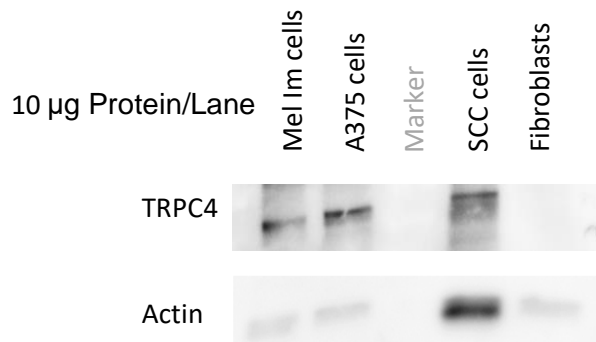
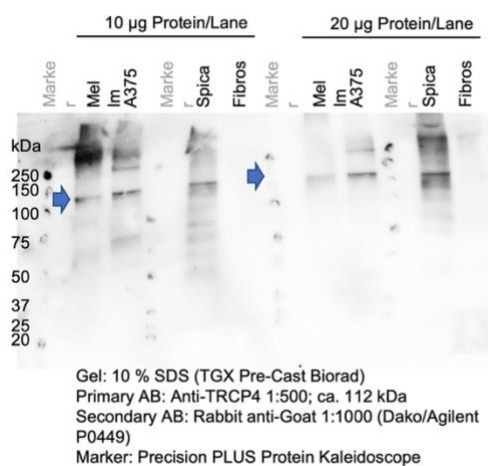


SUPPLEMENTARY INFORMATION

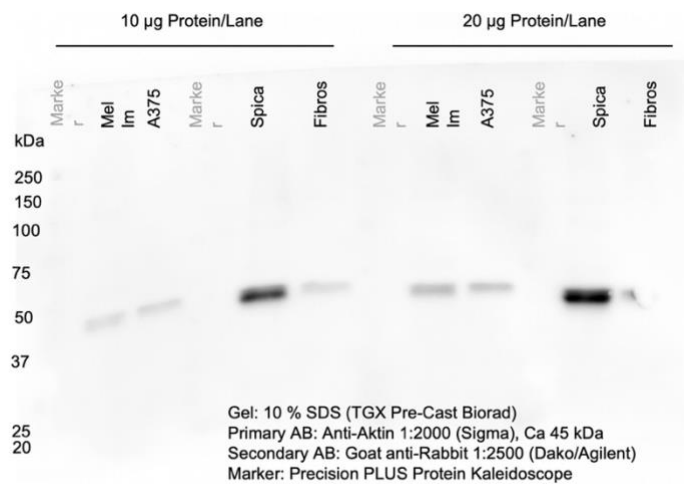
1



2



3



Supplementary Figure S1: Western Blot of TRPC4 antibody.

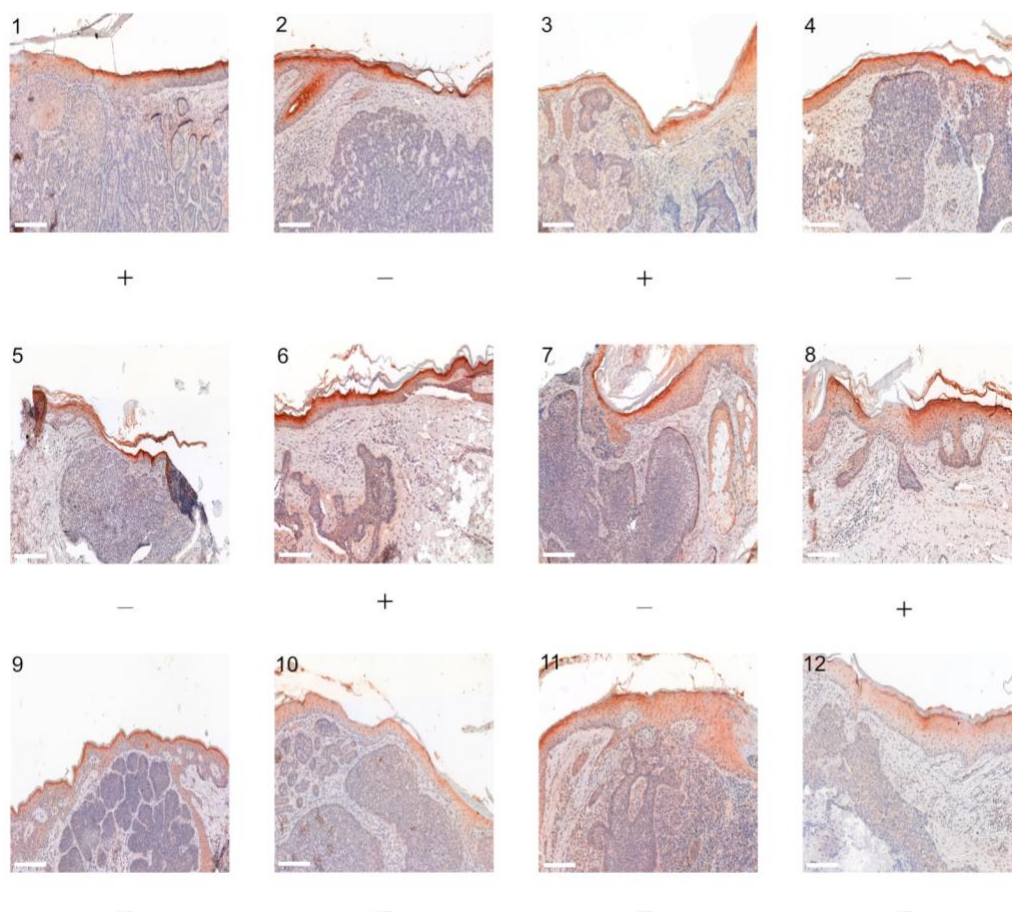
1 Determination of the specificity of the TRPC 4 antibody by western blot at a concentration of 10 µg per lane in Mel Im cells, A 375 cells, cells of squamous cell carcinoma (SCC), fibroblasts, in comparison to the housekeeper actin.

2, 3 Determination of the specificity of the TRPC 4 antibody by western blot at a concentration of 10 µg and 20 per lane in Mel Im cells, A 375 cells, cells of squamous cell carcinoma (SCC), fibroblasts, in comparison to the housekeeper actin.

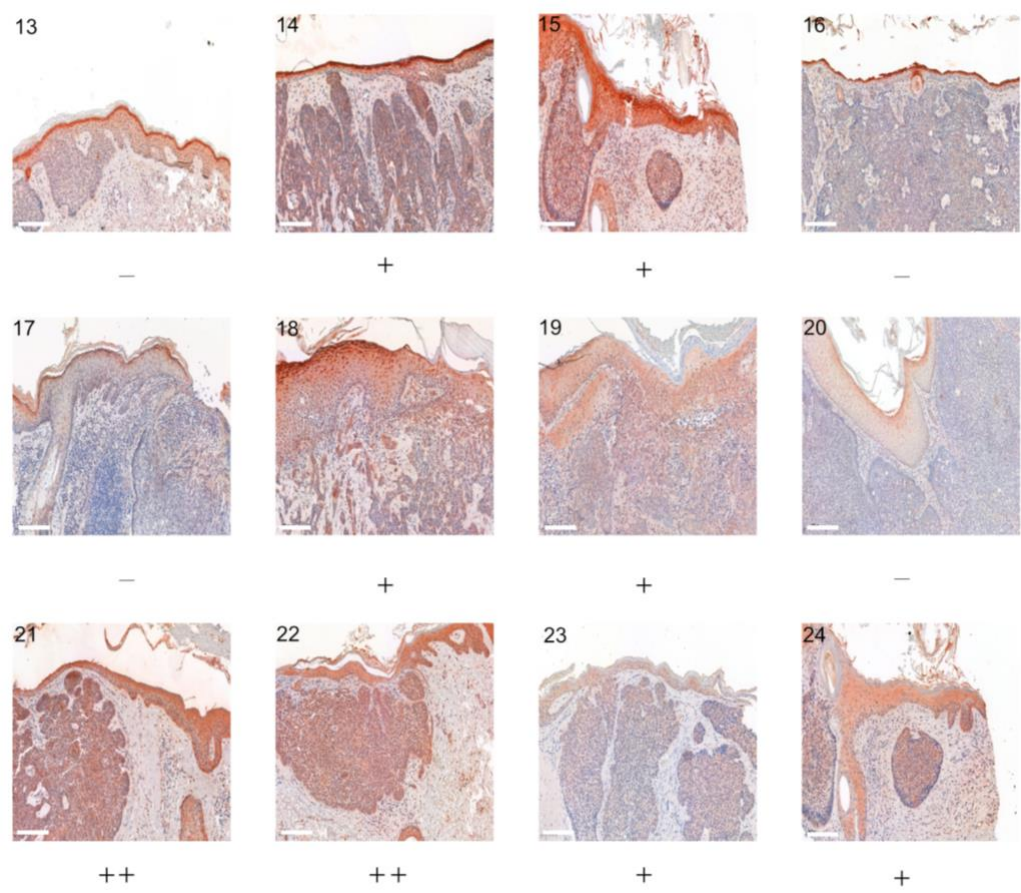
Supplementary Figure S2-S4: Immunohistochemistry for TRPC4 in BCC. Scale bars represent 200 μ m. In BCC, TRPC4 expression was weak positive for 16/39 samples (1, 3, 6, 8, 14, 15, 18, 19, 23, 24, 25, 30, 31, 33, 34, 35). 20/39 (2, 4, 5, 7, 9-13, 16, 17, 20, 26-28, 32, 36-39) showed a negative staining. 3/39 showed a strong positive reaction (21, 22, 29).

1 = A1M_1S_1, 2 = A1M_2S_1, 3 = A1M_3S_1, 4 = A1M_4S_1, 5 = A1M_5S_1, 6 = A1M_6S_1, 7 = A1M_7S_1, 8 = A1M_8S_1, 9 = A1M_9S_1, 10 = A1M_10S_1, 11 = , A1M_11S_1, 12 = A1M_12S_1, 13 = A1M_16S_1, 14 = A1M_17S_1, 15 = A1M_18S_1, 16 = A2M_1S_1, 17 = A2M_3S_1, 18 = A2M_4S_1, 19 = A2M_5S_1, 20 = A2M_6S_1, 21 = A2M_9S_1, 22 = A2M_11S_1, 23 = A2M_12S_1, 24 = A2M_13S_1, 25 = A2M_14S_1, 26 = A2M_18S_1, 27 = A2M_20S_1, 28 = A3M_1S_1, 29 = A3M_3S_1, 30 = A3M_4S_1, 31 = A3M_7S_1, 32 = A3M_10S_1, 33 = A3M_11S_1, 34 = A3M_12S_1, 35 = A3M_13S_1, 36 = A3M_14S_1, 37 = A3M_15S_1, 38 = A3M_16S_1, 39 = A3M_17S_1

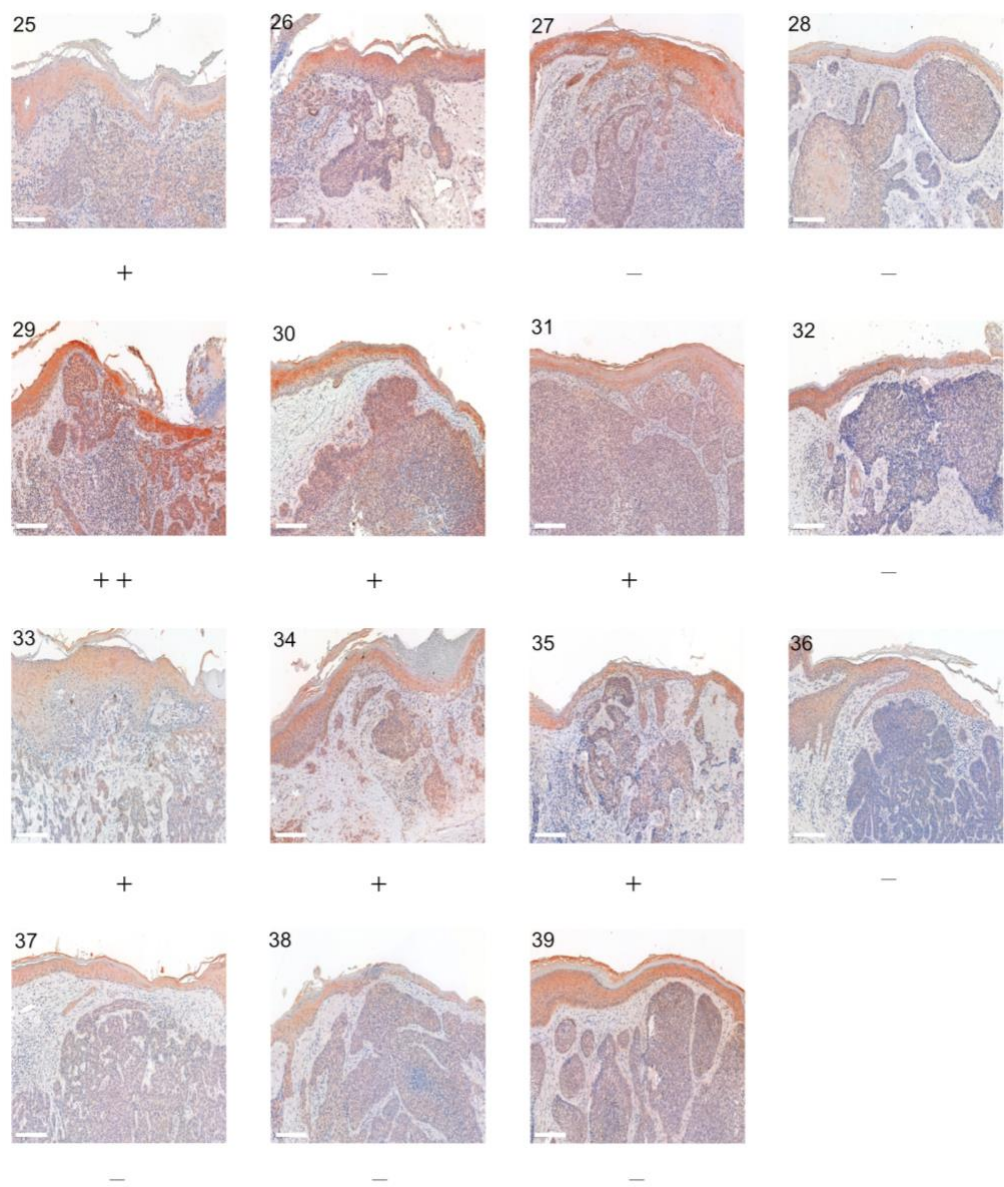
Supplementary Figure S2: Immunohistochemistry for TRPC4 in BCC (part 1)



Supplementary Figure S3: Immunohistochemistry for TRPC4 in BCC (part 2)



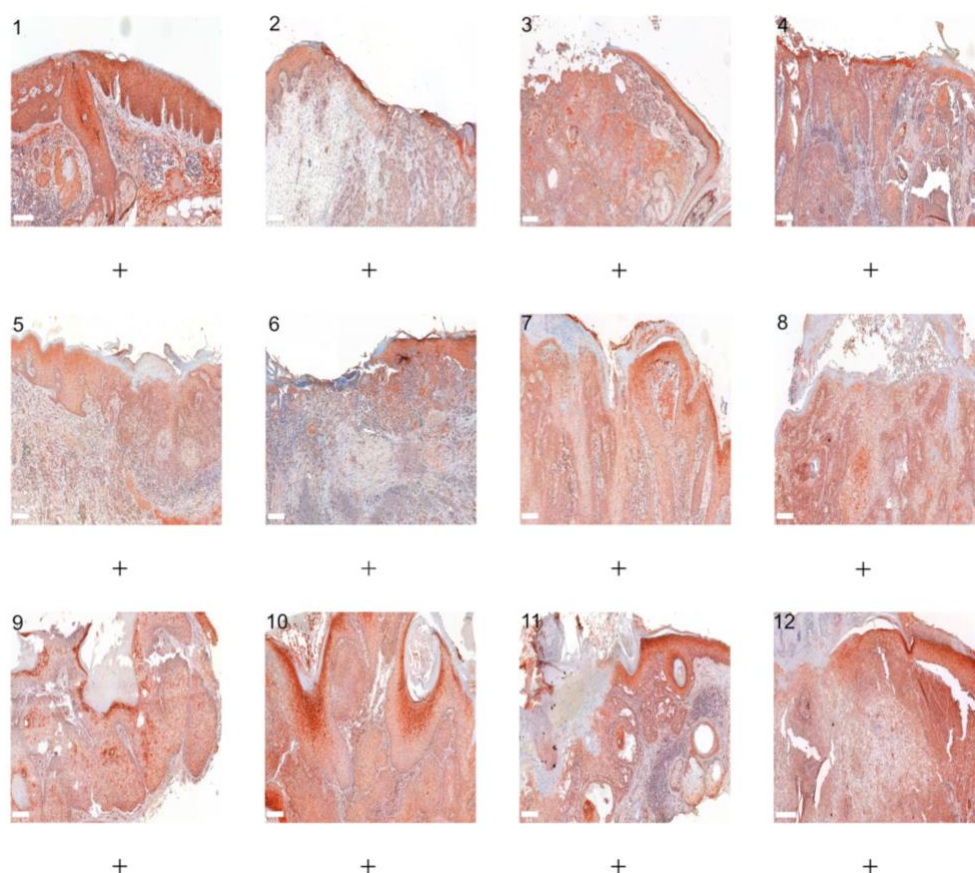
Supplementary Figure S4: Immunohistochemistry for TRPC4 in BCC (part 3)



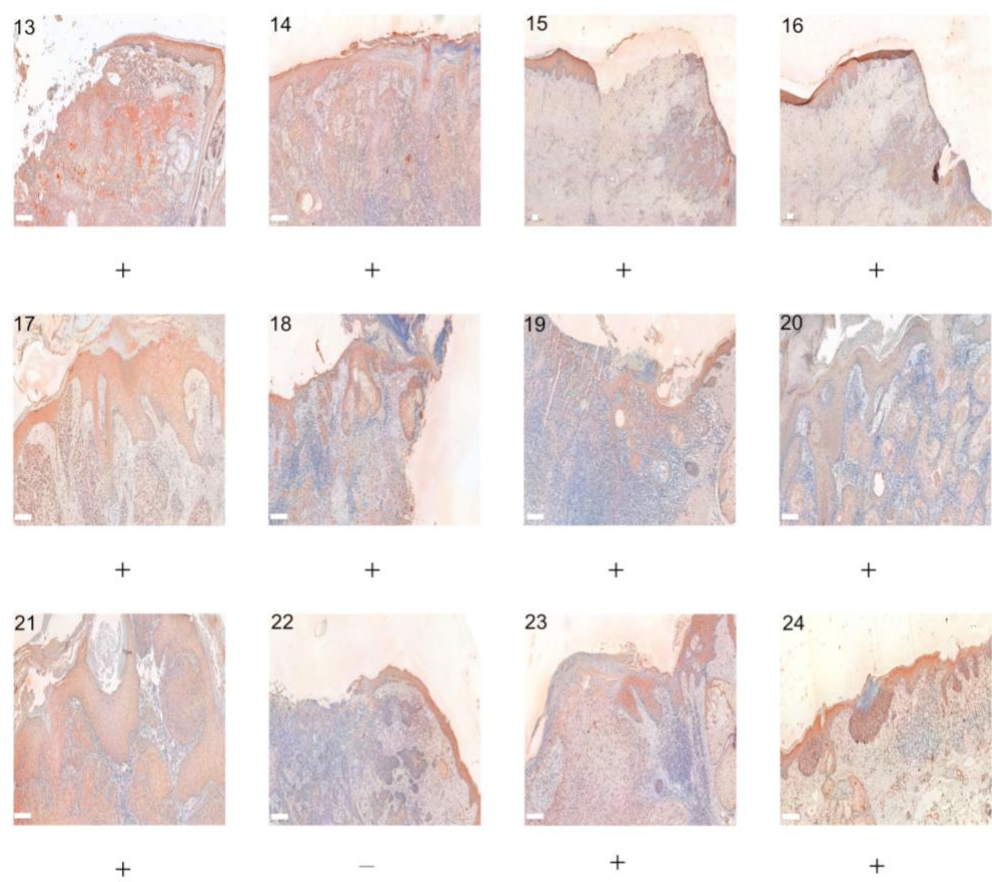
Supplementary Figure S5-S7: Immunohistochemistry for TRPC4 in SCC. Scale bars represent 200 μ m. SCC showed a rather homogeneous expression in all 25 samples (1-27), displaying a weak positive reaction.

1= A3M_19S_1, 2= A3M_20S_1, 3= A4M_1S_1, 4= A4M_3S_1, 5= A4M_4S_1, 6= A4M_7S_1, 7= A4M_8S_1, 8= A4M_10S_1, 9= A4M_12S_1, 10= A4M_15S_1, 11= A4M_16S_1, 12= A4M_17S_1, 13= A4M_18S_1, 14= A4M_19S_1, 15= A5M_1S_1, 16= A5M_2S_1, 17= A5M_5S_1, 18= A5M_6S_1, 19= A5M_9S_1, 20= A5M_11S_1, 21= A5M_12S_1, 22= A5M_14S_1, 23= A5M_16S_1, 24= A5M_17S_1, 25= A5M_18S_1, 26= A5M_19S_1, 27= A5M_20S_1

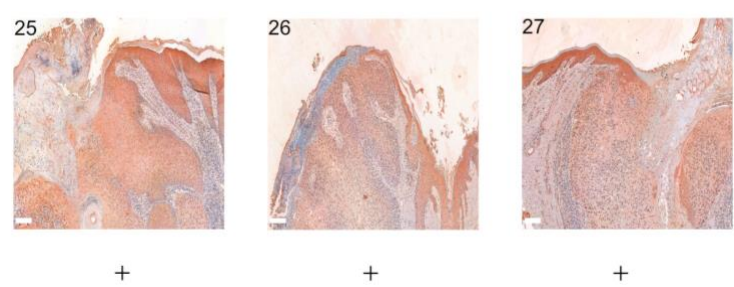
Supplementary Figure S5 Immunohistochemistry for TRPC4 in SCC (part 1)



Supplementary Figure S6 Immunohistochemistry for TRPC4 in SCC (part 2)

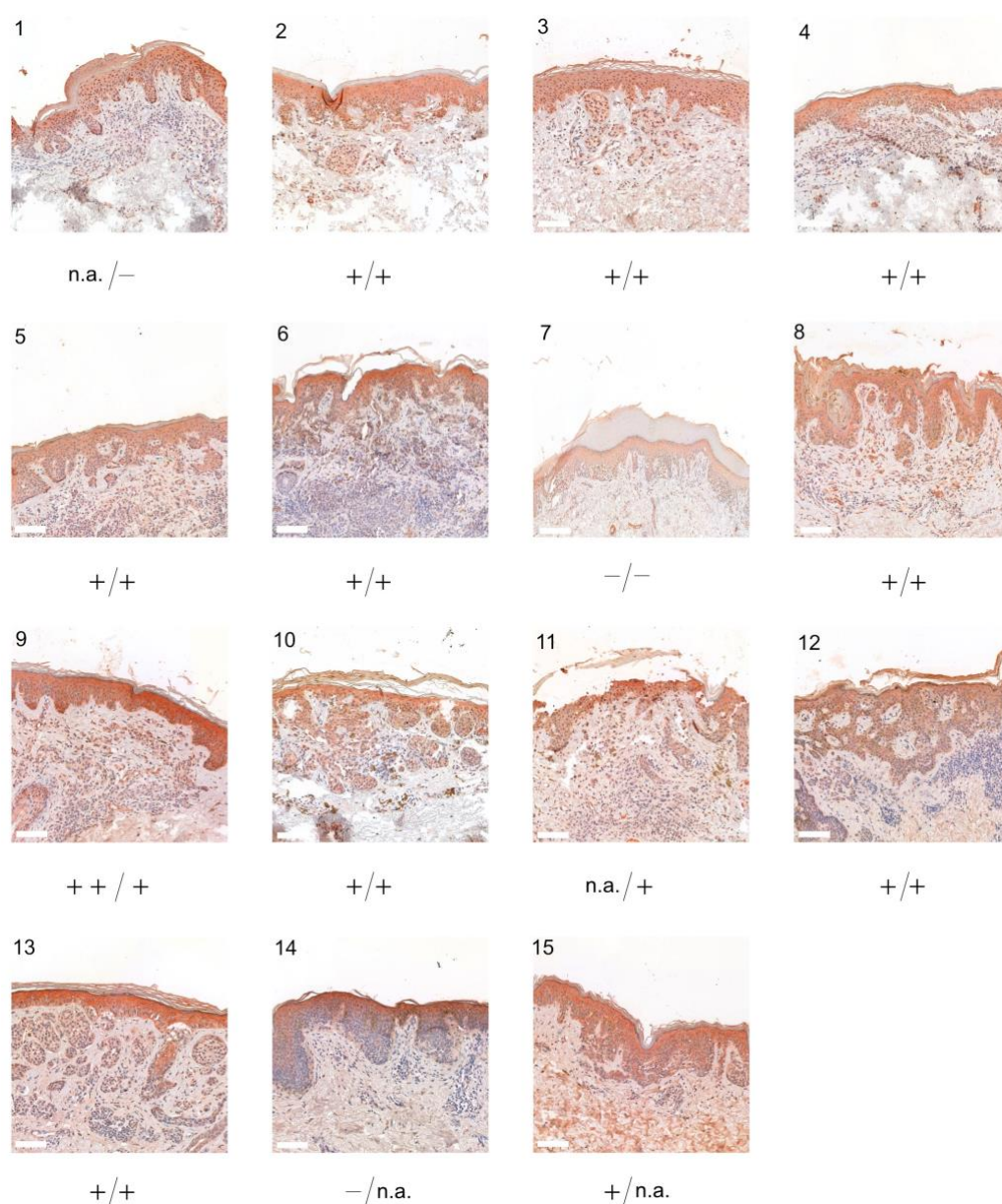


Supplementary Figure S7 Immunohistochemistry for TRPC4 in SCC (part 3)



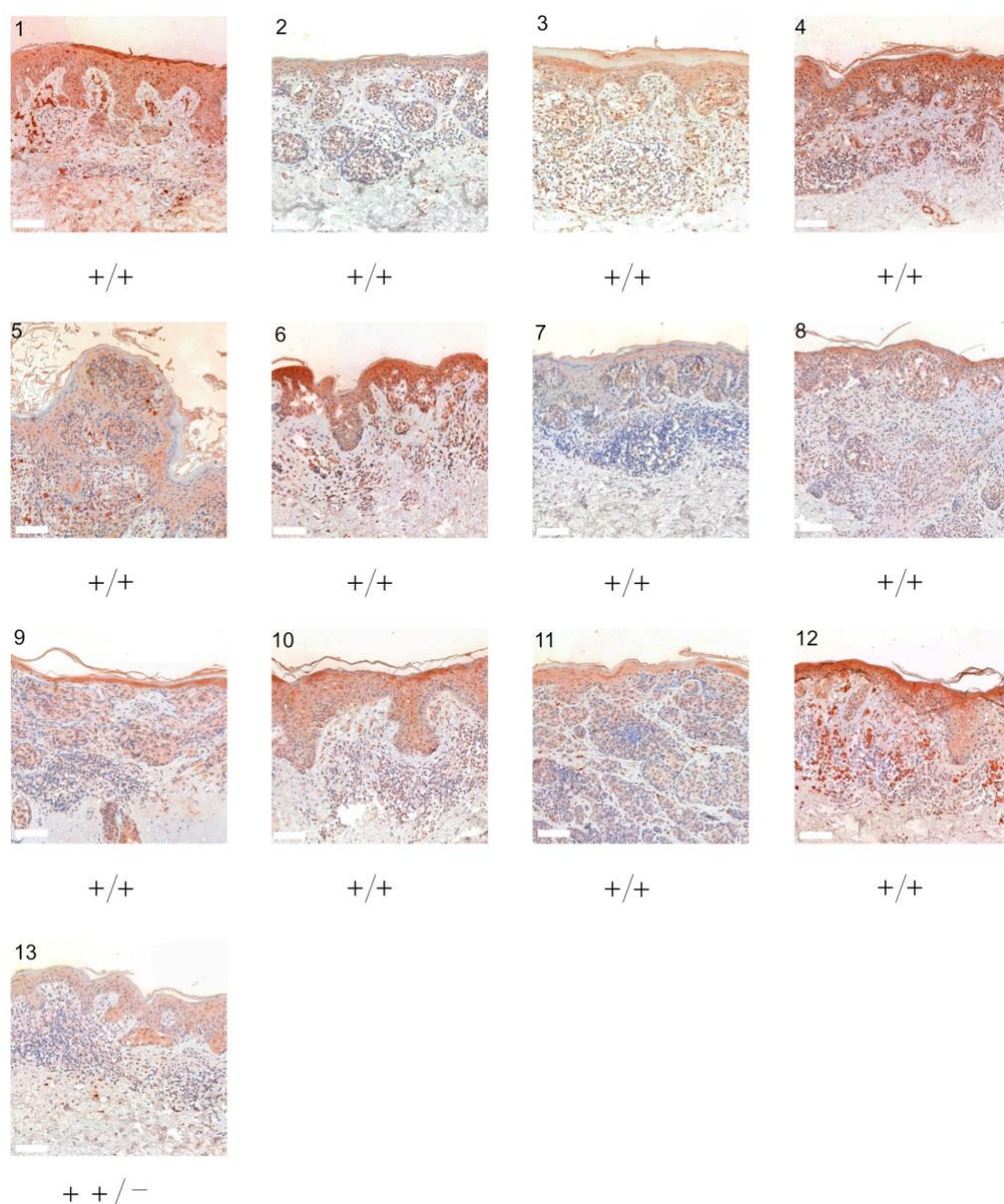
Supplementary Figure S8: Immunohistochemistry for TRPC4 in NCN. Scale bars represent 200 μ m. In epidermal parts, 10/13 showed a weak positive reaction for TRPC4 (2, 3, 4, 5, 6, 8, 10, 12, 13, 15), 1/13 reacted strong positive (9), and 2/13 (7,14) displayed a weak staining. The dermal portion showed a weak positive expression of TRPC4 in 11/13 (2, 3, 4, 5, 6, 8, 9, 10, 11, 12, 13). For number 7 and 13, a decreasing expression towards deeper tissue levels can be observed.

1= NZN TRPC4 27-11, 2= NZN TRPC4 30-11, 3= NZN TRPC4 30-11_24-9-2021_16-00-41, 4= NZN TRPC4 41-11, 5= NZN TRPC4 101-11, 6= NZN TPC4 109-11 2, 7= K. NZN TRPC4 117-11, 8= K. NZN TRPC4 121-11, 9= K. NZN TRPC4 122-11, 10= K. NZN TRPC4 265-11, 11= K. NZN TRPC4 496- 11, 12= K. NZN TRPC4 1496- 11, 13= K. NZN TRPC4 9629- 09, 14= K. NZN TRPC4 16892- 09, 15= K. NZN TRPC4 29215- 0

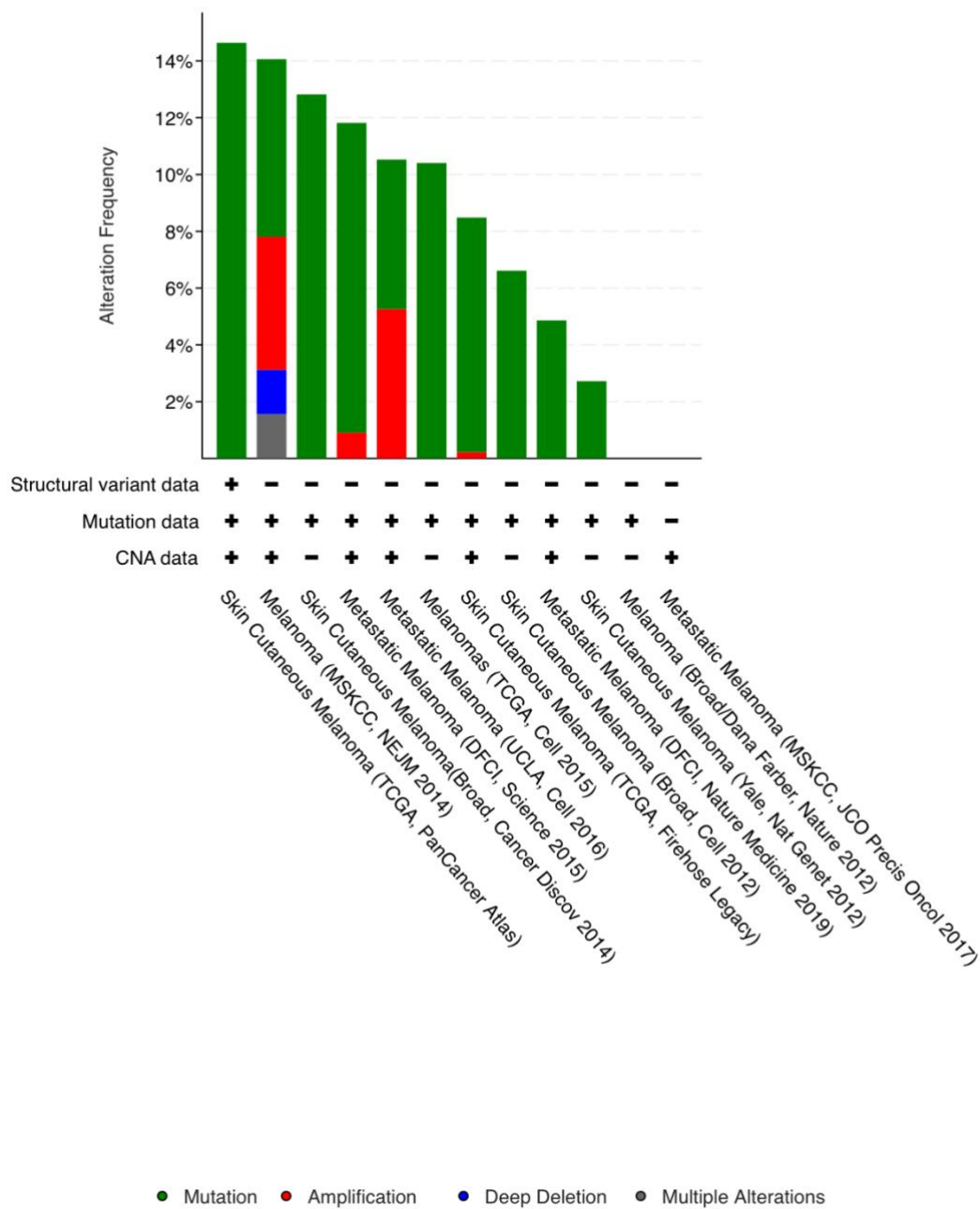


Supplementary Figure S9: Immunohistochemistry for TRPC4 in MM. Scale bars represent 200 μ m. 12/13 of the epidermal and dermal sections were weak positive for TRPC4 (1-12), whereas 1/13 of showed a strong positive epidermal and negative dermal staining reaction (13).

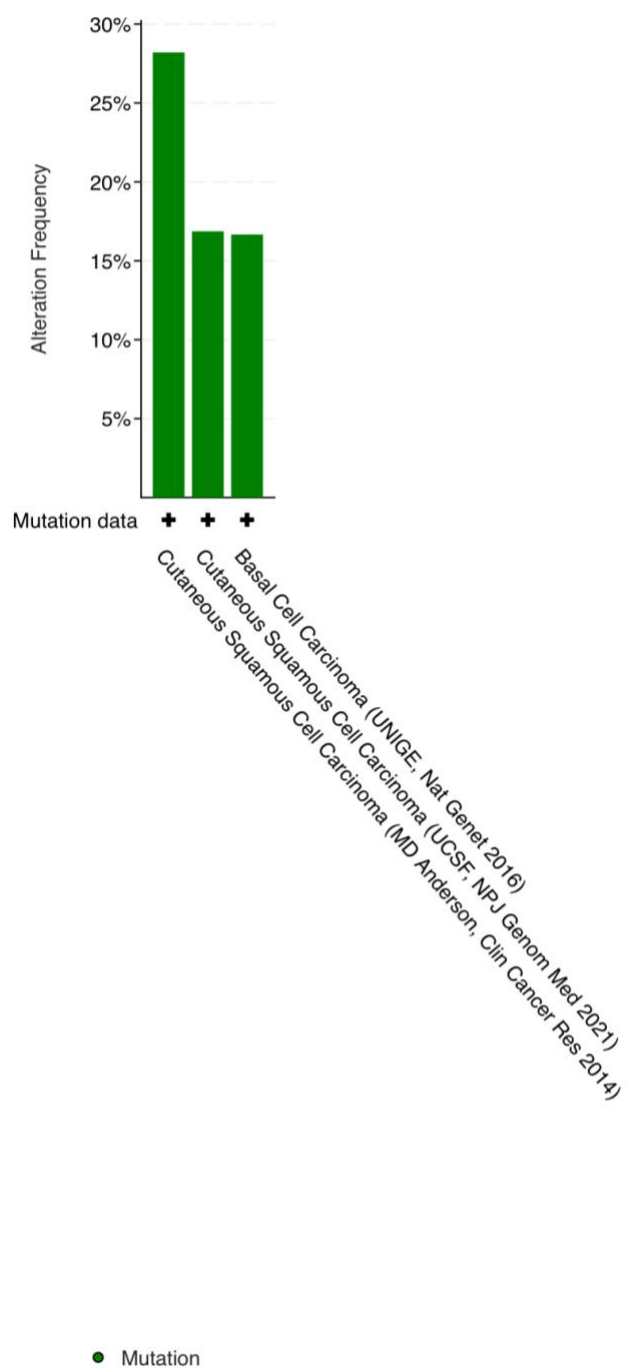
1= MM TRPC4 1043-11, 2= MM TRPC4 1730- 11, 3= MM TRPC4 1903-11, 4= MM TRPC4 1944-11, 5= MM TRPC4 2013-11, 6= MM TRPC4 2017-11, 7= MM TRPC4 2125- 11, 8= MM TRPC4 2668- 09, 9= MM TRPC4 7060- 09, 10= MM TRPC4 7104- 09, 11= MM TRPC4 7677- 09, 12= MM TRPC4 7802- 09, 13= MM TRPC4 7439-09



Supplementary Figure S10: TRPC4 mutation frequency in MM from cBioportal.org



Supplementary Figure S11: TRPC 4 Mutation frequency in non-melanoma skin cancer from cBioportal.org



Supplementary Table S1: Scoring results for TRPC4 in BCC

Number	Type of BCC	Scoring
A1M_1S_1	nodular	+
A1M_2S_1	nodular	-
A1M_3S_1	nodular	+
A1M_4S_1	nodular	-
A1M_6S_1	nodular	-
A1M_7S_1	nodular	+
A1M_8S_1	nodular	-
A1M_9S_1	superficial	+
A1M_11S_1	nodular	-
A1M_12S_1	nodular	-
A1M_13S_1	nodular	-
A1M_15S_1	nodular	-
A1M_16S_1	superficial	-
A1M_17S_1	nodular	+
A1M_18S_1	superficial	+
A2M_1S_1	nodular	-
A2M_3S_1	nodular	-
A2M_4S_1	sclerosing	+
A2M_5S_1	nodular / sclerosing (mixed)	+
A2M_6S_1	nodular	-
A2M_9S_1	nodular	++
A2M_11S_1	nodular	++
A2M_12S_1	nodular	+
A2M_13S_1	nodular	+
A2M_14S_1	nodular / sclerosing (mixed)	+
A2M_18S_1	nodular / sclerosing (mixed)	-
A2M_20S_1	nodular	-
A3M_1S_1	nodular	-
A3M_3S_1	nodular	++
A3M_4S_1	nodular	+
A3M_7S_1	nodular	+
A3M_10S_1	nodular	-
A3M_11S_1	nodular / sclerosing (mixed)	+
A3M_12S_1	nodular / sclerosing (mixed)	+
A3M_13S_1	nodular / sclerosing (mixed)	+
A3M_14S_1	nodular	-
A3M_15S_1	nodular	-
A3M_16S_1	nodular	-
A3M_17S_1	nodular	-

Supplementary Table S2: Scoring results for TRPC4 in SCC

Number	Scoring
A3M_19S_1	+
A3M_20S_1	+
A4M_1S_1	+
A4M_3S_1	+
A4M_4S_1	+
A4M_7S_1	+
A4M_8S_1	+
A4M_10S_1	+
A4M_12S_1	+
A4M_15S_1	+
A4M_16S_1	+
A4M_17S_1	+
A4M_18S_1	+
A4M_19S_1	+
A5M_1S_1	+
A5M_2S_1	+
A5M_5S_1	+
A5M_6S_1	+
A5M_9S_1	+
A5M_11S_1	+
A5M_12S_1	+
A5M_14S_1	-
A5M_16S_1	+
A5M_17S_1	+
A5M_18S_1	+
A5M_19S_1	+
A5M_20S_1	+

Supplementary Table S3: Scoring results for TRPC4 in NCN

Number	Type of NCN	Scoring Epidermal	Scoring Dermal
NZN TRPC4 27-11	dermal	n/a	-
NZN TRPC4 30-11	compound	+	+
NZN TRPC4 30-11_24-9-2021_16-00-41	compound	+	+
NZN TRPC4 41-11	compound	+	+
NZN TRPC4 101-11	compound	+	+
NZN TPC4 109-11 2	compound	+	+
K. NZN TRPC4 117-11	compound	-	-
K. NZN TRPC4 121-11	compound	+	+
K. NZN TRPC4 122-11	compound	++	+
K. NZN TRPC4 265-11	compound	+	+
K. NZN TRPC4 496- 11	dermal	n/a	+
K. NZN TRPC4 1496- 11	compound	+	+
K. NZN TRPC4 9629- 09	compound	+	+
K. NZN TRPC4 16892- 09	junctional	-	n/a
K. NZN TRPC4 29215- 09	junctional	+	n/a

Supplementary Table S4: Scoring results for TRPC4 in MM

Number	Scoring epidermal	Scoring dermal
MM TRPC4 1043-11	+	+
MM TRPC4 1730- 11	+	+
MM TRPC4 1903-11	+	+
MM TRPC4 1944-11	+	+
MM TRPC4 2013-11	+	+
MM TRPC4 2017-11	+	+
MM TRPC4 2125- 11	+	+
MM TRPC4 2668- 09	+	+
MM TRPC4 7060- 09	+	+
MM TRPC4 7104- 09	+	+
MM TRPC4 7677- 09	+	+
MM TRPC4 7802- 09	+	+
MM TRPC4 7439-09	++	-

Supplementary Table S5: Statistical analysis of TRPC4– comparison of all entities

		Scoring			total
		-	+	++	
SCC	number	0	25	0	25
	% of tumors	0%	100.0%	0%	100%
BCC	number	20	16	3	39
	% of tumors	51.3%	41.0%	7.7%	100%
NCN epidermal	number	2	10	1	13
	% of tumors	15.4%	76.9%	7.7%	100%
NCN dermal	number	2	11	0	13
	% of tumors	15.4%	84.6%	0%	100%
MM epidermal	number	0	12	1	13
	% of tumors	0%	92.3%	7.7%	100%
MM dermal	number	1	12	0	13
	% of tumors	7.7%	92.3%	0%	100%
Gesamt	number	25	86	5	116
	% of tumors	21.6%	74.1%	4.3%	100%

Supplementary Table S6: NCBI Geo gene expression analysis of TRPC4**BCC vs. SCC: Study GSE53462**

ID	adj.P.Val	P.Value	t	B	logFC	Gene.symbol	Gene.title
ILMN_1782295	0.945847	8.35e-01	-0.2115083	-6.17258	-0.01273726	TRPC4	transient receptor potential cation channel subfamily C member 4

NCN cs. MM: Study GSE4587

ID	adj.P.Val	P.Value	t	B	logFC	Gene.symbol	Gene.title
224220_x_at	0.2202	0.04481366	-2.2047613	-3.9612	-1.3656916	TRPC4	transient receptor potential cation channel subfamily C member 4
220818_s_at	0.5408	0.27021535	-1.1482785	-5.41951	-0.8524036	TRPC4	transient receptor potential cation channel subfamily C member 4
224219_s_at	0.9163	0.80658083	0.2495519	-6.02526	0.2283259	TRPC4	transient receptor potential cation channel subfamily C member 4
220817_at	581	0.31098903	-1.051415	-5.51844	-0.8847788	TRPC4	transient receptor potential cation channel subfamily C member 4

NCN cs. MM: Study GSE12391

ID	adj.P.Val	P.Value	t	B	logFC	Gene.symbol	Gene.title
19602	6.09e-01	3.72e-01	0.8958235	-6.0441039	0.01984097	TRPC4	transient receptor potential cation channel subfamily C member 4

NCN cs. MM: Study GSE46517

ID	adj.P.Val	P.Value	t	B	logFC	Gene.symbol	Gene.title
220817_at	6.26e-01	3.18e-01	1.010048	-5.803297	0.3355734	TRPC4	transient receptor potential cation channel subfamily C member 4
220818_s_at	9.58e-01	8.75e-01	0.158867	-6.289573	0.0550281	TRPC4	transient receptor potential cation channel subfamily C member 4

NCN cs. MM: Study GSE114445

ID	adj.P.Val	P.Value	t	B	logFC	Gene.symbol	Gene.title
220818_s_at	0.25245972	7.80e-02	-1.828659	-4.7264186	-0.11600316	TRPC4	transient receptor potential cation channel subfamily C member 4
224220_x_at	0.25438021	7.90e-02	-1.822226	-4.7368991	-0.13412296	TRPC4	transient receptor potential cation channel subfamily C member 4
220817_at	0.30558838	1.09e-01	-1.656632	-4.9965644	-0.10672587	TRPC4	transient receptor potential cation channel subfamily C member 4

NCN cs. MM: Study GSE183115

ID	adj.P.Val	P.Value	t	B	logFC	Gene.symbol	Gene.title
ADXECADA.22327_s_at	919	0.29257616	1.11	-5.20838	1.23e-01	TRPC4	transient receptor potential cation channel subfamily C member 4
ADXECNTDJ.362_s_at	963	0.58561657	-5.64e-01	-5.6313	-5.93e-02	TRPC4	transient receptor potential cation channel subfamily C member 4