

Mitchell B. Cohen, MD

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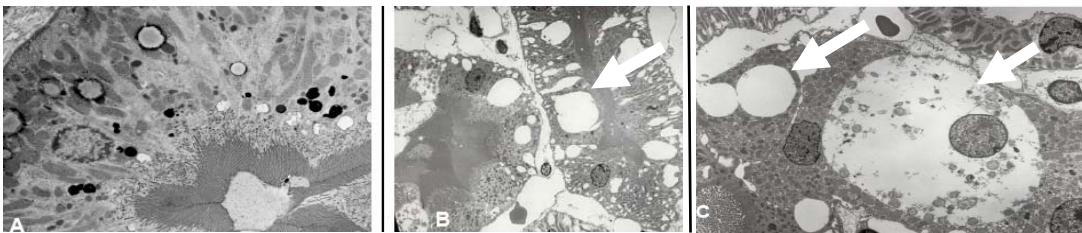
Description of Research:

Dr. Cohen focuses on host-pathogen interactions and intestinal secretion. His current work is investigating the mechanism of *E. coli* heat stable enterotoxin and its receptor guanylyl cyclase-C (GC-C). This receptor also binds the endogenous mammalian peptides, guanylin and uroguanylin, that are produced in the intestine. Dr. Cohen has generated two knock out strains of mice, one with a deletion of the guanylin gene and the other with a deletion of the uroguanylin gene. He is using these mice as well as GC-C knock out mice to identify other receptors for these peptides and to test the hypotheses that guanylin and uroguanylin are cytostatic and that removal of these ligands results in increased intestinal epithelial cell proliferation. In addition, he is testing the hypothesis that these peptides form a novel regulatory pathway to allow the intestine to communicate with the kidney to effect salt and water homeostasis.

Collaborations:

Dr. Cohen has used the **Bioinformatics, Microarray, and Integrative Morphology Cores** in collaboration with Drs. Aronow, Jiang, Lorenz, Matthews, Rudolph, Shull, Steinbrecher, and Witte to study the role of the guanylin/uroguanylin/GC-C circuit and of other intestinal peptides on secretory mechanisms in the intestinal tract. He has also used the same core services in collaboration with Drs. Denson and Rothenberg on studies investigating pathogenic mechanisms of pro-inflammatory and eosinophilic gastrointestinal disorders. Dr. Cohen serves as a mentor on Dr. Rudolph's K08 grant and Dr. Shroyer's K01 award.

Representative Figure:



Enteric renal axis of uroguanylin: Electron microscopy of proximal convoluted tubules after infusion of an enteral salt challenge. Prominent vacuoles are seen in uroguanylin knockout mice. A= wildtype animal. Small, mostly apical vacuoles are seen in the proximal convoluted tubule cells (Magnification X 2,500). B= A dramatic increase in number and size (arrow) of vacuoles is seen in uroguanylin knockout animals (Magnification X 3,500). Vacuoles compress the lumen of the tubule and are no longer confined to the apical pole. C= Higher power view of the vacuoles demonstrating no limiting membrane or electron dense composition of the vacuole (Magnification X 5,000). Figure 6 from *J Pediatr Gastroenterol Nutr* 2006 43:S74-S81