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SMALL CONDUCTANCE CALCIUM-ACTIVATED POTASSIUM (SK3) CHANNEL POSITIVE INTERSTITIAL CELLS IS PRESENT IN THE GAP OF DETRUSOR SMOOTH MUSCLE FIBER

Hypothesis / aims of study

Small conductance Ca^{2+}-activated K^+ channels (SK channels) are thought to be involved in the suppression of detrusor smooth muscle excitability and contractility, therefore the activation of SK channels might provide a novel therapeutic approach for controlling detrusor overactivity. These channels consist of three subtypes, SK1, SK2 and SK3. Above all, the suppression of SK3 induced an urinary bladder instability and SK3 is up-regulated and facilitatory function is observed after bladder outlet obstruction. On the other hand, SK3 is also a molecular marker detecting the some interstitial cells in the gastrointestinal musculature. In this study, we examined the distribution and structural feature of SK3 expressed interstitial cells in the bladder wall.

Study design, materials and methods

Male guinea pigs weighting 500 to 700 gm were anesthetized and transcardially perfused with heparinized saline followed by 500 ml of Zamboni solution. The urinary bladder was extirpated and post-fixed for 2 hours. After several rinse, the urinary bladder was incubated in the 0.1 M phosphate buffer containing 30% sucrose for cryoprotection. Five μm bladder wall section and 30 μm detrusor layer plate was made by cryostat. These sections were processed immunohistochemistry and examined by conforcal microscopy. These sections were labeled with antibody to SK3, double-immunolabeled by anti-αSMA, vimentin, and platelet-derived growth factor receptor-α (PDGFRα).

Results

The expression of SK3 was observed in interstitial cell in the smooth muscle bundle (Figure 1. red; αSMA, green; SK3). SK3 immunolabeled cell was not observed in the lamina propria. SK3 immunolabeled interstitial cell had a branched stellate or spindle morphology and connected each other like a mesh network (Figure 2). This network surrounded the smooth muscle bundle. Double labeling revealed that SK3 immunolabeled interstitial was co-labeled by vimentin and PDGFRα (Figure 3).

Figure 1

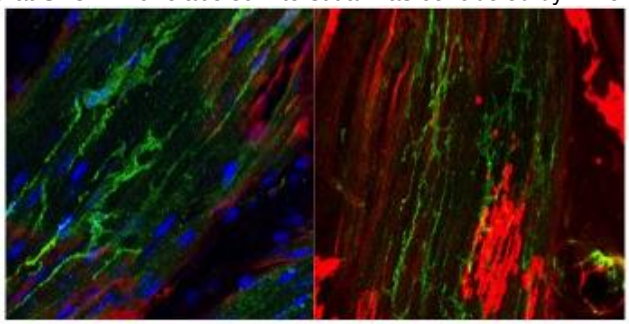


Figure 2, SK3; green, αSMA; red

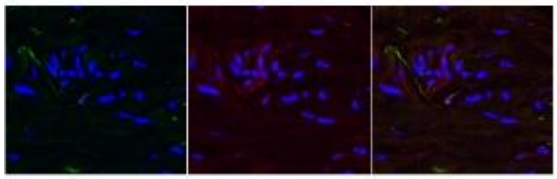
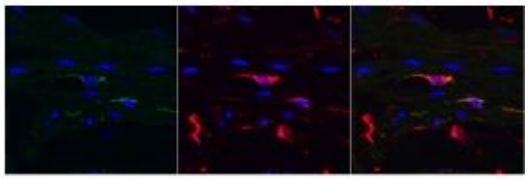


Figure 3, SK3; green, PDGFRα; red



SK3; green, vimentin; red

Interpretation of results

It has been reported SK3 is expressed in detrusor smooth muscle, however the immunoreactivity of SK3 in the smooth muscle cells was not observed in this study. SK3 is co-expressed with vimentin and PDGFRα, indicated that these cells are one type of interstitial cell. SK3 positive interstitial cells exist between the gap of detrusor smooth muscle fiber and are close to the detrusor smooth muscle cells.

Concluding message

SK3 positive interstitial cells are distributed in the detrusor smooth muscle layer. These cells are subfamily of mesenchymal cells. These cells might be involved in the regulation of motility of the urinary bladder detrusor smooth muscle. The structural feature (closeness to detrusor smooth muscle) of SK3 positive interstitial cells might be advantageous to modulate the electrical activity of the urinary bladder detrusor smooth muscle

References
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