

TITLE:

CaSR: linking nutrition to microbial ecology and gut inflammation

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RESEARCH PROJECT DESCRIPTION:

The mucosal surfaces are continuously exposed to microbes, both pathogenic and commensal organisms. Accordingly, nature has evolved an array of microbe-sensing mechanisms such as pattern-recognition receptors to impose balance between immunity and tolerance. In this way, the host can detect and react against invasion of potential pathogens with minimal harm to beneficial commensal microbes and host cells. Also, different from other mucosa, the primary function of the gut is to handle daily nutrients. Thus, the gut mucosa must develop additional mechanism(s) to balance nutrition, microbes and functional immune responses. Understanding this mechanism(s) may lead to development of novel therapeutic approaches not only for auto immune diseases but also for infections and nutritional disorders. Over the past years, we have generated evidence that the extracellular calcium/nutrient-sensing receptor (CaSR), a newly characterized unique G protein coupled receptor, is such a mechanism. Thus, candidate students will have the opportunity to address such basic questions as how the nutrient sensor interacts with bacteria sensors to maintain gut homeostasis and whether disruption of this interaction leads to disease. With this new knowledge, the students will be expected to participate in designing novel therapies or improving known treatments such as total enteral nutrition, a primary therapy widely used to induce Crohn's disease remission. Besides routine molecular cellular genetic and immunopathological techniques, students will have the opportunity to learn state of art cell-imaging and classical physiological and electrophysiological techniques including Ussing chamber/short-circuit current recording and pH stat measurement. The project is funded by NIH and UF funds.

Tang L, Cheng CY, Sun X, Pedicone AJ, Mohamadzaed M and Cheng SX. 2016. The Extracellular Calcium-Sensing Receptor in the Intestine: Evidence for Regulation of Colonic Absorption, Secretion, Motility, and Immunity. *Front. Physiol.* 7:245. doi: 10.3389/fphys.2016.00245

Cheng SX. 2016. Calcium-sensing receptor: A new target for therapy of diarrhea. *World Journal of Gastroenterology* 22(9):2711-24.

Owen JL, Cheng SX, Sahay B and Mohamadzaed M. 2015. The Role of the Calcium-Sensing Receptor in Gastrointestinal Inflammation. *Semin Cell Dev Biol* 49:44-51.
Cheng SX, Lightfoot YL, Yang T, Zadeh M, Tang L, Sahay B, Wang GP, Owen JL, and Mohamadzaed M. 2014. Epithelial CaSR Deficiency Alters Intestinal Integrity and Promotes Proinflammatory Immune Responses. *FEBS Lett.* 588: 4158-66.

Geibel J, Sritharan K, Geibel R, Geibel P, Persing JS, Seeger A, Roepke TK, Deichstetter M, Prinz C, Cheng SX, Martin D & Hebert SC (2006). Calcium-sensing receptor abrogates secretagogue-induced increases in intestinal net fluid secretion by enhancing cyclic nucleotide destruction. *PNAS*, 103: 9390-7.

Ring A*, Cheng SX*, Kahle KT, Leng Q, Rinehart J, Lalioti MD, Volkman HM, Wilson FH, Hebert SC & Lifton RP (2007). WNK4 regulates activity of the epithelial Na channel in vitro and in vivo. *PNAS*, 104:4020-4.

Cheng SX, Geibel JP & Hebert SC (2004). Extracellular polyamines regulate fluid secretion in rat colonic crypts via the extracellular calcium-sensing receptor. *Gastroenterology* 126(1):148-58.