velos mass spectrometry. Functional analysis of the data set was done using the Ingenuity GO (Gene Ontology) and Pathway Knowledge Base. Western blot and immunohistochemistry were performed for the expression validation.

Results

In the OAB urothelium, pathways involved in inflammation, such as the complement system, acute phase response signaling, LXR/RXR activation, and p38 MAPK signaling, were notably up-regulated. By contrast, signaling pathways related to cytoskeletal organization, including ILK signaling, RhoA signaling, and remodeling of epithelial adherens junctions, were commonly down-regulated. ER stress were down-regulated and proteins involved in death receptor signaling were up-regulated. 52 proteins involved in signaling molecules to communicate with closely located bladder nerves, detrusor muscles, and interstitial cells were identified. 7 ATP-related proteins were detected only in the OAB urothelium. Their expression pattern was validated by Western blot and immunohistochemistry experiments.

Interpretation of results

Signaling pathway analysis revealed that the differentially expressed proteins were mainly involved in the cytoskeletal organization, inflammatory response and apoptosis. These proteins may be associated with abnormal sensitivity and muscle contraction of the bladder.

Concluding message

Our findings will provide new insights understanding the development and pathophysiology of OAB.

References

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Disclosures

Funding: non **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Sprague-Dawley rat **Ethics Committee:** All animal experiments followed the guideline for care and use of animals and the protocols were approved by the Institutional Animal Care and Use Committee of Chungnam National University (IRB No. CNU-00706).