**Supplemental Materials and Methods**

***Animals.*** Animal Ethics Committees of Monash University, the University of Erlangen-Nürnberg and the University of Florence approved all studies on animals. C57BL/6 mice were from Monash Animal Research Platform. *Tgr5*$^{-/-}$, *tgr5-tg*, *trpa1*$^{-/-}$, *trpv1*$^{-/-}$ and *fos-tau-lacZ* mice have been described [1-4]. Male mice (6-10 weeks) were used. Male Sprague-Dawley rats (180-200 g) were from Harlan Laboratories (Italy). Mice and rats were maintained in a temperature-controlled environment with a 12 h light/dark cycle and free access to food and water. Mice and rats were killed by anesthetic overdose and bilateral thoracotomy.

***Materials.*** HC-030031, gallein, and GF109203X were from Tocris Biosciences (Minneapolis, MN, USA) and AMG-9810 was from Amgen Inc (Thousand Oaks, CA, USA). Unless stated otherwise, other reagents were from Sigma-Aldrich (St Louis, MO, USA). The concentrations of inhibitors and antagonists were selected from published studies examining regulation of TRP channel activation [5-7].

***Retrograde tracing.*** Mice (C57BL/6) were anesthetized with 5% isoflurane. A single intradermal injection of 1,1'-Dioctadecyl-3,3,3',3'-Tetramethylindocarbocyanine Perchlorate (DiI, 2%, 10 µl) was made to the nape of the neck. Mice recovered for 7 days before tissue collection.

***Immunofluorescence.*** After retrograde tracing, DRG (C1-C7) were removed and fixed in 4% paraformaldehyde (PFA), 100 mM PBS, pH 7.4 (overnight, 4°C). DRG were washed in PBS and cryoprotected in 30% sucrose, PBS, 0.1% sodium azide (overnight, 4°C). DRG were embedded in TissueTek Optimal Cutting Temperature compound (OCT, Sakura Finetek, Torrance, CA), and 12 µm frozen sections were prepared, with every third section mounted onto slides. Sections were incubated in blocking buffer (10% normal horse serum, 0.1% Triton X-100 in PBS containing 0.1% sodium azide; 1 h, room temperature), and were incubated with rabbit anti-TGR5 (1:500, [8]) or rabbit anti-NeuN (FOX3) (1:2,000, Abcam, Cambridge, UK, #104225) in blocking buffer (overnight, 4°C). Sections were washed in PBS and incubated with Alexa 488-conjugated donkey anti-rabbit IgG (1:1,000, Jackson ImmunoResearch, Westgrove, PA, USA) (1 h, room temperature). Sections were mounted in Prolong Gold (Invitrogen, Carlsbad, CA). Sections were observed using a Leica TCS SP8 confocal microscope. Images (1024x1024 pixels) were collected as z-stacks of the full diameter and thickness of each section. Ten sections were imaged per mouse, and images lacking detectable DiI were excluded. Z-stacks for individual channels were maximally projected using ImageJ (NIH). The threshold of images was set and DiI- or TGR5-positive neurons were identified independently and defined as regions of interest (ROIs). The ROIs were then combined and the relative overlap between DiI- and TGR5-positive neuronal populations was determined and expressed as a percentage of the total populations.

***In-situ hybridization and immunohistochemistry.*** A plasmid to prepare antisense cRNA complimentary to mouse TRPA1 mRNA was constructed using a partial mouse TRPA1 cDNA of 918 bp that was

amplified by RT-PCR from mouse DRG RNA using forward primer 5'acttcctggattacaacaatgctctg3' and reverse primer 3'attccacttgctgtgcatctgttc5' [9]. The PCR product was cloned into the pCRII-TOPO vector (Invitrogen) and its orientation was confirmed using M13 forward and reverse primers. Linear templates were prepared by PCR using M13 forward and reverse primers. Antisense and control sense digoxigenin-labeled cRNA was prepared by *in vitro* transcription with T7 and SP6 RNA polymerases (Roche Diagnostics, Indianapolis, IN), respectively. After retrograde tracing, cervical DRG were removed and fixed in 4% PFA (overnight, 4˚C). The ganglia were washed in diethylpyrocarbonate (DEPC) PBS, 4°C), incubated in 30% sucrose in DEPC-PBS (4 h, 4°C), embedded in OCT, and 12 µm frozen sections were prepared. Since the DiI fluorescence did not persist after the *in situ* hybridisation protocol, it was imaged beforehand. Sections were hybridised with TRPA1 probe in hybridisation buffer (50% formamide, 4x standard salt concentration [SSC]), pH 7.5, 10% dextran sulphate, 1x Denhardt's solution, 0.1 $mg.ml^{-1}$ yeast RNA) (overnight, 60°C) [10]. Bound probe was detected with alkaline phosphatase (AP)-conjugated sheep-anti-digoxigenin (DIG) Fab' using the NBD/BCIP substrate (Roche Diagnostics). Sections were then incubated with rabbit anti-TGR5 (1:500) or mouse anti-HuC/D (1:1,000, Invitrogen) (overnight, 4°C). Sections were washed and incubated with Alexa 488- or Alexa 647-conjugated donkey anti-rabbit IgG (Invitrogen) (1:1,000, 2 h, room temperature). Sections were observed using a Zeiss Axioskope.Z1 fluorescence microscope. The intensities of *in situ* hybridization and fluorescence signals and the extent of overlap were quantified using the ImageProPlus software (Media Cybernetics, Silver Spring, MD, USA), as described [11].

***Single cell RT-PCR.*** After retrograde tracing, DRG were collected from all spinal levels, and were dissociated as described [12]. Dissociated neurons were plated onto poly D-lysine- (0.1 $mg.ml^{-1}$) and laminin- (0.004 $mg.ml^{-1}$) coated cover slips, and were incubated in Leibovitz's L-15 medium containing 10% FBS in a humidified incubator (8 h, 37°C). Individual DiI-positive small diameter (<25 µm) neurons were selected and drawn into a glass-pipette (tip diameter 25-100 µm) by applying negative pressure [13]. The pipette tip was broken in a PCR tube containing 1 µl of resuspension buffer and RNAse inhibitor (RNAseOUT, 2 $U.\mu l^{-1}$, Invitrogen) and snap frozen. PCR reactions used the following intron-spanning mouse primers: TGR5 outer primer forward 5'-cactgcccttctctctgtcc-3', reverse 5'-tcaagtccaggtcaaatcctg-3'; TGR5 inner primer forward 5'-tgctcttcttgctgtgttgg-3', reverse 5'-gtccctcttggctcttcctc-3'; TRPV1 forward 5'-tcaccgtcagctctgttgtc-3', reverse 5'-gggtctttgaactcgctgtc-3'; TRPA1 forward 5'-ggagcagacatcaacagcac-3', reverse 5'-gcaggggcgacttcttatc-3'; or b-actin forward 5'-ctggtcgtcgacaacggctcc-3', 5'-reverse gccagatcttctccatg-3' [12]. As a negative control, superfusing fluid from the vicinity of the collected cells was amplified, or RT was omitted. Products were separated by electrophoresis (2% agarose), stained using ethidium bromide, and sequenced to confirm identity.

***Cell lines.*** HEK293 cell lines stably expressing human TGR5 have been described [8]. HEK293 cells expressing human TRPA1 were generated using a tetracycline-inducible system. Briefly, Flp-In™ T-Rex™ HEK293 cells were transfected with pcDNA5/FRT/TO containing TRPA1 using Lipofectamine 2000 (Invitrogen). Cells were grown in Dulbecco's Modified Eagle's Medium (DMEM) containing 10% tetracycline-free fetal bovine serum (FBS), blasticidin (5 $\mu g.ml^{-1}$) and hygromycin (100 $\mu g.ml^{-1}$). To generate cells co-expressing TRPA1 and TGR5, human TGR5 was cloned into pcDNA3.1 neo and then co-transfected into the HEK-TRPA1 cells using a calcium phosphate-DNA co-precipitation method. In brief, cells were incubated in 125 mM $CaCl_2$ plus HBSS with 1 µg TGR5 pcDNA3.1 overnight at 37°C and 5% $CO_2$. The transfection medium was replaced with selection medium (10% FBS, 5 $\mu g.ml^{-1}$ blasticidin, 100 $\mu g.ml^{-1}$ hygromycin, 400 $\mu g.ml^{-1}$ G418) and single clones isolated by limiting dilution. The clones were grown under selection, assayed for cAMP responses to the TGR5 agonist DCA, and one clone was selected based on its robust response. Cells were maintained in DMEM containing 10% tetracycline-free fetal FBS, 1% penicillin and streptomycin, 100 $\mu g.ml^{-1}$ hygromycin, 400 $\mu g.ml^{-1}$ G418 and 5 $\mu g.ml^{-1}$ blasticidin. To induce the expression of TRPA1, HEK-TRPA1 and HEK-TRPA1-TGR5 cells were incubated with tetracycline (100 $ng.ml^{-1}$) for 16 h before experiments.

***$[Ca^{2+}]_i$ assays in HEK cells.*** HEK-TGR5, HEK-TRPA1 and HEK-TRPA1-TGR5 cell lines were plated onto poly-D-lysine-coated 96 well plates (30,000 cells per well). Cells were loaded with Fura-2/AM (1.6 µM) in assay buffer (mM: NaCl 150, KCl 2.6, $CaCl_2$ 0.1, $MgCl_2$ 1.18, D-glucose 10, HEPES 10, pH 7.4) containing 4 mM probenecid and 0.5% BSA for 1 h at 37°C. Fluorescence were measured at 340 nm and 380 nm excitation with 530 nm emission using a FlexStation Microplate Reader (Molecular Devices, Sunnyvale, CA). Results are expressed as the 340/380 nm ratio, which is proportional to $[Ca^{2+}]_i$. To investigate the potential functional coupling between TGR5 and TRPA1, cells were challenged with DCA (100 µM, 5 min) and then AITC (100 µM, 5 min). To investigate the mechanism of TGR5 and TRPA1 functional coupling, cells were incubated with H89 (10 µM, PKA inhibitor), GF109203X (10 µM, PKC inhibitor), gallein (100 µM, Gβγ inhibitor), or vehicle (control) (60 min preincubation and inclusion through assays).

***Isolation and culture of DRG neurons.*** DRG were removed from all spinal levels from C57BL/6J, *tgr5*$^{-/-}$ and *trpa1*$^{-/-}$ mice, and were dissociated as described [12]. Neurons were plated onto poly D-lysine- (0.1 $mg.ml^{-1}$) and laminin- (0.004 $mg.ml^{-1}$) coated glass coverslips for $Ca^{2+}$ assays or onto poly-D-lysine- and laminin-coated 96 well plates for ERK1/2 and cAMP assays. Neurons were cultured for 24 h before assays.

***$[Ca^{2+}]_i$ assays in DRG neurons.*** Neurons were loaded with Fura-2-AM (2 µM) in assay buffer (mM: NaCl 150, KCl 2.6, $CaCl_2$ 0.1, $MgCl_2$ 1.18, D-glucose 10, HEPES 10, pH 7.4) containing 4 mM probenecid and 0.5% BSA for 30 min at 37°C. Neurons were mounted in an open chamber and were observed using a Leica DMI6000B microscope with a HC PL APO 20x NA0.75 objective. Fluorescence was measured at

340 nm and 380 nm excitation and 530 nm emission using an Andor iXon 887 camera (Andor, Ireland) and MetaFluor v7.8.0 software (Molecular Devices). Neurons were challenged sequentially with AITC (100 μM), DCA (100 μM), capsaicin (1 μM), and KCl (50 mM). In some experiments, neurons were incubated with GF109203X (10 μM), gallein (100 μM), HC-030031 (100 μM) or vehicle (control) (30 or 60 min preincubation and inclusion throughout), or were assayed in $Ca^{2+}$-free buffer containing 2 mM EDTA. Images were analyzed using a custom journal in MetaMorph v7.8.2 software (Molecular Devices). A maximum intensity image was generated and projected through time to generate an image of all cells. Cells were segmented and binarized from this image using the Multi Wavelength Cell Scoring module on the basis of size and fluorescence intensity. Neurons of interest (< 25 μm diameter) were selected, and responsive neurons were defined as those with an increase in fluorescence intensity standard deviation of >1.5 fold over the global baseline intensity standard deviation for all time points.

***ERK1/2 activation in DRG neurons***. Neurons were serum-starved for 6 h before assay. Neurons were challenged with DCA (100 μM) or phorbol 12,13-dibutyrate (PDBu, 200 nM, positive control) for 30 min at 37°C, and lysed in 30 μl 0.3% Tween 20, 5 mM HEPES, 0.1% BSA in water, pH 7.4. Activation of ERK1/2 was assessed using the AlphaScreen SureFire phospho-ERK assay (PerkinElmer Life Sciences).

***cAMP accumulation in DRG neurons.*** Neurons were serum-starved for 6 h before assay. Medium was replaced with activation buffer (phenol red-free DMEM containing 5 mM HEPES, 0.1% BSA, 1 mM 3-isobutyl-1-methylxanthine) for 45 min. Neurons were challenged with DCA (100 μM) or forskolin (10 μM, positive control) for 30 min at 37°C, and lysed. Accumulation of cAMP was assessed using the AlphaScreen cAMP assay (PerkinElmer Life Sciences).

***Measurement of TRPA1 currents in Xenopus laevis oocytes.*** Oocytes were collected from *Xenopus laevis* as described [14]. Defolliculated stage V-VI oocytes were injected (Nanoject II automatic injector, Drummond) with cRNA encoding human TRPA1 alone (0.5 ng) or both TRPA1 (0.5 ng) plus humanTGR5 (2 ng). The cRNAs were dissolved in RNase-free water and the total volume injected was 46 nl. Injected oocytes were stored at 19°C in ND9 solution (mM: N-methyl-D-glucamine-Cl 87, NaCl 9, KCl 2, $CaCl_2$ 1.8, $MgCl_2$ 1, HEPES 5, pH 7.4 with Tris) supplemented with 100 $units.ml^{-1}$ penicillin and 100 $\mu g.ml^{-1}$ streptomycin. Oocytes were studied two days after injection using the two-electrode voltage-clamp technique [14]. Individual oocytes were superfused with ND96 solution (mM: NaCl 96, KCl 2, $CaCl_2$ 1.8, $MgCl_2$ 1, HEPES 5, pH 7.4 with Tris) at a rate of 2-3 ml/min at room temperature. The TRPA1 activator AITC (50 μM) and antagonist HC-030031 (15 μM) were used to activate and inhibit TRPA1 currents, respectively. DCA (500 μM) was used to activate TGR5. Oocytes were clamped at a holding potential of -60 mV.

***Neuropeptide release.*** Slices (0.4 mm) of rat spinal cord with attached dorsal roots (combined cervical, thoracic, lumbar-sacral segments) were prepared at 4°C as described [1]. Slices (100 mg) were superfused

with Krebs solution (mM: NaCl 119, $NaHCO_3$ 25, $KH_2PO_4$ 1.2, $MgSO_4$ 1.5, $CaCl_2$ 2.5, KCl 4.7, D-glucose 11; 95% $CO_2$, 5% $O_2$, 37°C) containing 0.1% BSA and peptidase inhibitors (1 µM phosphoramidon, 1 µM captopril). Tissues were stabilized for 90 min and then superfusate was sampled at 10 min intervals. After collection of 2 basal samples, slices were stimulated with TLCA (500 µM), AITC (100 µM) or vehicle for 60 min. Some tissues were superfused with the TRPA1 antagonist HC-030031 (50 µM) or vehicle for 20 min before and during the stimulus. At the end of the experiment, tissues were blotted and weighed. Fractions (2 ml) were freeze-dried, reconstituted with assay buffer, and GRP and NPPB release were determined by enzyme immunoassays (Phoenix Pharmaceuticals, Burlingame, CA). Peptide concentrations were calculated as $fmol.g^{-1}$ tissue wet weight. TLCA, AITC and HC-030031 did not cross-react with GRP and NPPB antisera.

***Detection of c-fos in spinal neurons.*** FTL mice were habituated by daily handling for 2-3 weeks prior to experimentation. Mice were sedated (5% isoflurane) and DCA (25 µg, 10 µl, s.c.) or vehicle (0.9% NaCl) was injected into the nape of the neck. Other groups of mice were pretreated with the TRPA1 antagonist HC-030031 (100 $mg.kg^{-1}$) or vehicle by gavage (100 µl) 30 min before DCA injection. At 60 min after DCA injection, mice were anesthetized with isoflurane and transcardially perfused with 20 ml PBS and then 20 ml 4% PFA in PBS. The spinal cord was removed, fixed in 4% PFA (2 h, 4°C), and cryoprotected in 30% sucrose PBS (24 h, 4°C). The cervical spinal cord was frozen in OCT and 30 µm frozen sections were floated in 48 well plates in PBS. Sections were washed (PBS, 2 x 10 min) and incubated in 200 µl of β-galactosidase reaction buffer (1 mg/ml 5-bromo-4-chloro-3-indolyl-β-D-galactopyranoside in PBS, 20 mM $MgCl_2$, 10 mM potassium ferrocyanide, 10 mM potassium ferrocyanide, 24 h room temperature). The reaction was stopped with 200 µl of formalin. Sections were washed (PBS, 3 x 10 min), mounted onto slides and rinsed with $dH_2O$. Sections were dehydrated in 50%, 70%, and 100% EtOH, washed in xylene and mounted in DPX mounting medium (Electron Microscopy Sciences, Hattfield, PA, USA). Sections were observed with the ScanScope XT (Aperio, Vista, CA, USA). β-galactosidase- (*c-fos*-) positive cells in the dorsal horn laminae I-III were counted by an observer unaware of the treatment.

***Scratching behavior.*** C57BL/6J, *trpa1*$^{-/-}$ or *trpv1*$^{-/-}$ mice were removed from their home cage at 8 am and placed in individual cylinders on a plastic platform. Animals were acclimated to the experimental room, restraint apparatus and investigator for 2 h periods on three successive days before experiments. To evaluate the pruritogenic effects of DCA, mice were sedated (5% isoflurane) and DCA (25 µg, 10 µl, s.c.) was injected into the nape of the neck. To evaluate the contributions of TRP channels, mice were pretreated with the TRPA1 antagonist HC-030031 (100 $mg.kg^{-1}$, p.o., in 2% DMSO, 20% cyclodextrin), the TRPV1 antagonist AMG-9810 (40 $mg.kg^{-1}$, i.p., in 0.9% saline) or vehicle (100 µl) 30 min before DCA injection. Scratching behavior was recorded for 60 min after DCA injection. One scratch is defined as lifting of a hind limb to the nape of the neck and withdrawal from this site, regardless of the number of

strokes. Scratching was recorded by observers blinded to the experimental protocol. Scratching behavior was assessed at ~10 am, 2 h after removing mice from their home cage and withdrawal of food.

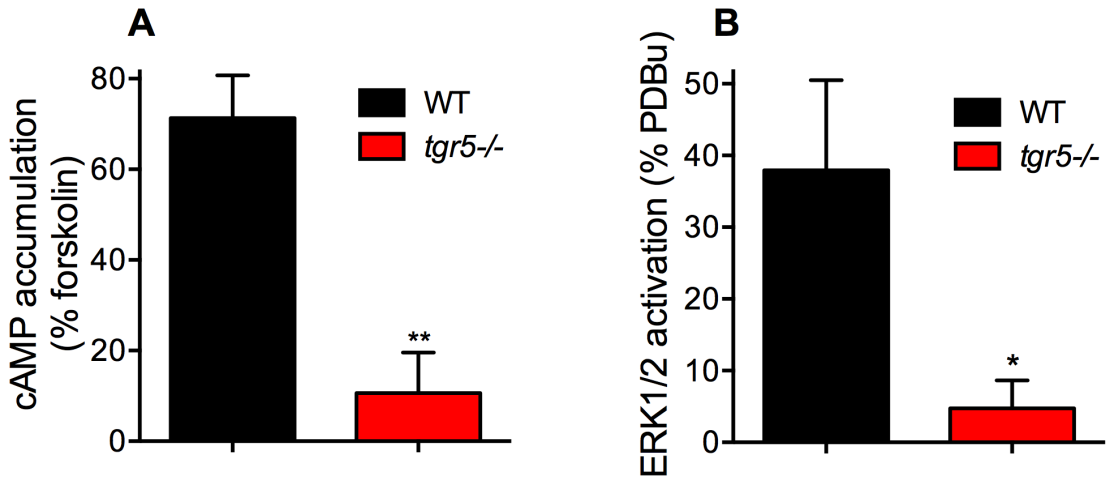
***Wiping behavior.*** The effectiveness of AMG-9810 as a TRPV1 antagonist was assessed by studying capsaicin-evoked wiping behavior [15]. Acclimatized C57BL/6J mice received AMG-9810 (40 $mg.kg^{-1}$, i.p., in 0.9% saline) or vehicle (100 µl) 30 min before injection of capsaicin (3 µg, 10 µl, s.c.) into the cheek. Wiping behavior was recorded at baseline and for 20 min after capsaicin injection by observers blinded to the experimental protocol. A wipe was defined as a singular motion of the ipsilateral (but not bilateral) forelimb beginning at the caudal extent of the injected cheek and proceeding in a rostral direction.

***Treatment of tgr5-tg mice with BA sequestrant and TGR5 antagonist.*** To determine the role of endogenous BAs to exacerbated spontaneous scratching, *tgr5-tg* mice were treated with the BA sequestrant colestipol hydrochloride (2.5 $mg.kg^{-1}$, p.o., Pfizer, Groton, CT) or vehicle (0.9% NaCl, p.o.), which were administered by gavage (100 µl) at 08:00 and 14:00 h for five consecutive days. During this treatment period, mice were habituated as described. After the final gavage treatment, spontaneous scratching behavior was recorded for 60 min. To determine the contribution of TRPA1 to exacerbated spontaneous scratching, *tgr5-tg* mice were treated with HC-030031 (100 $mg.kg^{-1}$) or vehicle 30 min before scratching behavior was recorded.

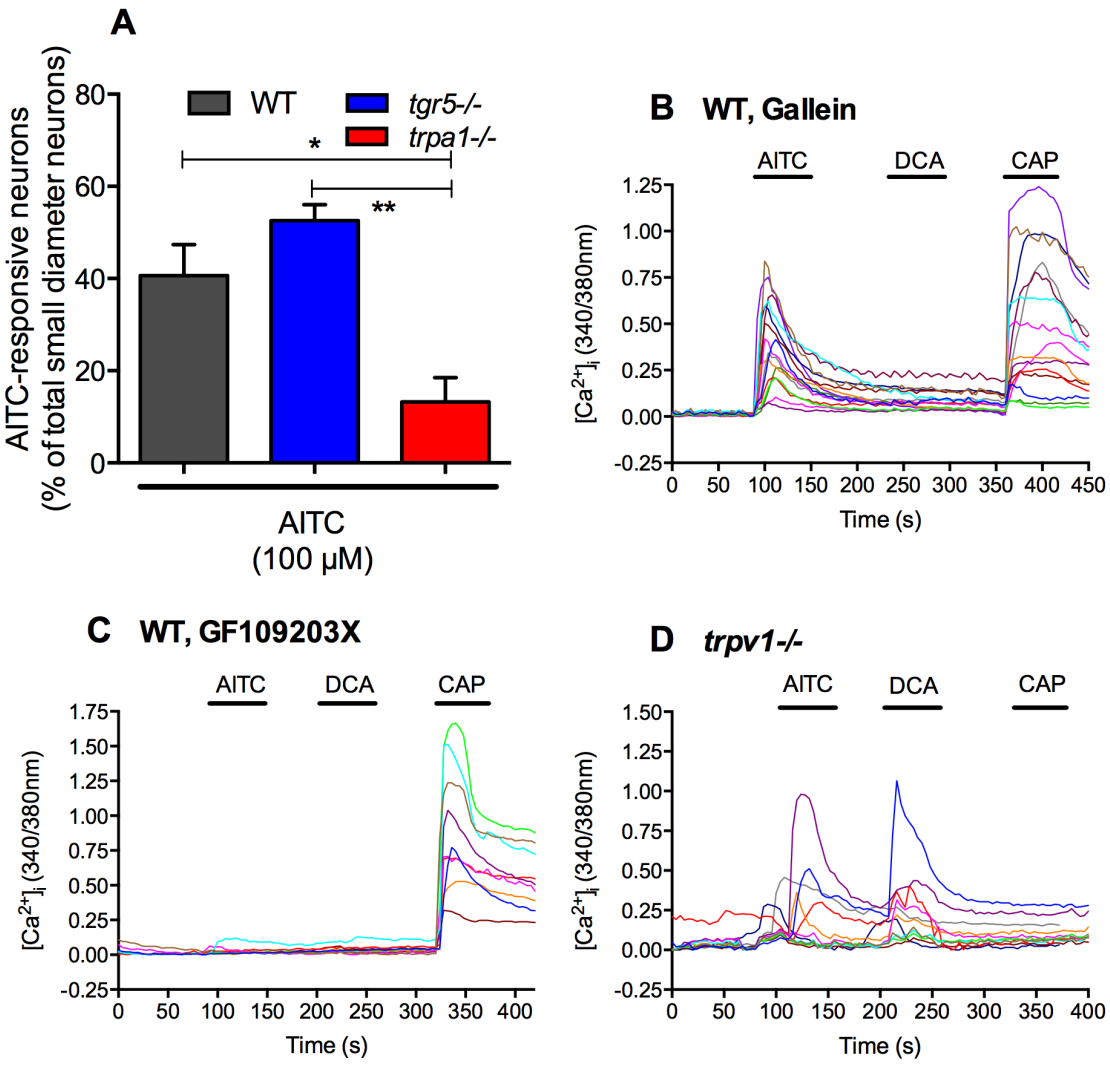
***Measurement of plasma BAs.*** *Tgr5-tg* mice treated with colestipol or vehicle were killed at the end of the scratching assays, ~4 h after food withdrawal. Blood was collected by cardiac puncture into Minicollect tubes (BD Bioscience, North Ryde, Australia) containing sodium EDTA, and plasma was immediately separated by centrifugation (5,000 g, 10 min, 4°C). Total BAs were measured using a Mouse Total BAs kit according to manufacturer's protocol (Crystal Chem, Downers Grove, IL) based on 540 nm absorbance of enzymatic property of 3-α-hydroxy-steroid dehydrogenase.

***Statistical analyses.*** Results are expressed as mean±SEM. Data were compared statistically using Graphpad Prism 6, with Student's t-test for comparisons of 2 groups and ANOVA and Bonferroni or Tukey-Kramer *post hoc* test comparisons of multiple groups. A *P*-value less than 0.05 was considered significant.

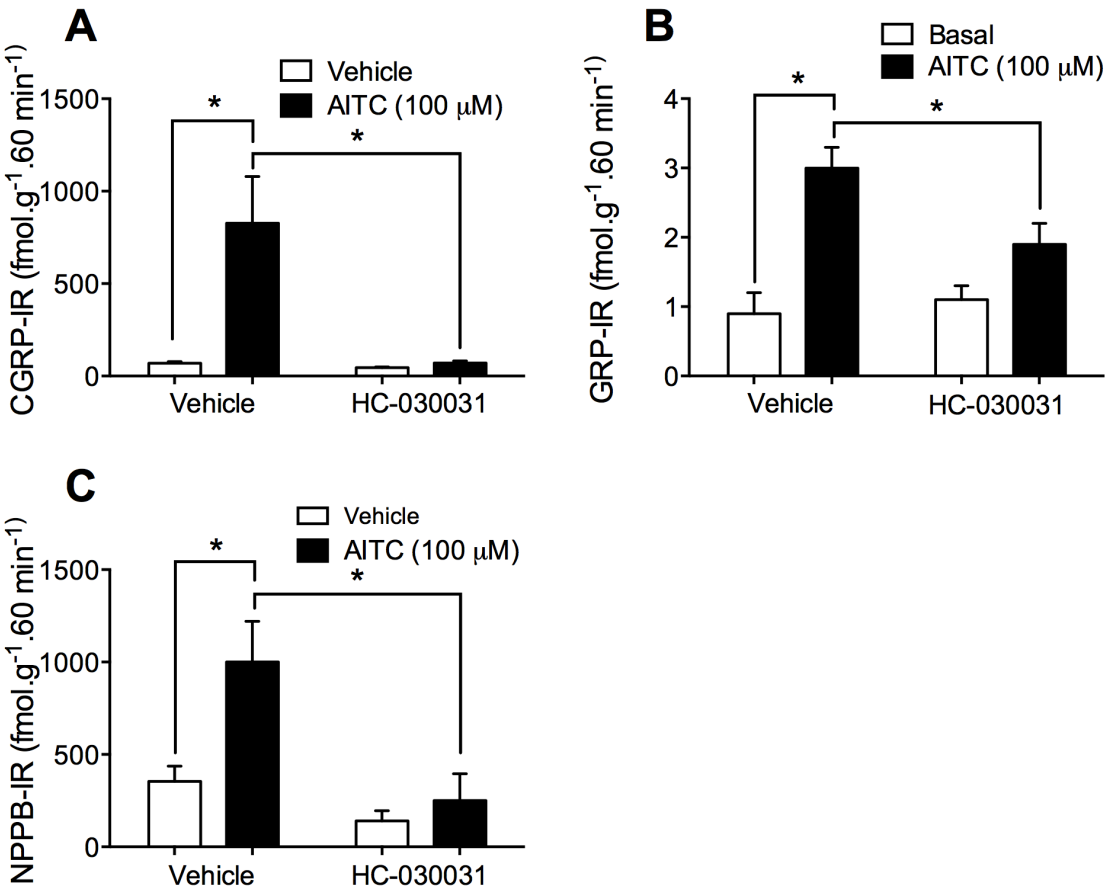
**Supplemental Figures**



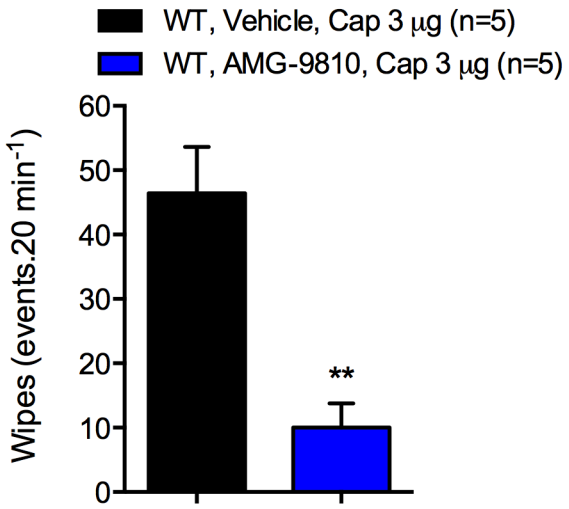

**Supplemental Figure 1. TGR5-dependent BA signaling in DRG neurons. A, B.** DRG neurons from wild-type (WT) and *tgr5*$^{-/-}$ mice were incubated with DCA (100 μM, 30 min). Generation of cAMP (**A**) and activation of ERK1/2 (**B**) were measured. n=3-6 mice. **P*<0.05, ***P*<0.01 to WT mice.



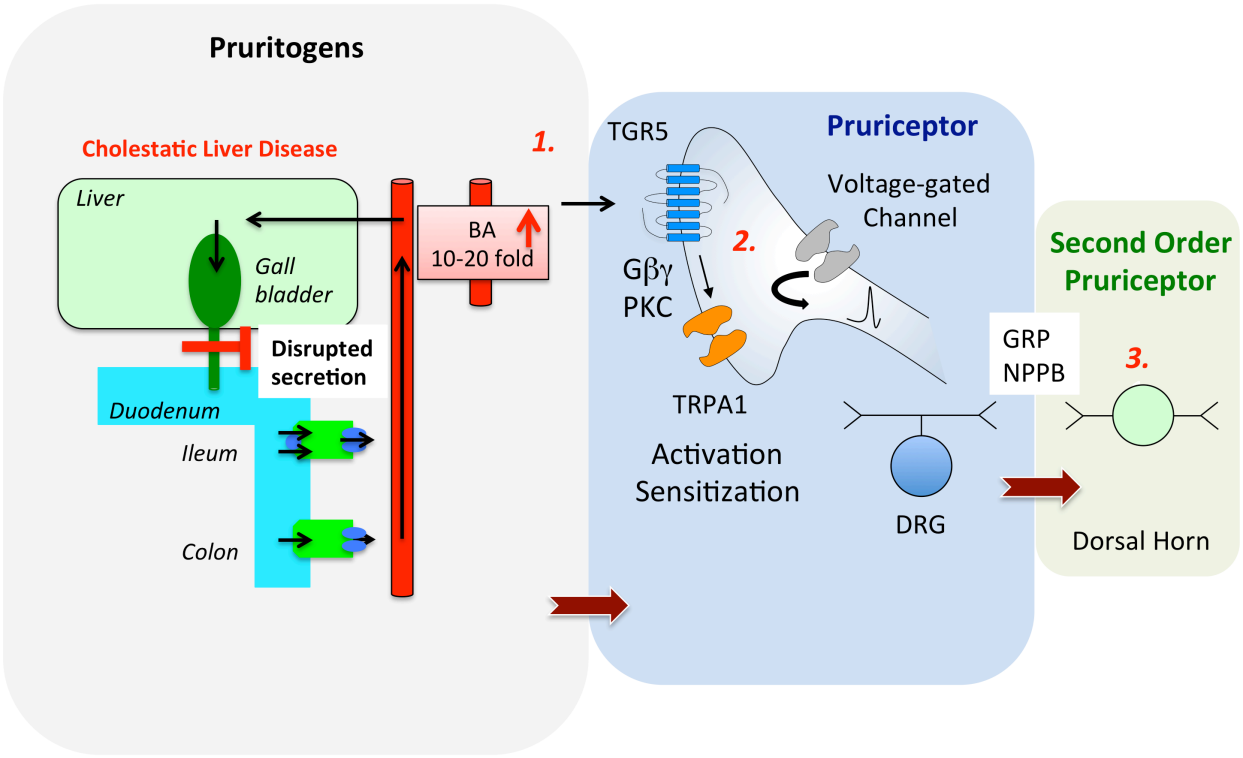

**Supplemental Figure 2. Gβγ- and PKC-dependent, but *trpv1*-independent, BA signaling in DRG neurons.** $[Ca^{2+}]_i$ was measured in small diameter neurons from WT mice, *tgr5*$^{-/-}$ mice, *trpa1*$^{-/-}$ mice and *trpv1-/-* mice challenged sequentially with AITC (100 μM), DCA (100 μM) and capsaicin (CAP, 1 μM). Responses of KCl (50 mM) -responsive neurons are shown. **A.** Pooled data showing the proportion of AITC-responsive neurons in different experimental groups (2453 neurons, n=22 mice). $^{**}P<0.01$, $^{*}P<0.05$ to AITC in WT or *tgr5*$^{-/-}$. **B.** WT mice treated with the Gβγ inhibitor gallein. **C**. WT mice treated with the PKC inhibitor GF109203X. **D.** *trpv1*$^{-/-}$ mice. In **B-D**, each line represents a single neuron.




**Supplemental Figure 3. AITC-evoked release of neuropeptides.** Release of CGRP-IR (**A**), GPR-IR (**B**) and NPPB-IR (**C**) from superfused slices of rat spinal cord treated with vehicle or the TRPA1 agonist AITC (100 μM, 60 min). Tissues were preincubated with vehicle or HC-030031 (50 μM). n=4, **P*<0.05.




**Supplemental Figure 4. Antagonism of capsaicin-evoked wiping.** Capsaicin was injected into one cheek of wild-type (WT) mice pretreated with the TRPV1 antagonist AMG-9810 or vehicle. Wiping behavior was recorded for 20 min. n=5 mice, $^{**}P<0.01$.




**Supplemental Figure 5. Hypothesized model for detection and transmission of BA-evoked itch.** ***1.*** Cholestatic liver diseases can induce increased circulating and tissue levels of BAs. ***2.*** BAs activate TGR5 on first order puriceptors. TGR5 couples to Gβγ and PKC, which activate and sensitize TRPA1, leading to influx of extracellular $Ca^{2+}$ ions. Activation of voltage sensitive channels results in central transmission to the dorsal horn of the spinal cord. ***3.*** GRP and NPPB, released within the dorsal horn, excite second order spinal pruriceptors, which transmit pruritogenic signals to higher centers.

**Supplemental References**


1. Amadesi S, Nie J, Vergnolle N, et al. Protease-activated receptor 2 sensitizes the capsaicin receptor transient receptor potential vanilloid receptor 1 to induce hyperalgesia. J Neurosci 2004;24:4300-4312.
2. Kwan KY, Allchorne AJ, Vollrath MA, et al. TRPA1 contributes to cold, mechanical, and chemical nociception but is not essential for hair-cell transduction. Neuron 2006;50:277-289.
3. Thomas C, Gioiello A, Noriega L, et al. TGR5-mediated bile acid sensing controls glucose homeostasis. Cell Metab 2009;10:167-177.
4. Wilson Y, Nag N, Davern P, et al. Visualization of functionally activated circuitry in the brain. Proc Natl Acad Sci USA 2002;99:3252-3257.
5. Bellono NW, Kammel LG, Zimmerman AL, et al. UV light phototransduction activates transient receptor potential A1 ion channels in human melanocytes. Proc Natl Acad Sci USA 2013;110:2383-2388.
6. Grant AD, Cottrell GS, Amadesi S, et al. Protease-activated receptor 2 sensitizes the transient receptor potential vanilloid 4 ion channel to cause mechanical hyperalgesia in mice. J Physiol 2007;578:715-733.
7. Wilson SR, Gerhold KA, Bifolck-Fisher A, et al. TRPA1 is required for histamine-independent, Mas-related G protein-coupled receptor-mediated itch. Nat Neurosci 2011;14:595-602.
8. Poole DP, Godfrey C, Cattaruzza F, et al. Expression and function of the bile acid receptor GpBAR1 (TGR5) in the murine enteric nervous system. Neurogastroenterol Motil 2010;22:814-825, e227-818.
9. Cho HJ, Callaghan B, Bron R, et al. Identification of enteroendocrine cells that express TRPA1 channels in the mouse intestine. Cell Tiss Res 2014;356:77-82.
10. Bron R, Wood RJ, Brock JA, et al. Piezo2 expression in corneal afferent neurons. J Comp Neurol 2014;522:2967-2979.
11. Needham K, Bron R, Hunne B, et al. Identification of subunits of voltage-gated calcium channels and actions of pregabalin on intrinsic primary afferent neurons in the guinea-pig ileum. Neurogastroenterol Motil 2010;22:e301-308.
12. **Alemi F, Kwon E**, Poole DP, et al. The TGR5 receptor mediates bile acid-induced itch and analgesia. J Clin Invest 2013;123:1513-1530.
13. Lieu T, Undem BJ. Neuroplasticity in vagal afferent neurons involved in cough. Pul Pharm Therap 2011;24:276-279.
14. Haerteis S, Krappitz M, Diakov A, et al. Plasmin and chymotrypsin have distinct preferences for channel activating cleavage sites in the gamma subunit of the human epithelial sodium channel. J Gen Physiol 2012;140:375-389.
15. Shimada SG, LaMotte RH. Behavioral differentiation between itch and pain in mouse. Pain 2008;139:681-687.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