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Cell Signaling Pathway in Renal Tubular Epithelial Cells

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Abstract

In diabetes patients and animal models, major cell morphology changes in renal tubules have been observed. The relationship between insulin and the microvillar structure of tubular epithelial cells, however, remains obscure. We used the Scanning Ion Conductance Microscope to image microvillars in the living cell to consider microvillar dynamic. Here, on the tubular epithelial cell surface, we found two layers of microvilli: short compact microvilli, and net-like long microvilli. The length and density of microvilli may be improved by insulin treatment. The PI3K/PLC γ signaling pathway, rather than the PI3K/Arp2/3 signal pathway, mediated this operation. In conclusion, our findings present a novel transduction mechanism for insulin signaling, which contributes to the understanding of complex regulation of renal tubular epithelial cell microvilli.

Introduction

Polarization, in which the plasma membrane is split into apical and basolateral membranes, is one of the features of renal tubular epithelial cells. To perform multiple functions, including glucose transport, ion channel control, signal transduction, volume regulation, the apical surface is filled with thickly packed microvilli. Changes in the composition of the microvillus are closely correlated with the development and progression of associated kidney/kidney diseases, such as type 2 diabetes, if not induced. As a result, it is important to recognize microvillar formation modulators for renal tubular cells and describe the mechanism for understanding kidney/kidney related diseases.

In the proximal renal tubule, insulin is known to control both metabolic and transport functions. A strong regulator of cell metabolism and energy homeostasis, the insulin signalling cascade appears to be involved in diabetic and non-diabetic kidney disease. Insulin also binds to receptors present in the proximal tubular basolateral membrane, in addition to the canonical insulin signal cascades, which initiate events leading to the phosphorylation of that receptor and the activation of downstream signal transduction.

Tanvi Pandey*

Department of Microbiology,
Delhi University, India

***Corresponding author:** Tanvi Pandey

 19ptanvi@gmail.com

Department of microbiology, Delhi
University, India
Tel: +917506147892

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Microvilli proteins mediate the transduction of cell signals and cell-cell contact. The cause of many pathological disorders are changes in cell microvilli. The existence of the insulin-to-renal proximal tubule relationship remains unclear.

An associated weight gain following insulin therapy can affect diabetic and cardiovascular morbidity and mortality in the treatment of type 2 diabetes. Antidiabetic medications have moderate weight loss properties, such as sodium/glucose cotransporter 2 (SGLT2) inhibitors. The major cotransporter involved in the reabsorption of glucose in the kidney, SGLT2, is expressed primarily at the brush border of renal tubular epithelial cells.

Based on the changes in the morphology of the insulin-induced cell surface and the underlying molecular changes in the present work. The Scanning Ion Conductance Microscope (SICM) was used in this research to investigate the continuous modifications of microvilli. A new insulin signal axis controlling the complex microvilli in renal tubular epithelial cells was revealed in our findings.

Discussion

A novel signaling axis involving the insulin-regulating microvilli network in epithelial renal tubule cells was seen in this study. The length and density of microvilli could be improved by insulin. The mechanism of the process was mediated by the activation of PI3K/PLC γ . Several microvillus mechanisms have been adequately studied in fundamental cell functions, including cell-surface enlargement, glucose transport/energy metabolism, ion channel control, membrane potential generation and modulation, volume regulation. It remains unclear, however, whether distinct microvilli perform distinct functions. We found two layers of microvilli presenting on the epithelial cells of the renal tubule. Microvilli contacts with cells in the vicinity were created by the more extended layer, indicating that the longer microvilli can mainly carry out cell-cell communication. In addition, when stimulating insulin, short compact microvilli could expand and form net-like microvilli, indicating that microvilli are versatile in the face of variable stimulation.

Conclusions

Collectively, our findings lead us to conclude that multiple insulin signaling pathways are involved in the regulation of microvilli of renal epithelial cells. This research provides important knowledge about the molecular signaling pathways involved in the renal epithelial cell's critical insulin-mediated processes. It demonstrates new drug targets for diabetes in the treatment of renal disease.