SUPPLEMENTRY METHODS:

Lactulose Breath Test: The lactulose breath test was used to exclude small bowel bacterial overgrowth as a potential cause of abdominal pain and diarrhea. Following an overnight fast, baseline breath samples were collected in bags to measure basal breath hydrogen using the Breath Tracker Analyzer (Quintron Instrument Co, Inc., Milwaukee, WI). Patients with a high basal value of breath hydrogen of >16 parts per million (ppm) were considered to be positive for bacterial overgrowth. Following the basal breath hydrogen measurement, patients ingested 10 grams of lactulose and breath samples were collected every 15 minutes for 3 hours. A rise in breath hydrogen by ≥20 ppm between any of the measured time points up to 120 minutes was considered positive for small bowel bacterial overgrowth.[19]

***TNBS Animal Model & Visceral Hypersensitivity Testing*:**
A balloon (3 cm long, 1.5 cm max diameter) made of polyethylene was secured to tubing attached to an automated distension device (IsoBar 3: G&J Electronics Corp; Willowdale, Ontario) and used to perform colonic distension. The balloon was lubricated and placed into the rat's distal colon so that the tip of the balloon was 1 cm from the anus. The rats were allowed to acclimatize 10 min before behavior testing began. The rats were restrained in a plastic containment device (RSTR544, Kent Scientific Corp, Torrington, CT) and received phasic distension (0–80 mmHg in 5 mmHg ascending increments of 10 s each) of the colon until the first contraction of the testicles, tail, or abdominal musculature occurred. This nociceptive threshold response was considered to reflect a behavioral index of visceral sensitivity in response to a nociceptive stimulus ("1st nociceptive response").[20] The colonic distensions were repeated 4 times with 5 min interstimulus intervals and the mean balloon pressure at the nociceptive threshold was recorded for each rat. Rats were categorized as hypersensitive to colonic distension (VH rats) if the 1st nociceptive response was at a calculated mean colonic distension pressure of <25 mmHg.[20]

Co-culture of human neuron cells / intestinal epithelial cells and single cell PCR:

LUHMES (human neuron cells: ATCC® CRL. 2927™) and epithelial cells (Human intestinal epithelial cells ATCC® CRL-1831™) were used for co-cell-culture study to elucidate the intercellular communications between neuronal and intestinal epithelial cells. GFP or RFP lentivirus was prepared with 293TN cells and SBI pPACK™ packaging systems(Cat # LV510A-1) according to manufacturer's protocol. Virus particles were precipitated with PEG-it reagent (SBI Cat# LV825A-1) and diluted with PBS and aliquoted. Lentiviral titers were measured with the Global UltraRapid™ Lentiviral Titer Kit(SBI Cat#: LV961A-1) by real-time PCR. Transduction of GFP - lenti-virus-199a to epithelial cells and transduction of RFP-lenti-virus (as dye) to neuron cells: Lentivirus was transduced to target cells with TransDux™ (SBI Cat# LV850A-1) according to manufacturer's protocol. 72 hours post transduction, the viral genome was integrated into the host cell genome. GFP and RFP were observed under the fluorescence microscope. Then, miR-199a-GFP-epithelial cells and RFP-neuron cells were co-cultured together for 48-72 hours. Co-cultured cells were observed under the

fluorescence microscope. A total of 5-10 of the red cells (neuron cells) were isolated and detached with a glass pipette tip and transfered to Single Cell Lysis/Dnase I solution. Single Cell PCR of TRPV1 mRNA was performed by using a Single Cell-to-CT™ Kit (Ambion cat# 4458237) to measure the TRPV1 expression in neuronal cells according to Ambion's protocol.

microRNA PCR Array and Assay

Human genome–wide microRNA PCR Array (Human miFinder 384HC miRNA PCR Array: SABiosciences/QIAGEN, MIHS-3001ZG) was performed on LightCycler 480 384-well block Real-Time PCR Detection System (Roche) as the 2nd platform in addition to microArray to compare the reproducibility between the training set (n=5) and testing set (n=5), as follows: 200 ng of enriched small RNA was converted into complementary DNA (cDNA) using miScript PCR System (SABiosciences/QIAGEN). The cDNAs were mixed with 2X QuantiTect SYBR Green PCR Master Mix (SABiosciences/QIAGEN) and dispersed into a 384-well human genome microRNA PCR Array with 10 uL/well reaction volume. MicroRNA PCR Array was used to monitor the expression of a panel of primer sets for 372 human microRNAs, with six housekeeping genes (RNU6-2, SNORD61, 68, 72, 95 and 96A) for small nuclear RNA as the endogenous controls to normalize raw data. Duplicate reverse transcription controls to test the efficiency of the microRNA reverse transcription reaction and duplicate positive PCR controls to test the efficiency of the PCR itself were also included in the array. The average of six housekeeping genes was used for normalization. Normalization of microRNA expression was conducted using SABiosciences Online PCR Array Data Analysis Web Portal. The 2^ ΔCt values from the original expression profiles were obtained.