Table 2 EC_{50} values for the hTRPV1 and hTRPA1 activation by Texanol and TXIB.

	hTRPV1		hTRPA1	
□	EC_{50} (μM)	Maximum Activation	EC_{50} (μM)	Maximum Activation
Texanol & TXIB	-	-	-	-
2,2,4-Trimethy-1,3-pentanediol	-	-	-	-
Trimethyl-1,3-pentanediol monoisobutyrate; Texanol	-	-	-	-
2,2,4-trimethyl-1,3-pentanediol diisobutyrate; TXIB	61 (43 - 86)	0.28 (0.24 - 0.33)	-	-

Maximum Activation ; Ratio to positive control

Table 3 EC_{50} values for the hTRPV1 and hTRPA1 activation by naphthoquinones.

	hTRPV1		hTRPA1	
	EC_{50} (μM)	Maximum Activation	EC_{50} (μM)	Maximum Activation
Naphthoquinones				
1,2-Naphthoquinone	15 (13 - 17)	0.40 (0.36 - 0.43)	0.20 (0.17 – 0.23)	1.34 (1.30 – 1.38)
1,4-Naphthoquinone	12 (11 - 13)	0.43 (0.40 - 0.46)	0.31 (0.27 – 0.34)	1.39 (1.33 – 1.42)
9,10-Phenanthrenequinone	-	-	1.8 (1.7 - 1.9)	1.22 (1.19 – 1.25)
Anthraquinone	-	-	-	-

Maximum Activation ; Ratio to positive control

Table 4 EC_{50} values for the hTRPV1 and hTRPA1 activation by microbial volatile organic compounds.

	hTRPV1		hTRPA1	
□	EC_{50} (μM)	Maximum Activation	EC_{50} (μM)	Maximum Activation
Microbial Volatile Organic Compounds; MVOC			-	-
2-Methyl-1-propanol	-	-	-	
2-Methyl-1-butanol	-	-	-	-
3-Methyl-1-butanol	-	-	-	-
3-Methyl-2-butanol	-	-	-	-
1-Pentanol	-	-	-	-
2-Pentanol	-	-	-	-
3-Octanol	-	-	230 (210 - 260)	0.93 (0.89 - 0.98)
1-Octen-3-ol	-	-	260 (240 - 290)	0.82 (0.78 - 0.87)
2-Octen-1-ol	130 (110 - 160)	0.64 (0.59 - 0.68)	230 (200 - 260)	0.85 (0.80 - 0.91)
1-Decanol	25 (17 - 37)	0.65 (0.59 - 0.71)	-	-
2-Methylfuran	-	-	-	-
3-Methylfuran	-	-	-	-
2-*n*-Pentylfuran	-	-	-	-
2-Hexanone	-	-	-	-
2-Heptanone	-	-	-	-
3-Octanone	-	-	-	-
1-Octen-3-one	440 (280 - 680)	1.0 (0.78 - 1.3)	9.7 (8.6 - 11)	0.98 (0.96 - 1.0)

Maximum Activation ; Ratio to positive control

Table 5-1 EC_{50} values for the hTRPV1 and hTRPA1 activation by disinfection by-product.

	hTRPV1		hTRPA1	
	EC_{50} (μM)	Maximum Activation	EC_{50} (μM)	Maximum Activation
Disinfection by-product			-	-
Trihalomethanes				
Chloroform	-	-	-	-
Bromodichloromethane	-	-	-	-
Dibromochloromethane	-	-	-	-
Bromoform	-	-	-	-
Halo-acetonitriles				
Chloroacetonitrile	-	-	-	-
Bromoacetonitrile	-	-	12 (8.7 - 15.6)	1.07 (1.02 - 1.11))
Dichloroacetonitrile	-	-	56 (47 - 67)	1.28 (1.19 - 1.36)
Dibromoacetonitrile	-	-	29 (23 - 35)	1.13 (1.07 - 1.19)
Bromochloroacetonitrile	-	-	50 (41 - 62)	0.87 (0.83 - 0.91)
Trichloroacetonitrile	-	-	179 (147 - 218)	1.00 (0.90 - 1.09)

Table 5-2 EC_{50} values for the hTRPV1 and hTRPA1 activation by disinfection by-product.

	hTRPV1		hTRPA1	
	EC_{50} (μM)	Maximum Activation	EC_{50} (μM)	Maximum Activation
Haloacetic acids			-	-
Chloroacetic acid	-	-	-	-
Bromoacetic acid	-	-	-	-
Dichloroacetic acid	-	-	-	-
Diboromoacetic acid	-	-	-	-
Bromochloroacetic acid	-	-	-	-
Trichloroacetic acid	-	-	-	-
Tribromoacetic acid	-	-	-	-
Haloacetones				
1-Chloro-2-Propanone	-	-	24 (22 - 25)	1.01 (0.99 - 1.04)
1,3-Dichloro-2-propanone	-	-	5.7 (5.1 - 6.3)	0.97 (0.96 - 1.00)
1,1-Dichloro-2-propanone	-	-	486 (453 - 522)	1.14 (1.06 - 1.22)
1,1,3-Trichloro-2-propanone	-	-	108 (99 - 118)	0.99 (0.95 - 1.02))

Maximum Activation ; Ratio to positive control

Table 6-1 The list of compounds assayed in this study. -Glycols/Glycol ethers-

	Compounds	Cas No
Glycols/Glycol ethers		
1	Propylene glycol	57-55-6
2	2-Methoxyethanol	109-86-4
3	2-(2-Methoxyethoxy)ethanol	111-77-3
4	2-[2-(2-Methoxyethoxy)ethoxy]ethanol	112-35-6
5	Polyethylene glycol monomethyl ether	9004-74-4
6	2-Isopropoxyethanol	109-59-1
7	2-Methoxyethyl acetate	110-49-6
8	2-Butoxyethanol	111-76-2
9	2-(2-Butoxyethoxy)ethanol	112-34-5
10	Triethylene glycol monobutyl ether	143-22-6
11	2-Isobutoxyethanol	4439-24-1
12	2-(2-isobutoxyethoxy)ethanol	18912-80-6
13	Ethylene glycol monohexyl ether	112-25-4
14	Diethylene glycol monohexyl ether	112-59-4
15	Ethyleneglycol mono 2-ethylhexylether	1559-35-9
16	Diethyleneglycol mono 2-ethylhexylether	1559-36-0
17	Allyloxyethanol	111-45-5
18	2-Ethoxyethyl acetate	111-15-9
19	2-Phenoxyethanol	122-99-6
20	2-(Benzyloxy)ethanol	622-08-2
21	2-[2-(Benzyloxy)ethoxy]ethanol	2050-25-1
22	1-Methoxy-2-propanol	107-98-2
23	Dipropylene glycol monomethyl ether	34590-94-8
24	Tripropylene glycol monomethyl ether	20324-33-8
25	1-propoxy-2-propanol	1569-01-3
26	Dipropylene glycol propyl ether	29911-27-1
27	1-Butoxy-2-propanol	5131-66-8
28	Dipropylene glycol monobutyl ether	29911-28-2
29	Tripropylene Glycol monobutyl ether	55934-93-5
30	1-Phenoxy-2-propanol	770-35-4

Table 6-2 The list of compounds assayed in this study. -Glycols/Glycol ethers-

	Compounds	Cas No
Glycols/Glycol ethers		
31	1,2-Propanediol 1-monomethyl ether 2-acetate	108-65-6
32	1,2-Dimethoxyethane	110-71-4
33	Bis(2-methoxyethyl)ether	111-96-6
34	1,2-Bis(2-methoxyethoxy)ethane	112-49-2
35	Ethylene glycol diethyl ether	629-14-1
36	Diethylene glycol diethyl ether	112-36-7
37	Bis(2-butoxyethyl)ether	112-73-2
38	Dipropylene glycol dimethyl ether	111109-77-4
39	2-Ethoxyethanol	110-80-5
40	2-(2-Ethoxyethoxy)ethanol	111-90-0
41	1-Ethoxy-2-propanol	1569-02-4
42	2-Propoxyethanol	2807-30-9
43	Diethylen glycol	111-46-6
44	Dipropylen glycol	110-98-5
45	1,3-Butanediol	107-88-0
46	2-Ethyl-1,3-hexanediol	94-96-2
47	2-Butyl-2-ethyl-1,3-propanediol	115-84-4
48	2,4-diethyl-1,5-pentanediol	57987-55-0
49	2-n-Butoxyethyl acetate	112-07-2
50	2-(2-n-Butoxyethoxy)ethyl acetate	124-17-4

Table 7 EC_{50} values for the hTRPV1 and hTRPA1 activation by glycol ethers.

□	hTRPV1		hTRPA1	
	EC_{50} (μM)	Maximum Activation	EC_{50} (μM)	Maximum Activation
Ethylene glycol monohexyl ether	-	-	-	-
Diethylene glycol monohexyl ether	-	-	-	-
Ethylene glycol mono 2-ethylhexyl ether	186 (148-233)	0.2 (0.2-0.2)	193 (172-217)	1.2 (1.1-1.3)
Diethylene glycol mono 2-ethylhexyl ether	63 (49-80)	0.6 (0.6-0.6)	198 (174-225)	1.2 (1.1-1.3)

Maximum Activation ; Ratio to positive control

Table 8-1 EC_{50} values for the hTRPV1 and hTRPA1 activation by aliphatic alcohols.

	hTRPV1		hTRPA1	
	EC_{50} (μM)	Maximum Activation	EC_{50} (μM)	Maximum Activation
1-Hexanol	529 (411-682)	0.4 (0.3-0.5)	-	-
3-Hexanol	-	-	-	-
1-Heptanol	299 (230-388)	0.8 (0.7-0.9)	-	-
3-Heptanol	-	-	-	-
1-Octanol	36 (31-41)	0.8 (0.7-0.8)	172 (133-222)	(1)
3-Octanol	428 (320-573)	0.6 (0.5-0.7)	190 (164-220)	(1)
1-Nonanol	14 (12-15)	0.8 (0.7-0.9)	88 (64-120)	1.0 (0.9-1.1)
3-Nonanol	146 (112-189)	0.5 (0.4-0.6)	81 (50-132)	1.3 (1.0-1.5)
1-Decanol	21 (18-25)	0.8 (0.8-0.9)	-	-
3-Decanol	55 (36-85)	0.5 (0.4-0.5)	66 (54-81)	0.9 (0.8-0.9)
3-Methyl-3-octanol	-	-	197 (169-231)	1.1 (1.0-1.2)

Table 8-2 EC_{50} values for the hTRPV1 and hTRPA1 activation by aliphatic alcohols.

	hTRPV1		hTRPA1	
	EC_{50} (μM)	Maximum Activation	EC_{50} (μM)	Maximum Activation
Tetrahydrolinalool	107 (88-129)	0.4 (0.3-0.4)	102 (93-111)	1.0 (0.9-1.0)
Dihydrolinalool	184 (148-228)	0.4 (0.4-0.5)	256 (221-295)	1.0 (0.9-1.1)
Linalool	342 (279-420)	0.4 0.4-0.5)	401 (362-444)	1.0 (0.9-1.0)
Tetrahydrogeraniol	15 (13-17)	0.7 (0.7-0.7)	71 (31-162)	0.7 (0.5-0.8)
(-)-b-Citronellol	20 (17-23)	0.7 (0.7-0.8)	136 (107-172)	0.9 (0.8-1.0)
Geraniol	34 (29-38)	0.6 (0.5-0.6)	211 (188-237)	0.9 (0.8-0.9)
Nerol	192 (130-285)	0.2 (0.2-0.3)	171 (142-205)	1.0 (0.9-1.1)
2-Ethyl-1-hexanol	468 (320-683)	0.4 (0.3-0.5)	172 (157-189)	1.1 (1.0-1.1)

Maximum Activation ; Ratio to positive control

Table 9 EC_{50} values for the hTRPA1 activation by metal compounds.

	EC_{50} (μM)	Maximum Activation	Hill Slope
$ZnCl_2$	7.7	0.59	2.3
	(6.7 – 8.8)	(0.55 - 0.62)	(1.6 – 2.9)
$CdCl_2$	0.95	0.83	3
	(0.9- 1.1)	(0.80 - 0.85)	(2.3 – 3.7)
$HgCl_2$	9.1	0.88	5.7
	(8.5 – 9.8)	(0.85 - 0.91)	(4.6 – 6.8)
CH_3HgCl	4.4	0.76	2.3
	(4.0 – 4.9)	(0.74 – 0.79)	(1.9 – 2.7)

Maximum Activation ; Ratio to positive control

Table 10 The list of compounds assayed in this study. -Neonicotinoids-

	Compounds	Cas No
Neonicotinoids		
1	Acetamiprid	135410-20-7
2	Clothianidin	210880-92-5
3	Dinotefuran	165252-70-0
4	Imidacloprid	138261-41-3
5	Nitenpyram	150824-47-8
6	Thiacloprid	111988-49-9
7	Thiamethoxam	153719-23-4

Table 11 EC_{50} values for the hTRPA1 activation by phthalate diesters.

□	hTRPA1	
	EC_{50} (μM)	Maximum Activation
Dimethyl phthalate	505 (478-532)	0.85 (0.78-0.92)
Diethyl phthalate	142 (112-181)	0.98 (0.85-1.10)
Di-*n*-propyl phthalate	39 (36-41)	0.97 (0.93-1.00)
Diisopropyl phthalate	48 (43-52)	1.10 (1.05-1.15)
Diallyl phthalate	39 (32-47)	0.98 (0.92-1.05)
Di-*n*-hexyl phthalate	487 (457-518)	0.86 (0.79-0.94)
Diisohexyl phthalate	27 (23-31)	1.03 (0.98-1.08)
Di-*n*-octyl phthalate	-	-

Maximum Activation ; Ratio to positive control

Table 12 EC_{50} values for the hTRPA1 activation by phthalate monoesters.

	hTRPA1	
	EC_{50} (μM)	Maximum Activation
Monobutyl phthalate	315 (289-344)	1.06 (0.99-1.14)
Monoisobutyl phthalate	-	-
Monobenzyl phthalate	419 (361-486)	0.92 (0.83-1.02)
Monohexyl phthalate	6.2 (5.9-6.6)	1.03 (1.00-1.06)
Monoethylhexyl phthalate	0.4 (0.3-0.4)	1.27 (1.22-1.32)
Monooctyl phthalate	0.4 (0.3-0.5)	1.21 (1.15-1.27)
Mono-2-octyl phthalate	2.5 (2.2-2.8)	1.24 (1.18-1.29)

Maximum Activation ; Ratio to positive control

Table 13 EC_{50} values for the hTRPV1 and hTRPA1 activation by Isothiazolinones.

Compounds	EC_{50} [μM] *EC_{50} [%]*	Maximum Activation
hTRPV1		
2-Methyl-4-isothiazolin-3-one (MIT)	-	-
5-Chloro-2-methyl-4-isothiazolin-3-one (CI-MIT)/2-Methyl-4-isothiazolin-3-one (MIT): 3.1	-	-
2-*n*-Octyl-4-isothiazolin-3-one (OIT)	49 (41-57) *1.0E-03*	0.88 (0.83-0.92)
4,5-Dichloro-2-*n*-octyl-4-isothiazolin-3-one (2Cl-OIT)	-	-
1,2-Benzisothizolin-3-one (BIT)	433 (404-464) *6.5E-03*	0.88 (0.82-0.93)
hTRPA1		
2-Methyl-4-isothiazolin-3-one (MIT)	66 (61-72) *7.6E-04*	1.04 (0.99-1.09)
5-Chloro-2-methyl-4-isothiazolin-3-one (CI-MIT)/2-Methyl-4-isothiazolin-3-one (MIT): 3.1	- *8.7.E-05*	0.83 (0.79-0.86)
2-*n*-Octyl-4-isothiazolin-3-one (OIT)	5.7(5.2-6.3) *1..E-04*	1.27 (1.23-1.30)
4,5-Dichloro-2-*n*-octyl-4-isothiazolin-3-one (2Cl-OIT)	2.3 (1.9-2.6) *1.3E-04*	1.05 (1.01-1.09)
1,2-Benzisothizolin-3-one (BIT)	3.4 (3.0-3.8) *5.1E-05*	1.15 (1.10-1.20)

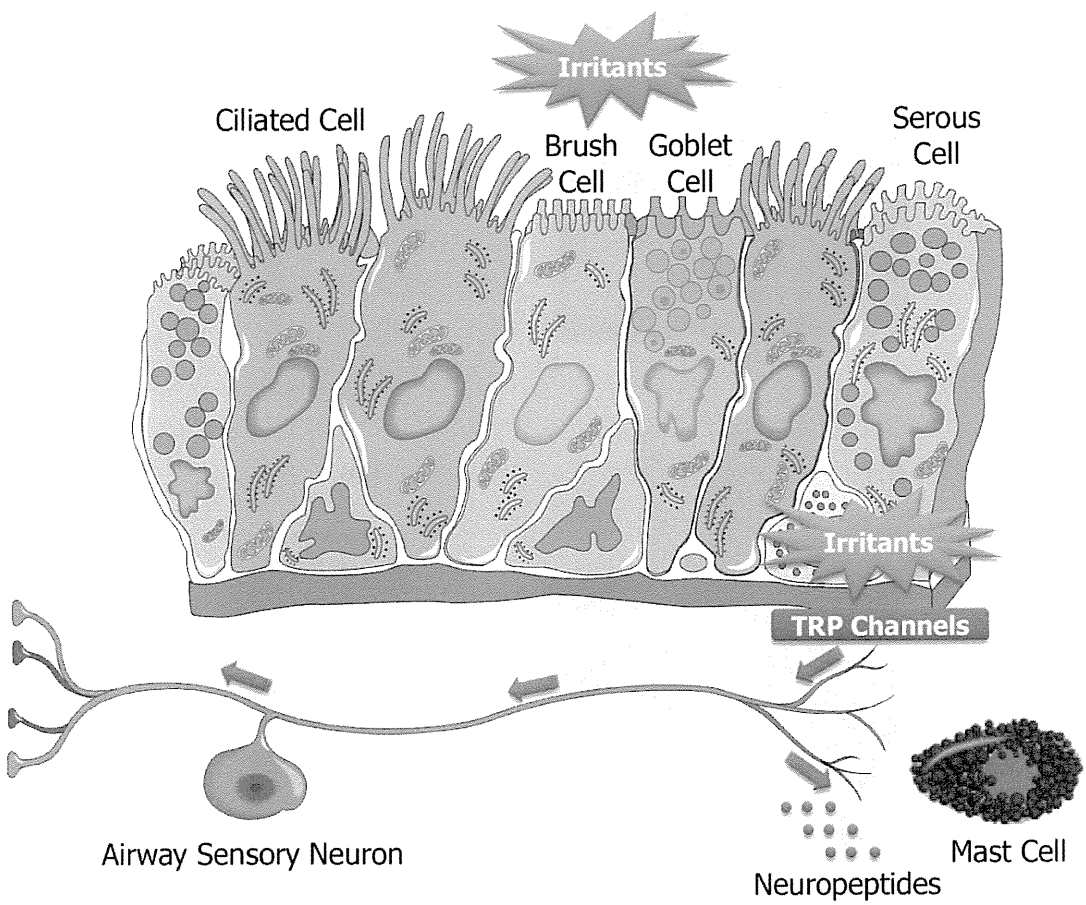


Fig. 1 Schematic presentation of airway hypersensitivity mediated by TRP ion channels.

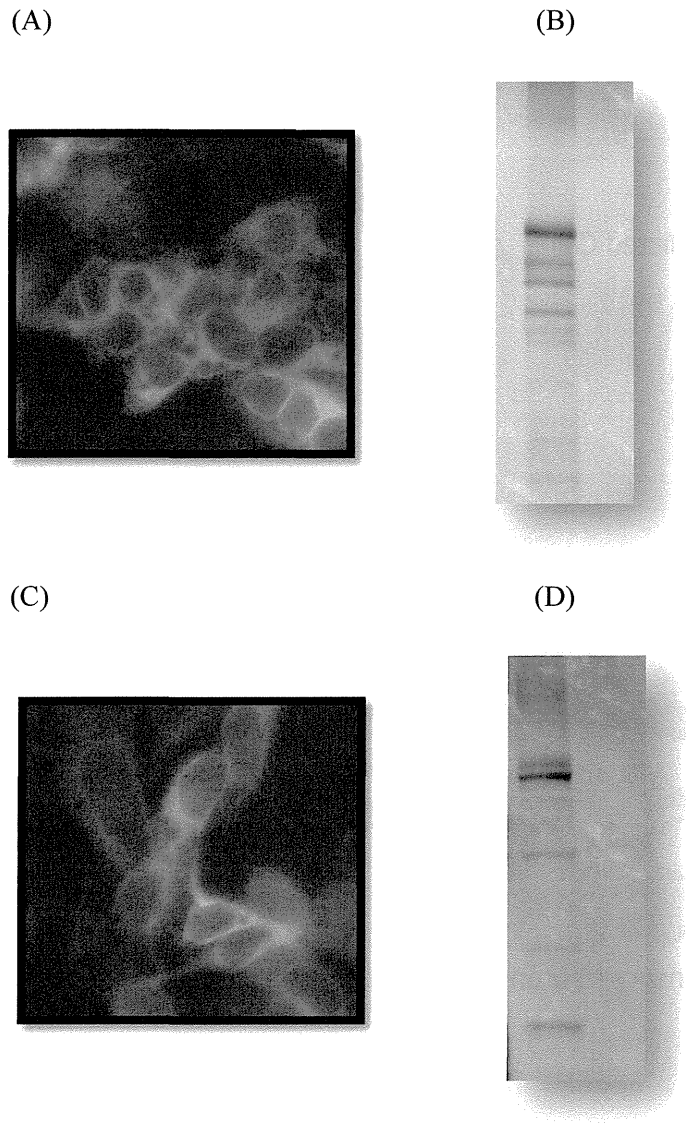


Fig. 2 Transient expression of human TRP ion channels in HEK 293 cells. Detection of ECFP-tagged hTRPV1(A) and hTRPA1 (C) by fluorescent microscopy and V5-tagged hTRPV1(B) and hTRPA1 (D) by Western blotting.

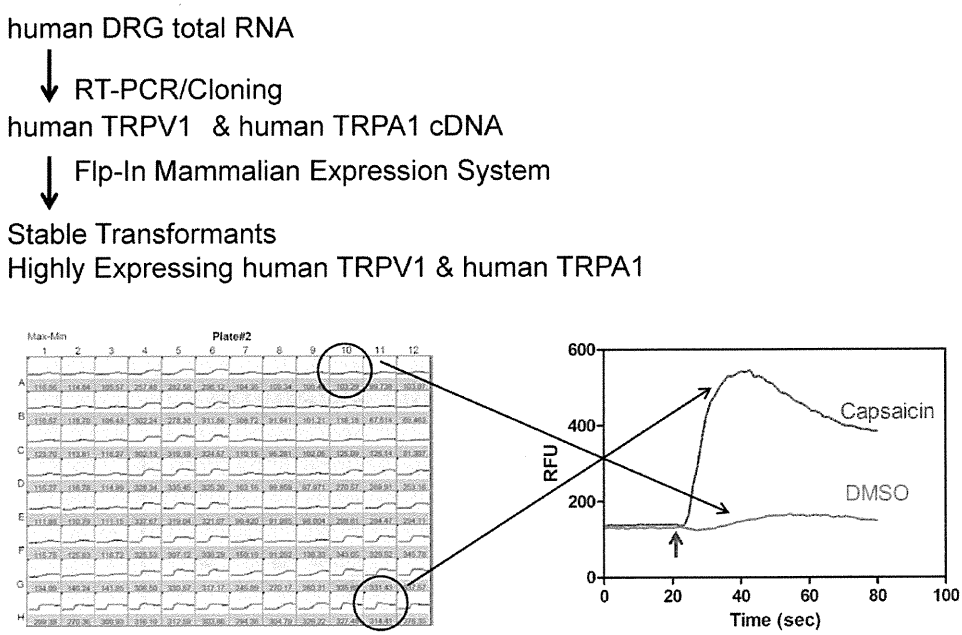


Fig. 3 High-throughput assay for TRP activation.

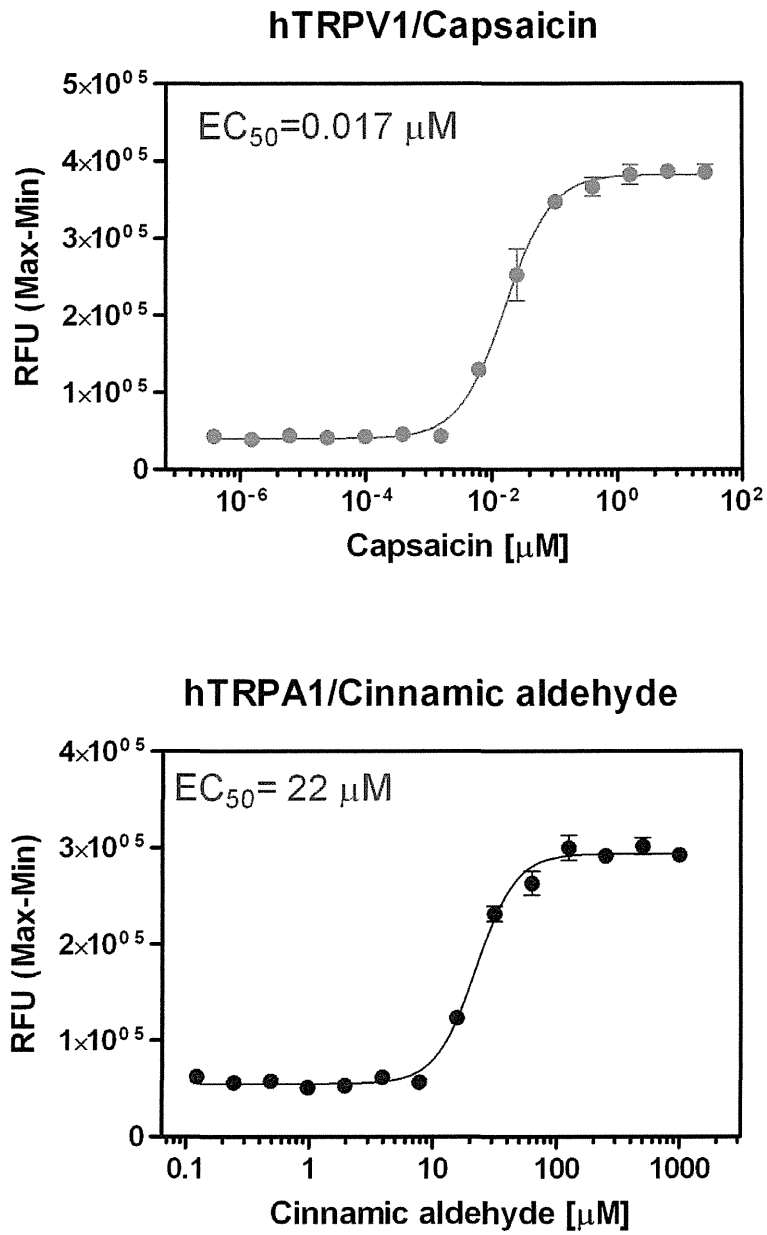
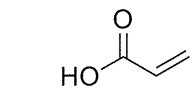
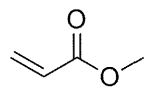


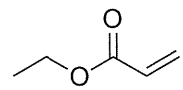
Fig. 4 Dose-response analysis of hTRP ion channels activation by typical agonist.



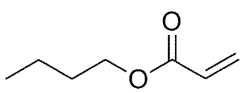
Acrylic acid



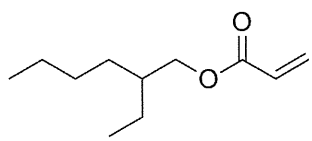
Methyl acrylate



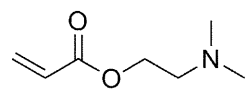
Ethyl acrylate



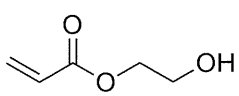
Butyl acrylate



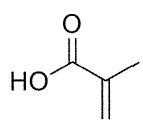
2-Ethylhexyl acrylate



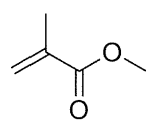
2-(Dimethylamino)ethyl acrylate



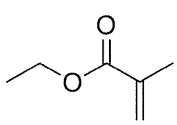
2-Hydroxyethyl acrylate



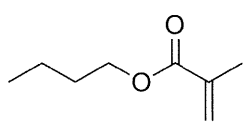
Methacrylic acid



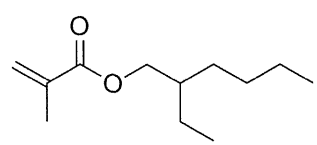
Methyl methacrylate



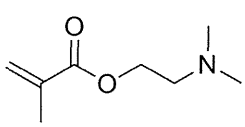
Ethyl methacrylate



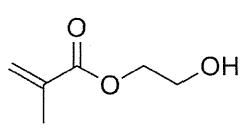
Butyl methacrylate



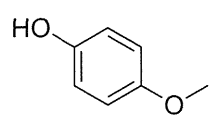
2-Ethylhexyl methacrylate



2-(Dimethylamino)ethyl methacrylate



2-Hydroxyethyl methacrylate



p-Methoxyphenol (Stabilizer)

Fig. 5 Chemical structures of acrylates/methacrylate and its esters assayed in this study..