	Ctrl (DMSO)	Cap 1 µM	Cap 2.5 µM	Cap 5 µM	Cap 10 µM	Cap 15 µM	Cap 20 µM	Cap 25 µM	Cap 30 µM	Cap 40 µM	Cap 50 µM	Cap 100 µM	Cap 300 µM
TER_{ini} ($\Omega.cm^2$)	1512.4 ± 114.6 n = 40	1696.8 ± 222.6 n = 16	2125.2 ± 168 n =12	1313.4 ± 139.1 n = 12	1140.5 ± 109.2 n = 16	2754.7 ± 220.9 n = 8	1556.6 ± 125.7 n = 13	2235.9 ± 164.9 n = 12	916.6 ± 36.0 n = 11	957.4 ± 46.2 n = 7	1091.6 ± 78.2 n = 11	2194.2 ± 272.9 n = 8	1892.8 ± 146.7 n = 8
Isc_{ini} ($\mu A/cm^2$)	0.99 ± 0.11	0.90 ± 0.15	0.63 ± 0.77	1.05 ± 0.17	1.03 ± 0.20	0.59 ± 0.64	0.81 ± 0.05	0.61 ± 0.05	0.64 ± 0.02	0.59 ± 0.03	0.62 ± 0.04	0.55 ± 0.04	0.64 ± 0.02
TER_{30} ($\Omega.cm^2$)	1523.7 ± 90.3^{NS}	1650.1 ± 166.2^{NS}	2117.5 ± 128.5^{NS}	1419.3 ± 156.9^{NS}	1173.7 ± 123.2^{NS}	2502.8 ± 90.5^{NS}	1597.4 ± 139.5^{NS}	2153.6 ± 108.5^{NS}	873.0 ± 34.6^{NS}	860.3 ± 55.6^{*}	1085.4 ± 102.3^{NS}	1926.1 ± 189.3^{NS}	1559.8 ± 167.9^{NS}
Isc_{30} ($\mu A/cm^2$)	1.20 ± 0.12^{***}	1.11 ± 0.20^{*}	0.72 ± 0.06^{*}	1.29 ± 0.24^{*}	1.35 ± 0.29^{**}	0.74 ± 0.07^{***}	0.96 ± 0.07^{**}	0.76 ± 0.05^{***}	0.60 ± 0.15^{NS}	0.73 ± 0.06^{*}	0.70 ± 0.08^{NS}	0.91 ± 0.09^{**}	1.70 ± 0.19^{***}

Table S1: Transepithelial resistance and short-circuit current during basolateral capsaicin exposure.

TER_{ini} and Isc_{in} represent the mean TER and Isc values at the beginning of the experiment and TER_{30} and Isc_{30} after 30 min incubation with vehicle (DMSO, control Ctrl) condition or basolateral capsaicin (Cap). ANOVA analysis showed a difference in the TER_{ini} ($P < 0.001$), Dunnett's post Hoc test

showed a difference between TER_{ini} Ctrl *vs* Cap 2.5 µM (P = 0.019), Ctrl *vs* Cap 15 µM (P < 0.0001), Ctrl *vs* Cap 25 µM (P = 0.003) and Ctrl *vs* Cap 100 µM (P = 0.031). Similarly a difference in Isc_{ini} was found by ANOVA (P = 0.03), Dunnett's Post hoc test showed that none were different from control. After 30 min in presence of capsaicin ANOVA analysis found a significant difference (P < 0.0001, one way ANOVA), Dunnett's Post Hoc test showed that Cap 2.5 µM TER_{30} (P < 0.0003), Cap 15 µM TER_{30} (P < 0.0001), Cap 25 µM TER_{30} (P = 0.001), Cap 30 µM TER_{30} (P = 0.001), Cap 40 µM TER_{30} (P = 0.01) were different from Ctrl. Similarly ANOVA analysis for Isc_{30} shows a significant difference (P = 0.002, one way ANOVA), Dunnett's Post Hoc test showed that none of the Isc_{30} were different from Ctrl. Stars represent paired t-test comparison of TER_{ini} *vs* TER_{30} and Isc_{ini} *vs* Isc_{30}. * P < 0.05, ** P < 0.01 and *** P < 0.001, NS non-significant.

	Ctrl (DMSO)	Cap 1 µM	Cap 2.5 µM	Cap 5 µM	Cap 10 µM	Cap 15 µM	Cap 20 µM	Cap 25 µM	Cap 30 µM	Cap 40 µM	Cap 50 µM	Cap 100 µM	Cap 300 µM
TER_{ini} ($\Omega.cm^2$)	1429.9 ± 122.6 n = 23	1375.9 ± 256.9 n = 11	1774.5 ± 209 n = 12	1420.5 ± 304.1 n = 11	1277.6 ± 218.4 n = 13	1709.7 ± 201.6 n = 12	1529.4 ± 201.0 n = 14	1966.3 ± 196.7 n = 8	1145.7 ± 117.7 n = 10	1022.4 ± 57.4 n = 9	855.5 ± 32.9 n = 10	1194.9 ± 134.6 n = 8	1436.7 ± 289.9 n = 8
Isc_{ini} ($\mu A/cm^2$)	0.75 ± 0.06	0.76 ± 0.05	0.62 ± 0.06	0.81 ± 0.06	0.69 ± 0.04	0.59 ± 0.06	0.90 ± 0.12	0.70 ± 0.06	0.69 ± 0.04	0.71 ± 0.05	0.51 ± 0.07	0.46 ± 0.05	0.62 ± 0.11
TER_{30} ($\Omega.cm^2$)	1393.8 ± 123.9^{NS}	1408.3 ± 268.8^{NS}	1349.7 ± 111.3^{*}	1405.8 ± 303.4^{NS}	1337.2 ± 250.2^{NS}	1428.2 ± 67.1^{NS}	1224.9 ± 96.9^{NS}	1243.0 ± 191.1^{*}	993.4 ± 99.3^{NS}	1053.9 ± 84.0^{NS}	917.9 ± 49.2^{NS}	955.6 ± 98.0^{NS}	898.0 ± 122.4^{NS}
Isc_{30} ($\mu A/cm^2$)	1.15 ± 0.24^{NS}	0.70 ± 0.06^{*}	1.51 ± 0.33^{**}	0.76 ± 0.07^{NS}	0.74 ± 0.06^{NS}	1.37 ± 0.31^{*}	2.04 ± 0.43^{**}	2.31 ± 0.27^{***}	0.95 ± 0.14^{NS}	0.72 ± 0.04^{NS}	0.49 ± 0.06^{NS}	0.83 ± 0.17^{*}	1.44 ± 0.40^{*}

Table S2: Transepithelial resistance and short-circuit current during apical capsaicin exposure.

TER_{ini}, Isc_{in}, TER_{30} and Isc_{30} have the same meaning as the one described in Table S1. ANOVA analysis shows a difference in TER_{ini} and Isc_{ini} ($P = 0.02$, and $P = 0.008$, one way ANOVA), but in each case they were not different from Ctrl as tested by Dunnett's post hoc. After 30 min incubation no

difference was found among the baseline values for TER_{30} (P = 0.18, one way ANOVA), but difference in Isc_{30} (P = < 0.0001, one way ANOVA). Dunnett's Post Hoc test shows that Cap 20 µM and 25 µM were different from Ctrl (P = 0.03 and P = 0.01) respectively. Stars represent paired *t*-test comparison of TER_{ini} *vs* TER_{30} and Isc_{ini} *vs* Isc_{30}.* P < 0.05, ** P < 0.01 and *** P < 0.001, NS non-significant.

	Ctrl	Cap 5 µM	AMG-9810 1 µM	AMG-9810 10 µM
TER_{ini} ($\Omega.cm^2$)	1602.3 ± 55.5 n =12	1621.3 ± 101.6 n =12	1534.8 ± 75.6 n =12	1710.7 ± 128.5 n =12
Isc_{ini} ($\mu A/cm^2$)	0.85 ± 0.03	0.82 ± 0.03	0.77 ± 0.05	0.81 ± 0.04
TER_{30} ($\Omega.cm^2$)	1688.2 ± 119.5^{NS}	1885.7 ± 154.5***	1874.1 ± 154.5**	1887.9 ± 258.8*
Isc_{30} ($\mu A/cm^2$)	1.26 ± 0.05***	1.22 ± 0.05***	1.24 ± 0.04***	1.13 ± 0.4***

Table S3: **Transepithelial resistance and short-circuit current during capsaicin and AMG-9810 exposure.**

TER_{ini}, Isc_{in}, TER_{30} and Isc_{30} have the same meaning as the one described in **Error! Reference source not found.**. No significant difference among the baseline values in TER_{ini} and Isc_{ini} was found P = 0.62 and P = 0.59, one way ANOVA respectively. After 30 min incubation in presence of capsaicin or DMSO, no significant difference in the TER_{30} values (P = 0.7, one way ANOVA) or Isc_{30} values was found (P = 0.2, one way ANOVA). Stars represent paired *t*-test comparison of TER_{ini} *vs* TER_{30} and Isc_{ini} *vs* Isc_{30}. * P < 0.05, ** P < 0.01 and *** P < 0.001, NS non-significant.

	Ctrl	Cap 20 µM	CPZ 10 µM
TER_{ini} ($\Omega.cm^2$)	1102.9 ± 40.9 n =19	1123.6 ± 32.6 n =16	1100.9 ± 41.39 n =19
Isc_{ini} ($\mu A/cm^2$)	1.03 ± 0.22	0.54 ± 0.02	0.81 ± 0.13
TER_{30} ($\Omega.cm^2$)	1098.8 ± 38.12^{NS}	1042.5 ± 38.2^{***}	1102.1 ± 41.5^{NS}
Isc_{30} ($\mu A/cm^2$)	$1.17 \pm 0.25^{*}$	$0.68 \pm 0.03^{***}$	$096 \pm 0.18^{*}$

Table S4: Transepithelial resistance and short-circuit current during capsaicin and capsazepine exposure

TER_{ini}, Isc_{in}, TER_{30} and Isc_{30} have the same meaning as the one described in Table S1. No significant difference in TER_{ini} and Isc_{ini} among the three groups was found P = 0.9 and P = 0.11, one-way ANOVA respectively. After 30 min incubation ANOVA comparison found no difference in the TER_{30} (P = 0.5, one way ANOVA) and Isc_{30} values (P = 0.22, one way ANOVA). Stars represent paired *t*-test comparison of TER_{ini} *vs* TER_{30} and Isc_{ini} *vs* Isc_{30}. * P < 0.05, and *** P < 0.001, NS non-significant.

	Ctrl (DMSO)	OLDA 10 µM	RTX 1 µM
TER_{ini} ($\Omega.cm^2$)	1551.2 ± 77.6 n = 24	1533.6 ± 76.8 n = 24	1664.4 ± 69.6 n = 24
Isc_{ini} ($\mu A/cm^2$)	0.64 ± 0.02	0.59 ± 0.02	0.64 ± 0.03
TER_{30} ($\Omega.cm^2$)	1786.9 ± 86.5***	1879.5 ± 87.4***	1820.3 ± 86.6***
Isc_{30} ($\mu A/cm^2$)	0.73 ± 0.09NS	0.78 ± 0.03***	0.93 ± 0.4***

Table S5: Transepithelial resistance and short-circuit current during capsaicin, *N*-Oleoyldopamine and resiniferatoxin exposure.

TER_{ini}, Isc_{in}, TER_{30} and Isc_{30} have the same meaning as the ones described in Table S1**Error! Reference source not found.**. No significant difference in the TER_{ini} and Isc_{ini} values was found among the groups (P = 0.41 and P = 0.37, one way ANOVA). At the end of the incubation period no difference in the TER_{30} and Isc_{30} was found among the groups (P = 0.74 and P = 0.057, one way ANOVA). Control (Ctrl), *N*-Oleoyldopamine (OLDA), resiniferatoxin (RTX). Stars represent paired *t*-test comparison of TER_{ini} *vs* TER_{30} and Isc_{ini} *vs* Isc_{30}. *** P < 0.001, NS non-significant.