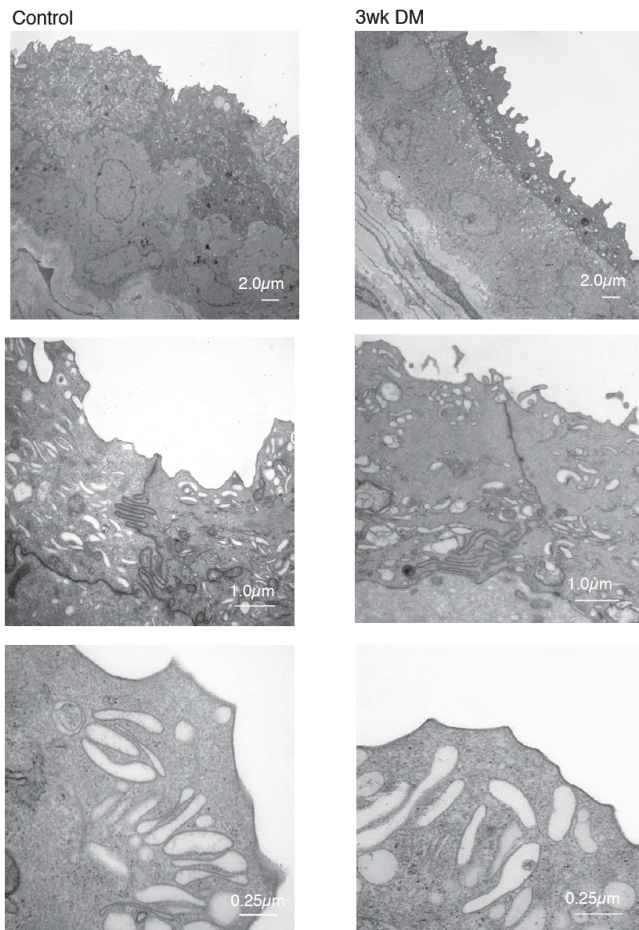


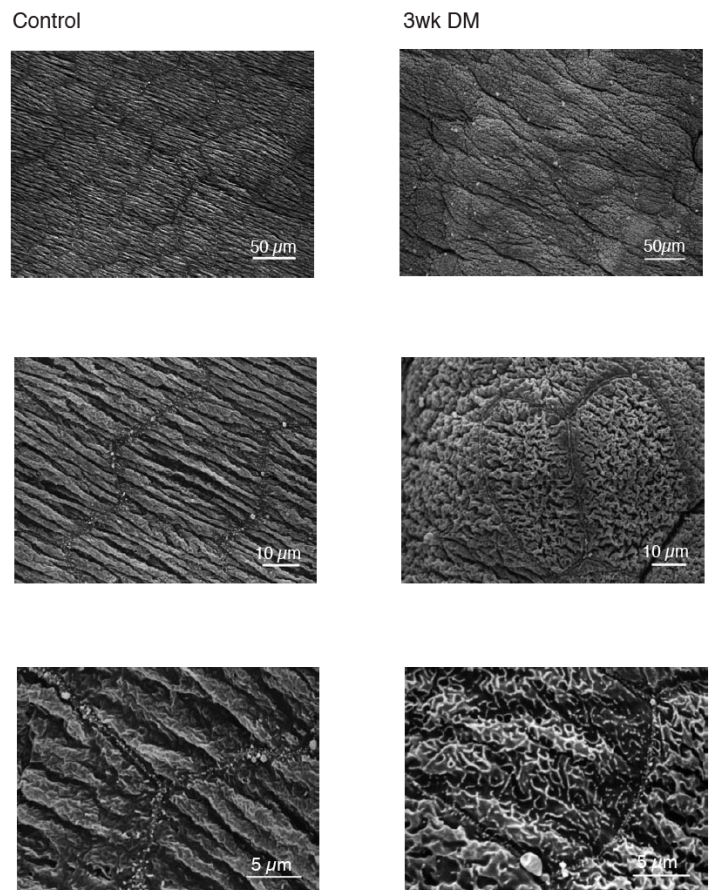
Studies and Results: There is a significant body of data indicating that the bladder urothelium exhibits both barrier as well as sensory properties. Defects in urothelial cells may play a significant role in diabetes-induced changes in bladder function. Additional findings support the general hypothesis that altered response of epithelial cells in the urinary bladder may contribute to symptoms of diabetes.

The goals of this proposal were to conduct a morphological examination of sensor molecules within the urothelium as well as changes in urothelial ultrastructure following treatment of rats with STZ for various time points (3, 9 and 20 weeks) as compared to untreated controls.

TEM images of control and 3 week old DM rats



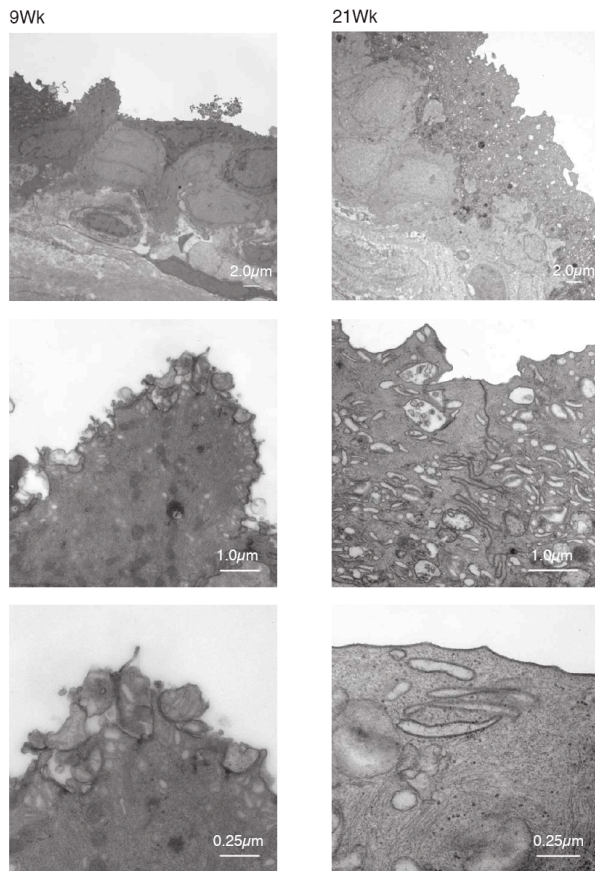
SEM images of control and 3 week old DM rats



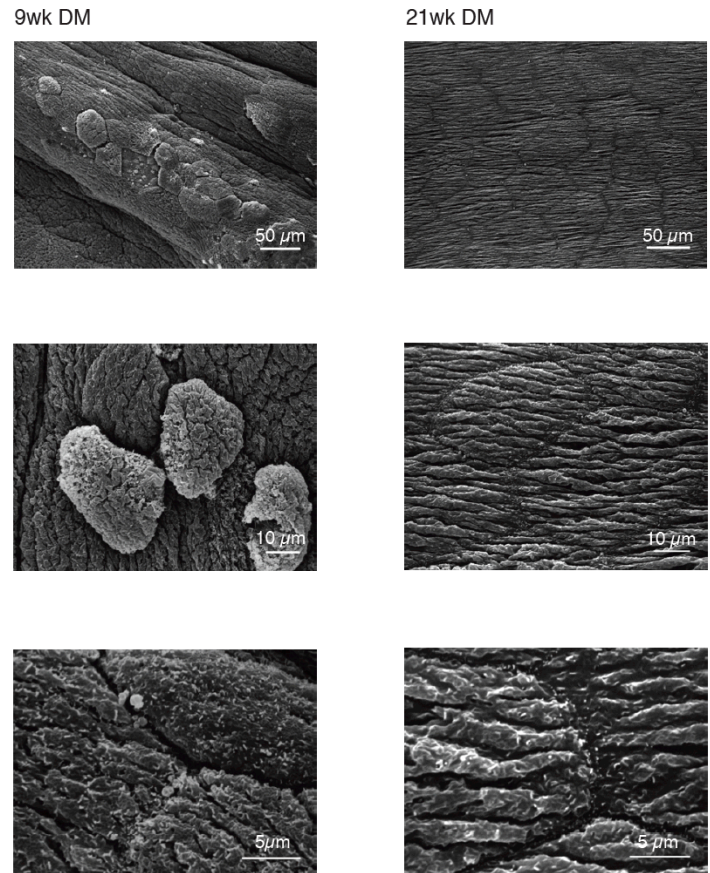
There is evidence that various animal models of diabetes are associated with morphological changes to the bladder urothelium. Even exposure to high glucose has the ability to alter various protein expression patterns within a number of cell types in the bladder wall. We have used (scanning and transmission) electron microscopy to examine the morphology of the bladder urothelium in STZ versus control rats. These experiments will provide information as to the morphological and chemical properties of normal and DM urothelial cells. Changes in the urothelium may impact on underlying bladder nerves and smooth muscle within the bladder wall---and ultimately impact bladder function.

These findings reveal significant changes to the urothelium as early as 3 weeks post STZ treatment. The following images show further alterations at 9 weeks and also at 20 weeks.

TEM images of 9 and 21 week old DM rats



SEM images of 9 and 21 week old DM rats



These findings are being compiled along with results in regard to molecular targets within the urothelium.

Ultrastructural Analysis of Bladder Epithelium: For conventional electron microscopy, samples of bladder or urethral epithelium are fixed and are en bloc- stained overnight with 0.5% (w/v) uranyl acetate in H₂O. Samples are dehydrated, embedded and sectioned with a diamond knife (Diatome; Fort Washington, PA), mounted on butvar-coated nickel grids and viewed at 80 kV in a Jeol 100 CX electron microscope. We will follow established design-based stereological methodology to count objects such as urothelial cells of different types, neurons and varicosities.

References in support of this grant:

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