# Supplementary Material

# **Drug Repurposing: The Anthelmintics Niclosamide and Nitazoxanide are Potent TMEM16A Antagonists that Fully Bronchodilate Airways**

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Supplementary Data

# **1** Supplementary Methods

# 1.1 Measuring antagonist effects on bronchial smooth muscle cell (BSMC) pro-contractile calcium flux.

Human BSMCs were obtained from Lonza, resuspended, cultured and serum starved for 24 hours as described for the histamine membrane potential assay. Compounds and dilutions were prepared in same manner, except they were serially diluted in Assay Buffer (2 mM CaCl2, 1 mM MgCl2, 4.5 mM KCl, 155 mM NaCl, 5 mM HEPES, 10 mM glucose, pH7.4) to 4X the final concentration. A Calcium Indicator Working Solution (10 ml) was prepared by adding 1ml BD PBX Signal Enhancer (Cat# 51-9006254) and 10  $\mu$ l of BD Calcium Indicator (BD Cat# 850000 resuspended in 100% DMSO) to 9 ml Assay Buffer. Following serum starvation of the BSMCs, culture media was aspirated off and 50 $\mu$ l of Calcium Indicator Working Solution was added to each well of microtiter plate. Twenty-five microliters of the 4X serially diluted compounds were then added and cells were incubated with compounds for 30 minutes at room temperature. Twenty-five microliters of a 4X histamine or methacholine solution (where 1X reflects EC<sub>80</sub>-EC<sub>100</sub> concentration from earlier validation of aliquot of cells from same donor) was then added and fluorescence changes were measured by a FLIPR-Tetra or internal FlashFluor instrument. In some experiments the TMEM16A opener, Eact, was used in place of histamine or methacholine.

# **1.2** Effects of the TMEM16A opener Eact on leukotriene secretion and Muc5AC mucin production from human bronchial epithelial air-liquid interface cultures.

Normal, asthma and COPD human bronchial epithelial (HBE) cells were from Lonza (Walkersville, MD). Cells were grown on 0.4 µM transparent PET transwell membranes insert (BD biosciences, San Diego). S-ALI air-liquid interface media (Lonza) was changed every other day until the cells reached confluence, at which time the apical medium was removed to establish an air liquid interface cultures. The basolateral medium was changed every other day. All experimentation was carried out on day 14-18 after ALI establishment. At this point, mature secretory cells are present in these differentiating cultures and the cells respond with maximal proliferation to IL-13 (10 ng/ml) (Peprotech, Rocky Hill, NJ, USA).

Human ALI cultures from a normal donor were treated with Eact, Eact vehicle and 10 ng/ml IL13 in basolateral medium for 48 hrs. After 48hr, 100 µl of basolateral medium were collected for determining leukotriene B4 and C4 secretion using ELISA kits from Enzo Life Sciences, Inc. and LSBio LifeSpan Biosciences Inc., respectively, and by following manufacture's protocols. There was a n of 3 replicate ALI cultures per condition.

The determine the effects of Eact on mucin secretion, mature human bronchial epithelial ALI cultures established from normal, asthma and COPD patients (2 donors, each) were treated with vehicle or 5  $\mu$ M Eact in basal media for 72 hours. To collect mucus, the apical side of ALI cultures (n = 2 ALIs per donor) was washed two times with 0.5 ml of 10 mM DTT (37°C for 15 min, each) and the washes were combined. Levels of Muc5AC protein in apical washes was then determined using a Muc5AC ELISA kit (Cosmo Bio USA, Carlsbad, CA) and following the manufacture's protocol.

# 2 Supplementary Tables

HTS Campaign Activity	Small molecule hits	Cell line	Assay modality	Test cpd. incubation/ stimulation	Hit cut-off	S/B	Avg. RZ/RZ'
Small molecule library of 581,849 compounds							
TMEM16A Primary Screen (n=1, 5μM final)	1,445	HEK293T:eYFP:TM EM16A(abc)	FI eYFP	30 min @ RT / 10mM Iodide, 2μM Ionomycin (final)	POC <72.6%	6.5	0.83 / 0.83
Hit Confirmation (n=3, 5µM final)	673	HEK293T:eYFP:TM EM16A(abc)	FI eYFP	same as above	POC <72.6%	6.5	0.76 / 0.80
Validation to remove compounds showing autofluorescence	491	HEK293T:eYFP:TM EM16A(abc)	FI	30 min @ RT	Baseline FI <10x STDV of neutral control	n.a.	n.a.
(n=1, 5µM final)							
Validate compounds not affecting calcium flux or [Ca <sup>2+</sup> ]i	328	HEK293T	FI Calcium 6	45 min @ RT / 1μM Ionomycin (final)	$IC_{50}\!>\!\!10\mu M$	29.5	0.74 / 0.81
(dose-response, 22-step, 1:2 dilution)							
TMEM16A Potency	145	HEK293T:eYFP:TM	FI	30 min @ RT / 10mM	$IC_{50} < 5 \mu M$	6.2	0.76/0.79
(dose response, 22-step, 1:2 dilution)		EM16A(abc)		Iodide, 2µM Ionomycin (final)			
Compound Quality Control	130	n.a.	Mass spec.	n.a.	≥50% purity, correct mass	n.a.	n.a.

#### 2.1 Supplementary Table 1. High-throughput-screening for TMEM16A antagonists and hit triaging.

High-throughput-screening of a small molecule library for TMEM16A antagonists using the halide-sensitive YFP (eYFP) assay was conducted in a fully automated and scheduled setup. The eYFP assay allows identification of TMEM16A inhibitors by measuring TMEM16A-dependent quenching of eYFP fluorescence intensity (FI). Cells were incubated with the test compound before the assay was started by addition of trigger solution containing ionomycin and iodide ions. Ionomycin triggers the  $Ca^{2+}$ -dependent activation of TMEM16A, which allows iodide ions to enter the cell and quench eYFP fluorescence intensity. Assay results were normalized based on the benchmark TMEM16A inhibitor benzbromarone (100% inhibition corresponding to 0% TMEM16A activity) and neutral control (0% inhibition corresponding to 100% TMEM16A activity) and reported as percent-of-control (POC). Hit cut-off is a statistical value that was calculated based on the results of all test wells (see Supplementary Figure 1). Compounds providing >27.4% inhibition corresponding to <72.6% POC TMEM16A activity were called hits. Statistical quality control parameters such RZ-factor and RZ'-factor and signal/background ratio (S/B) were determined throughout the HTS campaign. During primary screening the entire library was tested at a single concentration and yielded 1,445 primary hits. Confirmation screening tested all primary hits again in three independent, consecutive runs and delivered 673 confirmed hits. Auto-fluorescent compounds were eliminated based on the baseline fluorescence intensity recorded prior to addition of trigger solution and resulted in 491 non-fluorescent increase of intracellular calcium concentration. Dose response testing of the remaining hits revealed 145 hits with an IC<sub>50</sub><5 $\mu$ M and finally 130 validated hits, which passed quality control by mass spec analysis. Further details are provided in the materials and methods section.

Gender (Race)	Age (Years)	Cause of Death	Medical History - Respiratory Disease (Duration), Additional Comments	Medications (Respiratory)	Smoking History? (Yrs.; Packs/Day)
Male (C)	11	Accidental	None	None	No
Male (C)	60	Anoxic Event	None	None	No
Male (B)	4	Accidental	Asthma (unknown)	Albuterol	No
Female (H)	19	Anoxia/asthma	Asthma (17.5 yrs.), 2 prior admittances for severe asthma before death	None Specified	No
Male (C)	27	Accidental	Asthma (20 yrs.)	Proventil, Albuterol	No
Male (C)	44	Anoxic Event	COPD (unknown)	Advair, Combivent	Yes (25; 0.5)
Female (C)	48	Anoxic Event	COPD (unknown), diagnosed 6 months before death with emphysema	None Specified	Yes (34; 2-3)
Male (C)	49	Anoxic Event	COPD (unknown)	None Specified	Yes (34; 2-3)

#### 2.2 Supplementary Table 2. Patient Demographics (Cultured Human Bronchial Smooth Muscle Cells Used in RNA-Seq)

Cells were from Lonza Walkersville Inc., Walkersville, MD, USA. Bronchial cells were acquired from deceased donors and isolated from the bottom of the trachea and the bifurcation of the bronchi. Medical history was obtained from hospital records. Smoking refers to cigarettes, unless otherwise specified. Abbreviations are as follows: C, Caucasian; B, African-American; H, Hispanic. The RNA-Seq dataset containing primary human airway smooth muscle cells and bronchial epithelial cells has been described earlier (Aisenberg et al. 2016).

Gender Age Cause		Cause	Medical History - Respiratory	Medications	Smoking History?
(Race)	(Years)	of Death	Disease (Duration), Additional Comments	(Respiratory)	(Yrs.; Packs/Day)
Male (C)	11	Accidental	None	None	No
Female (B)	17	Anoxic Event	None	None	No
Male (C)	32	Drug Overdose	None	None	No
Male (C)	39	Drug Overdose	None	None	Yes (occasional)
Male (C)	46	Anoxic Event	None	None	Yes (30; 2)
Male (C)	47	Anoxic Event	None	None	Yes (30; 3 cigars/d)
Male (B)	54	Anoxic Event	None	None	Yes (30; 1)
Female (H)	19	Anoxia, Asthma	Asthma (17.5 yrs.), 2 prior admittances for severe asthma attacks prior to death	None Specified	No
Male (C)	52	Anoxic Event	Asthma (diagnosed as child), bronchitis x 3 months prior to death	Albuterol, Advair, Singulair, Prednisone, Decadron	No
Male (H)	57	Anoxia, Asthma	Asthma (unknown), admitted 1 day prior to death for asthmatic event	Inhaler, Prednisone, Albuterol	Yes (?, 1-2 cigs/d)
Female (B)	63	Anoxia, Asthma	Asthma (30+ yrs.)	Daily inhaled steroid	No
Male (C)	67	Anoxic Event	Asthma (10 yrs.)	None Specified	No
Male (C)	40	Drug Overdose	COPD (unknown)	None Specified	Yes (25, 1)
Male (C)	55	Drug Overdose	COPD (unknown)	None Specified	Yes (40, 1-2)
Female (C)	72	Anoxic Event	COPD (20 yrs.)	Prednisone	Yes (56, 2)

#### 2.3 Supplementary Table 3. Patient Demographics (Cultured Human Bronchial Epithelial Cells Used in RNA-Seq)

Cells were from Lonza Walkersville Inc., Walkersville, MD, USA. Bronchial cells were acquired from deceased donors and isolated from the bottom of the trachea and the bifurcation of the bronchi. Medical history was obtained from hospital records. Smoking refers to cigarettes, unless otherwise specified. Abbreviations are as follows: C, Caucasian; B, African-American; H, Hispanic; cigs, cigarettes. The RNA-Seq dataset containing primary human airway smooth muscle cells and bronchial epithelial cells has been described earlier (Aisenberg et al. 2016).

Gender (Race)	Age (Years)	Cause of Death	Medical History - Respiratory Disease (Duration), Additional Comments	Medications (Respiratory)	Smoking History? (Yrs.; Packs/Day)
Male (C)	64	Accidental	None	None	Yes (unknown)
Female (H)	40	Anoxic Event – CV Stroke	None	None	No
Male (C)	56	Unspecified	COPD (unknown), hospitalized one month prior to death for emphysema	None Specified	Yes (25; 1)
Male (B)	52	Unspecified	COPD (unknown)	None Specified	Yes (12; 1)
Female (B)	52	Anoxic Event	COPD (unknown)	Inhaler	Yes (25; 1)

# 2.4 Supplementary Table 4. Patient Demographics (Human Bronchial Epithelial Cells Used in ALI Cultures and RNA-Seq)

Cells were from Lonza Walkersville Inc., Walkersville, MD, USA. Bronchial cells were acquired from deceased donors and isolated from the bottom of the trachea and the bifurcation of the bronchi. Medical history was obtained from hospital records. Smoking refers to cigarettes, unless otherwise specified. Abbreviations are as follows: C, Caucasian; B, African-American; H, Hispanic. The RNA-Seq dataset containing primary human airway smooth muscle cells and bronchial epithelial cells has been described earlier (Aisenberg et al. 2016).

**3** Supplementary Figures

# 3.1 Supplementary Figure 1



A RZ'-factor and signal distribution per plate over entire HTS campaign

# B

Average HTS quality control metrics

Avg	S/B	Z' Factor	RZ' Factor	Z Factor	RZ Factor
HTS	6.5	0.76	0.83	0.74	0.83

**Supplementary Figure 1. Signal distribution and quality control metrics of the TMEM16A HTS campaign.** Data analysis of the entire HTS campaign was performed using Genedata Screener. (A) RZ'-factor and signal distribution per plate over entire HTS campaign. RZ'-factor was calculated per plate and is plotted per plate over the entire HTS campaign (top panel). Average RZ' was 0.83 and RZ' threshold was set at 0.5. Normalization of library compound activities was based on neutral control (0% inhibition) and on TMEM16A inhibitor control Benzbromarone (-100% inhibition) are are plotted as percent-of-control (POC)(bottom panel). Unbiased hit threshold is given as HALO (Hit Assessment and Lead Optimization) cut-off, which was calculated as Median+3xIQR+20% of all test wells. (B) Average HTS quality control metrics. Statistical quality control parameters such Z-factor, Z'-factor, RZ'-factor and signal/background ratio (S/B) were determined throughout the HTS campaign and are summarized as average values.

# 3.2 Supplementary Figure 2



Supplementary Figure 2. Composite dose-response data of compound impact in blocking ionomycin-induced TMEM16A (abc) eYFP quenching, where iodide was used as the permeant anion. Shown are the results of separate experiments run on differing days. Benzbromarone (A) and CaCCinh-A01 (B) fully blocked the iodide eYFP response, with  $IC_{50}$  ( $\mu$ M) of  $1.5081 \pm .504$  (n=58) and  $8.125 \pm 2.72$  (n=58), while niclosamide (C), Cpds 2-5 (D-G) and the benchmark TMEM16A antagonist 1PBC (H) showed potent but partial block of the ionomycin-induced eYFP response with  $IC_{50}$  ( $\mu$ M) values of  $0.13208 \pm 0.0671$  (n=42),  $0.19643 \pm 0.105$  (n=3),  $0.184 \pm 0.0891$  (n=4),  $0.95369 \pm 0.648$  (n=54),  $0.36967 \pm 0.131$  (n=42) and  $1.5233 \pm 1.36$  (n=17), respectively. Activity (%) is the same as Percent of Control (POC), where 100% is no block of the ionomycin-induced iodide quenching of the TMEM16A eYFP response, while 0% is full inhibition of the TMEM16A halide sensitive YFP response.

#### 3.3 Supplementary Figure 3



Supplementary Figure 3. Composite dose-response data of compound impact in blocking ionomycin-induced TMEM16A (abc) eYFP quenching, where iodide was used as the permeant anion. Shown are the results of separate experiments run on differing days with maximum concentration being 55.6  $\mu$ M. MONNA (A) and dichlorophen (B) fully blocked the iodide eYFP response, with IC<sub>50</sub> ( $\mu$ M) of 6.2947 ± 1.47 (n=19) and 4.3647 ± 1.21 (n=58), while niflumic acid (C) showed weak activity and IC<sub>50</sub> ( $\mu$ M) of 26.57 ± 11.8 (n=55). The benchmark antagonist NTTP (D), the approved drug nitazoxanide (E) and its metabolic product tizoxanide (F) showed potent, but partial inhibition with IC<sub>50</sub> values ( $\mu$ M) of 2.476 ± 1.236 (n=46), 1.23 (n=1) and 0.398 (n=1), respectively. The benchmark TMEM16A antagonist, T16Ainh-A01 (G), was inactive (IC<sub>50</sub> > 55.6  $\mu$ M, n= 16) in blocking the ionomycin-induced eYFP response. We were also unable to show any significant activity of this compound by QPatch electrophysiology using HEK293/TMEM16A (acd) cells and elevated intracellular calcium (Table 1 and Supplementary Figure 9), while all the other compounds were confirmed active in this ephys assay. The loss of dichlorophen activity at the highest doses is most likely due to poor compound solubility at higher concentrations. Activity (%) is the same as Percent of Control (POC), where 100% is no block of the ionomycin-induced iodide quenching of the TMEM16A eYFP response, while 0% is full inhibition of the TMEM16A halide sensitive YFP response.

#### 3.4 Supplementary Figure 4



Supplementary Figure 4. Distribution of potency of Niclosamide related compounds in the TMEM16A halide-sensitive YFP assay. A total of 304 distinct compounds from the niclosamide and Cpd 4 series had  $IC_{50} < 50 \ \mu\text{M}$  (A), with the 94 most potent compounds provided in (B). An additional 78 compounds aren't displayed as they were considered inactive having an  $IC_{50} > 50 \ \mu\text{M}$ . The compound identification number (root#) is listed on x-axis versus the potency ( $IC_{50}$ ,  $\mu$ M) on y-axis. It should be noted due to the large number of compounds shown, the x-axis only provides a subset of the root identification numbers that are plotted. The location of niclosamide (Cpd 1) (red, open square), Cpd 2 (blue, open triangle), Cpd 3 (84152 label on x-axis), Cpd 4 (brown, open circle) and Cpd 5 (purple, solid square) are shown in the plots.

#### 3.5 Supplementary Figure 5



Supplementary Figure 5. HEK293 / TMEM16A (acd) QPatch electrophysiology assay using 170 nM free  $[Ca^{2+}]_i$ . Representative current/voltage (I/V) traces of Cpd 2, Cpd 3, Nitazoxanide and Tizoxanide are shown in panels A-D, respectively. The voltage protocol involved 20 mV steps from -100 to +100 mV from a holding potential of 0 mV. The currents were voltage-dependent and outward rectifying as expected for TMEM16A recordings in the presence of low intracellular calcium.

#### 3.6 Supplementary Figure 6



**Supplementary Figure 6. Impact of benzbromarone on TMEM16A (acd) calcium-activated chloride currents as measured by QPatch electrophysiology.** Shown is a representative recording of the impact of progressive (5-fold) increases of benzbromarone on the TMEM16A current-voltage response. Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV for each sample addition, which allowed at least 60s incubation time per compound dose in our standard QPatch assay for determining potency (see Materials and Methods). The dots reflect the measured current (nA) after each 20 mV step from -100 to +100 mV. The currents were voltage-dependent in presence of 170 nM free intracellular calcium and benzbromarone inhibited both the outward and inward currents.

#### 3.7 Supplementary Figure 7



Supplementary Figure 7. Impact of CaCCinh-A01 on TMEM16A (acd) calcium-activated chloride currents as measured by QPatch electrophysiology. Shown is a representative recording of the impact of progressive (5-fold) increases of CaCCinh-A01 on the TMEM16A current-voltage response. Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV for each sample addition, which allowed at least 60s incubation time per compound dose in our standard QPatch assay for determining potency (see Materials and Methods). The channel exhibited the expected voltage-dependence with these recordings using 170 nM free intracellular calcium and CaCCinh-A01 inhibited both the outward and inward currents.

#### 3.8 Supplementary Figure 8



**Supplementary Figure 8. Impact of MONNA on TMEM16A (acd) calcium-activated chloride currents as measured by QPatch electrophysiology.** Shown is a representative recording of the impact of progressive (5-fold) increases of MONNA on the TMEM16A current-voltage response. Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV for each sample addition, which allowed at least 60s incubation time per compound dose in our standard QPatch assay for determining potency (see Materials and Methods). The channel exhibited the expected voltage-dependence with these recordings using 170 nM free intracellular calcium and MONNA inhibited both the outward and inward currents.

#### 3.9 Supplementary Figure 9



**Supplementary Figure 9.** Impact of T16Ainh-A01 on TMEM16A (acd) calcium-activated chloride currents as measured by QPatch electrophysiology. Shown is a representative recording of the impact of progressive (5-fold) increases of T16Ainh-A01 on the TMEM16A current-voltage response. Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV for each sample addition, which allowed at least 60s incubation time per compound dose in our standard QPatch assay for determining potency (see Materials and Methods). The channel exhibited the expected voltage-dependence with these recordings using 170 nM free intracellular calcium and the compound T16Ainh-A01 showed only slight effects in blocking the TMEM16A currents.

#### 3.10 Supplementary Figure 10



**Supplementary Figure 10. Impact of niflumic acid on TMEM16A (acd) calcium-activated chloride currents as measured by QPatch electrophysiology.** Shown is a representative recording of the impact of progressive (5-fold) increases of niflumic acid on the TMEM16A current-voltage response. Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV for each sample addition, which allowed at least 60s incubation time per compound dose in our standard QPatch assay for determining potency (see Materials and Methods). The channel exhibited the expected voltage-dependence with these recordings using 170 nM free intracellular calcium. Niflumic acid inhibited the outward current but showed a paradoxical stimulation of inward currents from -60 to -100 mV.

## 3.11 Supplementary Figure 11



**Supplementary Figure 11.** Impact of 1PBC on TMEM16A (acd) calcium-activated chloride currents as measured by QPatch electrophysiology. Shown is a representative recording of the impact of progressive (5-fold) increases of 1PBC on the TMEM16A current-voltage response. Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV for each sample addition, which allowed at least 60s incubation time per compound dose in our standard QPatch assay for determining potency (see Materials and Methods). The channel exhibited the expected voltage-dependence with these recordings using 170 nM free intracellular calcium. 1PBC inhibited the outward current but showed a paradoxical stimulation of inward currents from -60 to -100 mV.

#### 3.12 Supplementary Figure 12



Supplementary Figure 12. Impact of niclosamide on TMEM16A (acd) calcium-activated chloride currents as measured by QPatch electrophysiology. Shown is a representative recording of the impact of progressive (5-fold) increases of niclosamide on the TMEM16A current-voltage response. Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV for each sample addition, which allowed at least 60s incubation time per compound dose in our standard QPatch assay for determining potency (see Materials and Methods). The channel exhibited the expected voltage-dependence with these recordings using 170 nM free intracellular calcium. Niclosamide provided robust inhibition of the outward current but showed a paradoxical stimulation of the inward currents after voltage steps between -60 to -100 mV from a Vhold of 0 mV.

## 3.13 Supplementary Figure 13



Supplementary Figure 13. Effect of longer incubation times of niclosamide (Cpd 1, 1241157) on TMEM16A (acd) calcium-activated chloride currents at differing membrane potentials as measured by whole cell patch clamp electrophysiology. Shown is representative QPatch recordings over time after addition of 1.1  $\mu$ M (A), 3.3  $\mu$ M (B) and 10.0  $\mu$ M (C) of compound. Using a Vhold of 0 mV, niclosamide decreased the outward currents, but caused a paradoxical increase of the inward currents. The kinetics of niclosamide block of the outward current is delayed at lower concentrations indicating the standard QPatch recording time of ~60s per dose of our medium/high-throughput medchem QPatch assay may underestimate this compound's potency (see Suppl. Figure 12 and Materials and Methods).

#### 3.14 Supplementary Figure 14



**Supplementary Figure 14.** Impact of Compound 2 on TMEM16A (acd) calcium-activated chloride currents as measured by QPatch electrophysiology. Shown is a representative recording of the impact of progressive (5-fold) increases of Compound 2 on the TMEM16A current-voltage response. Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV for each sample addition, which allowed at least 60s incubation time per compound dose in our standard QPatch assay for determining potency (see Materials and Methods). The channel exhibited the expected voltage-dependence with these recordings using 170 nM free intracellular calcium. Compound 2 inhibited the outward current but showed a paradoxical stimulation of inward currents.

# 3.15 Supplementary Figure 15



Supplementary Figure 15. Effect of longer incubation times of Compound 2 (Cpd 2, 2717292) on TMEM16A (acd) calciumactivated chloride currents at different membrane potentials as measured by whole cell patch clamp electrophysiology. Shown is representative QPatch recordings over time after addition of 3.0  $\mu$ M Compound 2 using a voltage protocol with a Vhold of 0 mV where membrane potential was changed from -100 to +100 mV in 20 mV steps.

#### 3.16 Supplementary Figure 16



**Supplementary Figure 16.** Impact of Compound 4 on TMEM16A (acd) calcium-activated chloride currents as measured by QPatch electrophysiology. Shown is a representative recording of the impact of progressive (5-fold) increases of Compound 4 on the TMEM16A current-voltage response. Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV for each sample addition, which allowed at least 60s incubation time per compound dose in our standard QPatch assay for determining potency (see Materials and Methods). The channel exhibited the expected voltage-dependence with these recordings using 170 nM free intracellular calcium. Compound 4 showed robust inhibition of the outward currents, with effects observed even at low concentrations of 48-240 nM.

#### 3.17 Supplementary Figure 17



Supplementary Figure 17. Effect of longer incubation times and repeated pulses on Compound 4 (Cpd 4, 87057) block of TMEM16A (acd) calcium-activated chloride currents as measured by whole cell patch clamp electrophysiology. Shown are representative QPatch recordings over time after addition of  $1.1 \mu M$  (A) or  $10 \mu M$  Cpd 4 (B). The red rectangle of panel (A) is the typical time frame allowed for each compound dose in our standard cumulative concentration response protocol, which suggests our standard QPatch protocol for medium-/high-throughput medchem support may not allow sufficient time for some compounds to achieve steady-state block of the channel. The kinetics of Cpd 4 at  $10 \mu M$  reveal a progressive and stable inhibition of the outward current, but transient stimulation of the inward current which resolves over time (B).



#### 3.18 Supplementary Figure 18

**Supplementary Figure 18.** Impact of Compound 3 on TMEM16A (acd) calcium-activated chloride currents as measured by QPatch electrophysiology. Shown is a representative recording of the impact of progressive (5-fold) increases of Compound 3 on the TMEM16A current-voltage response. Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV for each sample addition, which allowed at least 60s incubation time per compound dose in our standard QPatch assay for determining potency (see Materials and Methods). The channel exhibited the expected voltage-dependence with these recordings using 170 nM free intracellular calcium. Compound 3 showed robust inhibition of the outward currents, with effects observed even at the lowest concentrations tested.

#### 3.19 Supplementary Figure 19



Supplementary Figure 19. Impact of NTTP (1289438) on TMEM16A iodide eYFP response and chloride currents. Panel (A) provides the structure of NTTP. Dose response results from the TMEM16A (abc) eYFP HTS assay (B) indicates NTTP provides potent (IC<sub>50</sub> = 2.84  $\mu$ M) but partial block of the ionomycin-induced eYFP quenching using iodide as the permeant anion and NTTP concentrations up to 55.6  $\mu$ M. In contrast, Panel (C) shows in a representative QPatch electrophysiology recording NTTP provides near complete block of the calcium-activated chloride current (IC<sub>50</sub> = 4.69  $\mu$ M; n=4). Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV for each sample addition, which allowed at least 60s incubation time per compound dose in our standard QPatch assay (see Materials and Methods). The channel exhibited the expected voltage-dependence with these recordings using 170 nM free intracellular calcium. NTTP inhibited the outward current but showed a paradoxical stimulation of inward currents from -60 to -100 mV.

#### 3.20 Supplementary Figure 20



Supplementary Figure 20. The approved drug nitazoxanide is a TMEM16A antagonist that is structurally similar to NTTP. The structures of NTTP and nitazoxanide are provided in Panels (A) and (B), respectively. Panel (C) shows representative results from our QPatch electrophysiology studies evaluating nitazoxanide inhibition of the TMEM16A (acd) calcium-activated chloride current in HEK293 cells after applying progressive (5-fold) increases in drug. The average nitazoxanide IC<sub>50</sub> from three separate QPatch recordings was 1.26  $\mu$ M. Shown are three I/V protocols run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV for each sample addition, which allowed at least 60s incubation time per compound dose in our standard QPatch assay for determining potency (see Materials and Methods). The channel exhibited the expected voltage-dependence with these recordings using 170 nM free intracellular calcium. Nitazoxanide showed robust inhibition of the outward currents, with effects observed even at low concentrations of 48-240 nM.

#### 3.21 Supplementary Figure 21



Supplementary Figure 21. Impact of NTTP-related compound, CID# 2806957 on TMEM16A (acd) calcium-activated chloride currents as measured by QPatch electrophysiology. Panel (A) provides the structure of NTTP, while Panel (B) provides the structure of CID# 2806957. A representative recording of progressive (5-fold) increases in concentration of CID# 2806957 on the TMEM16A current-voltage response is shown in Panel (C). This compound provided and average IC<sub>50</sub> of 0.67  $\mu$ M (n=3) for blocking the TMEM16A outward current. Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV for each sample addition, which allowed at least 60s incubation time per compound dose in our standard QPatch assay for determining potency (see Materials and Methods). The channel exhibited the expected voltage-dependence with these recordings using 170 nM free intracellular calcium. CID# 2806957 inhibited the outward current but showed a paradoxical stimulation of inward currents at negative membrane potentials.

#### 3.22 Supplementary Figure 22



Supplementary Figure 22. Impact of the TMEM16A antagonist 1PBC (676538) on endogenous calcium-activated chloride currents from colorectal cancer cell line COLO-205 as measured by QPatch electrophysiology. Shown is raw data from COLO-205 cells measuring the effect of 1PBC on the TMEM16A outward and inward currents. Using cells expressing TMEM16A endogenously, 1PBC caused the same paradoxical inhibition of the outward but stimulation of the inward current as observed earlier using HEK293 cells stably expressing the cloned TMEM16A (acd) variant (see Supplementary Figure 11). Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV per sample addition which allowed at least 60s incubation time at each compound dose (see Materials and Methods section). Using low free intracellular calcium (170 nM), the currents exhibited the expected voltage-dependence of TMEM16A.

#### 3.23 Supplementary Figure 23



Supplementary Figure 23. Impact of the TMEM16A antagonist benzbromarone on endogenous calcium-activated chloride currents from colorectal cancer cell line COLO-205 as measured by QPatch electrophysiology. Shown is raw data from a QPatch recording measuring concentration dependent effects on the TMEM16A current-voltage response. Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV per sample addition which allowed at least 60s incubation time at each compound dose (see Materials and Methods section). Using low free intracellular calcium (170 nM), the currents exhibited the expected voltage-dependence of TMEM16A. Benzbromarone inhibited both the outward and inward currents.





**Supplementary Figure 24**. **QPatch electrophysiology study of impact 1PBC on TMEM16A (abc) splice variant expressed in HEK293 cells.** Shown is raw data from a recording measuring the effect of 1PBC on the TMEM16A (abc) outward and inward currents. Using cells expressing the (abc) splice variant, 1PBC caused the same paradoxical inhibition of the outward but stimulation of inward current as observed earlier with the (acd) variant (see Supplementary Figure 11). Three I/V protocols were run from -100 to +100 mV (20 mV steps) from a Vhold of 0 mV per sample addition which allowed at least 60s incubation time at each compound dose and recordings used a low free intracellular calcium concentration of 170 nM (see Materials and Methods section).

#### 3.25 Supplementary Figure 25



Supplementary Figure 25. Niflumic acid and benzbromarone inhibit the ionomycin-induced inward current at -100 mV from HEK293 cells stably expressing the TMEM16A (abc) splice variant. The inward current over time is shown following the co-addition (time 0) of ionomycin (10  $\mu$ M) with the DMSO vehicle control (A), or various concentration of the antagonists benzbromarone (B) or niflumic acid (C) in perforated patch clamp electrophysiology studies using the IonWorks Barracuda. Benzbromarone (0.1 – 300  $\mu$ M) and niflumic acid (0.01 – 30  $\mu$ M) caused a concentration dependent inhibition of the inward current. The niflumic acid inhibition of the inward currents at -100 mV shown here by perforated patch clamp electrophysiology, contrasts markedly with the paradoxical stimulation shown earlier by QPatch planar whole cell patch clamp studies (see Supplementary Figure 10). Additionally, these perforated patch clamp studies reveal cloned TMEM16A currents in HEK293 cells show the same rapid inactivation described earlier for endogenous calcium-activated chloride currents recorded from tracheal smooth muscle cells following ionomycin or caffeine addition using similar perforated patch clamp electrophysiology methods; see (Wang and Kotlikoff 1997).

#### 3.26 Supplementary Figure 26



Supplementary Figure 26. Niclosamide and Compound 4 do not impact the CFTR chloride current. Panel (A) provides the voltage protocol for IonWorks Barracuda electrophysiology studies using CHO cells stably expressing the human CFTR gene. Red traces (B-D) show the baseline current, while grey traces show the current following addition of the Test Article (TA) or compound. While 10  $\mu$ M of the benchmark inhibitor, CFTRinh-172, fully inhibited the cAMP-activated chloride current (B), there were no significant effects on the CFTR chloride current following addition of 10  $\mu$ M niclosamide (C) or 10  $\mu$ M Compound 4 (D).

#### 3.27 Supplementary Figure 27



Supplementary Figure 27. Selectivity of benchmark TMEM16A antagonists in inhibiting TMEM16A (top panels) versus CFTR (bottom panels) chloride currents. The dose-response results in panels A-C are from QPatch electrophysiology studies using HEK293 / TMEM16A (acd) cells and 170 nM free intracellular calcium, while panels D-F show the results from IonWorks Barracuda studies using CHO / CFTR cells activated with 20 µM forskolin. Data shown are the mean and standard deviation of 6-7 recordings (A-C) or 3-4 recordings (D-F). Of the three TMEM16A antagonists shown, 1PBC appears the most selective in inhibiting TMEM16A vs CFTR.

#### 3.28 Supplementary Figure 28



Supplementary Figure 28. Representative histamine dose-response study in the FLIPR membrane potential assay using cultured primary human airway smooth muscle cells to determine the sensitivity to contractile agents. (A) Histamine induced a dose-dependent increase in fluorescence corresponding to ASM depolarization (Mean  $\pm$  SD, N = 4), a response which was sustained as shown in the representative kinetic traces provided in panel (B) of the fluorescent response following treatment with different concentrations of histamine. Routine experiments with TMEM16A antagonists involved pre-incubation of cells with compound for ~30 minutes and then treatment with an EC<sub>90</sub> concentration of histamine. RFU, relative fluorescence units. AUC, area under curve.

#### 3.29 Supplementary Figure 29



Supplementary Figure 29. The TMEM16A antagonists dichlorophen and benzbromarone fully inhibit the *histamine-induced* depolarization of primary human airway smooth muscle cells (donor 199524), while T16Ainh-A01 shows just partial effects. Panels (B-D) show raw fluorescence data from the membrane potential assay of buffer alone (dashed line), buffer plus 1  $\mu$ M histamine (open circles) and the combination of various concentrations of dichlorophen (B), benzbromarone (C) and T16Ainh-A01 (D) ranging from 0.05 – 100  $\mu$ M with histamine (solid lines, labeled). Panel (A) plots the dose-dependent changes in area under the curve (AUC) for the TMEM16A antagonists. Dichlorophen and benzbromarone fully reversed histamine depolarization and induced some hyperpolarization. RFU = relative fluorescence units.

#### 3.30 Supplementary Figure 30



Supplementary Figure 30. The TMEM16A antagonists dichlorophen and benzbromarone fully inhibit the *methacholine (Mch)-induced* depolarization of primary human airway smooth muscle cells (donor 199524), while T16Ainh-A01 showed little effect. Panels (B-D) show raw fluorescence data from the membrane potential assay of buffer alone (dashed line), buffer plus 20  $\mu$ M methacholine (open circles) and the combination of various concentrations of dichlorophen (B), benzbromarone (C) and T16Ainh-A01 (D) ranging from 0.05 – 100  $\mu$ M with methacholine (solid lines, labeled). Panel (A) plots the dose-dependent changes in area under the curve (AUC) of TMEM16A antagonists. Dichlorophen and benzbromarone fully reversed methacholine depolarization and induced some hyperpolarization. RFU = relative fluorescence units.

# 3.31 Supplementary Figure 31



Supplementary Figure 31. The small molecule TMEM16A activator,  $E_{act}$ , induces depolarization of primary human airway smooth muscle cells like the contractant carbachol. Kinetic traces from the FLIPR membrane potential assay indicate  $E_{act}$  (A) and carbachol (B) elicit a concentration dependent depolarization of human ASM cells which were serum starved for 4 hours [prf SmGM overnight + 4h prf SmBM]. The potency for  $E_{act}$  depolarization of ASM cells isolated from a normal, asthmatic or COPD patient is shown in panel (C). The average EC<sub>50</sub> of  $1 - 3 \mu$ M for depolarizing human ASM cells (C) compares favorably to the 3.0  $\mu$ M EC<sub>50</sub> which Namkung et al. (2011) report for activation of TMEM16A. RFU, relative fluorescence units. AUC, area under the curve.

#### 3.32 Supplementary Figure 32



Supplementary Figure 32. Primary human ASM cells treated with the TMEM16A opener,  $E_{act}$ , and the cholinergic methacholine (Mch) cause similar increases in the level of pro-contractile intracellular calcium (A). The TMEM16A antagonists benzbromarone, CaCCinh-A01 and dichlorophen block both the Mch (B) and  $E_{act}$  (C) ASM calcium flux (CaFlux), while the TMEM16A antagonist T16Ainh-A01 only showed effects in blocking the CaFlux induced by  $E_{act}$ .

# 3.33 Supplementary Figure 33



Supplementary Figure 33. Experimental procedure for determining the EC<sub>75</sub> of carbachol for contraction of mouse tracheal rings and an example of the efficacy of isoproterenol in relaxing carbachol pre-contracted airways. Panels (A) shows raw traces from the wire myograph studies on two tracheal rings showing ascending carbachol (CCh) concentrations (vertical dotted lines) cause progressive increases in force over time (each light blue block corresponds to 1 min). The calculated EC<sub>75</sub> for carbachol are shown in panel (B). After washing tissue and resetting baseline tension, the upper trace of panel (C) shows raw traces upon addition of an EC<sub>75</sub> level of CCh alone (open down arrows), while the lower trace of panel (C) shows force from EC<sub>75</sub> of carbachol followed by level of relaxation following increasing doses (up arrows) of isoproterenol. Carbachol causes sustained contraction over time of the tracheal rings (C) (each light blue block corresponds to 2 min) and isoproterenol induced potent relaxation which is plotted in panel (D).

# 3.34 Supplementary Figure 34



**Supplementary Figure 34**. **Mouse tracheal rings do not fatigue and maintain contraction for several hours.** DMT wire myograph study on six tracheal rings showing force changes over time following addition of an EC<sub>75</sub> concentration of carbachol. The contraction remained stable for the entire three-hour recording period shown.

#### 3.35 Supplementary Figure 35



Supplementary Figure 35. Efficacy of novel TMEM16A antagonists in bronchodilating mouse tracheal rings pre-contracted with carbachol. Compound 111758 is a structurally related analog of Compound 4 (87057), while 3179204 and 598689 are of the niclosamide series, with the former being a closely related analog of Compound 5. The compound 2100101 is a distinct chemotype from niclosamide or the Compound 4 series. The EC<sub>50</sub> of compounds in bronchodilating mouse airway rings is shown in the figure legend. Compounds 111758, 87057, 3179204, 598689, and 2100101 inhibited the TMEM16A halide-sensitive YFP response with an average IC<sub>50</sub> ( $\mu$ M) of 0.091±0.028 (n=3), 0.901±0.524 (n=53), 0.334 (n=1), 0.466±0.101 (n=3), and 3.330 (n=1), respectively.

### 3.36 Supplementary Figure 36



**Supplementary Figure 36**. **NTTP is efficacious in fully bronchodilating mouse tracheal rings.** The compound NTTP [CID: 19646] which only partially inhibited the TMEM16A *iodide* eYFP response but fully inhibited the calcium-activated *chloride* current (see Supplementary Figure 19), in physiological studies with tissue caused full relaxation of carbachol (EC<sub>75</sub>) pre-contracted mouse tracheal rings.

#### 3.37 Supplementary Figure 37



Supplementary Figure 37. TMEM16A antagonists fully relax airways and exhibit sustained action over several hours unlike the  $\beta$ -agonist isoproterenol which exhibited partial and transient bronchodilation. Panel (A) shows niclosamide, benzbromarone and isoproterenol caused dose-dependent relaxation of carbachol pre-contracted mouse tracheal rings. The airways were then washed to remove compounds and re-contracted with carbachol to evaluate if any of the compounds showed sustained effects (B). The isoproterenol efficacy was quickly lost, but niclosamide and benzbromarone provided sustained bronchodilation lasting several hours.

#### 3.38 Supplementary Figure 38



Supplementary Figure 38. Amongst benchmark TMEM16A antagonists, 1PBC is routinely one of the best bronchodilators of human bronchial rings. Cumulative concentration response curves (CCRC) for 1PBC (A), benzbromarone (B) and niflumic acid (C) relaxation of airways pre-contracted with carbachol was measured using a DMT wire myograph, with the potency (EC<sub>50</sub>) of each compound being listed. At the end of each recording and CCRC, theophylline was added to 2.2 mM final to induce maximal relaxation of the bronchial ring, which was considered 100 percent of control (POC) and used for normalization of compound effects. As a precaution, all recordings included 5  $\mu$ M indomethacin in the bath solution to eliminate any possible indirect effect due to prostaglandins.

#### 3.39 Supplementary Figure 39



Supplementary Figure 39. The  $\beta$ -agonist isoproterenol has a quick onset of action but does not fully relax maximally contracted mouse airways. The potency and maximal efficacy of isoproterenol in bronchodilating mouse tracheal rings is progressively reduced with increasing concentrations of carbachol ranging from EC25 to EC95 (A). The average efficacy (B), individual airway dose-response results (C), and raw wire myograph data of force changes over time (D) are shown for relaxation of airway rings pre-contracted with an EC75 concentration of carbachol. The hydrophilic compound isoproterenol (XLogP3 = -3.49) has a quick onset of action, taking just 2 – 4 min to relax the mouse tracheal tissue after applying a 10 nM dose (D).

#### 3.40 Supplementary Figure 40



Supplementary Figure 40. The niclosamide-related compound, Cpd 4, fully relaxes human bronchial rings pre-contracted with histamine, but exhibits a slow onset of action. The relative efficacy of niclosamide and Compound 4 (Cpd 4) compared to the  $\beta$ -agonist salbutamol is shown in panel (A) for relaxation of human 4<sup>th</sup> order bronchi pre-contracted with histamine. The average efficacy (B), individual airway dose-response results (C), and raw wire myograph data of force changes over time (D, E) are shown for the lipophilic molecule Cpd 4 (XLogP3 = 4.63) which exhibits a slow onset of action taking between 50 – 125 min at 10 µM before there is steady-state relaxation of the human bronchial tissue (D, E).

# 3.41 Supplementary Figure 41



**Supplementary Figure 41.** Array Studio visualization of RNA-Seq read coverage to validate expression and assess alternative splicing. Submerged bronchial epithelial cells (RLCP Epithelial Cells) and fully differentiated bronchial epithelial cells (CYTK) from untreated (red; Day5-or Day7-Ctrl) or IL-13 treated (purple; Day5 or Day7) ALI cultures express predominantly the 'abc' splice variant of *TMEM16A* (*ANO1*). In contrast, cultured (RLCP) human airway smooth muscle cells (ocher) and fibroblasts (gray) show a mixture of splice variants, with segments A and C detected in nearly all, but variable expression of segments B and D. Since ASM cells express lower levels of *ANO1* than the bronchial epithelium, it is difficult to decipher the exact variants expressed in ASM cells. The track entitled 'Variable Exon' shows the location of segments B, C and D. The four transcripts (blue) diagrammed at the topic of the image represent the most common permutations of segment B, C, and D inclusion (segment A appears to be almost universally retained). Thick bars denote exon sequences, and thin bars denote UTR sequences, which have been truncated to emphasize coding exon coverage. Intronic regions common to all transcripts are omitted. The individual RNA-Seq coverage tracks show aggregate read coverage for samples from the Amgen Lung dataset (RLCP) described earlier (Aisenberg et al. 2016) and the ALI culture IL-13 dataset (CYTK) described in the Supplementary Methods. The scale on the right side of the track indicates the maximum coverage of any base within the region. This visualization was made using the Array Studio gene browser (Omicsoft, NC).

## **3.42** Supplementary Figure 42



Supplementary Figure 42. The TMEM16A opener  $E_{act}$  induces Muc5AC and leukotriene secretion from human bronchial epithelial (HBE) air-liquid interface (ALI) cultures. Mature (14 day) HBE ALI cultures from normal, asthma or COPD patients (2 donors each, 2 ALI cultures per donor) were treated with vehicle or 5  $\mu$ M Eact in basal medium for 72 hours and then the apical side of ALI cultures were washed with 10mM DTT at 37°C for 15min to collect mucus for MUC5AC ELISA analysis (A). To measure effects on leukotriene secretion, normal HBE ALI cultures were treated with Eact vehicle (control), Eact opener, or 10ng/ml IL13 in basolateral medium for 48 hrs (n = 3 ALI cultures per condition), after which 100  $\mu$ l of basolateral medium was collected and leukotriene B4 and C4 were determined by ELISA (B). Shown is Mean ± SD. Unpaired students *t-test* to evaluate differences from untreated or control, with numeric P values listed or denoted as following: \* P<0.05, \*\* P<0.01, \*\*\*P<0.001, \*\*\*\*P<0.001, ns P>0.05

# 3.43 Supplementary Figure 43

Th1Th1Ch3Ch3Ch3Ch3Ch3Ch3Ch3MethodM	Cell Line	Aliases	Tissue	Cancer	ANO1 FPKM	Cell Line	Aliases	Tissue	Cancer	ANO1 FPKM
MMMMEMDMMEMendamCarringModeMachMode <td>TE11</td> <td>TE-11</td> <td>Esophagus</td> <td>Squamous Cell Carcinoma</td> <td>396.1</td> <td>CL11</td> <td>CL-11</td> <td>Colon</td> <td>Adenocarcinoma</td> <td>42.1</td>	TE11	TE-11	Esophagus	Squamous Cell Carcinoma	396.1	CL11	CL-11	Colon	Adenocarcinoma	42.1
TH.SOP10000TH.T.UnphysicSystems cell circumona10.54BCKRC-SBiederTextems cell circumona10.54VCRASEKCC-SHMargeSystems cell circumona10.54KCSerie SASerie	MDAMB415	MDA-MB-415	Breast	Carcinoma	194.4	SKCO1	SK-CO-1	Colon	Adenocarcinoma	42.0
SCC3SC 25TengelSeparation cell caronameJackTenEnglandSeparation cell caronameJackJackCMC10IndiaAnnore cell caronameIndiaColl IndiaAnnore cell caronameIndiaAnnore cell caronameIndiaCMC000Parce CAD [line cidlAnnore cell caronameIndiaNCISANCISARomanAnnore cell caronameIndiaCMC000Parce CAD [line cidlParce CaronameIndiaNCISANCISANCISANCISANCISAAnnore cell caronameIndiaCMC000Parce CAD [line cidlParce CaronameIndiaNCISA	TT_ESOPHAGUS	T.T T_T	Esophagus	Squamous Cell Carcinoma	162.8	BC3C	BC-3C	Bladder	Transitional Cell Carcinoma	41.5
BHC 2794BHC 2794ImageSegment fail controlment13.44MAINMain<	SCC25	SCC-25	Tongue	Squamous Cell Carcinoma	132.7	TE9	TE-9	Esophagus	Squamous Cell Carcinoma	41.2
VMCL01VMCL01VMCL01VMCL01VMCL01VMCL01VMCL01VMCL02VMCL	EPLC272H	EPLC-272H	Lung	Squamous Cell Carcinoma	130.4	CJM		Skin	Melanoma	40.4
COUDECOUDEColony and Advecaming20.52NUMMonto-MControlGenomeSelf PADVICADEPercessionPercession17.0NUMNUMNum <td>VMCUB1</td> <td>VM-CUB1</td> <td>Bladder</td> <td>Transitional Cell Carcinoma</td> <td>121.4</td> <td>HPAFII</td> <td>HPAF-II</td> <td>Pancreas</td> <td>Pancreatic Ductal Adenocarcinoma</td> <td>40.4</td>	VMCUB1	VM-CUB1	Bladder	Transitional Cell Carcinoma	121.4	HPAFII	HPAF-II	Pancreas	Pancreatic Ductal Adenocarcinoma	40.4
PANCORDPancoRD<	COLO201	COLO 201	Colon	Adenocarcinoma	120.5	HUG1N	HuG1-N	Stomach	Carcinoma	39.7
PATUBASC P	PANC0403	Panc 04.03   Panc 4.03	Pancreas	Adenocarcinoma	117.7	NCIH854	H854 NCI-H854	Lung	Adenocarcinoma	38.1
GP1For partnersEngingenSupartical ClaritorianP0.75MOMELLAPMode Train (March 2000)Restart antonameP3.00SVD10SVD10SVD10CLANSUD10CLANSUD10	PATU8902	PA-TU-8902 PATU8902T	Pancreas	Pancreatic Ductal Adenocarcinoma	113.4	RCM1	RCM-1	Rectum	Adenocarcinoma	38.1
SMALTSMALTColonAdvancementaLongColunColunColunAdvancementaColunAdvancementaColunColunAdvancementaColunColunAdvancementaColun </td <td>OE21</td> <td></td> <td>Esophagus</td> <td>Squamous Cell Carcinoma</td> <td>107.5</td> <td>MDAMB134VI</td> <td>MDA-MB-134 MDA-MB-134-VI</td> <td>Breast</td> <td>Ductal Breast Carcinoma</td> <td>38.0</td>	OE21		Esophagus	Squamous Cell Carcinoma	107.5	MDAMB134VI	MDA-MB-134 MDA-MB-134-VI	Breast	Ductal Breast Carcinoma	38.0
IS32ColonAdencarational Adencarational Adencar	SW1417	SW-1417	Colon	Adenocarcinoma	103.2	OCUM1	OCUM-1	Stomach	Adenocarcinoma	37.9
AbPC1ApPC-1Space should Advance intoma98.8MC 2019The State is an analysis of the	LS123		Colon	Adenocarcinoma	101.6	CAPAN1	Capan-1	Pancreas	Pancreatic Ductal Adenocarcinoma	37.8
IB3257IB 25.7 (alon 2 dataAde natronoma 4 denomer of the start of the star	ASPC1	AsPC-1	Pancreas	Pancreatic Ductal Adenocarcinoma	96.8	HCC1419		Breast	Ductal Breast Carcinoma	35.4
CAPAMECapamote CharlesParcetas	HS255T	Hs 255.T	Colon	Adenocarcinoma	96.1	HCT116	HCT 116 HCT-116	Colon	Carcinoma	35.3
BHYIncome Interal and NeckSysamos Cell Carcinoma98.40159Uncome Triate of the ExagenessAdenocarcinoma98.4NACASNarrobas <td>CAPAN2</td> <td>Capan-2</td> <td>Pancreas</td> <td>Pancreatic Ductal Adenocarcinoma</td> <td>95.8</td> <td>PK1</td> <td>PK-1</td> <td>Pancreas</td> <td>Carcinoma</td> <td>35.3</td>	CAPAN2	Capan-2	Pancreas	Pancreatic Ductal Adenocarcinoma	95.8	PK1	PK-1	Pancreas	Carcinoma	35.3
MACASIJournelOwaryMutational Cytatedinolarionna195.8V038V0-38Merodigitive TractSquamus Cell Carcinoma43.4ARX0813Partorski Lytatedinolarionna84.9SNL00NC-504 U-301 Nucl-50StorandCarcinoma31.6CD00250CD00CD00CD00Adenocarcinoma84.9SNL00NC-504 U-301 Nucl-50Merodistributiona31.6CD00250SNL400SNL400Nucl-50SNL400Nucl-51Merodistributiona31.0SNL50SNL400ColonAdenocarcinoma84.9SNL50Nucl-51IngenetistineAdenocarcinoma31.0SNL50SNL400ColonAdenocarcinoma85.9Nucl-51SNL50Nucl-51IngenetistineAdenocarcinoma30.9SNL52NUL53Nucl-54U-155NU-155IngenetistineCarcinoma30.3SNL52Nucl-54U-155NU-156IngenetistineCarcinoma30.3SNL52NUL53Nucl-54U-155NU-157IngenetistineCarcinoma30.3SNL52Nucl-54U-155NU-156IngenetistineCarcinoma30.3SNL52NUL53Nucl-54U-155NU-157IngenetistineSupamus Cell Carcinoma72.7HUT33HUT-33IngenetistineSupamus Cell Carcinoma22.9CORL2Colu-14IngenetistineSupamus Cell Carcinoma72.1CAL27CAL27CAL27IngenetistineSupamus Cell Carcinoma22.9CORL2Colu-14IngenetistineSupamus Cell Carcinoma62.0PAC-24.00 <td>ВНҮ</td> <td></td> <td>Head and Neck</td> <td>Squamous Cell Carcinoma</td> <td>94.7</td> <td>OE19</td> <td></td> <td>Lower Third of the Esophagus</td> <td>Adenocarcinoma</td> <td>34.8</td>	ВНҮ		Head and Neck	Squamous Cell Carcinoma	94.7	OE19		Lower Third of the Esophagus	Adenocarcinoma	34.8
PANCOBIAPancesia PancesiaPancesia Pancesia Contral Advances and Advances a	MCAS		Ovary	Mucinous Cystadenocarcinoma	89.5	YD38	YD-38	Aerodigestive Tract	Squamous Cell Carcinoma	34.3
COLD.265Colon.265Colon.AdenocarinomaBaskSNUCSSNUCSJarge IntestineAdenocarinomaB1.1INCLSNUBeskCarlonAdenocarinomaB8.0LUSSUnstall Intest CarlonB1.1INCLSNUBeskCarlonBeskCarlonB1.3Data Besk CarlonB1.1INCLSNUSNUCSSNUCSTensitivit of the ExplaysSamons Cell CarlonB1.3SNUSSANarcessCarlonanceB3.3SCC.5SC.15BeskCarlonanceB2.3SNUSSANarcessCarlonanceB7.0SNUCSNU SAL75[SNU-175]Large IntestineGarlonanceB2.5SNUSSANarcessCarlonance75.7SC.15SC.15Data Besk Carlonana29.5STATel-4BaderCarlonance72.1SS.00SI.00Adenocarlonana29.5STAColl-2UngCarlonana72.1SS.00SI.00Adenocarlonana28.0CORL2Coll-2UngGarlonana72.1JD.00RC.15DongSuamous Cell Carlonana28.0SCL4SC-4TogeSuamous Cell Carlonana72.1JD.00RC.15DongSuamous Cell Carlonana28.0SCL4SC-4TogeSuamous Cell Carlonana72.1JD.00Adenocarlonana28.0SUL50SUSSOBaderTossitoria Cell Carlonana72.1JD.00Adenocarlonana28.0SUL50SUSSOSuamous Cell Carlonana72.1JD.00 </td <td>PANC0813</td> <td>Panc 08.13   Panc8.13</td> <td>Pancreas</td> <td>Pancreatic Ductal Adenocarcinoma</td> <td>88.9</td> <td>SN U620</td> <td>NCI-SNU-620 SNU-620</td> <td>Stomach</td> <td>Carcinoma</td> <td>33.6</td>	PANC0813	Panc 08.13   Panc8.13	Pancreas	Pancreatic Ductal Adenocarcinoma	88.9	SN U620	NCI-SNU-620 SNU-620	Stomach	Carcinoma	33.6
IRBR/CAD2RERPLUngMark denocaritomaB830LUGSungLungNon-Small Cell Carinoma31.1SVA80SW-480ColonAdenocaritomaB830G23Exect Third The ExplaseAdenocaritoma30.9SVA80SW-480ColonAdenocaritomaB836G23SC:15TongueSeatAdenocaritoma30.9ND-8015241[SUL-322ParcensCaritomaB836SC:15SC:15TongueSeatScintilitiiSci	COLO205	COLO 205	Colon	Adenocarcinoma	88.1	SNUC5	SNU-C5	Large Intestine	Adenocarcinoma	31.1
HCC1954Junctal BreaktDuckal Breakt CarcinomaMALAMDA.MB172/I MDA.MB-175/WII. RestDuckal Breakt Carcinoma31.0133L3.3ColonAdencoarcinoma645.0CE33Uner Thir of the Space Advanced Carcinoma30.8134L3.3NursesPancreastCarcinoma83.2SCC1.5SC.15Tongue Carcinoma30.8NursesPancreastic Ducfal Adencarcinoma83.2SCL1.5Nc1.5NU-15[SNU-15Large IntestineCarcinoma31.0SNURSNc1.5NU-25[SNU-15Large IntestineCarcinoma73.7ZR7.5RestBreastDuctal Breast Carcinoma29.9SNURSCR1-13BadderSquamous Cell Carcinoma73.7ZR7.6RUP3.3PancreastPancreastPancreast29.9SCC4CSC-4BadderSquamous Cell Carcinoma73.1LARRUP3.8NursestSquamous Cell Carcinoma23.0SCC4SCC4Squamous Cell Carcinoma73.1RUP3.8RUP3.8NursestSquamous Cell Carcinoma27.1BFC095BadderPancreastPancreastPancreastPancreastPancreast27.9SVI930PancreastPancreastPancreastPancreastPancreast27.9SVI930PancreastPancreastPancreastPancreastPancreast27.9SVI930PancreastPancreastPancreastPancreastPancreast27.9SVI930PancreastPancreastPancreastPancreast	RERFLCAD2	RERF-LC-Ad2	Lung	Adenocarcinoma	88.0	LU65		Lung	Non-Small Cell Carcinoma	31.1
SW480SW480ColonAdenotarcinoma#46OE33Lower Third of the EophagyAdenotarcinoma33.913313.3PancesatCarcinoma88.3SCC15SC-15SC-15Inague Carcinoma33.1PATUB885PA TU8885PancesatPancesatCarcinoma78.2SU175K1-SU1-S1SU1-75Large IntestineCarcinoma33.1PATUB805PATUB885PancesatCarcinoma78.2SU175ZVS-1BresstDamots Cell Carcinoma33.1SGATPATUB805PancesatCarcinoma78.1SU50ZUS-1Damots Cell Carcinoma29.0SGATCORL23UngLarge Clarcinoma72.1K150SU50CarcinomaSupanous Cell Carcinoma29.0SCG4SC-4TongueBadderTransicol Cell Carcinoma72.1HOK38HOK38PancesatGancoux Cell Carcinoma28.7SNB99NC-54U-S91SVL99PancesatPancesat Cell Carcinoma72.0PALCPALCDamotsQancoux Cell Carcinoma28.7SNB99NC-54U-S91SVL99PancesatSupanous Cell CarcinomaGAUPALCPALCDamotsAdenocarcinoma28.7SNU390NC-54U-S91SVL197Lage IntestineCarcinomaGAUPALCPALCDamotsCalcinoma28.7SNU390NC-54U-S91SVL197Lage IntestineCarcinomaGAUPALCSVL18U-SVL167Lage Calcinoma28.7SNU390NC-54U-S91SVL197Lage Intestine	HCC1954		Breast	Ductal Breast Carcinoma	85.9	MDAMB175VII	MDA-MB-175 MDA-MB-175-VII	Breast	Ductal Breast Carcinoma	31.0
13313.3PancressCarcinoma83.3SCG1.5SCG1.5SCG1.5TongueSquamos Cell Carcinoma30.3PATU8985PancressPancressPancressCarcinoma78.7ZR73.1Large InterineCarcinoma29.9SNU324N15.40U-37[SNU-12]RestDuctal Iterast Carcinoma29.9ZR75.1BreastPancressPancressPancress29.9S0.7HUF3PancressPancressPancressPancress29.9ZR75.1Large Interst Carcinoma29.5S0.7LungLarge Clarcinoma72.1I.S180Li S180ColonAdenocarcinoma29.5S0.7SCG.50SCG.50PancressPancressPancressSquamos Cell Carcinoma29.5S0.8Staff ColonPancressPancressPancressPancress29.7S0.8PancressPancressPancressPancressPancressPancress29.7S0.9N.S.NU-890 [SNU-899PancressPancressPancressAdenocarcinoma27.8S0.9NU-1995 [SNU-1990PancressPancressPancressAdenocarcinoma27.8S0.9NU-1995 [SNU-1990PancressPancressPancressPancressPancress27.8S0.9NU-1995 [SNU-1995 [SNU-1990PancressPancressPancressPancress27.8S0.9NU-1995 [SNU-1990 PancressPancressPancressPancressPancressPancress27.8S0.9N	SW480	SW-480	Colon	Adenocarcinoma	84.6	OE33		Lower Third of the Esophagus	Adenocarcinoma	30.9
PATUB885PAncesPancreatic Quickl Adenocaritoma83.2SNU75NC/5-NU-35(SNU-75Large IntestineGracinomaC33.3SNU324NC-SNU-324(SNU-324)PancreasPancreasPancreasPancreasQ29.9TE14TE-14EophagusSquamous Cell Carcinoma75.7HUPT3HUP-73PancreasPancreasPancreasPancreasQ29.9CORL3CORL3LungLarge Cell Carcinoma72.3CAL27CAL27TongueSquamous Cell Carcinoma28.9SCC4SC-4Tongue Cell Carcinoma72.3LARL8UR18.8Large NamousSquamous Cell Carcinoma28.9SCC4SC-4Tanstional Cell Carcinoma72.1JHOM2BJHOM2BJHOM2BVaryMonious Adenocarcinoma28.7TSM4TSM4TSM4PancreasPancreasAdenocarcinoma28.7PCA19414(NoRC12)Oral CarvinySquamous Cell Carcinoma63.0PARCSO4Panc Cs.04PancreasAdenocarcinoma28.7SNU350NSV1509PancreasPancreasAdenocarcinoma63.0PARCSO4Panc Cs.04PancreasAdenocarcinoma28.9SNU350NSV1509PancreasPancreasSquamous Cell Carcinoma63.0PARCSO4Panc Cs.04PancreasAdenocarcinoma28.9SNU350NSV1509PancreasPancreasPancreasSquamous Cell Carcinoma53.0HEM3HEM3HEM3HEM3HEM3HEM3HEM3HEM3HEM3HEM3	L33	L3.3	Pancreas	Carcinoma	83.3	SCC15	SCC-15	Tongue	Squamous Cell Carcinoma	30.8
SNU324No.54.PancesCarcinoma78.72875.2875.2875.BreastOutal Breast Carcinoma29.95637TE-14EcolpagusSogumous Cell Carcinoma74.1LS18015.80ColonAenocarcinoma29.95637OCR-12UngLorg Cell Carcinoma72.1LS180LS180ColonAenocarcinoma28.95646SC-4TongueSquamous Cell Carcinoma72.3BICR18BICR18BaynSquamous Cell Carcinoma28.787050BidderTantional Cell Carcinoma72.0PC14PC14UNO-28UngMucinous Adenocarcinoma28.778040NG-5NL-8951NU-899NareascPancesci Ucal Adenocarcinoma72.0PC14PC-14LungMucinous Adenocarcinoma27.9870505BidderTanomaGC1PC14PC-14LungAdenocarcinoma27.9870507VI-5NL-9951NU-1970Large InterstinoGarcinoma62.7PECA-P151PECA-P151TongueSquamous Cell Carcinoma27.88NU1970Nc1-SNL-1951NU-1970Large InterstinoGarcinoma62.7PECA-P151VI-5NLAdenocarcinoma28.7SNU1970Nc1-SNL-1951NU-1970Large InterstinoSquamous Cell Carcinoma58.0HUEN3HUEN3HUEN3UterusAdenocarcinoma28.6SNU1950Nc1-SNL-1951NU-198Large Interstino Carcinoma55.2HT29HT24BrastCalcinoma28.6SNU1950Nc1-SNL-1	PATU8988S	PA-TU-8988S	Pancreas	Pancreatic Ductal Adenocarcinoma	83.2	SNU175	NCI-SNU-175 SNU-175	Large Intestine	Carcinoma	30.3
TE14TE-14ExophagusSquamous Cell Carcinoma75.7HUPT3HUPT3PincreasPancreasPancreatic Duch Aldenocarinoma28.5CORL23CORL23LungLarge Cell Carcinoma7.21CAL27CAL27TongueSquamous Cell Carcinoma28.9CORL3SCC-4TongueSquamous Cell Carcinoma7.21JHOM28BIR38LanynkSquamous Cell Carcinoma28.9BTC050BTC-055BladderTransitional Cell Carcinoma7.21JHOM28DVaryMucinous Adenocarcinoma28.7SNU89NC15NU-299[SNU-390PancreasPancreasi Ducin Aldenocarcinoma7.21JHOM28DVaryMucinous Adenocarcinoma28.7SNU89NC15NU-299[SNU-390Pancreasi Ducin Aldenocarcinoma6.30PANCD504Panc C5.04PancreasiAdenocarcinoma27.8SNU190Pancreasi Ducin Aldenocarcinoma6.14SW1116SW1116[SW-1116ColonAdenocarcinoma28.5SNU190PancreasiPancreasi Ducin Aldenocarcinoma5.66B174B1-44BreastDucin BreastAdenocarcinoma28.5SNU190SNU190PancreasiAdenocarcinoma5.66B174B1-44BreastDucin BreastDucin Breast28.5SNU190NC1-SNU-1905[SNU-190Balay TractCarcinoma5.66B174B1-44BreastDucin Breast28.5SNU190NC1-SNU-1905[SNU-190Adenocarcinoma5.61B174B1-45B1-45B1-45B1-45B1-45	SNU324	NCI-SNU-324 SNU-324	Pancreas	Carcinoma	78.7	ZR751	ZR-75-1	Breast	Ductal Breast Carcinoma	29.9
5637oraceBladerCarcinoma74.1S180S180ColonAdenocarciona230CORL23CORL3LungLung cell Carcinoma7.33CAL27CAL27TongueSquamous cell Carcinoma7.28SCC4SCC4TongueSquamous cell Carcinoma7.21JHOM28HICM.28LarynxSquamous cell Carcinoma7.28T3M4TM4-4PancreasPancreatic Ductal Adenocarcinoma7.20PC14PC14LungNor-Small Cell Carcinoma7.28SUBS9NCI-SNU-S99J SNU-B9Acrodigetive TractSquamous cell Carcinoma6.20PC14Pc14LungNor-Small Cell Carcinoma7.28SUBS9NCI-SNU-S99J SNU-B9Acrodigetive TractSquamous cell Carcinoma6.27PECAPJ24 (clone C12)Colo Andenocarcinoma7.28SNU159NCI-SNU-S99J SNU-197arge InterstineCarcinoma6.27PECAPJ24PLCAPJ34 (clone C12)Colo Adenocarcinoma7.28SNU159NCI-SNU-S19SJ SNU-197arge InterstineCarcinoma6.50N1116 (SNU-116)SW-1116Colon Adenocarcinoma7.26SNU150NCI-SNU-S19SJ SNU-197Bilary TarciaCarcinoma5.27HT29HT2-9Colon Adenocarcinoma7.26SNU150NCI-SNU-S19SJ SNU-197Bilary TarciaCarcinoma5.27HT29Nor-Small Cell Carcinoma7.26SNU150NCI-SNU-S1SJ SNU-198Bilary TarciaCarcinoma5.27HT29Nor-Small Cell Carcinoma7.26SNU150NCI-SNU-S1SJ S	TE14	TE-14	Esophagus	Squamous Cell Carcinoma	75.7	HUPT3	HUP-T3	Pancreas	Pancreatic Ductal Adenocarcinoma	29.5
CORL32CORL33LungLarge cell Carcinoma7.2CAL27CAL27TongueSquamous cell Carcinoma28.9SCG4SCC4TongueSquamous cell Carcinoma7.2JHCM28BICR18BaryntSquamous cell Carcinoma28.8BFTC905BFC905BladderTransitional cell Carcinoma7.2JHCM28JHCM28OvaryMainstal Cell Carcinoma28.5SNU890NC-SNU-899[SNL-899Areodigestive TractSquamous cell Carcinoma7.0PC14PC14LungNon-Small Cell Carcinoma28.5SNU190NC-SNU-199[SNL-899]Areodigestive TractSquamous cell Carcinoma6.27PECAPJ15TongueSquamous cell Carcinoma27.8SNU190NC-SNU-1907[SNL-1907Lage InstitueCarcinoma6.20PECAPJ15PECAPJ15TongueAdenocarcinoma26.9SNU190NC-SNU-1907[SNL-1907PancrestoPancrestoSquamous cell Carcinoma5.0H744BractDerastAdenocarcinoma26.9BICR32NCR3VU-1905[SNL-1196Bilary TractCarcinoma5.2H729H7-29ColonAdenocarcinoma26.7BICR31NCR3VU-1905[SNL-1168Bilary TractSquamous cell Carcinoma5.2H724H724BractDucla Breast Carcinoma26.7BICR32PancrestoSquamous cell Carcinoma5.2H724H724BractDucla Breast Carcinoma26.7BICR31PancrestoSquamous cell Carcinoma5.2H724H724Bra	5637		Bladder	Carcinoma	74.1	LS180	LS 180	Colon	Adenocarcinoma	29.0
SCC4SCC4TongueSquamous Cell Carcinoma7.2.1JRCR3BICR3BICR3LarymxSquamous Cell Carcinoma28.8BTC950BladderTransitional Cell Carcinoma7.2.1JHOM2.8UM-28UanguMucinous Cell Carcinoma28.7T3M4T3M-4PancreasPancreasic Ductal Adenocarinoma7.2.1JHOM2.8UM-28.0UanguMucinous Cell Carcinoma28.7PECAP34CUDNE20PCCAP.314 (clone C12)Oral CavitySquamous Cell Carcinoma63.0PANCG504Pancre50.4PancreasAdenocarcinoma27.8SVM390NCI-SNU-3991/SNU-139Large InterstineCarcinoma61.4SV1116SV1116/SW-1116ConconAdenocarcinoma27.8SVM390NU190/SNU-1990Large InterstineCarcinoma61.4SV1116HUEM3UterusAdenocarcinoma26.9SNU1196Billary TactCarcinoma55.2HT29HT-29ColonAdenocarcinoma26.4SNU1196NL196 [SNU-1196] SNU-1196Billary TactCarcinoma52.7RERFLCAd1RERFLC-Ad1LungAdenocarcinoma26.4SNU1196PancreasPancreasPancreasAdenocarcinoma52.7RERFLCAd1RERFLC-Ad1LungAdenocarcinoma26.4SNU1196SNU1196PancreasPancreasPancreasPancreasSactarcinoma25.7RERFLC-Ad1LungAdenocarcinoma25.4SNU1196PancreasPancreasPancreasPancreasPancreas<	CORL23	COR-L23	Lung	Large Cell Carcinoma	72.3	CAL27	CAL 27	Tongue	Squamous Cell Carcinoma	28.9
BFTC305BFTC305BildderTrasitional Cell Carcinoma7.21JHOM23JHOM236OvaryMuchous Adenocaricinoma28.7TAMATaM4Pancreatic Ouclai Adenocaricinoma7.20PC14PC14LungNon-Sintal Cell Carcinoma7.27SNUB90NI-SNU-S991 SNU-S991Oral GavinySquamous Cell Carcinoma6.27PCACPA151TongueSquamous Cell Carcinoma7.20SNU1907NI-SNU-1097 [SNU-1997Jarge IntestineGarcinoma6.27PKCAP1415ColonAdenocarcinoma7.20SNU1909SNU9909Pancreatic Ouclai Adenocaricinoma5.60JHUEM3JHUEM3-3UterusAdenocarcinoma2.62BICR2NCI-SNU-195 [SNU-196Billairy TractCarcinoma5.62H74BT-474BreastDuclai Breast carcinoma2.62BICR3NCI-SNU-195 [SNU-196Billairy TractCarcinoma5.62H74H74BreastDuclai Breast carcinoma2.62BICR3NCI-SNU-195 [SNU-196Billairy TractCarcinoma5.62H74BT-474BreastDuclai Breast carcinoma2.62BICR3Panceast OpenacoPanceastAdenocarcinoma5.27PK2PC-2PancreastDuclai Breast carcinoma2.62BICR3CarlairePancreast Carcinoma5.27PK8PK-16-CArl 1UngAdenocarcinoma2.52CAL142BreastPancreast Carcinoma5.24PC-14Statt 1.62Statt 1.62Statt 1.62PK50Pancreast Carc	SCC4	SCC-4	Tongue	Squamous Cell Carcinoma	72.3	BICR18	BICR 18	Larynx	Squamous Cell Carcinoma	28.8
TBM4TBM4Pance pance	BFTC905	BFTC-905	Bladder	Transitional Cell Carcinoma	72.1	JHOM2B	JHOM-2B	Ovary	Mucinous Adenocarcinoma	28.7
SNUB99No.1SNU-8999Acrodigestive fractSquamous Cell Carcinoma6.3.0PANC05 APanC 50.4PancresAdencarcinomaC27.9PCCAP312C0122PCACP312C0122PCACP312C0122CarcinomaCarcinomaCAPCACP312C0120SVI105ColonAdencarcinomaZ7.8SNU1970NCI-SNU-1097/SNU-1197Large IntestineCarcinomaCASVI116SVI1116/SVI-116ColonAdencarcinomaZ7.8SNU1900SWI 9900PancreasPancreasic Ductal AdencarcinomaS6.6FT474FT44BreastDuctal Resat CarcinomaZ6.5SNU1190NCI-SNU-1195/SNU-1196Billary TractCarcinomaS5.2HT29HT-29ColonAdencarcinomaZ6.7SNU1900No1-SNU-1195/SNU-1196Billary TractCarcinomaS2.7RFRFLCAD1HTP-29PancreasAdencarcinomaZ6.3PANC0201PancreasPancreasAdencarcinomaS2.7RFRFLCAD1RFR-LC-Ad1LargAdencarcinomaZ5.7PANC0201PancreasPancreasPancreasic Ductal AdencarcinomaS2.0NCH4576BreastLarge AdencarcinomaZ5.7CAL127CAL-148BreastPancreasic Ductal AdencarcinomaS2.0NCH4584H5481NC-H1648Large AdencarcinomaZ5.7PC3PancreasPancreasicQarcinomaS2.0NCH4576NCH5163Large AdencarcinomaZ5.7CAL127CAL-148BreastPancreasic Ductal AdencarcinomaS2.0NCH4575NCH5163	T3M4	T3M-4	Pancreas	Pancreatic Ductal Adenocarcinoma	72.0	PC14	PC-14	Lung	Non-Small Cell Carcinoma	28.5
PECAP.134 CLONEC12     PECAP.134 Clone Cl.21     Oragle awnows Cell Carcinoma     C2.78       SWU1397     NCI-SNU-1097 JNL 1378 Intestinie     Carcinoma     C5.4     SW1136     SW1136     Concol     Adenocarcinoma     Z7.8       SW1990     W1990 JNV-1990     Pancreas     Pancreatic Ductal Adenocarcinoma     S6.0     HPUEM3     Uterus     Adenocarcinoma     Z6.9       SNU196     NCI-SNU-1196 JSNU-1196     Bilary Tract     Carcinoma     S5.2     HP2.4     H7.40     Breast     Ductal Breast Carcinoma     Z6.7       SNU196     NCI-SNU-1196 JSNU-1196     Bilary Tract     Carcinoma     S5.2     HT2.9     H7.40     Pancreas     Adenocarcinoma     Z6.7       BICR31     SICR 31     Ongue     Pancreas     Adenocarcinoma     S5.2     HT2.9     NCI-SNU-164     Adenocarcinoma     Z6.3       PANC0203     Pancreas     Pancreas     Adenocarcinoma     S2.7     RERFLCAFL     Ling MSCI-H164     Ling MSCI	SNU899	NCI-SNU-899 SNU-899	Aerodigestive Tract	Squamous Cell Carcinoma	63.0	PANC0504	Panc 05.04	Pancreas	Adenocarcinoma	27.9
SNU119/NUC1-SNU-109/ISNU-119/Large IntestineCarinomaCari	PECAPJ34CLONEC12	PE/CA-PJ34 (clone C12)	Oral Cavity	Squamous Cell Carcinoma	62.7	PECAPJ15	PE/CA-PJ15	Tongue	Squamous Cell Carcinoma	27.8
SM13901     SM13901     Pancreas     <	SNU1197	NCI-SNU-1097 SNU-1197	Large Intestine	Carcinoma	61.4	SW1116	SW 1116 SW-1116	Colon	Adenocarcinoma	27.8
BicR 2BicR 2IongueSquamous cell carcinoma56.6BitA 4BitA 4BreastDuctal Breast carcinoma26.5SNU1196NCI-SNU-1196 [SNU-1196Billary TractCarcinoma55.7HT-29HT-29ColonAdenocarcinoma26.7BICR31BICR 31TongueSquamous Cell Carcinoma52.7RERFLCAD1HT-29PancreasTubular Adenocarcinoma26.8PANC0203PancreasPancreasAdenocarcinoma52.7RERFLCAD1RERFLCAD1LungAdenocarcinoma25.8CAL148CAL-148BreastDuctal Breast Carcinoma52.0NCH1648HERFLC-AD1LungAdenocarcinoma25.7CAL127CAL127LungNon-Small Cell Carcinoma51.4IM95StomachAdenocarcinoma25.1PCSPancreasPancreasCarcinoma51.4IM95StomachPancreasAdenocarcinoma25.1PCSPC-3PancreasPancreasic Ductal Adenocarcinoma49.1Stw837Stw837Stw837StomachSquamous Cell Carcinoma23.7YAPCPancreasPancreasic Ductal Adenocarcinoma47.4Stw837Stw837Stw837StenaduSquamous Cell Carcinoma23.1YAPCBreastAdenocarcinoma47.4Stu0176Ntl-Stp15Ub-170.6Adenocarcinoma23.1YAPCBreastAdenocarcinoma47.4Stu0176Ntl-Stp15Ub-170.6Adenocarcinoma23.1YAPCBreastAdenocarcinoma47	SW1990	SW 1990   SW-1990	Pancreas	Pancreatic Ductal Adenocarcinoma	58.0	JHUEM3	JHUEM-3	Uterus	Adenocarcinoma	26.9
SNU196NL-SNU-195NU-196Billary TractCardonaS.2H1.29LotonLotonAdenocationa26.7BICR31BICR31TongueSquamous Cell CarcinomaS2.7H1.29N2-2PancreasUublar Adenocarinoma26.3PANC2039Pance30PancreasAdenocarinomaS2.7RERFLCA1RERF-LCA1LungAdenocarinoma26.3HPACPanceasPancreasDuctal Breast CarcinomaS2.0DU4475BreastDuctal Breast Carcinoma25.7CAL124CAL-148BreastDuctal Breast CarcinomaS1.4IM95BreastStomachAdenocarinoma25.7CAL127CAL127LungNon-Small Cell CarcinomaS1.4IM95StomachAdenocarinoma25.1PK59PK-50PancreasPancreasCarcinoma49.1SW837SW-837RectumAdenocarinoma23.7YAPCPancreasPancreasAdenocarinoma47.9KYSE-140KYSE-140EsophagusSquamous Cell Carcinoma23.4YAPCBreastAdenocarinoma47.9KYSE-140KYSE-140LungNon-Small Cell Carcinoma23.4SNU3105NCI-SNU-31[SNU-81]Large IntestineCarcinoma46.6RERFLCK1RERF-LC-K1LungNon-Small Cell Carcinoma23.1DANGDAN-GPancreasMucoepidermid Carcinoma46.6RERFLCK1RERFLC-K1LungAdenocarinoma23.1SNU3105NCI-SNU-31[SNU-81]Jarge Intestine <td>BICR22</td> <td>BICR 22</td> <td>longue</td> <td>Squamous Cell Carcinoma</td> <td>56.6</td> <td>B14/4</td> <td>B1-4/4</td> <td>Breast</td> <td>Ductal Breast Carcinoma</td> <td>26.5</td>	BICR22	BICR 22	longue	Squamous Cell Carcinoma	56.6	B14/4	B1-4/4	Breast	Ductal Breast Carcinoma	26.5
Bick 31Bick 31LongueSquamus Cell Carcinoma54.3KP2KP-2ParceParcesIubular Adenocaricoma26.4PANC0203Panc 203] Panc2.03PancreasAdenocaricoma52.7RERFLCA1RERFLCA41LungAdenocaricoma52.8CAL148CAL-148BreastDuctal Breast Carcinoma52.0NCH1648H1648]NCI-H1648LungAdenocaricoma25.7CAL127CAL127LungNon-Small Cell Carcinoma51.4IM95StomachAdenocaricoma25.7PC3ParceasPancreasCarcinoma49.2CFPAC1CFPAC-1PancreasPancreasic Ductal Adenocaricoma25.1PC3PancreasPancreastCarcinoma49.2CFPAC1CFPAC-1PancreasAdenocaricoma23.7YAPCPancreasPancreastCarcinoma49.1SW837SW-837ReturnAdenocaricoma23.7YAPCPancreastPancreastAdenocarinoma49.1SW837SW-837ReturnAdenocaricoma23.7YAPCPancreastPancreastAdenocarinoma49.1SW837SW-837ReturnAdenocaricoma23.7YAPCPancreastPancreastAdenocarinoma49.1SW1076NCI-SNU-1076] SNU-1076Supanus Cell Carcinoma23.7YAPCPancreastPancreastAdenocarinoma47.4SNU1076NCI-SNU-1076] SNU-1076SkinAdenocarinoma23.7SNU30NCI-SNU-81]SNU-81Large Intestine </td <td>SNU1196</td> <td>NCI-SNU-1196 SNU-1196</td> <td>Biliary Iract</td> <td>Carcinoma</td> <td>55.2</td> <td>H129</td> <td>H1-29</td> <td>Colon</td> <td>Adenocarcinoma</td> <td>26.7</td>	SNU1196	NCI-SNU-1196 SNU-1196	Biliary Iract	Carcinoma	55.2	H129	H1-29	Colon	Adenocarcinoma	26.7
PARCU20sPanc PancesAdenocarinomaS2.7RERF-LCAD1RERF-LCAD1LungAdenocarinoma22.5CAL128CAL-148BreastDuctal Breast CarcinomaS2.2DU4475FreastDuctal Breast Carcinoma25.7CAL127CAL-127LungNon-Small Cell CarcinomaS1.4ILM55FreastDuctal Breast Carcinoma25.7CAL127CAL-127LungNon-Small Cell CarcinomaS1.4ILM55StomachAdenocarinoma25.1PC3PG-3PancreastCarcinoma49.2CFPAC1PancreastPancreastPancreast23.7PC4PC-3Prostate GlandAdenocarinoma49.1SW837SW-837Return Adenocarinoma42.3PC4PancreastPancreastAdenocarinoma49.1SW837SV-837Return StanceSquamous Cell Carcinoma23.3PK1C429PancreastPancreastAdenocarinoma47.4SNU1076NCI-5NU-1076 [SNU-1076Aerodigestive TractSquamous Cell Carcinoma23.3SNU81NCI-SNU-81]SNU-81Large IntestineCarcinoma46.5RERFLCKJRERF-LC-KJLungMelanocarinoma23.1AV53A-6Submantibular GlandMucoepidermid Carcinoma45.9NUGC3NUGC-3StomachAdenocarinoma21.8SNU79NCI-SNU-79[SNU-795StomachAdenocarinoma45.9NUGC3NUGC-3StomachAdenocarinoma21.5ACC238Warantibular GlandMucoepidermid Carcin	BICR31	BICR 31	Iongue	Squamous Cell Carcinoma	54.3	KP2	KP-2	Pancreas	lubular Adenocarcinoma	26.4
HHACPancesPancesPanceta Ductal Adenocarinoma52.2DU44/5BareatDuctal Breast Carcinoma25.8CAL148CAL-148BreastDuctal Breast Carcinoma52.0NCH1648H1648 NCI-H1648LungAdenocarinoma25.4CAL127CAL-127LungNon-Small Cell Carcinoma51.4IM95StomachAdenocarinoma25.4PK59PK-59PancreasCarcinoma49.2CFPAC1CFPAC-1PancreasPancreatic Ductal Adenocarinoma25.1YAPCPancreasPostate GiandAdenocarinoma49.1SW837SW-837RectumAdenocarinoma23.4YAPCPancreasPancreasPancreatic Ductal Adenocarinoma47.9SW1076NCI-SNU-1076 SNU-1076Aerodigestive TractSquamous Cell Carcinoma23.4YAPCPancreasPancreasCarcinoma47.4SNU1076NCI-SNU-1076 SNU-1076Aerodigestive TractSquamous Cell Carcinoma23.4YAPCPancreasCarcinoma47.4SNU1076NCI-SNU-1076 SNU-1076Aerodigestive TractSquamous Cell Carcinoma23.4SNU81NA-6PancreasCarcinoma46.5H5695TH5695TH5695TSkinMoreasAdenocarinoma21.8SNU719NCI-SNU-119/SNU-719StomachMcencarinoma45.9NUGC3NUGC-3StomachAdenocarinoma21.8SNU719NCI-SNU-179/SNU-707StomachMcencarinoma45.9HUCCT1UMUC1BieloutCarcinom	PANCU2U3	Pane 02.03 Pane 2.03	Pancreas	Adenocarcinoma	52.7	RERFLCADI	RERF-LC-Ad1	Lung	Adenocarcinoma	26.3
CAL148CAL-148LargeMeda Nucl-148LungAdenocarcinoma2.2.7CAL127LungNon-Small Cell Carcinoma51.4IM95MC StomachAdenocarcinoma25.4PK59PK-59PancreasCarcinoma49.2CFPAC1CFPAC-1PancreasPancreasPancreatic Ductal Adenocarcinoma25.1PC3PC-3Prostate GiandAdenocarcinoma49.1SW837SW-837RetumAdenocarcinoma23.7YAPCPancreasPancreasPancreatic Ductal Adenocarcinoma47.9KYSE140KYSE140StomachAdenocarcinoma23.3SNU81NCI-SNU-81[SNU-81Large IntestineCarcinoma47.4SNU1076NCI-SNU-1076[SNU-1076Aerodigestive TractSquamous Cell Carcinoma23.3SNU81NCI-SNU-81[SNU-81Large IntestineCarcinoma46.6RER/LCXRER-LC-K1LungNon-Snail Cell Carcinoma23.1ADAGDAN-GPancreasCarcinoma45.9NUGC3NUGC-3StomachAdenocarcinoma23.1ADASA-253Submandibular GlandMucoepidermoid Carcinoma45.9NUGC3NUGC-3StomachAdenocarcinoma21.5NUC2218ParcaBreastDuctal Breast Carcinoma45.9HUCC11HUCC11Bile DuctCarcinoma21.5NUC2218BreastDuctal Breast Carcinoma44.4FE15EsophagusSquamous Cell Carcinoma20.1PANC03271Panc 03.271/Panc3.27PancreasPancr	HPAC		Pancreas	Pancreatic Ductal Adenocarcinoma	52.2	DU4475		Breast	Ductal Breast Carcinoma	25.8
CALL21CAL-121CAL <td>CAL148</td> <td>CAL-148</td> <td>Breast</td> <td>Ductal Breast Carcinoma</td> <td>52.0</td> <td>NCIH1648</td> <td>H1648 NCI-H1648</td> <td>Lung</td> <td>Adenocarcinoma</td> <td>25.7</td>	CAL148	CAL-148	Breast	Ductal Breast Carcinoma	52.0	NCIH1648	H1648 NCI-H1648	Lung	Adenocarcinoma	25.7
PK-59PK-59PAGCesPancreasPancreasPancreasPancreasPancreasPancreatic Ductal Adenocarcinoma49.1SW837SW-837RectumAdenocarcinoma2.3YAPCPancreasPancreasPancreasPancreatic Ductal Adenocarcinoma47.9SW837SW-837RectumAdenocarcinoma23.4HCC128BreastAdenocarcinoma47.4SNU1076NCI-SNU-1076[SNU-1076Acrolugestive TractSquamous Cell Carcinoma23.3DANGDAN-GPancreasCarcinoma46.6RERFLCKJRERFLCKJRedetNon-Small Cell Carcinoma23.3DANGDAN-GPancreasCarcinoma46.5HS695THs 695TSkinAdenocarcinoma22.7A253A-253Submandibular GlandMucepidemoid Carcinoma45.9NUCG.3NUGC-3StamachAdenocarcinoma21.8SNU719NCI-SNU-719[SNU-719StomachCarcinoma45.9NUCC1UMUC1UMUC1Bile DuctCarcinoma20.1UACC893MCC-893BreastDuctal Breast Carcinoma44.5HUCC11HUCC11Bile DuctCarcinoma20.1PANC20327Panco3.27[Panc3.27PancesPanceatic Ductal Adenocarcinoma43.5NUR37NU-407[NU-4077]Large IntestineCarcinoma20.1DV90Dv-90LungAdenocarcinoma43.5SNU407NCI-SNU-407[NU-4077]Large IntestineCarcinoma20.1	CALIZI	CAL-121	Lung	Non-Small Cell Carcinoma	51.4	IIVI95	CED4.C.4	Stomacn	Adenocarcinoma	25.4
PC-3PC-3Prostate GaladAdenocarcinoma49.1SW837SW-837Ref Cum mAdenocarcinoma23.7YAPCPancreasPancreasiPancreasiPancreasiVX5E140KYSE140KSE140Eduna SophagusSquamus Cell Carcinoma23.4HCC1428BreastAdenocarcinoma47.4SVU1076NCI-SNU-1076]SNU-1076Aerodigestive TractSquamus Cell Carcinoma23.3SNU81NCI-SNU-81[SNU-81Large IntestineCarcinoma46.6REFLCXREF-LC-KJLugNon-Snall Cell Carcinoma23.1DANGDAN-GPancreasCarcinoma46.5HS695THS695THS695TSkinAdenocarcinoma21.8A253A-253Submandibular GlandMucoepidermoid Carcinoma45.9NUGC3NUGC-3StomachAdenocarcinoma21.5SNU719NCI-SNU-719[SNU-719StomachCarcinoma45.1UMUC1UM-U-C1BladerCarcinoma21.5VACC893UACC893BreastDuctal Breast Carcinoma44.4FL5HUCCT1HCC11BladerCarcinoma20.1PANC0327Pance3.27PancesPanceasic Ductal Adenocarcinoma43.5NUR237H23/FNU-4077Large IntestineCarcinoma20.1PANC0327Pance3.27PancesPanceasic Ductal Adenocarcinoma43.5SNU407NLC3NU-407[SNU-4077Large IntestineCarcinoma20.0DV90Dv-90LungAdenocarcinoma43.5SNU407NLC3NU-407[SNU-4077 </td <td>PK59</td> <td>PK-59</td> <td>Pancreas</td> <td>Carcinoma</td> <td>49.2</td> <td>CFPACI</td> <td>CFPAC-1</td> <td>Pancreas</td> <td>Pancreatic Ductal Adenocarcinoma</td> <td>25.1</td>	PK59	PK-59	Pancreas	Carcinoma	49.2	CFPACI	CFPAC-1	Pancreas	Pancreatic Ductal Adenocarcinoma	25.1
MACPancreasPancreasPancreasPancreasAdenocarcinoma47.9NTS-140NTS-140ExophagusSquamos Cell carcinoma23.4MCC1428BreastAdenocarcinoma47.4SNU107NCI-SNU-1076[SNU-1076Acordigestive ractSquamos Cell Carcinoma23.3SNU81NCI-SNU-581[SNU-81Large IntestineCarcinoma46.6RERLCKJRER-LC-KJLungNon-Small Cell Carcinoma23.1DANGDA-S3Submandibular GlandMucoepidemoid Carcinoma46.5RERF-LCKJRER-LC-KJLungNon-Small Cell Carcinoma23.1A253A-253Submandibular GlandMucoepidemoid Carcinoma45.9NUGC3NUGC-3StomachAdenocarcinoma21.8SNU719NCI-SNU-719[SNU-719StomachCarcinoma45.9NUGC3NUGC-3StomachAdenocarcinoma21.9VACC893MACC 893BreastDuctal Breast Carcinoma45.9HUCC11UM-UC-1BladerTransitional Cell Carcinoma25.0HCC218BreastDuctal Breast Carcinoma44.4TE15EsophagusSquamos Cell Carcinoma20.1PANC0327Panc 03.27[Panc3.27PancreasPancreaic Ductal Adenocarcinoma43.5NHL9247NL-14247[NCI-H2247Lung Cell Carcinoma20.0DV90Dv-90LungAdenocarcinoma43.5SNU407NL-67.0N-407[SNU-407Large IntestineCarcinoma20.0	PC3	PC-3	Prostate Gland	Adenocarcinoma	49.1	SW837	SW-837	Rectum	Adenocarcinoma	23.7
Incl.420Area <t< td=""><td>TAPC</td><td></td><td>Pancreas</td><td>A de acesso in a ma</td><td>47.9</td><td>KT5E140</td><td>NT3E-140</td><td>Esophagus</td><td>Squamous Cell Carcinoma</td><td>23.4</td></t<>	TAPC		Pancreas	A de acesso in a ma	47.9	KT5E140	NT3E-140	Esophagus	Squamous Cell Carcinoma	23.4
SND81 NLF-SND-81 Large intestine Carcinoma 46.5 RERFLEX RERFLEX Lung Nomail Cell Carcinoma 23.1   DANG DANG Pancreas Carcinoma 46.5 HS695T HS69T SNin Melanotic Nucleanoma 23.2   A253 A-253 Submandibular Gland Mucoepidermoid Carcinoma 45.9 NUGC3 NUGC-3 Stomach Adenocarcinoma 21.8   SNU719 NCI-SNU-719[SNU-719 Stomach Carcinoma 45.1 UMUC1 UM-UC-1 Bidebuc Carcinoma 21.6   VACC893 UACC893 Breast Ductal Breast Carcinoma 44.5 HUCC11 HUCC11 Bide Duct Carcinoma 20.1   PANC0327 Panc 03.27 [Panc3.27 Pancreas Pancreatic Ductal Adenocarcinoma 43.5 NIH2347 H2347[NCI-H2347] Lung entestine Carcinoma 20.1   PAN0327 Panc 03.27 [Panc3.27] Panc easity Ductal Adenocarcinoma 43.5 SNU407 NCI-SNU-407 [SNU-407] Lung entestine Carcinoma 20.0	HUC1428		Breast	Adenocarcinoma	47.4	SNU1076	NCI-SNU-10/6 SNU-10/6	Aerodigestive fract	Squamous Cell Carcinoma	23.3
DarkedDarke	SNU81	NCI-SNU-81 SNU-81	Large Intestine	Carcinoma	46.6	RERFLCKJ	RERF-LC-KJ	Lung	A malanatia Malanama	23.1
Ac2s Ac2s Submanifold and build of and Mode of an interval of a control Acs Notes Notes Stora Stora Action Action Action Action   NU719 NCI-SNU-719 [SNU-719 Stomach Carcinoma 45.1 UMUC1 UMUC1 Bidder Transitional Cell Carcinoma 21.5   UACC893 UACC-893 Breast Ductal Breast Carcinoma 44.5 HUCCT1 HuCCT1 Bile Duct Carcinoma 20.5   HCC218 Breast Ductal Breast Carcinoma 44.4 TE15 Esophagus Squamous Cell Carcinoma 20.1   PANC0327 Panc Cas27 [Panc3.27 Pancreasic Ductal Adenocarcinoma 43.5 SNU407 NCI+SNU-407 Lunge Intestine Carcinoma 20.0   DV90 DV-90 Lung Adenocarcinoma 43.5 SNU407 NCI-SNU-407 [SNU-407 Lunge Intestine Carcinoma 20.0	A252	DAN-G	PallCleas	Carcinoma Museepidermeid Carcineme	40.5	H30951	NUCC 2	Skill	Adependencia	22.7
SND 19 NCF-SND - / 19 SND - / 19 SND - / 19 SND - / 19 SND - / 10 SND - / 19 SND	A200	A-200	Submanulbular Glanu	Mucoepidermola Carcinoma	45.9	INUGCS	NUGC-3	Diaddar	Adenocarcinoma	21.6
Account	110/19	110CC-803	Breast	Ductal Breast Carcinoma	45.1	HUCCT1	Huccr1	Bile Duct	Carcinoma	21.5
PARC03270     Parc03.27   Panc3.27   Panc4     Panceas     Panceatic Ductal Adenocarcinoma     43.5     NCH2347     H2347   NCI-H2347     Lung     Adenocarcinoma     20.1       Dy90     Dy-90     Lung     Adenocarcinoma     43.5     SNU407     NCI-SNU-407   SNU-407     Large Intestine     Carcinoma     20.0	UCC2219	0.000	Broast	Ductal Proact Carcinoma	44.5	TE1E	HUCCII	Ecophague	Squamous Coll Carsinoma	20.3
PANCUG2/ Partus// Par	DAN(C0227	Dana 02 271 Dana2 27	Diedst	Ductar breast carcinoma	44.4	1610	U2247 NCL U2247	Luna	A de se servine me	20.1
DV-50 Long Adenotationina 45.5 Silve407 Inclusion407 Joint-407 Large Incestine Calcinolina 20.0	DV90	DV-90	Lung	Adenocarcinoma	43.5	SNU 407	NCI-SNI L407 SNI L407	Lung	Carcinoma	20.1
HCC1500 Breast Divital Breast Carcinoma 42.1 IS411N Corum Adoparationna 20.0	HCC1500	54.50	Breast	Ductal Breast Carcinoma	43.5	IS/11N	1401-5140-407 [5140-407	Cocum	Adenocarcinoma	20.0

Supplementary Figure 43. *TMEM16A* (*ANO1*) expression in cancer cell lines. The RNA-Seq *ANO1* expression level is reported for cell lines from the Cancer Cell Line Encyclopedia (Barretina et al. 2012), one cell line present in both CCLE and Amgen (HT-29; average FPKM shown) and a single cell lines assayed at Amgen, COLO205. The results for cancer cell lines exhibiting the highest expression (FPKM  $\geq$  20) are shown, and in all cases except HT-29 sample size is one.

#### 3.44 Supplementary Figure 44



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Compound No. (RM#)	TMEM16A eYFP Assay (IC50, μM)	Mook et al. Wnt/β-catenin TopFlash (IC50, μM)	IC50 Ratio, Wnt/TMEM16A
1	0.13	0.34	2.62
2	1.04	11.81	11.36
3	0.20	0.99	5.50
4	2.62	6.42	2.45
6	4.72	7.66	1.62
11	0.13	0.89	6.85
13	0.37	1.30	3.51
14	0.09	1.65	18.33
15	0.33	3.05	9.24
16	0.09	0.42	4.67
18	0.20	0.70	3.50
19	0.09	0.73	8.11
20	3.08	>12	NA
21	0.25	3.84	15.36
22	0.31	4.02	12.97
23	13.4	>12	NA

Supplementary Figure 44. Activity of sixteen niclosamide compounds on TMEM16A versus Wnt/ $\beta$ -catenin. Mook et al. (2015) describe the structure and activity of various niclosamide analogs for inhibition of Wnt/ $\beta$ -catenin transcription using a TopFlash assay. Sixteen of these compounds we have also tested for activity in our halide-sensitive TMEM16A eYFP assay and the activity is compared in the plot provided in panel (A). Pearson's analysis of correlation (n=14) using GraphPad Prism 7.03, provided an r of 0.8046 and P (two-tailed) of 0.0005. The raw IC<sub>50</sub> values from each compound are provided in the table (B), where compound numbering is as provided by Mook et al. (2015), with Compound No. 1 being niclosamide.

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